

The **17th** **ISEI Symposium**

ISEI 2026 Tokyo

The International Society of Exercise and Immunology



Exercise Immunology:
From Scientific Basis to
Practical Applications

August 27-30, 2026

Waseda University
International Conference Center
Tokyo, Japan

Co-sponsored by:

Waseda University, Faculty of Sports Sciences



Schedule

Thursday 27 Aug. 2026		Friday 28 Aug. 2026	Saturday 29 Aug. 2026	Sunday 30 Aug. 2026
09:00 10:30		Session 1 Immune mechanisms & regulation	Session 5 Nutrition, metabolism & immunometabolism	Session 9 Environmental & physiological stress
10:30-11:00		Coffee break	Coffee break	Coffee break
11:00-12:30		Session 2 Host defence, infection & vaccination	Session 6 Ageing, growth & development	Session 10 Clinical issues
12:30-14:00	Registration 13:00-18:00	Lunch Luncheon Seminar 1 Board meeting	Lunch Luncheon Seminar 2	Closing & Awards
14:00-15:30		Session 3 Inflammation & resolution	Session 7 Lifestyle & metabolic disease	
15:30-16:00		Coffee break	Coffee break	
16:00-17:30	Opening & Keynote	Session 4 Methods, omics & systems approaches	Session 8 Cancer & tumour Immunology	
18:00-20:00	Welcome reception* Refreshments provided	Poster presentation Refreshments provided		

*Welcome Reception Venue: 2nd Floor, Okuma Garden House, Waseda University

Day 1 - Thursday, 27 August

Registration Desk : 13:00 - 18:00

Tokyo Tourist Information Desk: 13:00 - 18:00

Opening Ceremony	16:00 – 17:30
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Barbara Wessner	ISEI President University of Vienna
Masashi Miyashita	Deputy Dean, Faculty of Sports Sciences, Waseda University

Keynote	* : Invited speakres
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Chair	Katsuhiko Suzuki	Waseda University
	Masashi Miyashita	Waseda University

KN-1	Ryoichi Nagatomi	*	How can exercise immunology contribute to everyday life? A suggestion for need-oriented exercise immunology
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KN-2	Chin Leong Lim	*	Exploring current evidence on the drivers of heat stress and injury: Can heat stroke be triggered by immne disturbance?
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KN-3	Masaki Inada		Differential gene responses for slow-twitch and fast-twitch muscles in muscular atrophy and hypertrophy
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Welcome Reception	18:00 – 20:00
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Venue: 2nd Floor, Okuma Garden Terrace, Waseda University (5-minute walk)

Day 2 - Friday, 28 August

Registration Desk : 8:30 - 18:00

Tourist Information Desk: 8:30 - 17:30

* YIA: Candidates of the
young investigator
award

Session 1 - Immune mechanisms & regulation	9:00 - 10:30
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Chair	Chin Leong Lim	Nanyang Technological University, VinUniversity
	Cláudia Regina Cavaglieri	University of Campinas

OP-1	Emily LaVoy	*	T cell metabolism and function differs by cardiorespiratory fitness level and with acute exercise
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OP-2	Masato Kawashima		Neutrophil depletion alters early repair responses and delays skeletal muscle regeneration following crush injury
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OP-3	Heejae Lee	YIA*	High-intensity interval training (HIIT) induces persistent and divergent remodelling of T cell immunity
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OP-4	Julian Moser	YIA	Acute exercise and extracellular vesicle responses: Immunological and methodological insights from a systematic review sub- analysis
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Coffee break	10:30 - 11:00
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Conference Rooms 1 and 2 on the 3rd Floor

Session 2 - Host defence, infection & vaccination			11:00 - 12:30
Chair	Richard J. Simpson	The University of Arizona	
	Nicholas West	Griffith University	
OP-5	James Turner	*	The influence of latent Cytomegalovirus infection on adipose tissue in healthy men
OP-6	Katharina Leuchte		Acute HIIT widely modifies immunity: Dynamics of virus-specific CD8+ T cells, immunomodulatory serum proteins and chemokine receptor expression on lymphocytes
OP-7	Seiichi Sato		Mechanical lung expansion triggers antiviral innate immune responses in vivo
OP-8	Tung-Lin Lu	YIA	Effects of long-term glutamine supplementation on gut microbiota during training periodization of cross-country skiers
Lunch & Luncheon Seminar			12:30 - 14:00
Conference Rooms 1 and 2 on the 3rd Floor Board Meeting Held at Lunchtime The luncheon seminar will be held in Conference Room 3. (12:50 - 13:50)			
LS-1	Sihui Ma Gen Tanabe		The application of immune protein intake to the field of sports medicine (Sponsored by: Ortho Corporation)
Session 3 - Inflammation & resolution			14:00 - 15:30
Chair	Brandt Pence	University of Memphis	
	Yuri Hosokawa	Waseda University	
OP-9	Jonathan Peake	*	Multi-omics assessment of responses to resistance exercise
OP-10	Ivan Bautmans		Strength training affects intracellular stress response in peripheral immune cells
OP-11	Cong Wu	YIA	Disuse-induced muscle atrophy impairs inflammatory regulation and delays skeletal muscle regeneration following acute injury
OP-12	Fumi Asanuma	YIA	Self-assessed immune function and associated risk factors among Japanese firefighters
Coffee break			15:30 - 16:00
Conference Rooms 1 and 2 on the 3rd Floor <u>Start time for poster display in Conference Room 3</u>			
Session 4 - Methods, omics & systems approaches			16:00 - 17:30
Chair	Jonathan Peake	Queensland University of Technology	
	Barbara Wessner	University of Vienna	
OP-13	Nicholas West	*	Divergent peripheral (muscle) and systemic (whole blood) immune gene expression following prolonged intense exercise: A spatial and transcriptomic analysis
OP-14	Brandt Pence	*	Comprehensive proteomic profiling in the WELCOM cohort identifies reduced inhibin/activin betaC in physically active women

OP-15	Jongbok Lee	Precision-prescribed HIIT at 110% RCP abolishes plasma multi-omic heterogeneity across training backgrounds
OP-16	Timothy M. Kistner	CITE-seq reveals rare immune cell populations while maintaining concordance with flow cytometry in exercise-mobilized PBMCs

Poster Presentation	18:00 -20:00
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Conference Room 3 on the 3rd Floor

- Light refreshments are available in Conference Room 1.

- The poster presentation program is listed on the following pages.

Chair	Armin Paravlić	University of Ljubljana
	Kumpei Tanisawa	Waseda University

Day 3 - Saturday, 29 August

Registration Desk : 8:30 - 18:00

Tokyo Tourist Information Desk: 8:30 - 17:30

Session 5 - Nutrition, metabolism & immunometabolism	9:00 - 10:30
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Chair	Emily LaVoy	University of Houston
	Masashi Miyashita	Waseda University

OP-17	Ana Maria Teixeira	*	Lifelong exercise is associated with metabolic capacity and remodeling in cytotoxic and unconventional T cells
OP-18	Ruheea Taskin Ruhee		Short-term sulforaphane intake modulates exercise-induced oxidative stress in healthy adults
OP-19	Therdtham Chawrai	YIA	The effects of four weeks of ketone ester supplementation on systemic and adipose tissue inflammation in healthy older adults: a randomised controlled trial
OP-20	Emily C. Fraschetti	YIA	Feeding recovery: Post-exercise nutrition influences immune cell dynamics

Coffee break	10:30 - 11:00
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Conference Rooms 1 and 2 on the 3rd Floor

Session 6 - Ageing, growth & development	11:00 - 12:30
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Chair	Barbara Wessner		University of Vienna
	Guillaume Spielmann		Louisiana State University
OP-21	Zsolt Radák	*	Exercise slows epigenetic aging, whereas pro-inflammatory gut bacterial species accelerate it
OP-22	Paulo F. de Almeida-Neto	YIA	Biological maturation modulates neutrophil mobilization and IL-8 responses following repeated sprint exercise in adolescent athletes
OP-23	Yishan Tong	YIA	Effects of 3-(4-hydroxy-3-methoxyphenyl)propionic acid on regulating oxidative stress and muscle fiber composition
OP-24	Xiang Pan	YIA	Gut microbiota and childhood mental health through a physical-fitness versus physical-activity decoupling lens: a microbiota–gut–brain study in children aged 6–9 years

Lunch & Luncheon Seminar	12:30 - 14:00
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Conference Rooms 1 and 2 on the 3rd Floor
The luncheon seminar will be held in Conference Room 3. (12:50 - 13:50)

LS-2	Mitsuru Higuchi Yasuhiro Seki	Rowing: as a promising geroprotector for senior people (Sponsored by: Wismerll Co., Ltd.)
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Session 7 - Lifestyle & metabolic disease	14:00 - 15:30
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Chair	Ana Teixeira	University of Coimbra
	Llion Roberts	Griffith University
OP-25	Cláudia Regina Cavaglieri	* Regular physical activity and reduction of neurogenic obesity may mitigate premature immunosenescence in people with spinal cord injury
OP-26	Brian J. Andonian	Exercise training and hypocaloric diet modulate markers of lymphocyte aging and inflammation in older adults with rheumatoid arthritis
OP-27	Gabriela Mandú Gimenes	YIA Effect of gut microbiota depletion on glucose tolerance and T lymphocytes profile in a model of non-obese type 2 diabetes
OP-28	Chuwen Xue	YIA Metabolic improvements in obese mice induced by combined black ginger extract supplementation and endurance exercise

Coffee break	15:30 - 16:00
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Conference Rooms 1 and 2 on the 3rd Floor

Session 8 - Cancer & tumor immunology	16:00 -17:30
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Chair	Cláudia Regina Cavaglieri	University of Campinas
	James Turner	The University of Birmingham
OP-29	Richard J. Simpson	* Exercise as an immune adjuvant for allogeneic cell therapies: An overview of the Allo-X trial
OP-30	Gitte Holmen Olofsson	High-intensity interval training enhances immunotherapy efficacy in metastatic non-small cell lung cancer: results from the randomized HI AIM trial with integrated translational analyses
OP-31	Forrest L. Baker	Exercise-expanded $\gamma\delta$ T cells show in vitro and in vivo anti-myeloma potential and daratumumab-mediated ADCC
OP-32	Moe Sugasaki	YIA Inflammatory cytokine interleukin-1 induced bone formation in the model of bone metastasized cancer

Day 4 - Sunday, 30 August

Registration Desk : 8:30 - 14:00
Tokyo Tourist Information Desk: 8:30 - 14:00

Session 9 - Environmental & physiological stress	9:00 - 10:30
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Chair	Zsolt Radák	Hungarian University of Sports Science, Waseda University
	Paulo Francisco de Almeida-Neto	Federal University of Rio Grande do Norte Natal

OP-33	Llion A Roberts	*	Redox perspectives to recovery and adaptation from acute and chronic post-resistance exercise cold water immersion
OP-34	Armin Paravlić	*	Aerobic exercise, systemic inflammation, and endothelial function: Insights from systematic review and meta-analysis of randomized controlled trials
OP-35	Sandro M. Hirabara		Determination of metabolic parameters and lymphocyte profile in military police officers with metabolic syndrome
OP-36	Kristina Drole	YIA	Immune-endocrine responses across a competitive season and their association with illness occurrence in elite athletes
Coffee break			10:30 - 11:00
Conference Rooms 1 and 2 on the 3rd Floor			
Session 10 - Clinical issues			11:00 - 12:30
Chair	Ryoichi Nagatomi	Tohoku University	
	Eisuke Ochi	Hosei University	
OP-37	John Sullivan	YIA	Exercise mobilized T-cells upregulate CD137 after blinatumomab stimulation and have enhanced effector function against B-ALL
OP-38	Randy Chou	YIA	Exercise-expanded $\gamma\delta$ T cells show enhanced responsiveness to bispecific antibody redirection in hematological malignancies
OP-39	Ken-ichi Okada		Effects of adjuvant /neoadjuvant chemotherapy combined with exercise therapy in pancreatic cancer
OP-40	Michiya Tanimoto		Activities of the cancer and exercise working group: Bridging evidence and practice in exercise oncology
Closing Ceremony			12:30 - 13:30
Public Lecture by the Cancer and Exercise Working Group			14:30 - 16:20
<u>The event will be held in Japanese.</u> Free admission. We welcome everyone to attend.			

Day 2 - Friday, 28 August, Evening

Poster Presentation

* YIA: candidates of the young investigator award

Chair	Armin Paravlić	University of Ljubljana
	Kumpei Tanisawa	Waseda University
PP-1	Yuzuru Sakamoto	Effects of long-term voluntary running exercise on allergy-related immune cell dynamics and immune checkpoint receptor-mediated immunoregulation
PP-2	Amara Cassandra dos Anjos Alves	YIA* The influence of bone marrow hematopoietic activity in low-grade inflammation in lean type 2 diabetes
PP-3	Linda Ericsson	YIA Immunophenotype characterization of CD8+ T cells and NK cells following aerobic exercise and resistance exercise in healthy individuals
PP-4	Muhammad Arkan Rahmat	YIA The effects of high-intensity interval training on T-cell activation in patients with rheumatoid arthritis: A scoping review
PP-5	Ting-Cheng WU	YIA Probiotic and prebiotic supplementation for respiratory immune modulation in athletes versus asthma: A comparative meta-analysis
PP-6	Ena Yoshida	YIA Leukocyte, interleukin-6, and chemokine responses to moderate-intensity aerobic exercise during the menstrual and luteal phases
PP-7	Ming-Ru Chiang	Transient alterations of salivary mucosal immunity following vaccination in adolescent female athletes
PP-8	Rui Curi	Neutrophil function in elite athletes with high-intensity exercise induced bronchospasm
PP-9	Cheng-Lin Tsai	Effects of pre-maximal isometric contraction on eccentric exercise induced muscle damage and pulse wave velocity of the knee extensor
PP-10	Emelyn Mathot	YIA Strength training as an immune rejuvenation strategy: Evidence from the SPRINT project
PP-11	Zong-Jia Wu	YIA Reduced glucose availability elevates electrical pulse stimulation-induced oxidative stress in C2C12 myotubes
PP-12	Shiva Ebrahimpour Nosrani	YIA Exercise-induced inflammatory modulation and muscle endurance in older women at risk of sarcopenia
PP-13	Yutaka Matsumoto	Dose optimization of topical methyl salicylate: 10% wintergreen oil attenuates exercise-induced soleus inflammation without impairing performance
PP-14	Rio Yagi	Age-related differences in gene expression following percutaneous absorption of wintergreen oil in mice
PP-15	Yutaro Hara	YIA Acute systemic inflammatory responses induced by transdermal absorption of wintergreen oil in mice
PP-16	Daisuke Shiiba	Development of a patch-free murine model of epicutaneous sensitization using a highly viscous carboxymethyl cellulose solution
PP-17	Haruki Kobori	YIA The utility of a small animal grip strength measurement device as a model for studying exercise-induced muscle damage

PP-18	Muhammad Sulthan Arya Rasyad	YIA	Immunometabolic reprogramming by GLP-1 receptor agonists in inflammatory skin diseases: A scoping review of omics, immune regulation, and exercise-technology interactions
PP-19	Naufal Reginald Abiyasa	YIA	Wearable technology for monitoring immune stress and exercise-induced physiological responses: A scoping review
PP-20	Kayla Anindya	YIA	Wearable sweat biosensors and saliva-based biomarker monitoring in exercise immunology: A scoping review
PP-21	Hoi Yee Chan	YIA	Can exercise-associated leukocytosis be used as a surrogate screening biomarker for exercise-induced gastrointestinal syndrome? - A feasibility exploration
PP-22	Kayla Henningsen	YIA	The impact of a polyphenol rich sugarcane extract nutrition intervention on exercise-associated bacteraemia in response to exertional-heat stress
PP-23	Isao Okayasu		Prostaglandin E-major urinary metabolite as a potential biomarker of muscle inflammation following physical exercise, considering gender difference
PP-24	Hung-Wen Liu		Sex differences in appetite regulation and energy intake following moderate-load resistance exercise
PP-25	Hayato Tsukamoto		No effect of flavanol-rich cocoa on salivary cortisol and secretory immunoglobulin A concentrations at rest and after exercise under cognitive fatigue
PP-26	Hsin-Hua Li		Epigallocatechin gallate attenuates hydrogen peroxide-induced atrophy-related responses in C2C12 myotubes
PP-27	Chin Hsu		Metabolomic profiling of immunometabolic responses following antrodia camphorata supplementation and prolonged exercise
PP-28	Tania Pithon-Curi		Effects of cardiovascular rehabilitation in plasma lipidome profiles of myocardial infarction patients with and without type 2 diabetes mellitus
PP-29	Jiapeng Huang	YIA	8-week kaempferia parviflora extract administration improves submaximal exercise capacity in mice by enhancing skeletal muscle antioxidant gene expression and plasma antioxidant capacity
PP-30	Chung-Kai Wang	YIA	Glutamine and iron supplementation optimizes mucosal immunity against high-intensity resistance exercise stress in women during the mid-luteal phase
PP-31	Angelika Pritama Naldita Haloho	YIA	Beyond moderate-to-vigorous physical activity: Low-intensity physical activity and immunometabolic regulation — A scoping review
PP-32	Chieh-Yu Yang	YIA	Probiotic effects on immunity, cytokines, and URTI in athletes: A systematic review and meta-analysis
PP-33	Queennyva Rumaisya	YIA	Probiotic supplementation for endurance and athletic performance in athletes: A scoping review
PP-34	Ryo Miyazaki		Comparative analysis of the discriminative ability of GDF-15 and FGF21 for prefrailty and frailty in community-dwelling older adults
PP-35	Jai-Sing Yang		Association between serum creatinine-to-body weight ratio, exercise, and muscle mass: A large-scale cross-sectional study in the Taiwan biobank
PP-36	Shuji Sawada		miR-4423-3p and miR-191-5p as exploratory candidates for phase angle response after bodyweight-based resistance training in Japanese older adults
PP-37	Hui Lyu		Effect of subcutaneous adipose tissue on ultrasound echo intensity of rectus femoris: Implications for region of interest selection

PP-38	Junqiang Jia	YIA	Age-related divergence between muscle thickness and strength differs across upper and lower limbs
PP-39	Sohrab Rezaei	YIA	Effects of taurine supplementation combined with exercise training on inflammatory and oxidative stress biomarkers in older women with sarcopenia
PP-40	Kaan Akalp	YIA	The influence of simultaneous aerobic and cognitive training (Activ4Brain) intervention on cognition, inflammatory markers and neuroprotective factors
PP-41	Nasda Aliatus Sya'bana	YIA	The role of exercise in modulating immunosenescence-related mechanisms in brain aging and neuroprotection: A scoping review
PP-42	Tomoya Kasugai	YIA	Cellular senescence induced by the DNA alkylation damage response on myoblast differentiation
PP-43	Orgesa Qipo	YIA	Impact of acute blood flow restriction training and high intensity resistance training on BDNF and IGF-1 levels in healthy older men
PP-44	Ayumi Goto		CREG1 ameliorates diabetic pathology and enhances voluntary exercise in a mouse model of diabetes mellitus
PP-45	Thomas G. Bissen	YIA	The association between body composition and immune cell mobilization during acute exercise in young adults
PP-46	Luiz Eduardo Ferraz Rodrigues	YIA	Effect of resistance exercise on insulin resistance in skeletal muscle in a non-obese type 2 diabetic animal model
PP-47	Megan M. Lo	YIA	Habitual physical activity patterns of children are related to NK cell mobilization following high-intensity intermittent exercise
PP-48	Eloise May	YIA	β -adrenergic sensitivity is preserved in circulating peripheral blood mononuclear cells in young adults with obesity
PP-49	Hong Shik Park	YIA	The effects of inspiratory muscle strength training on β 2-adrenergic mediated cAMP signaling in young adults with obesity
PP-50	Kyoma Sasaoka	YIA	Associations of meditation, budo, and geido with mindfulness-related measures: WASEDA'S health study
PP-51	Shuo Wang	YIA	Time-of-day exercise and redox adaptation in obese mice: muscle-derived extracellular vesicle miRNAs as candidate regulators
PP-52	Noriaki Kawanishi		Aging alters the microRNA expression profile of extracellular vesicles derived from skeletal muscle-resident CD45-positive cells and their effects on gene expression in skeletal muscle cells
PP-53	Tomoko Fukazawa		Effects of 6-month Chios Mastiha resin supplementation alone or combined with physical activity on glycemic control and lipid metabolism in middle-aged Japanese men
PP-54	Michelle Burr	YIA	Acute exercise enhances the potency of cytokine-induced killer cells against hematological malignancies
PP-55	Xue-Hua Ling	YIA	Phenotypic landscape mapping by multiparametric high-content screening reveals divergent modulators of cancer cachexia-associated muscle atrophy
PP-56	Laurence Poirier	YIA	Immune signatures of exercise-mobilized NK cells in aging cancer patients undergoing treatment identified by single-cell RNA sequencing
PP-57	Helena Batatinha		Impact of heat exposure on immune responses during endurance exercise in triathletes

PP-58	Yoshitaka Ohno		The effect of environmental heat stress on the morphological changes in cultured skeletal muscle cells during proliferation
PP-59	Shinsuke Tamai		Effects of high-concentration carbon dioxide hot water immersion and contrast water therapy on salivary human herpesvirus 6 and 7 levels
PP-60	Yichang Wang	YIA	Effects of menopausal status on body temperature responses during exercise in the heat
PP-61	Yun-Ru Wu	YIA	LGG attenuates PM2.5- and allergen-induced airway inflammation through immune rebalancing: A co-exposure model for exercise-associated airway disease
PP-62	Hiyori Nogawa	YIA	Effects of acute resistance exercise combined with hypoxic exposure maintained until immediately after exercise on metabolic and hormonal responses
PP-63	Eriko Iino	YIA	The effects of different beverage intake during field sports exercise in severe heat on dehydration and secretory immunoglobulin A
PP-64	Audinny Putri Prettisia	YIA	Exercise-induced immune responses in tropical hot-humid environments: A scoping review
PP-65	Kazuma Izumi	YIA	Effects of knee joint angle on intramuscular blood flow and muscle deoxygenation during fatiguing isometric contractions
PP-66	Gen Tanabe		Nonlinear relationship between salivary flow rate and secretory IgA concentration in athletes
PP-67	Sofia Botelho Teixeira	YIA	Breathing better, living better? Functional and patient-reported outcomes of pulmonary rehabilitation in interstitial lung disease
PP-68	Tatsuya Moteki	YIA	Effects of hip and knee flexion angle combinations on hamstring muscle activity and knee flexion torque during maximal voluntary isometric knee flexion

Keynote

How Can Exercise Immunology Contribute to Everyday Life?

A Suggestion for Need-Oriented Exercise Immunology

Ryoichi Nagatomi, Professor Emeritus Tohoku University

Director of Designing Future Health Initiative, Center for Promotion of Innovation Strategy, Tohoku University

Abstract

Exercise immunology has greatly advanced our understanding of the interactions between physical activity and the immune system. Over the past four decades, research has elucidated the mechanisms by which exercise influences immune surveillance, inflammation, infection susceptibility, and tissue repair, providing scientific foundations for health promotion and disease prevention. However, much of the field has been driven by scientific curiosity and physiological questions rather than by the practical needs encountered in everyday life.

In this keynote lecture, I propose the concept of **Need-oriented Exercise Immunology**, an approach that places real-world health concerns at the center of research and practice. The purpose of exercise immunology should not be limited to describing immunological responses to exercise, but should extend to addressing problems that people actually face, such as return to play or work after infectious diseases, physical activity and sports for immunocompromised patients and others.

Need-oriented Exercise Immunology emphasizes the translation of mechanistic findings into practical solutions tailored to individuals and communities. It should be noted that once Exercise Immunology is emphasized, it may also deprive an opportunity to meet the unmet need with other disciplines of science.

By reviewing representative findings from exercise immunology and discussing future perspectives, this lecture aims to explore how the discipline can evolve from a science that explains physiological phenomena to one that actively contributes to healthier daily living. Such a transition may help establish exercise immunology as a truly people-centered science for the twenty-first century.

Exploring current evidence on the drivers of heat stress and injury: Can heat stroke be triggered by immune disturbance?

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Abstract

Environmental heat affects human physiology and functions in the forms of discomfort, limitations in work performance and increased risks of heat injury. The aetiology underlying these effects of heat are not the same and are not necessarily connected. However, the strategies to mitigate the risks of these condition are often broad and non-specific, targeting primarily at controlling the rise in body temperature and limiting exposure to environmental heat. These approaches in mitigating the effects of heat stress are grounded on the classical models of heat injury, which dates back more than a century. This presentation will explore evidence to suggest that thermoregulation and heat intolerance are different both in concept and physiology, and that heat is not the only driver of heat injury. Current evidence suggests that fatigue during physical performance may be triggered centrally by a critical threshold body temperature, which in itself is a self-limiting mechanism against excessive heat load storage. A more effective thermoregulatory system in limiting the extent of positive thermal balance is also advantageous for endurance performance, suggesting that heat is regulated to preserve homeostasis and to sustain physical work, and may not be associated with risks of heat injury. Although all victims of heat injury have elevated body temperature, not everyone with elevated temperature suffers from heat injury - which is more often the case. There is also growing evidence from animal models and pathology reports that heat stroke is associated with a compromised immune system, gut-related endotoxemia and systemic inflammation, which is not totally associated with heat stress. The exploration of this evidence should lead to more effective design of strategies to mitigate the effects of heat on human function and health.

References

Lim C.L. and L. Mackinnon. The role of exercise-induced immune disturbances in the pathology of heat Stroke: The dual pathway model of heat stroke. *Sports Med* 36: 39–64, 2006.

Lim C.L. Heat sepsis precedes heat toxicity in the pathophysiology of heat stroke. *Antioxidants* 2018 25;7(11):149. doi: 10.3390/antiox7110149

Lim C.L. Fundamental concepts of human thermoregulation and adaptation to heat: A review in the context of global warming. *Int J. Env Res Pub Health* doi:10.3390/ijerph17217795, 2020

Differential gene responses for slow-twitch and fast-twitch muscles in muscular atrophy and hypertrophy

Urara KASUGA^{1,2}, Tomoya KASUGAI¹, Keisuke IKEDA¹, Moe SUGASAKI¹, Yoshifumi ITOH³, Michiko HIRATA¹, Masaki INADA^{1,2}

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Abstract

INTRODUCTION: Disuse muscular atrophy represents a clinically significant consequence of physical unloading, characterized by the progressive loss of skeletal muscle mass and functional capacity (Tominari et al., 2019). Mechanical unloading is widely recognized; however, the precise molecular pathways governing muscle plasticity under altered gravitational forces remain to be elucidated. This investigation aims to clarify these mechanisms by analyzing the contrasting transcriptional responses of skeletal muscle to artificially produced physical unloading (1G) and mechanical loading via 2G hypergravity within a mouse model.

METHODS: Mice were subjected to either hindlimb unloading (HLU) or a 2G hypergravity environment, the latter generated using a newly developed, advanced centrifugal device. To comprehensively evaluate the global transcriptional profile, high-throughput RNA-sequencing (RNA-seq) was performed on two phenotypically distinct muscle tissues: the slow-twitch fiber-dominant soleus (SOL) and the fast-twitch fiber-dominant tibialis anterior (TA), focusing specifically on myogenic and myo-atrophic gene expression networks.

RESULTS: RNA-seq analysis revealed distinct, diametrically opposed transcriptional adaptations under unloading and loading conditions. Under hindlimb unloading (HLU), rapid muscle atrophy occurred, which was selectively pronounced in the slow-twitch fiber-dominant SOL. Within 1 day of HLU, atrogenes were rapidly upregulated, whereas growth factors, such as insulin-like growth factor (IGF), were downregulated. Disuse atrophy in slow-twitch muscles is driven by the suppression of myogenic transcription factors, decreased myokine expression, reduced mitochondrial bioenergetics, and impaired angiogenesis and apoptosis (Matsunobe et al., 2022). Conversely, 2G hypergravity elicited robust hypertrophic adaptations. At the molecular level, 2G hypergravity enhanced the mRNA expression of pivotal myogenic regulatory factors (Myod1, Myog, Myf5, Myf6, Pax7), anabolic myokines (Igf1, Fstl1, Sparc), and Yap1/Taz transcription factors. In contrast to HLU, hypergravity mitigated muscle protein degradation by downregulating key ubiquitin ligases (Atrogin1, Murf1) and significantly suppressing autophagy-related genes (Lc3b, Atg5, Atg7, Atg16l) (Takatoya et al., 2025).

CONCLUSION: In conclusion, skeletal muscle mass and phenotypic identity are bidirectionally governed by gravitational and mechanical forces. Disuse atrophy is driven by the coordinated suppression of myogenic factors and the activation of proteolytic and apoptotic pathways, specifically targeting slow-twitch fibers. Conversely, hypergravity-induced hypertrophy is mediated by the activation of myogenic and oxidative gene networks alongside the concurrent suppression of atrophic degradation machinery, highlighting the adaptive capacity of muscle to altered gravitational loads.

References

Matsunobe, M., Motohashi, N., Aoki, E., Tominari, T., Inada, M., & Aoki, Y. (2022). Caveolin-3 regulates the activity of Ca²⁺/calmodulin-dependent protein kinase II in C2C12 cells. *American Journal of Physiology-Cell Physiology*, 323(4), C1137–C1148. <https://doi.org/10.1152/ajpcell.00077.2022>

Takatoya, M., Kasugai, T., Arai, D., Kasuga, U., Miyaara, C., Hirata, M., Itoh, Y., Tominari, T., Aoki, Y., & Inada, M. (2025). Glutamine Promotes Myogenesis in Myoblasts Through Glutaminolysis-Mediated Histone H3 Acetylation That Enhances Myogenin Transcription. *Nutrients*, 17(23), 3673. <https://doi.org/10.3390/nu17233673>

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Oral Presentation

T cell metabolism and function differs by cardiorespiratory fitness level and with acute exercise

Emily LAVOY¹, Charlie HODGMAN¹, Justin CRANE¹, Rebekah MADDUX¹, and Okechukwu OFORKA¹

¹ Health and Human Performance, University of Houston, Houston, USA
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Abstract

INTRODUCTION: Cardiorespiratory fitness (CRF) is associated with enhanced leukocyte metabolism, yet the effects of CRF on the metabolism of specific leukocytes such as CD8+ T cell subsets or regulatory T cells (Tregs) are not fully understood. The extent to which T cell metabolism changes acutely with exercise is also unknown. As T cell metabolism and function are linked, metabolic changes associated with higher CRF or acute exercise could impact Tc function. Here, we asked whether T cell metabolism and function differed by CRF level or by acute exercise.

METHODS: Participants (n=45: 18 female; 29.8 ± 6.3 years) completed a VO_{2max} test to determine CRF and donated resting blood. A subset (n=18: 9 female) with average CRF values (33.8 ± 3.9 ml/kg/min) returned twice to cycle 30 minutes at moderate and heavy intensity and donated blood before, after, and 2h after exercise. CD8+ T cell subsets and Treg fatty acid and amino acid oxidation (FAO and AAO) capacity, glycolytic capacity, and IFN-γ or IL-10 expression were assessed via flow cytometry. Linear regression assessed CRF as predictor of cell metabolism and function. Effects of acute exercise and intensity were analyzed by linear mixed models. Analyses were conducted within CD8+ T cell subsets and Tregs.

RESULTS: CRF predicted FAO and AAO capacity of each CD8+ T cell subset (p<.05). CRF also predicted glycolytic capacity of CD8+ central memory and effector memory re-expressing CD45RA (EMRA) subsets, and Tregs (p<.05). As CRF values increased, so did FAO and AAO and glycolytic capacities of each cell type. CRF predicted IFN-γ expression by naive and EMRA CD8+ T cells (p<.05). Post-exercise, CD8+ T cell subsets and Tregs had lowered metabolic activity and glycolytic capacity (p<.05). These changes returned to or exceeded resting values by 2h post-exercise. Despite lowered metabolic parameters post-exercise, Treg IL-10 expression was greatest post-exercise, and CD8+ T cell IFN-γ expression negatively correlated with post-exercise metabolic activity (p<.05). No significant effects of exercise intensity on CD8+ T cell metabolism were detected. Yet, changes in FAO and AAO capacity among Tregs were greater following heavy intensity compared to moderate intensity exercise.

CONCLUSION: These data provide evidence that greater CRF is associated with increased CD8+ T cell oxidative and glycolytic metabolism and enhanced function, as well as increased Treg glycolytic capacity. Further, both moderate and heavy intensity acute exercise transiently lowered metabolic activity and glycolytic capacity, but not functional capacity, of CD8+ T cell subsets and Tregs. The data indicate that T cell subsets differ in the degree to which their metabolic properties are impacted by CRF or acute exercise, highlighting the importance of examining metabolic responses to exercise within cell subsets. These results suggest that T cell metabolism may be modified by exercise training; this requires more study.

Neutrophil depletion alters early repair responses and delays skeletal muscle regeneration following crush injury

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Abstract

INTRODUCTION: Skeletal muscle regeneration is orchestrated by a complex inflammatory response in which neutrophils rapidly accumulate at the injury site during the early phase of regeneration. However, whether neutrophils exert beneficial or detrimental effects on muscle repair remains controversial, partly because previous studies (e.g., Teixeira et al., 2003) have been limited by the use of non-specific depletion strategies and/or toxin-induced injury models that may not adequately reflect physiological muscle injury. Therefore, this study investigated the effects of neutrophil depletion on muscle regeneration and injury-induced gene expression profiles using a neutrophil-specific depletion approach in a crush injury model.

METHODS: Male ICR mice (12-wk-old) were divided into depletion (Dep) and control (Con) groups. For neutrophil depletion, anti-Ly6G and isotype control antibodies were intraperitoneally administered to mice in the Dep and Con groups, respectively, 24 h before muscle injury. Muscle injury was induced by crushing the extensor digitorum longus muscle for 30 s using forceps, as previously described (Kawashima et al., 2020) with some modifications. Muscle regeneration was evaluated by measuring the cross-sectional area (CSA) of regenerating myofibers on day 14 post-injury. Transcriptomic profiling of injured muscle using mRNA sequencing was conducted during the early phase of regeneration, and KEGG pathway analysis was performed using genes showing >1.5-fold differential expression between groups.

RESULTS: Administration of anti-Ly6G antibody reduced neutrophil accumulation in injured muscles by approximately 90% and 63% on days 1 and 3 after injury, respectively. The CSA of regenerating myofibers on day 14 was significantly smaller in the Dep group than in the Con group ($P < 0.05$). Transcriptomic profiling revealed marked alterations in early tissue remodeling and regenerative pathways in the Dep group. On day 1, pathways associated with ubiquitin-mediated proteolysis and cell cycle were downregulated, whereas pathways related to endocytosis and lysosome biogenesis were upregulated. On day 3, TNF and mTOR signaling pathways were downregulated.

CONCLUSION: These findings suggest that neutrophils contribute to muscle regeneration after injury. The delayed regeneration observed following anti-Ly6G treatment may be associated with altered early tissue remodeling and regenerative responses.

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High-intensity interval training (HIIT) induces persistent and divergent remodelling of T cell immunity

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Abstract

INTRODUCTION: Adoptive cellular therapy (ACT) is an immune cell-based cancer therapy, in which the patient's immune cells are extracted, equipped with anti-cancer properties, and re-infused. The quality of immune cells used for ACT determines the therapeutic outcome¹, yet patient immune cells are often compromised due to chemotherapy and on-going disease. Exercise is known to strengthen immune function², and thus, has the potential to improve immune cell quality at the source as an upstream intervention in ACT development. However, mechanistic insights into the exercise-immunity axis remain underexplored³, limiting our ability to leverage exercise to enhance ACT. Here, we used a multi-omics approach to uncover the immune impact of acute HIIT.

METHODS: Healthy males (N=12; 18-36 years) performed a bout of HIIT comprising 4 x 4-min cycling at 110% of their power output at VT₂, determined from a VO₂max test, with 3-min recovery intervals. Peripheral blood samples were collected at rest (T⁰), immediately post-exercise (T'), 1 hr- (T¹), 5 hr- (T⁵), and 24 hr-post (T²⁴). We profiled time-course transcriptional changes in PBMCs at the single-cell level using scRNAseq, with a focus on CD8⁺ T cells. Plasma metabolomics, lipidomics, and proteomics were used to identify exercise-induced changes and their correlative networks. Omics-based findings were validated through immunophenotyping and SCENITH metabolic assay using spectral flow cytometry.

RESULTS: CD8⁺ T cell number increased by 1.76-fold at T' (p<0.001), which returned to baseline by T²⁴. In contrast to this transient change in cell number, transcriptional changes persisted, with naïve-like and cytotoxic signature scores progressively increasing and peaking at T²⁴ (p<0.001). To determine how both scores concurrently increase, we tracked TCR clonotypes and found divergent remodeling between singleton and expanded clonotypes. Increased naïve-like signature score, including *TCF7*, was more pronounced in singleton clonotypes, whereas cytotoxic signature score, including *PRF* and *GZMB*, preferentially increased in expanded clonotypes. GSEA also identified immediate and persistent metabolic remodeling towards OXPHOS (p<0.05) and FAO (p<0.05). Consistent with this, the plasma metabolome, lipidome, and proteome showed dynamic changes across the time-course, including significant changes in TCA cycle intermediates, amino acids, and lipid-associated molecules. Using SCENITH, we confirmed exercise-induced changes in OXPHOS dependence of CD8⁺ T cells, which progressively increased by 28% from T⁰ to T²⁴ (p<0.001).

CONCLUSION: Acute HIIT induces persistent remodeling of CD8⁺ T cells, reinforcing naïve-like and cytotoxic signature scores in a subset-specific manner. Exercise-altered milieu also elicits metabolic reprogramming of CD8⁺ T cells towards OXPHOS. These functional changes support the potential of exercise as an upstream intervention to develop more potent, long-lasting, and metabolically flexible ACT products.

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Acute Exercise and Extracellular Vesicle Responses: Immunological and Methodological Insights from a Systematic Review Sub-Analysis

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Abstract

INTRODUCTION: Acute exercise induces physiological and immunological adaptations that support systemic homeostasis. Extracellular vesicles (EVs) may mediate these adaptations by transferring bioactive cargo between tissues and immune cells [1,2,3]. However, evidence on acute exercise-induced EV responses remains fragmented due to methodological heterogeneity. This review synthesised biological and methodological evidence on EV responses to acute exercise in healthy adults, focusing on immunology-relevant outcomes.

METHODS: PubMed, Scopus, Web of Science, Cochrane Library and SPORTDiscus were searched systematically (PROSPERO: CRD420261294279). Studies investigating blood-derived EV responses before and after a single exercise bout in healthy adults were eligible. This sub-analysis included studies reporting immune-cell-derived EVs, inflammatory or immunoregulatory EV cargo, or immune-related EV phenotypes following acute endurance exercise. Study quality was assessed using a validated NIH quality assessment tool. Findings were synthesised narratively.

RESULTS: Among 75 studies included in the full review, 20 studies comprising 308 participants were eligible for this endurance exercise immunology-focused sub-analysis. Participants ranged from sedentary to endurance-trained individuals (age: 33.8 ± 15.8 years, 23.4% females). Interventions included cycling (n=12), treadmill exercise (n=5) and walking (n=3), performed at moderate to maximal intensity and lasting 10–90 min.

Acute exercise induced heterogeneous but predominantly positive effects on circulating EV abundance with increases in 11 studies, no significant change in 5 and decreases in specific EV subpopulations in 4. More consistently, exercise influenced EV phenotype and cellular origin, with frequent increases in platelet-, leukocyte-, monocyte- and neutrophil-derived EV populations. Several studies also reported changes in EV-associated proteins, miRNAs and other cargo linked to immune regulation, inflammation, coagulation and vascular homeostasis, suggesting that exercise may remodel EV composition more consistently than total EV abundance.

Methodologically, plasma was the predominant matrix (n=17), but studies varied in anticoagulant use (EDTA n=11; citrate n=6; heparin n=1), pre-analytical processing, EV isolation, characterisation and cargo profiling workflows. Isolation methods included differential centrifugation (n=5), SEC (n=6) and ultracentrifugation (n=4). While most studies employed canonical recommended EV markers [2], EV purity assessment was inconsistent.

CONCLUSION: Acute endurance exercise remodels the circulating EV landscape through changes in EV abundance, cellular origin and molecular cargo. However, methodological heterogeneity limits comparability across studies and precludes causal conclusions on EV-mediated exercise adaptations. Future cargo-focused analyses using harmonised analytical workflows may enhance mechanistic insight into EV-mediated exercise adaptations.

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The influence of latent Cytomegalovirus infection on adipose tissue in healthy men

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Abstract

INTRODUCTION: Adipose tissue is an endocrine and immunological organ that has roles in host defense. We have shown that adipose tissue changes substantially with ageing in the absence of obesity, including an accumulation of effector memory T cells and exacerbated inflammatory protein secretion. It is known that adipose tissue can be infected by pathogens, such as *Cytomegalovirus* (CMV), but the influence CMV sero-status has on adipose tissue immunometabolic profiles is unknown.

METHODS: We undertook secondary analyses of data from 24 non-obese, healthy men (age 23-73 years) stratified by CMV sero-status ($n=9$ CMV+, $n=15$ CMV-) from a previous study (Trim et al., 2022). Using flow cytometry, blood and adipose tissue CD4+/CD8+ T cells were characterised from Naïve (NA; CD27+CD45RA+) to Effector Memory subtypes (EMRA; CD27-CD45RA+) and adipose tissue macrophages (CD14+CD206+) were quantified. Inflammatory proteins were assessed in plasma and supernatant from 3 hour adipose tissue cultures with multiplex immunoassays. Transcriptional profiles were established via bulk RNA-sequencing of adipose tissue, and interactions between age, CMV sero-status and all variables were explored. Antigen specificity of adipose tissue T cells was assessed with interferon-gamma (IFN- γ) Enzyme-Linked Immunospot assays in a separate cohort of healthy non-obese people (5 men, 4 women, age 18-52 years).

RESULTS: Age, anthropometrics, and habitual physical activity were not different between CMV+ and CMV- participants ($p \geq 0.194$). CMV+ participants exhibited immunosenescent profiles in blood and adipose tissue: counts and/or proportions of CD4+/CD8+ EMRA cells were higher and CD4+/CD8+ NA cells were lower compared to CMV- participants ($p < 0.04$). Unstimulated T cell activation was not different in blood or adipose tissue between CMV+ and CMV- participants. Adipose tissue macrophage counts were not different, but their proportion among CD45+ cells and their activation was lower in CMV+ participants ($p < 0.040$). In cultured adipose tissue supernatant, Serum Amyloid Alpha (SAA) was higher, and leptin was lower in CMV+ participants ($p \leq 0.032$). Adipose tissue RNA-sequencing revealed an interaction between CMV-serostatus and age, with a CMV-associated accelerated ageing phenotype present in both younger and older participants, characterized by inflammation and immune activation across pathways within lymphocytes, granulocytes and myeloid cells. These features were significantly associated with inflammatory protein secretion from cultured adipose tissue and the accumulation of adipose tissue T cells. Lastly, IFN- γ producing CMV-specific T cells recognizing the antigens pp65 and IE1 were present in adipose tissue.

CONCLUSION: We show for the first time that latent CMV infection alters the profile of human adipose tissue and is associated with higher acute-phase protein secretion and lower leptin production accompanied by an inflammatory transcriptome characteristic of adipose tissue ageing.

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Acute HIIT widely modifies immunity: Dynamics of virus-specific CD8⁺ T cells, immunomodulatory serum proteins and chemokine receptor expression on lymphocytes

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Abstract

INTRODUCTION: Physical activity induces rapid, selective leukocyte mobilization. Among the most responsive cell types to high-intensity exercise are NK and CD8⁺ T cells, key effectors of immune defense against infected and malignant cells. However, comprehensive characterization of acute high-intensity interval training (HIIT)-induced immune modulation is limited.

METHODS: We collected peripheral blood from 23 healthy participants undergoing a supervised, group-based HIIT session at baseline, immediately post-exercise (ex02), and one hour post-exercise (ex60). Cell counts were quantified using clinical-grade flow cytometry. CD8⁺ T cells were analyzed for memory and differentiation status and virus peptide reactivity using DNA-barcoded peptide-MHC multimer staining targeting 250 peptides. Associations between individual characteristics (fitness, sex, body composition, and age) and CD8⁺ T cell mobilization were analyzed to identify potential modulators of this response. Chemokine receptor expression (CX3CR1, CXCR2, CXCR4, CCR2, CCR5) on CD8⁺, CD4⁺, γδ T cells, NK cells, and monocytes was profiled using flow cytometry and FlowSOM clustering. Serum proteomics for a panel of immunomodulatory proteins were performed using the Olink platform, and associations with individual characteristics were evaluated using linear regression and variation analysis.

RESULTS: A single HIIT bout induced robust cell type-specific mobilization followed by substantial egress, consistent across fitness levels, body composition and age. NK, γδ and CD8⁺ T cells were the most HIIT-responsive cell types. Catecholamines NE and EPI peaked post-exercise, and NE was selectively associated with CD8⁺ T cell mobilization. CD8⁺ T cell memory subsets were reorganized, reducing terminally differentiated and CD57⁺, PD-1⁺, and CD28neg cells at ex60 post exercise. Circulating virus-reactive CD8⁺ T cells increased across 12 virus types and decreased below baseline at ex60. HIIT modulated chemokine receptor profiles in a cell type-specific manner – HIIT preferentially mobilized CX3CR1⁺ CXCR2⁺ CD56dim NK cells, CD4⁺ T cells expressing CX3CR1hi and CCR5⁺, and CX3CR1⁺ CD56⁺ γδ T cells, and two populations of CD8⁺ T cells with distinct chemokine receptor patterns, indicating mobilization of immune cells phenotypically associated with migratory and cytotoxic potential. Immunomodulatory serum proteins are highly HIIT-reactive, with 79 proteins increased immediately post-exercise, and 47 proteins decreased one hour after exercise compared to bsl, including proteins related to tissue migration

and cytolysis. Responses were largely independent of sex, VO_2 peak, lean body mass and body fat mass, while age discriminated low and high responders and predicted selected proteins (Pleiotrophin, MMP7).

CONCLUSION: Acute HIIT mobilizes functional, virus-reactive CD8^+ T cells with enhanced migratory and activation potential. Transient remodeling of the immunomodulatory serum proteome demonstrates strong immune modification by HIIT, in conclusion highlighting its potential as a broadly applicable immune-activating intervention.

The study is registered at clinicaltrials.gov (NCT05826496).

Mechanical lung expansion triggers antiviral innate immune responses *in vivo*

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Abstract

INTRODUCTION: We are constantly exposed to infectious threats such as seasonal influenza viruses and pandemic-causing pathogens including SARS-CoV-2. Although preventive strategies such as vaccination are widely implemented worldwide to reduce the risk of infectious diseases, access to medical resources remains limited due to finite supply and economic cost. As a result, many people each year are unable to benefit sufficiently from infection prevention measures. Witnessing the global SARS-CoV-2 pandemic firsthand, this study aimed to identify a universally accessible method for infection prevention and to elucidate its underlying mechanism.

METHODS: Using $\Delta\beta$ -Luc mice (in which the *Ifnb* gene is replaced with a luciferase reporter gene), wild-type (WT) mice, and cGAS/STING knockout mice, we investigated whether lung expansion stimulation could induce *Ifnb* production and exert antiviral effects against Influenza A virus (IAV) infection.

RESULTS: Our analyses revealed that mechanical lung expansion stimulation robustly induces *Ifnb* expression *in vivo*. Importantly, mice subjected to lung expansion stimulation exhibited enhanced resistance to IAV infection, demonstrating that this mechanically induced immune response possesses functional antiviral activity. These findings indicate that physical stimulation of the respiratory system can activate innate antiviral immunity independently of conventional pathogen-derived immune activation signals. To further elucidate the mechanism underlying this phenomenon, we investigated the involvement of innate immune signaling pathways using knockout mouse models. Interestingly, the induction of *Ifnb* following lung expansion stimulation was markedly impaired in cGAS-deficient and STING-deficient mice, demonstrating that the cGAS–STING signaling axis plays a critical role in this response. The cGAS–STING pathway is traditionally recognized as a cytosolic DNA sensing pathway that detects pathogenic or damaged self-DNA and subsequently induces type I interferon production. Our findings therefore suggest that mechanical stimulation generated by lung expansion may trigger endogenous danger-associated molecular signals capable of activating cGAS–STING-mediated innate immunity.

CONCLUSION: Our results suggest that mechanical lung expansion stimulation robustly induces *Ifnb* expression mediated by the cGAS-STING pathway *in vivo*.

Effects of Long-term Glutamine Supplementation on Gut Microbiota During Training Periodization of Cross-country Skiers

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Abstract

INTRODUCTION: Gut microbiota play a key role in host metabolism, immune regulation, and intestinal barrier function, contributing to the health and performance of athletes. Endurance training imposes physiological stress on athletes that may disrupt the intestinal homeostasis and alter the microbial composition. L-glutamine has been reported to support the intestinal function of endurance athletes under physiological stress. Previous studies in non-athletic populations reported that glutamine supplementation may influence the gut microbiota composition and metabolic activity; however, the findings were not consistent and the evidence in athletic populations, particularly during training period, is still limited. Therefore, this study aimed to determine whether L-glutamine supplementation influences gut microbiota composition during the training period in endurance athletes.

METHODS: Nineteen collegiate cross-country skiers were recruited in a randomized, double-blind, placebo-controlled crossover trial during the training period. They consumed 4-week L-glutamine or placebo (10 g/day), respectively. Stool samples were collected at three time points during each intervention period (baseline, week 2, and week 4). Gut microbiota composition was analyzed using 16S rRNA gene sequencing targeting the V4 region. Fecal calprotectin concentrations were measured as a marker of intestinal inflammation. Gastrointestinal symptoms were assessed weekly using the Gastrointestinal Symptom Rating Scale (GSRS), and stool consistency was evaluated using the Bristol Stool Form Scale (BSFS).

RESULTS: Shannon α -diversity increased over time ($p = 0.011$), and beta diversity also showed significant time-related changes (PERMANOVA $p = 0.004$), with no evident supplementation or interaction effects. At the genus level, significant time $\times$ supplementation interactions were observed for *Faecalibacterium* and *Collinsella*, with a higher relative abundance of *Faecalibacterium* ($p = 0.010$) and a lower relative abundance of *Collinsella* ($p = 0.020$) at week 2 during glutamine supplementation. Significant positive correlations among short-chain fatty acids (SCFAs) producing bacteria across time intervals were observed under glutamine supplementation, particularly between *Anaerostipes* and *Blautia* (baseline–week 2: $p = 0.76$, FDR = 0.002; baseline–week 4: $p = 0.64$, FDR = 0.039) and also between *Anaerostipes* and *Bifidobacterium* (baseline–week 4: $p = 0.69$, FDR = 0.032). L-glutamine supplementation did not significantly affect fecal calprotectin concentrations, GSRS and BSFS scores. *Blautia* showed a negative correlation tendency with fecal calprotectin ($p = -0.553$, $p = 0.026$, FDR = 0.158). Among GSRS subscales, only abdominal pain showed a significant time effect ($p = 0.020$), while reflux showed a trend over time ($p = 0.082$).

CONCLUSION: L-glutamine supplementation may have contributed to transient genus-level changes and enhanced SCFA-producing bacterial interactions.

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Multi-omics assessment of responses to resistance exercise

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Abstract

INTRODUCTION: Intense resistance exercise induces microtrauma within skeletal muscle. This microtrauma has been characterized by investigating changes in force-generating capacity, subjective ratings of delayed onset muscle soreness, circulating muscle enzymes and proteins (e.g., creatine kinase, myoglobin), and circulating cytokines. By contrast, less is known about changes in the serum proteome, salivary microRNAs and the transcriptional profile of peripheral blood mononuclear cells.

METHODS: Twenty-two resistance-trained adults (10 males, 12 females; age 18–45 years) volunteered to take part in the study. The exercise protocol involved three sets of 10 repetitions of 10 upper and lower body exercises performed at 50% 1-RM, with 1.5 minute rest between sets and exercises. The participants performed this exercise protocol twice on the same day, with 1 hour between each bout. Blood and saliva samples were collected at rest 1–2 weeks before exercise, 2 hours before exercise, soon after the first and second bouts of exercise, and 24 hours after exercise. The serum proteome was analysed using liquid-chromatography tandem mass spectrometry. Saliva samples were analysed for microRNAs. The transcriptional profile of peripheral blood mononuclear cells were analysed by NextGen Sequencing. Ratings of perceived exertion, repetitions in reserve, maximal isometric strength and exercise completion rates were recorded throughout the protocol.

RESULTS: Data analysis of the serum proteome, salivary microRNAs and the transcriptional profile of peripheral blood mononuclear cells is ongoing. Final results will be presented at the conference.

Strength training affects intracellular stress response in peripheral immune cells

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Abstract

INTRODUCTION: The aim of the present study was to examine the impact of a three-month resistance exercise intervention on the expression of inflammation related genes in peripheral blood mononuclear cells (PBMCs) of older adults, after an acute infection mimicked by an in-vitro challenge by lipopolysaccharide (LPS) in PBMCs.

METHODS: Adults aged 65 years, or more were randomized to three-month intervention, 2 to 3 times a week: an intensive strength training (IST, 3 sets of 10 reps. at 80% 1RM), strength endurance training (SET, 2 sets of 30 reps. at 40% 1RM) or a flexibility training (CON, 3 sets of 30 sec.). Whole blood was collected by a venipuncture at baseline and after three months intervention. PBMCs were isolated and cultured with and without LPS challenge for 24 hours. RNA was extracted from isolated PBMCs (blanco) and isolated PBMCs cultured without and with LPS (respectively control and LPS samples). A core set of 36 genes was investigated with Quantigene method.

RESULTS: No statistical differences were observed in the participants' characteristics between the three intervention groups at baseline. Both men and women showed comparable exercise-induced gene expression patterns after an LPS immunochallenge, however different genes were affected. In CMV seronegative men and women a more pro-inflammatory genes were downregulated after the exercise intervention regarding the LPS-induced gene expression in PBMCs. In the CMV seronegative men a more pronounced exercise-induced effect is visible in the SET group compared to the CON group than in seropositive men.

CONCLUSION: A confirmatory analysis via Quantigene of a core gene set identified after RNA sequence analyses showed that different resistance exercise intensities impacted the gene expression linked to inflammation, immunosenescence, and ageing in PBMCs after an LPS challenge. Both gender and CMV status have an impact on the immune function at the genetic level. In which CMV seronegative men benefit more from exercise regarding an immunochallenge. Thus, resistance exercise induces effects on gene expression after an immunochallenge, however a balanced resistance exercise program is recommended for optimal immune adaptations in older adults.

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Disuse-Induced Muscle Atrophy Impairs Inflammatory Regulation and Delays Skeletal Muscle Regeneration Following Acute Injury

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Abstract

INTRODUCTION: Skeletal muscle has a substantial capacity for regeneration after acute injury [1]. Efficient muscle repair depends on the timely coordination of myogenic and inflammatory responses [2]. Muscle atrophy is associated with impaired mobility, increased fall risk, and a greater incidence of fractures and musculoskeletal injury. However, little is known about how pre-existing muscle atrophy influences inflammatory responses and regenerative processes following subsequent injury. Therefore, the aim of this research was to investigate the inflammatory responses and regenerative processes following acute skeletal muscle injury in disuse-induced atrophied muscle. A mouse hindlimb immobilization model was used to induce disuse-associated muscle atrophy, followed by cardiotoxin injection to mimic acute muscle injury under prolonged disuse conditions.

METHODS: Eleven-week-old mice were randomly divided into 2 groups on Day 0: (1) control group (CON group) and (2) immobilization group (IM group). For those in the CON group, 7 mice were kept feeding without injection for 14 days until sacrifice. The other mice were injected with cardiotoxin on Day 14 and sacrificed at 6 hours, 3 days and 7 days after injection. Mice in the CON group were allowed to move freely within the cage during the experiment period. For those in the IM group, all mice were immobilized with bilateral lower limbs to induce disuse-associated atrophy. Seven mice were sacrificed on Day 14 without injection. The other mice were injected with cardiotoxin on Day 14 and sacrificed at 6 hours, 3 days and 7 days after injection. The immobilization was maintained throughout the post-injury regeneration period. Histological analysis was performed at each sacrificial time point. Myogenic gene expressions and inflammatory gene expressions were accessed at 3 and 7 days after injury.

RESULTS: Hindlimb immobilization successfully induced characteristic features of disuse atrophy, including reductions in muscle mass, myofiber size, and grip strength, indicating that a skeletal muscle wasting condition had been established before injury. When acute injury was subsequently introduced, atrophied muscle exhibited delayed tissue repair compared with non-atrophied control muscle. This was characterized by prolonged persistence of necrotic fibers, altered macrophage dynamics during regeneration, reduced formation and growth of regenerating myofibers, and changes in regeneration-related gene expression. Overall, these findings indicate that constant disuse condition disrupted the coordinated inflammatory and myogenic responses required for efficient muscle regeneration.

CONCLUSION: These findings indicate that skeletal muscle atrophy is not only a condition of reduced tissue mass, but also a biological state characterized by impaired immunoregulatory capacity that compromises subsequent muscle repair through partial inflammatory reactions [3].

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Self-assessed Immune Function and Associated Risk Factors among Japanese Firefighters

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Abstract

INTRODUCTION: Firefighters experience chronic physical and psychological stress that can impair immune function. Although regular immunological assessment would benefit firefighters, invasive biomarker measurement is impractical in the work setting. This study examined subjective immune function using the Immune Status Questionnaire (ISQ) and explored associated risk factors for low ISQ scores.

METHODS: An online survey was administered to Japanese firefighters using Microsoft Forms to examine their health status over the preceding 12 months. Completion of the survey indicated consent for participation in the study. Survey items included demographics, occupational information, lifestyle habits, health status, and subjective immune function measured by the ISQ (maximum score 10 with a cut-off score at ≤ 6 for poor status). For the purpose of this study, ISQ was translated to Japanese (FA) and checked by bilingual researcher (YH). Valid responses collected between May 11–14, 2026 were analyzed. Data are presented as mean (median) $\pm$ standard deviation (range). Kruskal-Wallis and Mann-Whitney U tests were used to identify risk factors for reduced subjective immune function.

RESULTS: A total of 471 responses were collected (461 male [97.88%], 9 female [1.91%]). The majority were aged 30–40 years (38.85%). Mean height, weight and BMI were 171.26 ± 5.49 cm, 70.34 ± 8.97 kg, and 24 ± 3 kg/m², respectively. Median ISQ score was 2 (range, 0–6) with no participants above the cut-off value). Age groups showed significant associations with ISQ scores ($\chi^2[5] = 28.28$, $p < .001$), with the 20–30 year group demonstrating significantly low ISQ scores compared to the 60–65 year age group ($p = .006$) and the 30–40 year group ($p = .005$). Similarly, both the 20–30 year group and the 30–40 year group had significantly low ISQ scores than the 50–60 year age group (the 20–30 year group, $p = .020$; the 30–40 year group, $p = .015$). Subjective sleep quality was also significantly associated with ISQ scores ($\chi^2 [4] = 13.87$, $p = .008$), with participants reporting "good" sleep quality demonstrating significantly higher ISQ scores compared to those reporting "poor" sleep quality ($p = .021$). ISQ scores were significantly lower in non-drinkers compared to drinkers ($U=30807.50$, $p=.016$). In contrast, BMI, exercise habits, dietary habits, and concurrent job positions were not significant factors contributing to ISQ score differences.

CONCLUSION: Firefighters demonstrated lower subjective immune function compared to the general population that observed 82.5% of the participants scoring $ISQ \geq 7$. Implementing appropriate conditioning strategies and ensuring adequate sleep may enhance immune function assessment.

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Divergent Peripheral (Muscle) and Systemic (Whole Blood) Immune Gene Expression Following Prolonged Intense Exercise: A Spatial and Transcriptomic Analysis

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Abstract

INTRODUCTION: Prolonged intense exercise provokes substantial perturbations in the immune system (1). While systemic immune responses have been characterised extensively using blood-based measures, our understanding of local immune responses within skeletal muscle remains limited (2). Spatial transcriptomic technologies now enable in situ, cell-type-resolved profiling within tissue (3). These approaches allow for simultaneous comparison of peripheral (muscle) and systemic (blood) immune responses with improved resolution.

METHODS: A single-arm prospective trial was employed to quantify the acute 0–3 h post-exercise immune response to a 2-hour bout of cycling on an ergometer at 110% of gas exchange threshold (GET). Vastus lateralis muscle biopsies and peripheral blood samples (x ml) were collected pre-exercise, immediately post-exercise, 30 min post-exercise and 3 h post-exercise from 11 healthy well-trained cyclists (3 female; 8 male). GeoMx® Digital Spatial Profiling (DSP) with the 1,812-plex Cancer Transcriptome Atlas was used to examine the expression of immune genes in non-segmented regions of interest in-situ within each muscle biopsy, and the nCounter® Digital Analyser with the PanCancer Immune Profiling Panel used to quantify the expression of immune genes in whole blood samples, which contained a set of 731 overlapping genes for cell typing and pathway profiling. Data analysis involved quality control assessment, filtering, normalisation, differential expression, pathway profiling and cell typing.

RESULTS: The pre-trial maximum $\dot{V}O_2$ uptake ($\dot{V}O_{2peak}$) was 55 (12) mL/kg/min (mean (SD)) with a peak power output of 384 (73) W. The power output attained at GET was 202 (51) W 110% of this GET was equivalent to 60 (9) % of $\dot{V}O_{2peak}$. The group mean power output sustained during the 2-h cycling bout was 205.0 (60) W, while heart rate averaged 134 (10) bpm (76 (3)) % of maximum heart rate). There were no significant differentially expressed genes at an adjusted p-value observed post-exercise in muscle tissue. Endurance exercise induced distinct changes in whole blood immune gene expression at all three post-exercise timepoints. Based on transcriptomic deconvolution of cell-specific genes, there were increases from pre-exercise to the post-exercise timepoints in the abundance of neutrophils (10-14% $\pm$ 7.5-17%; mean $\pm$ 95%; $p < 0.001$) confidence intervals) and CD45 cells (3.8-7.8% 1.8-9.4%; $p < 0.001$). Lymphocyte (T-cell, Th1, CD8 cells) cell abundance scores all decreased (~5%) from pre-exercise to the post-exercise timepoints. Immediately after exercise, gene sets associated with stress response, inflammation and leucocyte chemotaxis increased (>10%), while at 30 min and 3 h post-exercise, gene sets associated with inflammation, pathogen defence (~5%) and cytokine signalling increased compared to pre-exercise.

CONCLUSION: Distinct systemic and peripheral differences in the acute exercise-induced immune response emerge after 2 hours of prolonged intense cycling. Minimal changes in peripheral post-exercise immune gene expression is evidence of only modest perturbations in immunity.

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Comprehensive proteomic profiling in the WELCOM cohort identifies reduced inhibin/activin betaC in physically active women

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Abstract

INTRODUCTION: The WELCOM study (Weight Loss and Cancer Outcomes in the Mid-South) is a multi-omics project aimed at identifying potential cancer risk biomarkers associated with physiological characteristics in women in the greater Memphis area. A variety of approaches aimed at quantifying proteomic, metabolomic, and immune profiling data are being collected alongside traditional anthropometric, physiological, and clinically-relevant variables. Here, we present a secondary analysis of proteomic data using self-reported physical activity levels as an example of biomarker discovery possible in this rich dataset.

METHODS: A cohort of healthy female subjects was recruited across a full factorial design based on age group (>65 vs. <35), obesity status (lean vs. obese), and race (Black vs. white). Outcomes in this phase of the study are collected in women without cancer or other major chronic diseases and are intended to be discovery analyses for later application to cancer prediction. Physical activity level self-report was collected as a part of VioScreen questionnaires for dietary analysis, and subjects were categorized into low activity (sedentary or low active) or high activity (active, highly active, or extremely active) based on daily energy expenditure estimates. A comprehensive proteomic dataset was generated examining plasma levels of 5,540 proteins using the Olink platform, on which independent samples Student's t tests were performed to identify differentially expressed proteins (adj. $p < 0.05$) with Benjamini-Hochberg correction for false discovery rate (FDR). Data were analyzed using R v. 4.6.0.

RESULTS: Olink analysis identified several proteins which were significantly downregulated in active subjects after control for FDR. Of these, inhibin subunit beta C (INHBC) encodes a preproprotein which is processed to a TGF-beta superfamily protein. INHBC is associated with pro-inflammatory state and promotes tumor growth and migration, and the protein may modulate muscle myostatin signaling [1].

CONCLUSION: A preliminary analysis of comprehensive proteomics data found five proteins significantly downregulated in active subjects compared to less active counterparts after stringent correction for FDR (644 proteins were differentially regulated when considering raw p-values). These associations were independent of race, obesity, or age group status. INHBC, the gene for which encodes a TGF-beta superfamily protein, was the most notable of these proteins. Previous research has found significant negative correlations between the protein and VO2 max [2], but little is known about links between exercise and INHBC. Previous research has also suggested links between INHBC and various cancers [3], suggesting further study into the role of exercise in its expression. These results also demonstrate the potential for biomarker discovery in the WELCOM cohort.

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Precision-Prescribed HIIT at 110% RCP Abolishes Plasma Multi-Omic Heterogeneity Across Training Backgrounds

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Abstract

BACKGROUND: The classification of individuals as exercise "non-responders" has long been attributed to biological heterogeneity. Yet when exercise intensity is prescribed using generalized frameworks (i.e. a fixed percentage of VO_2max or maximum heart rate) two individuals at nominally the same intensity may be experiencing fundamentally different metabolic stimuli. The molecular heterogeneity that follows may therefore reflect the noise of imprecise prescription rather than true biological individuality.

METHODS: To test this, we recruited trained ($n = 4$) and untrained ($n = 3$) adults and delivered a high-intensity interval exercise (HIIT) protocol anchored to each individual's respiratory compensation point (RCP), adjusted for mean response time and VO_2 kinetics. Despite large differences in absolute VO_2max and power output, respiratory exchange ratio during exercise did not differ between groups ($p = 0.61$), confirming delivery of a metabolically equivalent relative stimulus. We profiled the acute plasma response using semi-targeted metabolomics and lipidomics (pre and post-exercise; $n = 7$) and Olink Explore HT proteomics (pre, post, 1h, 5h, and 24h; $n = 6$, 3 trained, 3 untrained).

RESULTS: Within-donor metabolomic analysis revealed a directionally concordant response across all participants regardless of training status, characterized by TCA cycle intermediate accumulation (fumarate, succinate, aconitate), purine catabolite release (hypoxanthine, xanthine), and broad amino acid clearance. In contrast, the plasma lipidome showed minimal net remodeling immediately post-exercise, pointing to the specificity of the water-soluble metabolic response at this acute timepoint and the buffering of opposing lipid mobilization and uptake fluxes in plasma. Olink proteomics revealed that all participants' immediate post-exercise proteomes converged to a uniform molecular state, independent of training background. Across recovery, a temporally organized adaptive program including cytokine and chemokine signaling, extracellular matrix remodeling, vascular endothelial growth factor receptor activity, and neurotrophic signaling emerged at 24 hours regardless of fitness level.

CONCLUSION: These findings reframe the exercise non-responder as a prescription artifact and establish precision exercise prescription as a methodological imperative for exercise molecular biology research and a clinical opportunity to harness the therapeutic potential of exercise across the population.

CITE-seq Reveals Rare Immune Cell Populations while Maintaining Concordance with Flow Cytometry in Exercise-Mobilized PBMCs

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Abstract

INTRODUCTION: Acute exercise is well known to preferentially mobilize and redistribute effector lymphocyte subsets, which is hypothesized to enhance immunosurveillance¹. However, there are a dearth of studies which assay the acute immune response to exercise at single cell resolutions, potentially obscuring exercise-induced changes in rare immune cell populations. In addition, it is not well known how closely single cell techniques align with conventional flow cytometry approaches on exercise mobilized cells.

METHODS: 9 healthy individuals performed a stepwise ~20 minute exercise trial that ranged in intensity from moderate to vigorous activity (50%-80% VO₂max). Peripheral venous blood was drawn at rest, during vigorous activity (80%) and 1 hour post exercise cessation. Whole blood samples were immediately run through an automated hematology analyzer to obtain a complete blood count and phenotyped on a 14-color flow cytometer to characterize major lymphocyte and monocyte lineages as well as T-cell differentiation states. PBMCs were isolated from whole blood and frozen for later analysis. Cellular Indexing of Transcriptomes and Epitopes by Sequencing (CITE-seq) was performed on thawed PBMCs. This approach combines single cell RNA sequencing with surface antibody staining to investigate cell identity and function. CITEseq files were processed for quality control metrics and then clustered twice using multimodal unsupervised weighted nearest neighbor analysis. In both clustering rounds, clusters were manually annotated using a combination of gene and surface protein expression. In both phenotyping modalities, cell type percentages were calculated and multiplied by absolute cell counts from the automated hematology analyzer to get absolute cell numbers. Absolute cell numbers from each method were then correlated with one another to measure the degree of concordance between the samples.

RESULTS: Using the CITEseq clustering, 31 unique celltypes were identified including rare populations such as hematopoietic stem cells, plasmablasts and various subsets of dendritic cells. Correlations between absolute numbers derived from flow cytometry and those derived from CITEseq varied significantly. Total T-cells, total CD8+T-cells, total NK cells, γδ T-cells and classical monocytes were significantly correlated between the analysis types with Pearson's R values ranging from 0.68 to 0.97. CD4+ T-cells, B-cells and non-classical monocytes were not significantly correlated between the two analysis methods. For most T-cell subsets and nonclassical monocytes, CITEseq overestimated absolute cell numbers while it underestimated the number of NK cells, B-cells and γδ T-cells.

CONCLUSION: These results suggest that while CITEseq analysis excels at identifying rare cell types during exercise and accurately reflects changes in many effector lymphocyte populations, parallel flow cytometry may be necessary accurately quantify changes in CD4+ T-cells and B-cells.

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Lifelong exercise is associated with metabolic capacity and remodeling in cytotoxic and unconventional T cells

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Abstract

INTRODUCTION: Lifelong exercise has been proposed to attenuate immunosenescence by preserving immune-cell function, mitochondrial health, and metabolic flexibility (Minuzzi et al, 2025). However, the cellular energetic adaptations associated with lifelong exercise training remains incompletely characterized in cytotoxic and unconventional lymphocyte subsets. Single-Cell Energetic Metabolism by Profiling Translation Inhibition (SCENITH) was used to investigate whether master athletes (MA) display distinct immune-cell metabolic profiles compared to age-matched untrained individuals (UNTR).

METHODS: Peripheral blood (PB) was obtained from 14 MA and 12 UNTR. Protein levels of Cytc c and PGC-1 α were quantified by western blot. SCENITH was performed in a subset of subjects using puromycin incorporation combined with metabolic inhibitors targeting glycolysis, mitochondrial ATP production, and combined pathway blockade. PBMC-based assays were performed after overnight IL-2 stimulation and co-culture with K562 cells. Data were analyzed using two-way ANOVA followed by Bonferroni's multiple comparisons test.

RESULTS: Cytc and PGC-1 α levels were higher in MA. Basal protein synthesis/cell was higher in selected PB subsets from MA. They showed higher basal translational levels in NKT-like cells ($p=0.030$) and $\gamma\delta$ T cells ($p=0.019$). Within-group comparisons further indicated that $\gamma\delta$ T cells displayed higher basal translation than bright NK cells in both UNTR ($p=0.022$) and MA ($p=0.004$) indicating that lifelong exercise may be associated with higher basal protein synthesis, particularly in unconventional lymphocyte.

Among T-cell and unconventional T-cell subsets, MA showed higher absolute FAO/amino-acid oxidation capacity across all analyzed populations. Absolute glycolytic capacity was selectively increased in NKT-like cells ($p=0.007$) and $\gamma\delta$ T cells ($p<0.001$). Percentage-derived parameters further supported a subset-specific metabolic shift with $\gamma\delta$ T cells from MA showing lower mitochondrial dependence than UNTR ($p=0.006$).

CONCLUSION: Preliminary findings indicate that lifelong exercise is associated with enhanced basal translational activity and subset-specific metabolic remodeling of human cytotoxic and unconventional lymphocytes. The most consistent exercise-associated signatures were observed in NK and dim NK cells in peripheral blood, and in NKT-like and $\gamma\delta$ T cells within the unconventional T-cell compartment. The $\gamma\delta$ T-cell profile was particularly distinctive, combining higher basal translation, increased absolute glycolytic capacity, and lower mitochondrial dependence, supporting the hypothesis that MA maintain greater immune-cell metabolic readiness and plasticity, particularly in lymphocyte subsets involved in rapid immune responses, cytotoxicity, and immune surveillance. Larger cohorts and integration with functional cytotoxicity and molecular markers are warranted to confirm these findings.

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Short-term Sulforaphane Intake Modulates Exercise-Induced Oxidative Stress in Healthy Adults

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Abstract

INTRODUCTION: Endurance exercise is known to induce excessive production of reactive oxygen metabolites due to enhanced metabolic activity, leading to oxidative stress and related injuries. Sulforaphane, an isothiocyanate, is broadly acknowledged for its potential antioxidant and anti-inflammatory properties along with other protective functions. Sulforaphane enhanced the production of endogenous antioxidant defense system, thereby attenuating exercise-induced oxidative stress. The purpose of this study was to investigate the effects of short-term sulforaphane supplementation on maximal exercise-induced muscle damage, oxidative stress and endurance capacity in healthy adults.

METHODS: In a randomized double-blind placebo-controlled crossover design, 14 healthy participants (7 males, 7 females; age, 25.07 ± 1.04 years, weight, 65.28 ± 4.13 kg, height, 170.07 ± 3.46 cm, BMI, 22.48 ± 0.91) received either sulforaphane (85 mg/day) or placebo for two weeks at the first trial. Following a three-week washout period, participants crossed over to the alternate treatment. Maximal exercise tests were performed following each supplementation (sulforaphane or placebo) period. Blood samples were collected at baseline (before treatment), pre-exercise, post-exercise and 2 h after each exercise session. All the capsules used in this experiment were provided by Murakami Farm Co., Ltd. and were designed to be indistinguishable from each other. Subjects' body composition was obtained using a bioelectrical impedance analysis. The exercise protocol used here comprised an incremental cycling exercise test to measure maximal oxygen uptake, which has been broadly accepted as a powerful way to provoke oxidative stress and physiological strain among healthy-untrained people.

RESULTS: Sulforaphane supplementation did not alter body weight and composition, endurance capacity, or total and differential blood cell counts; however, it significantly attenuated serum creatine kinase (CK) activity ($p < 0.034$) and myoglobin (Mb) concentration ($p < 0.011$) following exercise. Analysis of oxidative stress markers showed no significant changes in the absolute values in d-ROMs ($p < 0.038$) and OXY adsorbent tests ($p < 0.032$); however, percent changes from baseline showed significant interaction with the supplement intervention. Besides, CK and Mb were negatively correlated ($P < 0.001$) with OXY levels in the sulforaphane group.

CONCLUSION: Short-term sulforaphane supplementation modulated selected circulating markers of oxidative stress and muscle damage following maximal exercise without affecting endurance performance. These findings provide proof-of-principle human evidence that sulforaphane may influence the magnitude of acute exercise-induced alterations in systemic redox homeostasis. In conclusion, sulforaphane intake may be a beneficial, non-invasive strategy to prevent muscle damage via antioxidant defense system in untrained physically active individuals.

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The Effects of Four Weeks of Ketone Ester Supplementation on Systemic and Adipose Tissue Inflammation in Healthy Older Adults: A Randomised Controlled Trial

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Abstract

INTRODUCTION: Ageing is associated with low-grade chronic inflammation that contributes to age-related diseases (Franceschi et al., 2017). Supplementation with exogenous ketone bodies, particularly ketone esters, has been reported to exert anti-inflammatory effects (Neudorf et al., 2024) but the mechanisms are not fully understood, especially among older adults who are not obese. This study investigated whether four weeks of ketone ester supplementation in healthy older adults alters cytokine secretion from immune cells in adipose tissue and peripheral blood, while also influencing inflammatory and metabolic protein secretions from adipocytes

METHODS: Thirty-two healthy older adults (aged 68 ± 5 years, BMI 24.5 ± 3.2 kg/m²) were randomised to receive either ketone ester drinks (0.282g ketone ester/kg body mass/serving) (ketone group) or taste-matched placebo (placebo group) three times daily for 28 days. Blood and abdominal subcutaneous adipose tissue biopsies were collected before and after the intervention. IFN- γ production by T cells and IL-1 β and TNF- α production by monocytes/macrophages were assessed in peripheral blood mononuclear cells (PBMCs) and adipose tissue stromal-vascular-fraction (SVF) under basal conditions and following LPS stimulation using spectral flow cytometry (SONY ID7000). In proof of principle experiments, IFN- γ , IL-1 β and TNF- α secretion were measured in ex vivo whole blood cultures prior to the intervention under basal conditions and with LPS or PMA stimulation with and without β -hydroxybutyrate (BHB). Adipocyte secretion of inflammatory and metabolic markers was also measured using multiplex immunoassays.

RESULTS: Exogenous ketone ester supplementation did not significantly alter cytokine production or activation markers in monocytes and T cells in PBMCs or in adipose tissue SVF macrophages and T cells ($p > 0.05$). However, in LPS-stimulated SVF, time $\times$ group interaction effects showed that the number of adipose resident macrophages (CD45⁺CD14⁺CD206⁺) declined in the ketone group pre- to post-intervention, whereas these cells increased in the placebo group ($p = 0.048$). Analysis of the primary adipocyte secretions, revealed that there were no time $\times$ group interaction effects between the ketone and placebo groups from pre- to post-intervention ($p > 0.05$). In ex vivo whole blood cultures at baseline, BHB significantly reduced LPS-stimulated IFN- γ secretion by 18% ($p = 0.013$), IL-1 β by 61% ($p < 0.001$), as well as basal TNF- α by 63% ($p < 0.001$).

CONCLUSION: While BHB exhibits anti-inflammatory effects in ex vivo whole-blood assays, the impact of exogenous ketone ester supplementation on inflammation in healthy, non-obese older adults (in vivo) is limited with a 4-week intervention. However, the observed changes in adipose tissue macrophage counts might imply that ketone ester supplementation could partly influence aspects of adipose tissue inflammation.

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Feeding Recovery: Post-exercise nutrition influences immune cell dynamics

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Abstract

INTRODUCTION: Post-exercise nutrition can modulate systemic cytokine concentrations. However, limited research has investigated the influence of post-exercise nutrition on circulating leukocyte populations. We aimed to determine whether post-exercise dairy consumption modulates the circulating leukocyte response to high-intensity exercise.

METHODS: 20 healthy males and females participated in this four-arm crossover. Participants underwent a high-intensity, multi-modal exercise bout. Following exercise, participants consumed either 500ml milk, 200g Greek yogurt (GY), an isoenergetic (to milk) carbohydrate (CHO) beverage, or isovolumetric water. Supplements were provided 5m and 1h post-exercise, and before bed. Blood samples were obtained pre-exercise, 1h, 4h, and 24h post-exercise. Peripheral leukocytes were isolated from the buffy coat and incubated with and without lipopolysaccharide (LPS) for 4h. Cells were stained for surface markers, fixed, permeabilized and analyzed using spectral flow cytometry. Both cell counts and proportions (%) of total live or parent cells were examined. Linear mixed models with fixed effects of time*trial*sex, a random effect of participant ID, and covariates (trial order, total cell counts, baseline values) were conducted. Post-hoc testing was corrected using false discovery rate.

RESULTS: In unstimulated cells, beginning 1h post-exercise, neutrophils increased, and lymphocytes decreased in cell counts and proportions (B cells, total T cells [CD3+], CD4+ T cells, CD8+ T cells, Tregs, natural killer (NK) cells and NKT cells), with no differences between trial arms. CD4+ cells, as a % of total T cells, were lower in CHO vs. other arms at 24h post-exercise. NKT cells, as a % of total T cells, increased at 4h and 24h in males, and 24h in females, vs. pre-exercise. Monocyte cell counts decreased post-exercise, with decreases observed in classical, intermediate, and non-classical populations. Among males, there were greater total monocyte counts in MILK vs. WATER. There was also a decrease in total monocyte proportions, however, subpopulation analyses revealed a sex-specific response, with a more sustained reduction in monocyte subpopulations in females. Further, among males, there was a greater % of intermediate monocytes in CHO vs. other arms. Similar results were observed in cell counts and proportions with LPS stimulation.

CONCLUSION: Exercise induced increases in neutrophils and decreases in lymphocyte and monocyte populations. Post-exercise nutrition differentially modulated this response, with a preservation of monocyte counts following MILK (vs. WATER) in males, a reduction of CD4+ T cells (% total T cells) following CHO (vs. other interventions) at 24h post-exercise, and a greater % of intermediate monocytes following CHO (vs. other interventions) in males. Future analyses will examine whether these nutritional effects translate to altered cytokine responses, which may influence exercise recovery.

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Exercise slows epigenetic aging, whereas pro-inflammatory gut bacterial species accelerate it

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Abstract

INTRODUCTION:

Although aging is an unavoidable process, its rate is heavily influenced by lifestyle choices. Higher levels of physical fitness are linked to a decreased incidence of a wide range of diseases.

METHODS: DNA methylation and microbiome analyses were used to assess the rate of aging in sedentary and physically active subjects and Olympic Champions. In animal experiments, we used high-intensity interval training (HIIT), lactate, and MCT1 blocking five times a week for six weeks to study the possible effects of lactate on DNA methylation.

RESULTS: Physically active individuals have slower levels of DNA methylation-based aging than the sedentary population, while Olympic Champions are about 6.3 years younger than their chronological age. We could not find a relationship between the methylation of mtDNA and nuclear DNA. Aging and fitness modify the gut microbiome; however, an increased abundance of pro-inflammatory bacterial species is associated with epigenetic aging. In animal studies, HIIT, lactate injection, and lactate transporter blockade altered DNA methylation, miRNA and mRNA expression, and certain protein levels.

CONCLUSION: A higher level of physical fitness is associated with slower DNA methylation-based aging, and even elite sport can suppress the aging process. Increased abundance of pro-inflammatory species in gut microbiome accelerates the aging process. Lactate is a potential epigenetic modulator via DNA methylation.

Biological Maturation Modulates Neutrophil Mobilization and IL-8 Responses Following Repeated Sprint Exercise in Adolescent Athletes

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Abstract

INTRODUCTION: Repeated sprint exercise (RSE) is a common training modality in intermittent sports, such as combat and court-based disciplines (Billat, 2001). RSE induces substantial physiological stress, which may trigger neutrophil mobilization and increase plasma levels of interleukin-8 (IL-8) (Suzuki et al., 1999). RSE is frequently employed in youth sports teams, where athletes are still undergoing the process of biological maturation (BM) (Almeida-Neto et al., 2023). Thus, this quasi-experimental study investigates whether the dynamics of circulating neutrophils and IL-8 responses after RSE are dependent on the stage of BM in adolescent athletes.

METHODS: Adolescent athletes were categorized according to their BM stage based on Peak Height Velocity (PHV): pre-PHV (n=10) and circum-PHV (n=10). An additional group of adult athletes (n=10) was included as a biologically mature reference. Participants performed an RSE protocol consisting of 3 sets of 6 x 35m sprints (10-s intra-sprint and 5-min inter-set passive recovery). Blood samples were collected before, immediately after, and at 2h and 24h post RSE. Total leukocytes were determined via automated hematology analyzer. Neutrophil phenotypes were assessed via optical microscopy to classify segmented (mature) and band (immature) cells, and pseudopod formation (activation marker). Plasma IL-8 was measured by ELISA and serum lactate by enzyme assay.

RESULTS: RSE induced a transient increase in circulating leukocytes and neutrophils across all groups (After-RSE: $p < 0.05$). However, the magnitude and temporal recovery profile were strongly influenced by BM. Adults and Circum-PHV athletes exhibited a more robust and prolonged neutrophil mobilization compared to Pre-PHV peers ($p < 0.05$). Regarding phenotypic activation, segmented neutrophils peaked after-RSE ($\eta^2 p = 0.236$), while pseudopod formation showed a pronounced delayed increase, peaking at 2h post ($\eta^2 p = 0.815$). Notably, Pre-PHV athletes demonstrated significantly lower activation levels (pseudopods) than adults at both immediately after-RSE and 2h post ($p < 0.001$). Plasma IL-8 concentrations rose acutely following exercise ($\eta^2 p = 0.140$), paralleling the neutrophil kinetics. Lactate levels confirmed the high-intensity nature of the effort, being significantly higher in adults and least pronounced in the Pre-PHV group ($p < 0.001$), reflecting differences in glycolytic capacity related to maturation.

CONCLUSION: BM significantly modulates the magnitude and temporal dynamics of neutrophil mobilization and morphological responses following RSE. Less mature athletes exhibit an attenuated neutrophilic response and diminished cellular activation compared to more mature and adult counterparts. The integrated assessment of neutrophil counts, phenotypes, and IL-8 responses provides novel insights into maturation-dependent immune adaptations to RSE, potentially improving the monitoring of physiological stress and recovery in athletes at different developmental stages.

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Effects of 3-(4-Hydroxy-3-methoxyphenyl)propionic Acid on Regulating Oxidative Stress and Muscle Fiber Composition

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Abstract

INTRODUCTION: Dietary plant-derived bioactive compounds hold promise for supporting muscle performance and structural adaptation [1]. While the plant-derived hydroxycinnamic acid 4-hydroxy-3-methoxycinnamic acid, also known as ferulic acid, has been reported to promote skeletal muscle hypertrophy and attenuate oxidative stress, its gut microbiota-derived metabolite, 3-(4-hydroxy-3-methoxyphenyl)propionic acid (HMPA), remains insufficiently explored with respect to its specific mechanisms in muscle adaptation. Our previous study demonstrated that HMPA administration improved grip strength and reduced blood urea nitrogen levels, but the precise mechanisms by which HMPA regulates skeletal muscle redox homeostasis and fiber-type remodeling remain unclear [2,3]. Therefore, this study aimed to investigate the effects of HMPA on oxidative stress and muscle fiber composition, with particular focus on its role in modulating redox signaling pathways and muscle development-related responses.

METHODS: Eight-week-old male C57BL/6 mice (n = 48) received vehicle, low-dose HMPA (50 mg/kg/day), or high-dose HMPA (500 mg/kg/day) by oral gavage for 14 days. Mice were further subdivided into sedentary and exhaustive treadmill exercise groups. Plasma oxidative stress and antioxidant status were assessed using d-ROMs (oxidative stress marker), BAP (reducing antioxidant capacity), OXY-adsorbent (hypochlorous acid-scavenging antioxidant capacity), and nitrite/nitrate assays. MDA levels, antioxidant enzyme and NOS mRNA expression, MHC isoform expression, mitochondrial biogenesis-related genes, and mTOR/AMPK phosphorylation were analyzed in gastrocnemius and soleus muscles using biochemical assays, qPCR, and Western blotting. Data were analyzed by two-way ANOVA with Tukey's post hoc test.

RESULTS: HMPA significantly decreased plasma d-ROMs at both doses, indicating reduced systemic oxidative stress. High-dose HMPA increased post-exercise OXY-adsorbent levels and attenuated the exercise-induced rise in plasma nitrite/nitrate. In the soleus, high-dose HMPA increased *Sod1* expression and reduced *Nos2* and *Nos3* expression, whereas no significant change was observed in muscle MDA content. Notably, low-dose HMPA significantly upregulated *Myh4* and *Igf1* gene expression, suggesting an IGF-1-mediated promotion of fast-twitch fiber hypertrophy. Furthermore, low-dose HMPA uniquely increased post-exercise AMPK phosphorylation and Sirt1 and Nrf1 expression, indicating enhanced mitochondrial biogenesis and metabolic adaptation.

CONCLUSION: These findings suggest that HMPA may serve as a dietary supplement to regulate redox balance, enhance antioxidant defenses, and promote fast-twitch fiber-related adaptation.

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Gut microbiota and childhood mental health through a physical-fitness versus physical-activity decoupling lens: a microbiota-gut-brain study in children aged 6–9 years

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Abstract

INTRODUCTION: Childhood internalizing symptoms and low resilience are increasingly common, and the microbiota-gut-brain axis is a leading candidate substrate. Positive associations have been reported in preschool cohorts but tend to fade above age 10, leaving the 6-9-year window and positive constructs such as resilience under-studied. Whether physical fitness and physical activity (PA) leave distinguishable microbiota signatures, and whether the microbiota relates to mental health in this window, remains unresolved.

METHODS: From a 2023 fitness cohort of 6,074 children aged 6-9 in Weifang, China, we drew an extreme-quartile subsample of the PA x physical-fitness (PF) distribution; 113 children with complete faecal 16S rRNA sequencing (V4; QIIME2 2022.02 / DADA2 / SILVA 138), seven-day accelerometry, six z-standardized fitness items and five validated scales (CES-DC, SCARED, SDQ, CD-RISC-10, WHO-5) formed the analytic sample. Placing the microbiota-mental-health relationship at the centre and the physical phenotype as an upstream correlate, we combined partial Spearman correlation, four-method differential abundance, DIABLO integration, cross-validated prediction, bootstrap mediation with inverse-probability re-weighting and partial Mantel tests, adjusted for age, sex, BMI, diet and wear days.

RESULTS: Gut microbial richness (Chao1) was robustly associated with resilience (CD-RISC; Spearman rho=0.51, 0.35 after full adjustment, p=0.0002) and generalized out of sample (cross-validated incremental R²=17%; random-forest out-of-bag R²=25%, p<0.001). Community composition tracked the broader psychological profile across three distance metrics and two omnibus tests, independent of physical fitness (partial Mantel r=0.156), and a short-chain fatty acid-producer guild predicted well-being out of sample (incremental R²=11.5%). A genus-level pathobiont (*Escherichia-Shigella*, *Klebsiella*) versus commensal (*Subdoligranulum*, *Fusicatenibacter*) axis was directionally coherent but did not survive genus-wide FDR. Richness correlated most strongly with physical fitness (grip strength rho=0.74), not activity volume; a cross-sectional mediation indicated the fitness-resilience association was partly carried by richness (indirect effect +0.17 [0.08, 0.33]). Bulk faecal SCFA did not differ across cells, redirecting candidate mechanisms toward immune and vagal routes.

CONCLUSION: In school-age children, gut microbial richness, driven by physical fitness rather than activity volume, is associated with resilience and the broader mental-health profile, and under the cross-sectional design the fitness-related microbial signature statistically mediates resilience. The findings extend prior preschool associations into school age and support pre-pubertal fitness as a candidate target for psychoneuroimmune intervention. Because only joint exposure extremes were sampled, magnitudes reflect the extreme-quartile contrast and all associations are cross-sectional.

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Regular physical activity and reduction of neurogenic obesity may mitigate premature immunosenescence in people with spinal cord injury

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Abstract

INTRODUCTION: Neurogenic obesity is a problem that affects people with spinal cord injury (SCI), a prevalent risk factor for cardiometabolic diseases. In healthy populations, obesity is considered an anticipatory factor for immunosenescence, while higher physical activity levels (PAL) have been shown to be effective in improving parameters related to early immunosenescence in obese individuals. Therefore, our aim was to characterize the impact of PAL on markers of T cell early immunosenescence in individuals with SCI.

METHODS: The study included 33 male subjects, aged between 18 and 50 years, 19 had SCI with a neurological level of tetraplegia. They were divided into three groups: a control group without SCI and irregularly active (Control, n=14), a group with physically active SCI (SCI-PA, n=11), and a group with irregularly active SCI (SCI-IA, n=8). Assessments included completing the Godin-Shephard Leisure-Time Physical Activity Questionnaire (GSLTPAQ), blood collection for circulating cytokine analysis and T cell phenotype (assessed via flow cytometry), maximum oxygen consumption test (VO₂max), and body composition assessment by dual-energy X-ray absorptiometry (DEXA). For statistical analyses, the Shapiro-Wilk test was applied to assess data normality, one-way ANOVA followed by Tukey's post-hoc test, as well as Pearson's correlation, was used for parametric data, and corresponding analyses for non-parametric data.

RESULTS: The SCI-PA group showed higher proportions of naïve CD4⁺ and CD8⁺ T cells (35.90±3.74 vs 28.90±7.73, 53.30±6.50 vs 39.20±8.06 respectively), and CD28⁻ expression (6.18±2.25 vs 10.80±3.27, 7.30±9.11 vs 50.40±11.70 respectively), and lower proportions of effector memory (EM) T cells (9.07±1.65 vs 13.4±3.94, 7.99±2.40 vs 26.9±4.47 respectively), terminal effector memory (EMRA) cells (5.35±1.09 vs 11.90±2.51 for CD8⁺) and expression of KLRG1⁺ (43.80±3.81 vs 67.40±8.26 for CD8⁺) compared to the SCI-IA group. Additionally, we performed multiple linear regression analyses, with senescence indicators of T cells as independent variables. Among the most significant results, approximately 75% of the frequency of CD8⁺EMRA cells can be jointly explained by serum concentration of IL-6, TNF-α, and hours of training practiced per week (p=0.002); 77% of the frequency of CD4⁺CD28⁻CD57⁺ cells by VO₂max and % Visceral Fat; 99% of CD8⁺CD28⁻CD57⁺ cells jointly by serum concentration of IL-6, TNF-α, VO₂max, and % Visceral Fat; 70% and 93% of CD4⁺ and CD8⁺KLRG1⁺ cells can be explained by serum concentration of IL-6, % Visceral Fat, and hours of training practiced per week (p=0.050 and p=0.009 respectively).

CONCLUSION: Higher levels of physical activity (PAL) and VO₂max in individuals with spinal cord injury exert a positive impact on neurogenic obesity and the immunosenescence phenotype. Furthermore, the restoration of immune health associated with these factors may contribute to reducing the risk of developing chronic non-communicable diseases.

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Exercise Training and Hypocaloric Diet Modulate Markers of Lymphocyte Aging and Inflammation in Older Adults with Rheumatoid Arthritis

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Abstract

INTRODUCTION: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic systemic inflammation. Physical inactivity is common in RA and linked with accelerated immune aging. In older adults with RA and overweight/obesity, we showed a remotely-supervised weight loss and exercise training (SWET) intervention, compared to a lifestyle counseling intervention, improves RA, physical, and patient-reported health (Andonian et al., 2023). Lifestyle modification after either intervention led to sustained reductions in RA inflammatory disease activity with less need for medications (Collins-Bennett et al., 2025). In this ancillary study of the SWET RA randomized controlled trial, our goal was to identify the effects of lifestyle modification on peripheral Senescence-Associated Secretory Phenotype (SASP), immune signaling, and markers of lymphocyte aging to inform mechanisms of exercise benefit for RA.

METHODS: Older (age 60-80 years) participants with RA and overweight/obesity were randomized to 16 weeks of SWET or lifestyle counseling. Target lifestyle prescription for both groups included 150 min/week moderate-to-vigorous aerobic exercise, 2 days/week resistance exercise using resistance bands, and a hypocaloric diet. Ancillary study assessments included SASP and immune signaling profiles via immunoassay and lymphocyte profiles via flow cytometry. Within group and between group pre- versus post-intervention changes were assessed using Wilcoxon non-parametric testing. Relationships were assessed using Spearman's correlations. Significance was established at $p < 0.05$.

RESULTS: Among all participants ($n=20$), lifestyle modification led to increased frequencies of peripheral CD4+CCR7+CD45RA+ naïve helper T cells (relative change= $7.9 \pm 19.1\%$, $p=0.04$) and decreased frequencies of CD4+CD25hiCD127low Treg ($-11.1 \pm 22.6\%$, $p=0.03$), CD3+CD56bright NK T cells ($-19.5 \pm 32.3\%$, $p=0.01$), CD3-CD56brightKLRG1+ senescent NK cells ($-7.4 \pm 15.4\%$, $p=0.04$), and KLRG1+ senescent NK T cells ($-2.0 \pm 7.6\%$, $p=0.02$). Relative increases in naïve helper T cells associated with decreases in erythrocyte sedimentation rate ($\rho=-0.51$, $p=0.02$). Decreases in Treg associated with decreases in IL-3, IL-17, and MCP-1 ($\rho > 0.49$, $p < 0.03$ for all). Changes in immune signaling and lymphocyte profiling were similar between SWET and lifestyle counseling groups ($p > 0.05$ for all). Absolute counts of peripheral leukocytes and lymphocytes did not change post-intervention in total or for either group ($p > 0.05$ for all).

CONCLUSION: In older adults with RA and overweight/obesity, exercise training combined with hypocaloric diet modulates markers of peripheral Treg and lymphocyte aging in association with dampening of inflammation and senescence signaling. Results of this exploratory study highlight the potential for lifestyle modification to improve immune competence, biological aging, and, ultimately, the clinical care of patients with RA and other chronic autoimmune and inflammatory diseases.

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Effect of Gut Microbiota Depletion on Glucose Tolerance and T Lymphocytes Profile in a Model of Non-Obese Type 2 Diabetes

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Abstract

INTRODUCTION: The gut microbiota has a close relationship with host immune system and inflammatory response. The GK rat develops type 2 diabetes mellitus (T2DM) without obesity and presents constipation with altered gut microbiota composition and increase of pro-inflammatory profile of T lymphocytes from mesenteric lymph node (MLN) as early as 21 days old (pre-diabetic state). We hypothesized that gut microbiota alterations in GK rats contribute to glucose intolerance and impair T lymphocyte profiles. To investigate this relationship, microbiota depletion was induced in GK rats using broad-spectrum antibiotics.

METHODS: An antibiotic (ABX) cocktail containing ampicillin, neomycin, metronidazole (1 g/L) and vancomycin (0.5 g/L) was given in the drinking water of the ABX groups from 40 to 60 days of age. The rats were divided into four groups: twelve WT^{CT} (control rats that received only water), eleven WT^{ABX} (control rats that received antibiotics), twelve GK^{ABX} (T2DM rats that received antibiotics) and twelve GK^{CT} (T2DM rats that received only water). Glucose tolerance test (GTT), fecal metabolome and profile of T lymphocytes from Peyer patches (PP) and MLN were studied.

RESULTS: The depletion of gut microbiota resulted in an improvement in glucose tolerance in GK^{ABX} was seen in GTT, with decrease in area under the curve (AUC), when compared to GK^{CT}. Metabolomics analysis shows that the composition of fecal metabolites in the control groups (WT^{CT} vs GK^{CT}) is distinct, with a notable increase in pyrimidines, purines, mevalonate and nicotinate, and a decrease in deoxycholate in the GK^{CT} group. Regarding T lymphocytes from PP, immunophenotyping results show a decrease in Tregulatory (Treg) and T helper 17 (Th17) profiles in WT^{ABX}, while GK^{ABX} exhibit an increase of Th1 compared to GK^{CT}. Despite limited changes in MLN T-cell subsets, the expression of mRNA of IL-10 in GK^{CT} is increased compared to WT^{CT}. However, gut microbiota depletion was associated with decrease of IL-10 in GK^{ABX}.

CONCLUSION: The depletion of GK rats gut microbiota highlighted its association with glucose intolerance rather than insulin resistance. There was no complete reversal of glucose intolerance, as the model presents genetic alterations that favor dysfunction in glucose-stimulated insulin secretion. The distinguished composition of fecal metabolites between GK^{CT} and WT^{CT} is characterized by increased levels of purines and pyrimidine and metabolization of amino acids. The effect of gut microbiota on T lymphocytes was observed in both groups of rats; in both cases, intestinal immunotolerance was lost due to the absence of gut microbiome, leading to a more pronounced pro-inflammatory profile on GK, whereas the main protective cells populations was reduced in WT. However, evidence indicates that, despite its genetic background, gut microbiota exerts influence on non-obese T2DM and T lymphocyte profiles.

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Metabolic Improvements in Obese Mice Induced by Combined Black Ginger Extract Supplementation and Endurance Exercise

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Abstract

INTRODUCTION: Obesity induced by a high-fat diet (HFD) is closely associated with chronic low-grade inflammation, metabolic inflexibility, and insulin resistance. While exercise and nutritional interventions independently confer metabolic benefits, their combined effects remain incompletely understood. This study investigated whether supplementation with *Kaempferia parviflora* extract (KPE) enhances the metabolic effects of endurance exercise training in HFD-fed mice, with a particular focus on inflammatory and immune-related responses.

METHODS: Male C57BL/6 mice were fed an HFD and subjected to an 8-week intervention consisting of KPE supplementation, endurance exercise training, or their combination (n=8). Systemic metabolic parameters, tissue-specific gene expression, and signaling pathways related to inflammation, mitochondrial regulation, and insulin sensitivity were assessed in the liver, white and brown adipose tissues, and skeletal muscle.

RESULTS: The combined intervention attenuated HFD-induced body weight gain and significantly improved insulin resistance, as indicated by reduced fasting insulin levels and HOMA-IR.

These systemic improvements were accompanied by normalization of hepatic lipid metabolic gene expression and marked modulation of inflammatory gene expression in both the liver and white adipose tissue. In the liver, HFD-induced upregulation of inflammatory cytokine genes (*Ccl2*, *Tnf*, and *Il1b*) was significantly reduced at the mRNA level by exercise training and more prominently by the combined intervention, whereas KPE supplementation alone showed a modest, non-significant effect.

Similarly, in white adipose tissue, inflammatory gene expression remained elevated in the HFD and single-intervention groups but was markedly attenuated in the combined intervention group, approaching levels observed in the Chow group. In parallel, the mRNA expression of macrophage-related markers (*Cd68*, *Adgre1*, *Itgax*, and *Mrc1*) was significantly increased in HFD-fed mice, while both exercise training and the combined intervention suppressed these elevations, indicating reduced macrophage infiltration at the transcriptional level.

Additionally, enhanced expression of genes related to mitochondrial regulation and insulin signaling was observed in skeletal muscle. In the liver, KPE supplementation and exercise training enhanced signaling pathways involved in cellular energy metabolism, indicating a shift toward improved metabolic regulation.

CONCLUSION: Combining KPE supplementation with endurance exercise training confers broader metabolic benefits than either intervention alone. These effects appear to be mediated primarily through metabolic and tissue-specific regulatory mechanisms, rather than uniform suppression of systemic inflammatory responses. This study highlights the potential of integrated nutritional and exercise strategies for mitigating obesity-associated metabolic dysfunction.

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Exercise as an Immune Adjuvant for Allogeneic Cell Therapies: An Overview of the Allo-X Trial

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Abstract

Allogeneic adoptive cell therapies, including donor lymphocyte infusion, cytokine-induced killer cells, $\gamma\delta$ T cells, natural killer cell therapies, and engineered T-cell products, hold considerable promise for preventing and treating relapse after allogeneic hematopoietic cell transplantation. However, their efficacy is limited by variable donor cell composition, inadequate persistence, impaired trafficking, immune escape, and the need to enhance graft-versus-leukemia effects without increasing graft-versus-host disease. A single bout of moderate-to-vigorous exercise rapidly mobilizes large numbers of highly differentiated effector lymphocytes into the circulation, including NK cells, $\gamma\delta$ T cells, CD8⁺ T cells, and cytokine-induced killer cell precursors with phenotypic and molecular features associated with cytotoxicity, tissue trafficking, immune synapse formation, and anti-tumor activity. Published and emerging studies from our group indicate that exercise-mobilized lymphocytes can be used to generate enhanced allogeneic cell therapy products, including cytokine-induced killer cells, NK-cell and $\gamma\delta$ T-cell products, and may also improve synergy with combination therapies such as bispecific T-cell engagers (BiTEs) and monoclonal antibodies (Baker et al., 2024; Batatinha et al., 2026; McDougal et al., 2025).

This presentation will provide an overview of the Allo-X trial, “Exercise as an Immune Adjuvant for Allogeneic Cell Therapies,” which investigates whether immune cells collected after acute exercise can generate superior therapeutic products compared with cells collected under resting conditions from the same donor. A central focus is DLI-X, defined as donor lymphocyte infusion from exercise-mobilized peripheral blood mononuclear cells. The trial evaluates the effects of 20 minutes of graded cycling exercise on immune cell number, phenotype, transcriptomic profile, secretome, and anti-leukemia function. It also examines the role of catecholamine–adrenergic receptor signaling using selective and non-selective β -blockade, phosphodiesterase modulation, and isoproterenol infusion as an exercise-mimetic stimulus. Emerging data from the Allo-X platform suggest that DLI-X and related exercise-enhanced allogeneic products exhibit superior anti-leukemia activity, including improved activity in combination with BiTEs and monoclonal antibodies. Collectively, these studies support exercise as a novel, scalable, and biologically targeted strategy to improve allogeneic cell therapies for hematologic malignancies.

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High-intensity interval training enhances immunotherapy efficacy in metastatic non-small cell lung cancer: results from the randomized HI AIM trial with integrated translational analyses

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Abstract

INTRODUCTION: Lifestyle factors are increasingly recognized as modifiers of cancer outcomes, yet prospective clinical evidence remains limited. Here, we report results from the randomized controlled HI AIM trial, designed to test whether structured exercise can improve treatment efficacy in patients with metastatic non-small cell lung cancer (mNSCLC), alongside a translational research program.

METHODS: Patients receiving immunotherapy or chemotherapy were randomized to 6 weeks of supervised high-intensity interval training (HIIT; three sessions weekly) or usual care without exercise modification. Clinical endpoints included treatment tolerance, psychological distress, and survival outcomes, complemented by longitudinal immune profiling from peripheral blood sampled before and after acute exercise.

RESULTS: Between August 2020 and October 2023, 54 patients were enrolled. HIIT was safe and feasible, reduced treatment-related toxicity, and alleviated anxiety. Notably, HIIT improved progression-free survival (PFS, hazard ratio [HR] 0.7), with a pronounced and statistically significant benefit in patients receiving immunotherapy (n=19; HR 0.2, 95% CI 0.05–0.77; p=0.01). Mechanistically, HIIT induced transient catecholamine elevations and mobilization of cytotoxic lymphocytes, including a sustained increase in circulating natural killer cells.

CONCLUSION: These findings provide clinical and mechanistic evidence that high-intensity exercise augments immunotherapy efficacy in mNSCLC, supporting its integration into multimodal cancer care.

Clinicaltrials.gov Identifier: NCT04263467

Exercise-Expanded $\gamma\delta$ T Cells Show In Vitro and In Vivo Anti-Myeloma Potential and Daratumumab-Mediated ADCC

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Abstract

INTRODUCTION: Gamma delta ($\gamma\delta$) T cells are MHC-independent cytotoxic lymphocytes with promise for allogeneic immunotherapy in multiple myeloma (MM), but durability is limited by the immunosuppressive tumor microenvironment. Our previous work showed that acute exercise mobilizes PBMCs that support robust *ex vivo* $\gamma\delta$ T-cell expansion, increased CD16 expression, and enhanced *in vitro* cytotoxicity against hematological tumor targets, including U266 myeloma cells. Therefore, we further investigated the *in vitro* and *in vivo* anti-myeloma potential of exercise (EX)-expanded $\gamma\delta$ T cells and tested whether clinically relevant zoledraonate (ZOL) exposure and daratumumab-mediated ADCC augment their anti-MM activity.

METHODS: 23 healthy adults completed a graded cycling protocol with blood collected at rest and during exercise at 80% VO_2max . Peripheral blood mononuclear cells (PBMCs) were isolated and $\gamma\delta$ T cells were expanded for 14 days with IL-2 and ZOL. Expanded products were phenotyped by flow cytometry and tested in 4-hour cytotoxicity assays against MM cell lines (MM1.S & MM1.R) under untreated, ZOL-sensitized, DARA-treated, and ZOL+DARA conditions. CD16-blocking assays assessed ADCC contribution from DARA treatment. *In vivo* efficacy was evaluated in NSG-IL15 mice bearing MM1.S-luc tumors using prophylactic and therapeutic REST- or EX-expanded $\gamma\delta$ T-cell transfer, with and without DARA treatment.

RESULTS: EX-expanded $\gamma\delta$ T cells showed greater lysis of MM1.S ($p<0.0001$) and MM1.R ($p=0.0004$), with ZOL sensitization further enhancing cytotoxicity against both targets (MM1.S: $p=0.0007$; MM1.R: $p=0.0008$) compared with REST-expanded $\gamma\delta$ T cells. A single prophylactic injection of EX-expanded $\gamma\delta$ T cells delayed tumor growth ($p<0.05$) and increased tumor-free survival ($p=0.007$) in NSG-IL15 mice bearing MM1.S tumors compared with REST-expanded $\gamma\delta$ T cells. In a therapeutic model of established disease, four weekly injections of EX-expanded $\gamma\delta$ T cells plus ZOL improved tumor control ($p<0.05$) in mice with 14-day established MM1.S tumors compared with REST-expanded $\gamma\delta$ T cells plus ZOL. We next tested DARA-mediated ADCC by targeting CD38 on MM cell lines. DARA augmented EX-expanded $\gamma\delta$ T-cell cytotoxicity against MM1.S ($p<0.001$) and MM1.R ($p<0.01$), including ZOL-sensitized targets, while CD16 blockade significantly reduced DARA-enhanced killing. However, this enhancement did not translate *in vivo*, as DARA failed to synergize with $\gamma\delta$ T-cell infusions.

CONCLUSION: Acute exercise primes expanded $\gamma\delta$ T cells toward an activating, ADCC-competent phenotype with improved anti-myeloma cytotoxicity *in vitro* and therapeutic activity *in vivo*. While DARA enhanced cytotoxicity *in vitro*, it did not improve *in vivo* durability. These data support exercise as a practical immune adjuvant for $\gamma\delta$ T-cell-based immunotherapy and highlight the need to optimize monoclonal antibody pairing, timing, and dosing for MM.

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Inflammatory cytokine interleukin-1 induced bone formation in the model of bone metastasized cancer

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Abstract

INTRODUCTION: Excessive exercise and overtraining are known to elevate levels of inflammatory cytokines, such as interleukin-1 (IL-1), both systemically and locally within bone tissues. Under physiological bone metabolism, characterized by predominant inflammation, IL-1 (specifically IL-1 alpha and beta) and its primary receptor (IL-1R1) directly stimulate osteoclast formation, thereby accelerating bone resorption. We recently discovered that the new model of bone formation is paradoxically enhanced in close association with increased IL-1 production in the local microenvironment of bone-metastatic cancer. This study investigated the specific role of IL-1 in osteogenesis induced by prostate cancer cells.

METHODS: A new model of bone formation was established by injecting a human prostate cancer cell line, PC3, and structural alterations were assessed via micro-computed tomography (micro-CT) image analysis. To evaluate osteogenesis in vitro, a co-culture system consisting of PC3 cells and primary mouse osteoblasts was used, and bone formation was analyzed. The mRNA expression levels of osteogenesis-related genes within the co-culture system were quantified using reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Furthermore, the activation and phosphorylation cascades of extracellular signal-regulated kinases were evaluated via Western blotting.

RESULTS: In the PC3 bone graft model, marked bone formation was observed within the bone marrow cavity, and quantitative morphometric analysis via micro-CT confirmed a significant increase in bone parameters associated with osteogenesis (Yoshinouchi et al., 2023). Investigation into the involvement of PC3 cell-surface factors revealed the specific production of membrane-bound IL-1 alpha. The additional treatment of an IL-1 receptor antagonist (IL-1Ra) to the PC3-osteoblast co-culture system significantly suppressed ARS-positive mineralized bone formation. Treatment of recombinant IL-1 α to osteoblast stimulated mRNA expression of both IL-1 α and Runx2, while concurrently promoting phosphorylation of JNK, ERK, and p38. IL-1 alpha-mediated enhancement of osteoblast differentiation and bone formation was effectively abolished by pharmacological inhibitors of JNK and p38 (Sugasaki et al., 2025).

CONCLUSION: The present study indicates that hyperproduction of IL-1, associated with cancer metastasis, triggers a diametrically opposed effect, strongly inducing osteogenesis. These findings demonstrate that prostate cancer cells induce IL-1 α production through direct intercellular adhesion with osteoblasts, thereby promoting osteogenesis via downstream MAPK signaling. Further research will need to clarify the regulatory mechanisms of IL-1 in bone metabolism, focusing on the shared MAPK signaling pathophysiology between exercise-induced inflammation and the bone formation microenvironment in cancer.

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Redox perspectives to recovery and adaptation from acute and chronic post-resistance exercise cold water immersion

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Abstract

INTRODUCTION: Cold applications are regularly used post-exercise as recovery therapies, theorized by practitioners to reduce inflammation and muscle damage induced oxidative stress, thus enhancing recovery. Evidence of such responses, however, is limited. Further, evidence is largely based on indirect measures and assumptions of different forms of cold applications indicating similar responses. Herein, we explored whether evidence of such responses exist after post-exercise cold water immersion (CWI) in humans.

METHODS: Part A was an acute cross-over study of nine males completing two unilateral strength exercise sessions on separate days with each session followed by 10 min of CWI or active recovery (ACT) control. Part B was a parallel-group study, where twenty-one males completed chronic strength training, twice weekly, for 12 weeks. Ten mins of CWI or ACT was performed after each session. Blood and vastus lateralis muscle biopsies were collected at rest, over 48 hrs post-exercise in the acute study, whilst resting muscle biopsies, strength performance, and a near infrared spectroscopy-derived measure of muscle oxygen consumption, were collected, before, and after the 12 weeks' training. Biological markers, including blood markers of oxidative stress and defence were assessed alongside intramuscular transcription factors in the acute study, whilst intramuscular protein markers of mitochondrial and metabolic adaptation were measured in the chronic study.

RESULTS: Acute Resistance exercise influenced blood redox and antioxidant markers (time effects $p < 0.05$). Plasma F₂-isoprostanes changed due to exercise and were different between conditions being lower after exercise and CWI, compared with ACT ($p < 0.05$). However, derivatives of reactive oxygen metabolites (d-ROMs) and protein carbonyl responses did not differ between CWI and ACT. Glutathione peroxidase activity and biological antioxidant potential (BAP) changed over time (time effects $p < 0.05$); however, only BAP differed between conditions, being higher after CWI than ACT, 2 h post exercise ($p < 0.05$). Resistance exercise influenced muscle redox genes over time, e.g., NRF2, HMOX1 and Thioredoxin; however, there were no differences between CWI and ACT (all $p > 0.05$). Chronic training increased citrate synthase, mitochondrial enzyme complexes I and IV, and AMPK activity ($p < 0.05$), but the responses were not different between CWI and ACT groups. Maximal strength adaptation to training with regular CWI was impaired, which coincided with slower oxygen desaturation rate (static contractions), and higher oxygen consumption quantity (dynamic), all $p < 0.05$.

CONCLUSION: Post-exercise CWI did not broadly alter intramuscular or consistently augment markers of the redox milieu, or markers of mitochondrial electron transport chain adaptation. Regular CWI, however, did reduce strength adaptation, which was accompanied by altered muscle oxygen kinetics.

Aerobic Exercise, Systemic Inflammation, and Endothelial Function: Insights from Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

INTRODUCTION: Chronic low-grade inflammation contributes to endothelial dysfunction and cardiovascular disease progression. Aerobic exercise may partially improve vascular health by attenuating systemic inflammation and restoring the balance between endothelial vasodilatory and vasoconstrictive signalling. However, whether improvements in endothelial function occur alongside reductions in systemic inflammation remains unclear, limiting understanding of the mechanisms underlying exercise-induced vascular adaptation.

METHODS: A systematic review and meta-analysis was conducted in accordance with PRISMA and PERSiST guidance. Randomized controlled trials involving adults were eligible when they compared aerobic exercise with a non-exercise control and reported brachial artery flow-mediated dilation (baFMD) together with at least one cardiovascular, metabolic, endothelial, or inflammatory marker. Random-effects models were used to estimate pooled intervention effects. Meta-regression examined whether changes in eligible secondary outcomes were associated with changes in baFMD.

RESULTS: Seventy-two studies, comprising 99 exercise comparisons and 3,357 participants, were included. Aerobic exercise increased baFMD by 2.35 percentage points compared with non-exercise control (95% confidence interval: 1.98 to 2.73; $p < 0.001$), representing a clinically meaningful improvement in endothelial function. Exercise also produced a small reduction in C-reactive protein, while tumour necrosis factor- α showed a moderate reduction that did not reach statistical significance in the random-effects model but was significant in the fixed-effects analysis. No consistent change was observed for interleukin-6. Alongside these inflammatory responses, aerobic exercise increased nitric oxide and nitrogen oxide concentrations and reduced endothelin-1, indicating a shift towards a more favourable endothelial environment. Greater improvements in baFMD were associated with reductions in body weight, body fat, systolic and diastolic blood pressure, as well as with improvements in maximal oxygen uptake and changes in insulin levels. The available evidence was insufficient to determine whether changes in inflammatory markers directly moderated baFMD adaptations.

CONCLUSION: Aerobic exercise improves endothelial function while concurrently producing favourable changes in systemic inflammation and endothelial signalling. The reduction in C-reactive protein, together with increased nitric oxide bioavailability and reduced endothelin-1, supports an interconnected immunovascular response to chronic aerobic exercise. Further trials should concurrently assess inflammatory, oxidative stress, and vascular outcomes to clarify whether attenuation of chronic inflammation mediates exercise-induced endothelial adaptation.

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Determination of metabolic parameters and lymphocyte profile in military police officers with metabolic syndrome

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Abstract

INTRODUCTION: Brazilian military police officers (MPOs) are submitted to several stressing conditions that negatively impact their quality of life and positively increasing the incidence of inflammatory and non-communicable chronic diseases, including the metabolic syndrome (MS). However, the relationship between metabolic and inflammatory risk factors in MPOs are not known yet. Thus, the objectives of this work were: a) to characterize and compare the risk factors for metabolic syndrome (MS) in MPOs of the Sao Paulo city; and b) to compare the T CD4⁺ lymphocyte profile in MPOs with and without MS.

METHODS: Active MPOs from the Sao Paulo city (Brazil) were invited to participate of the study. After an initial screening of the participants, 209 MPOs were eligible for the work, of which 151 did not present metabolic syndrome (control group = CO) and 58 had the syndrome (metabolic syndrome group = MS), according to the criteria of the NCEP-ATP III. Anthropometric parameters (body weight, height, waist circumference, and body composition) and level of physical activity (IPAQ) were determined in all participants. T CD4⁺ lymphocyte profile (Th1, Th2, Th17, and Treg) was evaluated in a subgroup of 27 MPOs from the CO group and 25 from the MS group.

RESULTS: All parameters related to MS were significantly altered in the group with the syndrome: increased glycemia (93.8±9.1 vs 99.2±14.9; p<0.01), reduced HDL-cholesterol content (50.2±12.5 vs 41.1±6.6; p<0.001), elevated triglyceride concentration (108.0±47.8 vs 218.4±113.2; p<0.001), high systolic blood pressure (131.1±13.5 vs 139.3±15.9; p<0.001) and diastolic blood pressure (82.2±9.2 vs 89.3±11.6; p<0.001), as well as increased waist circumference (92.0±10.5 vs 103.4±9.3; p<0.001). MPOs with MS presented increased body weight (85.8±10.3 vs 101.2±15.6; p<0.001) and BMI (28.2±3.0 vs 32.9±4.9; p<0.001), greater muscle mass (37.6±4.4 vs 39.9±4.4; p<0.05), and increased body fat percentage (23.2±6.2 vs 30.0±7.5; p<0.001) total body fat mass (20.4±7.3 vs 31.3±11.0; p<0.001). We did not observe differences between the physical activity level (28.7% of sedentary and irregularly active MPOs in CO group and 28.9% in MS group). We found significant alterations in the profile of Th1, Th17, and regulatory T lymphocytes, suggesting immunological dysregulation associated with the metabolic syndrome. A significant increase in Th1 (CD4⁺INF-γ⁺ lymphocytes; 5.45±0.8 vs 10.9±1.5; p<0.05) and Th17 (CD4⁺IL-17⁺; 12.5±1.2 vs 20.5±1.7; p<0.01), no change in Th2 (CD4⁺IL-4⁺; 10.0±1.0 vs 9.6±0.9; NS), and a significant reduction in Treg (CD4⁺Foxp3⁺; 12.3±0.2 vs 6.3±0.5; p<0.001) were found in the MS group in comparison to the CO group.

CONCLUSION: Our results suggest that the worsen metabolic and anthropometric parameters in MPOs with MS are directly associated with a lower “regulatory signature” (increased Th1 and Th17, and reduced Treg lymphocytes), which is consistent with a scenario of a pro-inflammatory condition in MS patients.

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Immune-endocrine responses across a competitive season and their association with illness occurrence in elite athletes

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Abstract

INTRODUCTION: Sport-related and non-sport-related stressors impose physiological and psychological demands on athletes, creating a continuum of adaptation ranging from homeostasis to acute fatigue, functional overreaching, overtraining syndrome, subtle immune alterations, clinical symptoms and illness. Yet, the ability to identify early signs of impaired adaptation before illness manifests remains a major challenge in athlete health monitoring. Although longitudinal monitoring of immune-endocrine responses may provide insights into athlete homeostasis and help identify periods of increased vulnerability to illness, large-sample studies combining repeated immune and endocrine assessments with training stress and illness occurrence across an entire competitive season remain limited.

METHODS: A prospective cohort study was conducted in 189 elite male handball players competing in the 1st Slovenian Handball League. Athletes were monitored over one competitive season (45 weeks). Blood samples were collected at five time points to determine IgA, testosterone and cortisol, from which the testosterone to cortisol (T:C) ratio was calculated. Weekly loads and illnesses were collected using Oslo Sports Trauma Research Centre Questionnaire on Health Problems. Linear mixed-effects models were used to evaluate longitudinal biomarker changes, while logistic regression was used to examine associations between biomarkers and illness occurrence.

RESULTS: Testosterone concentrations increased significantly at three follow-up assessments compared with baseline, whereas cortisol showed only a transient increase during the middle of the competitive season. Consequently, the T:C decreased significantly at the same time point, indicating a temporary alteration in anabolic-catabolic balance. In contrast, IgA remained stable throughout the season. T:C was significantly associated with illness occurrence (OR = 0.976, 95% CI 0.956–0.993, $p = 0.010$), indicating that each percent in the T:C ratio decrease is associated with a 2.4% increase in the odds of getting ill. Moreover, IgA was associated with illness (OR = 1.05, 95% CI 1.01–1.10, $p = 0.030$), suggesting that IgA may reflect an ongoing immune response rather than susceptibility to illness.

CONCLUSION: The observed variations in testosterone, cortisol, and the T:C ratio indicate that these biomarkers are responsive to changes in physiological demands throughout the season. A lower T:C ratio was associated with increased illness occurrence, suggesting its potential relevance for monitoring immune-related vulnerability. Furthermore, the positive association between IgA concentrations and illness highlights the complexity of longitudinal monitoring and immune biomarker interpretation. These findings suggest that immune-endocrine markers may contribute to athlete health monitoring, however, their selection and interpretation require consideration of the broader context and individual responses to training stress.

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Exercise Mobilized T-cells Upregulate CD137 after Blinatumomab Stimulation and have enhanced Effector Function against B-ALL

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Abstract

INTRODUCTION: Donor Lymphocyte Infusions (DLI) are used to prevent and treat leukemic relapse after allogeneic hematopoietic cell transplantation, but efficacy against lymphoid malignancies is limited¹. Blinatumomab (Blina), a CD3/CD19 bispecific T-cell engager, promotes T-cell mediated killing of malignant B cells and is emerging as an important combination therapy to augment DLI efficacy against acute lymphoblastic leukemia (ALL)². CD137 is a surface marker induced on effector lymphocytes after tumor antigen exposure and has been targeted to harness tumor-reactive cells for immunotherapy³.

PURPOSE: We have shown previously that exercise-mobilized DLI (DLI-X) combined with Blina is more effective against B-ALL than standard DLI+Blina, and that exercise-mobilized lymphocytes upregulate CD137 upon stimulation with Blina and target cells with greater capacity than resting lymphocytes. Here, we tested the hypothesis that CD137⁺-enriched cells from DLI-X display enhanced cytotoxicity against CD19⁺ malignancies in vitro and synergize with Blina.

METHODS: Healthy participants enrolled in the Allo-X trial (NCT06643221) completed 20-minutes graded cycling exercise up to 80% VO₂max. Lymphocytes were isolated at rest and during the final exercise stage. To select CD137⁺ cells, lymphocytes were co-cultured overnight with RS4;11 tumor cells and Blina, then positively selected for surface CD137 expression for functional and phenotypic analysis. Protein expression was assessed by 8-color flow cytometry. Cytotoxicity assays were performed in vitro using CD19⁺ RS4;11 cells as a B-ALL model.

RESULTS: 24 hour co-culture of DLI/DLI-X products with CD19⁺ RS4;11 cells and Blina induced CD137 expression, with DLI-X lymphocytes expressing significantly more as a percentage (~10%) among all lymphocytes compared to standard DLI. CD137⁺ cells from DLI-X were proportionally shifted toward an effector phenotype compared to resting CD137⁺ cells, with CD8⁺ T cells containing higher proportions of EM and EMRA subsets, and increased KLRG1 expression (~30%). CD137⁺-selected cells showed enhanced cytotoxicity compared to whole PBMCs and CD137⁻ cells, and exercise-mobilized CD137⁺ cells demonstrated amplified cytotoxicity with Blina compared to resting CD137⁺ cells. Exercise-mobilized CD137⁺ T cells produced more TNF-α and IFN-γ and expressed more CD107a upon tumor challenge in the presence of Blina.

CONCLUSION: Exercise mobilizes lymphocytes with increased capacity for CD137 upregulation upon activation with CD19⁺ tumor cells and Blina. CD137⁺ cells activated from exercise-mobilized lymphocytes are proportionally enriched for CD8⁺ T cells with a more differentiated effector phenotype, and show increased tumor cytolysis, cytokine release, and degranulation with Blina compared to CD137⁺ cells activated from resting lymphocytes. This suggests CD137 selection from DLI-X after short-term pre-exposure to CD19 antigen and Blina represents a strategy for improving DLI-X and Blinatumomab combination therapy to treat leukemic relapse after allogeneic hematopoietic cell transplantation.

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Exercise-Expanded $\gamma\delta$ T Cells Show Enhanced Responsiveness to Bispecific Antibody Redirection in Hematological Malignancies

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Abstract

INTRODUCTION: CD3-engaging bispecific antibodies (bsAbs), including CD19 $\times$ CD3 and BCMA $\times$ CD3 agents, redirect T cells toward malignant B cells and plasma cells but remain limited by variable effector-cell fitness and incomplete patient responses. Allogeneic $\gamma\delta$ T cells are an attractive off-the-shelf effector platform because they retain CD3-dependent signaling capacity, recognize tumors in a non-MHC-restricted manner, and have low graft-versus-host disease risk. Our laboratory has previously shown that acute exercise mobilizes $\gamma\delta$ T cells with a more favorable tumor-recognition and cytotoxic profile, including increased NKG2D, DNAM-1, CD56, and CD16 expression, and that these phenotypic features are preserved following ex vivo expansion. Here, we tested whether exercise-expanded $\gamma\delta$ T cells acquire additional phenotypic features that may support enhanced responsiveness to bsAb-mediated tumor engagement and improve bsAb-directed anti-tumor function.

METHODS: Healthy participants enrolled in the Allo-X trial (NCT06643221) completed a 20-minute graded cycling protocol up to 80% VO_2max . Lymphocytes were isolated from blood collected at rest and during the final stage of the graded exercise challenge. PBMCs were expanded into $\gamma\delta$ T-cells over 14 days prior to their use in downstream assays. Expanded $\gamma\delta$ T cells were assessed by flow cytometry for phenotypic features associated with tumor recognition, cytotoxic potential, and bsAb-directed responsiveness. Cytotoxicity was evaluated in 4-hour co-culture assays across five hematologic malignancy cell lines: three CD19+ models (RS4;11, Nalm-6, and Jeko-1) treated with blinatumomab and two BCMA+ multiple myeloma models (MM1.S and U266) treated with teclistamab. Effector-to-target ratios ranged from 1.25:1 to 10:1. Functional responsiveness was further assessed by CD107a degranulation and intracellular TNF α and IFN γ production following bsAb-directed stimulation against representative CD19+ and BCMA+ tumor models. Cytotoxicity data were analyzed by three-way ANOVA, and degranulation/cytokine data were analyzed by two-way ANOVA in Graphpad Prism.

RESULTS: Exercise-expanded $\gamma\delta$ T cells displayed increased expression of adhesion-related molecules, including ICAM-1(CD54) and β 2-integrin-associated adhesion markers such as LFA-1. These findings support a phenotype more compatible with bsAb-directed tumor engagement. Across CD19+ leukemia/lymphoma models, blinatumomab increased tumor lysis, with exercise-expanded $\gamma\delta$ T cells showing consistently greater bsAb-directed cytotoxicity than rest-expanded $\gamma\delta$ T cells. Similar enhancement was observed in BCMA+ multiple myeloma models treated with teclistamab. Statistical analysis demonstrated significant main effects of exercise and bsAb treatment, as well as a significant exercise $\times$ bsAb interaction, indicating that exercise-expanded $\gamma\delta$ T cells were more responsive to bsAb-mediated redirection. Functional assays further supported this pattern: following bsAb stimulation, exercise-expanded $\gamma\delta$ T cells showed increased CD107a degranulation and TNF α production compared with rest-expanded cells, with IFN γ showing a similar directional increase. These responses were minimal in unstimulated controls, suggesting that the enhanced functional activity was most apparent under bsAb-directed tumor engagement.

CONCLUSION: Acute exercise may improve the therapeutic fitness of expanded $\gamma\delta$ T cells by preserving a favorable tumor-recognition phenotype, promoting adhesion-associated features, and enhancing bsAb-directed cytotoxic and cytokine responses. These findings support a potential synergy between exercise-expanded $\gamma\delta$ T cells and bispecific antibody redirection, providing a rationale for further development of exercise-informed allogeneic $\gamma\delta$ T-cell platforms for hematologic malignancies.

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Effects of adjuvant /neoadjuvant chemotherapy combined with exercise therapy in pancreatic cancer

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Abstract

INTRODUCTION: Improvement of the completion rate of postoperative adjuvant chemotherapy is a key to obtaining favorable prognosis in patients who undergo macroscopically curative pancreatectomy for pancreatic ductal adenocarcinoma (PDAC). We investigate the effect of supervised exercise therapy on improvement of the rate of completion of adjuvant therapy by a prospective phase II trial of patients undergoing pancreatectomy for PDAC.

METHODS: This clinical trial evaluated the completion rate of four courses of S-1 adjuvant chemotherapy in combination with supervised exercise therapy in patients who underwent macroscopically curative pancreatectomy for PDAC. Secondary endpoints were dose intensity of S-1, recurrence-free survival time, overall survival time, and safety of the protocol therapy used in this study. Frailty was evaluated with the Kihon checklist and the G8 questionnaire. Forty-three patients were included in the study.

RESULTS: The completion rate of S-1 therapy, the primary endpoint, was 93%, which exceeded the threshold completion rate of 53% ($P < 0.001$). As secondary endpoints, the relative dose intensity of S-1 was $91.8 \pm 19.6\%$, the median recurrence-free survival was 20.4 months, and the median overall survival was not reached, confirming the safety of protocol treatment. The assessment of frailty status showed significant decrease in the Kihon checklist score ($P = 0.002$) and significant increase in G8 questionnaire score ($P < 0.001$), indicating that exercise therapy reduced frailty. There were no incidences of serious adverse events except for one case of grade 3 febrile neutropenia. The differences between before/after therapy (between 6 months/baseline) of mean muscle mass, mean body fat mass, and mean body fat percentage were 1.52 ($P < 0.001$), -1.18 ($P = 0.007$), and -2.47 ($P < 0.001$), respectively.

CONCLUSION: Adjuvant chemotherapy combined with supervised exercise therapy for PDAC was confirmed to improve the completion rate of S-1 adjuvant chemotherapy.

FUTURE PROSPECTS: Currently a phase II study of the safety and efficacy of the neoadjuvant chemotherapy with home-based exercise program for pancreatic cancer is on going. To investigate the efficacy and safety of neoadjuvant chemotherapy for pancreatic cancer combined with home-based exercise therapy on the lymphocyte-to-monocyte ratio (LMR) and other inflammatory based prognostic scores (IBPS). In addition, we will examine whether the practice of exercise therapy contributes to a decrease in postoperative complications, an increase in the completion rate of adjuvant chemotherapy, and a prolongation of recurrence-free survival. In addition, we will examine how exercise therapy changes the tumor microenvironment and how it correlates with IBPS. We will introduce the concept and protocol of this study and discuss the future prospects of exercise therapy in multidisciplinary treatment of pancreatic cancer.

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Activities of the Cancer and Exercise Working Group: Bridging Evidence and Practice in Exercise Oncology

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Abstract

INTRODUCTION: Exercise Oncology has emerged as a rapidly growing multidisciplinary field spanning cancer prevention, treatment, and survivorship. Exercise contributes to cancer prevention, supports cancer treatment through the mitigation of treatment-related side effects and maintenance of physical function, and is associated with improved prognosis after treatment. Increasing attention has also been paid to the potential role of exercise in modulating inflammation, immune function, and the tumor microenvironment. However, despite the growing body of evidence, public awareness and implementation of exercise for people affected by cancer remain insufficient. To bridge the gap between evidence and practice, the Cancer and Exercise Working Group was established through a multidisciplinary collaboration among healthcare professionals, researchers, and exercise specialists. This abstract reports the activities and outcomes of the Working Group rather than the results of an original research study.

METHODS: The Working Group consists of physicians, researchers, and exercise professionals with expertise in cancer rehabilitation, oncology, exercise physiology, and sports science. To promote awareness of the benefits of exercise among cancer patients, their families, healthcare providers, and exercise instructors, educational materials including posters and web-based content were developed. The contents were created based on national and international guidelines and relevant scientific evidence through multidisciplinary discussion and consensus.

RESULTS: An educational poster and website on exercise and cancer were developed. The poster provides concise messages regarding the importance of exercise and includes a QR code linking to the website. The website summarizes scientific evidence broadly supported by current guidelines and review articles regarding exercise for cancer prevention, exercise during cancer treatment, and exercise after treatment, together with practical recommendations and safety considerations. In addition, home-based exercise videos were made accessible through the website.

CONCLUSION: Although evidence supporting Exercise Oncology continues to accumulate, its translation into public practice remains limited. This initiative represents an effort to disseminate evidence-based information to the public and healthcare settings. Future activities will focus on expanding collaboration with healthcare institutions, local governments, and exercise facilities to further promote exercise in cancer care.

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Luncheon Seminar

Immune Protein Supplementation in Athletes: Attenuating Exercise-Induced Renal Stress, Intestinal Barrier Damage, and Inflammation

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Abstract

Prolonged strenuous exercise can challenge fluid balance, renal function, intestinal barrier integrity, and immune homeostasis in athletes. Dehydration may compound renal stress, while splanchnic hypoperfusion and thermal strain can disrupt the intestinal barrier and promote inflammation. These interconnected responses are important targets for nutritional support. Immune protein (IMP), a concentrated product of hyperimmunized cow milk, is a candidate nutritional strategy with barrier-protective and anti-inflammatory potential.

In a double-blind, randomized, placebo-controlled crossover study, seven healthy male long-distance runners consumed IMP (10 g twice daily) or a matched placebo for 8 weeks, separated by a 1-month washout. Participants completed 3000-m time trials before supplementation and after 4 and 8 weeks. Urine obtained before and after each trial was analyzed for renal and dehydration-related indices, including N-acetyl- β -D-glucosaminidase (NAG), osmotic pressure, and specific gravity; intestinal fatty acid-binding protein (I-FABP), a marker of intestinal epithelial injury and permeability; and inflammatory mediators, including interferon-gamma (IFN- γ), interleukin-1 beta (IL-1 β), and tumor necrosis factor-alpha (TNF- α).

The 3000-m time trial increased urinary NAG, consistent with acute renal tubular stress, but IMP did not modify NAG. In contrast, after 8 weeks of IMP supplementation, the exercise-associated changes in urinary osmotic pressure and specific gravity were attenuated, suggesting preservation of renal concentrating function under dehydration-related stress. IMP also significantly attenuated the exercise-induced rise in creatinine-corrected urinary I-FABP, supporting protection of intestinal barrier integrity. Exercise-related increases in urinary IFN- γ and TNF- α were inhibited, while IL-1 β showed an inhibitory trend. Race performance, perceived exertion, and body composition did not differ between conditions, and no adverse events were self-reported or observed.

These findings support an integrated model in which IMP may help athletes maintain renal concentrating function, limit exercise-induced intestinal epithelial injury, and dampen inflammatory responses. Improved barrier integrity may reduce lipopolysaccharide translocation and thereby contribute to the lower cytokine response, although this mechanism was not directly tested. In this lunch seminar, I will discuss the physiological links among dehydration, renal dysfunction, intestinal permeability, and inflammation; the translational relevance of IMP supplementation; and the need for confirmation in larger cohorts and under more strenuous or heat-stress conditions.

Immune Proteins in Sports: Effects on Salivary Mucosal Immunity in Athletes

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Abstract

Immune proteins (IMP), also known as hyperimmune milk, are protein-rich milk powder produced by vaccinating dairy cows with multiple antigens to produce pathogen-specific antibodies. The milk obtained from these hyperimmunized cows was concentrated, resulting in a supplement enriched with immunoglobulins directed against specific pathogens, including *Escherichia coli*, *Salmonella*, *Shigella*, and *Staphylococcus aureus*.

Previous studies have shown that IMP causes a direct antigen-antibody response to pathogens and inhibits increased intestinal permeability. These mechanisms suggest that IMP supplementation exerts protective effects via a dual-layer passive immune system comprising IgG-mediated pathogen neutralization and IgA-mediated mucosal barrier stabilization.

In competitive sports, maintaining optimal physical condition and immune function is essential for athletes seeking to sustain high training loads and maximize their performance. However, athletes who engage in repeated high-intensity training are exposed to physiological stressors that can provoke systemic inflammation, organ damage, transient immunosuppression, and an increased incidence of upper respiratory tract infections (URTIs). Among the mechanisms underlying disruptions in inflammatory signaling, exercise-induced disruption of intestinal barrier function ("leaky gut") has attracted attention as a potential initiating factor.

Accordingly, there is growing demand for effective strategies to mitigate training-induced immune dysfunction in athletes. Among the various approaches proposed, nutritional interventions have attracted attention because of their feasibility and applicability in daily training environments. In this context, our research has focused on the potential role of immune proteins in sports. In this seminar, we will present our findings on the eight weeks effects of IMP supplementation on salivary mucosal immunity in athletes, focusing particularly on secretory IgA and changes in the microbiota.

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Rowing: as a promising geroprotector for senior people

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Abstract

Both aerobic and resistance exercise have been recommended for senior people to prevent metabolic syndrome (high blood sugar, blood lipid abnormality, and high blood pressure) and locomotive syndrome (low bone mineral density, and low muscle mass and strength). Rowing is one of the oldest sports in the world, and it offers a combination of both aerobic and resistance exercise. Rowing is practiced on a seat, less impact is placed upon the knee joints, making it safe for senior people. Masters rowers have higher cardiorespiratory fitness and a lower risk of metabolic and locomotive syndromes than age-matched sedentary individuals. Our joint study performed together with Waseda University and Hungarian Sport Science University for senior rowers, who participated in World Rowing Masters Regatta in Hungary, 2019, suggested that senior rowers have higher anti-oxidative capacity than sedentary controls. Our search for the mechanisms suggested that habitual rowing exercise is associated with lower oxidative stress and higher anti-oxidative capacity compared with sedentary controls. In addition, trained rowers demonstrated favorable fatty acid profiles, including lower n-6/n3 and AA/EPA (Arachidonic acid/Eicosapentaenoic acid) ratios, together with altered interrelationships between telomere length, epigenetic aging markers, and chronological age, suggesting enhanced biological resilience against aging processes. Oxidative stress and anti-oxidative capacity were evaluated using the d-ROMs (derivatives of reactive oxygen metabolites) test and BAP (biological antioxidant potential) test, which are widely utilized redox biomarkers for assessing systemic oxidative balance in clinical and sports science research. The seminar will also introduce the scientific background and practical applicability of these redox assessments as accessible tools for monitoring physiological responses to exercise and healthy aging. Collectively, these findings support the concept that lifelong rowing exercise may contribute to the maintenance of redox homeostasis and healthy longevity. These observations further highlight the potential value of rowing as a multimodal lifestyle intervention targeting biological aging pathways. Therefore, rowing exercise could be expected as a promising geroprotector to delay biological aging associated with lengthening of health lifespan for the senior people.

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Poster Presentation

Effects of long-term voluntary running exercise on allergy-related immune cell dynamics and immune checkpoint receptor-mediated immunoregulation

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Abstract

INTRODUCTION: Exercise is widely recognized as an important factor in maintaining health and preventing disease, and recent evidence suggests that it may suppress inflammation and allergic responses. However, the molecular mechanisms underlying the immunomodulatory effects of exercise remain unclear, particularly regarding immune checkpoint molecules. LILRB4, known as gp49B in mice, is an inhibitory immune checkpoint receptor expressed on various immune cells, including mast cells, macrophages, dendritic cells, and NK cells¹. gp49B transmits inhibitory signals through ITIM-mediated recruitment of SHP-1/2 and has been implicated in the regulation of allergic and inflammatory responses^{1,2}. Therefore, this study aimed to investigate the effects of long-term voluntary exercise on immune cell dynamics and gp49B-mediated immunoregulation in the bone marrow (BM) and spleen.

METHODS: C57BL/6 wild-type (WT) and gp49B-deficient mice were subjected to eight weeks of voluntary running exercise using running wheel systems. Serum, BM, and spleen samples were collected before and after the exercise period. Cells isolated from the BM and spleen were analyzed by flow cytometry. Serum cytokine levels were also measured to assess exercise-induced changes in circulating cytokines.

RESULTS: Body weight increased with age in both WT and gp49B-deficient mice during the exercise period; however, no significant difference in body weight was observed between the two genotypes at the end of the exercise period. Exercise volume was also comparable between the two groups throughout the study period. After the exercise period, gp49B expression was detected in BM and spleen cells, particularly in macrophages and basophils. In gp49B-deficient mice, exercise significantly altered the proportions of macrophages and basophils in both the BM and spleen. Exercise also induced significant changes in the splenic localization of CD8⁺ T cells, and M1-type macrophages. In contrast, no marked changes were observed in B cells, CD4⁺ T cells, or NK cells in either tissue.

CONCLUSION: These findings suggest that long-term voluntary exercise may influence allergic responses by altering immune cell dynamics and immune checkpoint receptor-mediated regulation.

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The Influence of Bone Marrow Hematopoietic Activity in Low-Grade Inflammation in Lean Type 2 Diabetes

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Abstract

INTRODUCTION: The obesity derived low grade chronic inflammation triggers the insulin resistance (IR) development and consequently the type 2 diabetes *mellitus* (T2DM). Nonetheless, a rising population of diabetic individuals do not present obesity, especially in Japan, where non-obese diabetic individuals represent around 60% of T2DM cases. The bone marrow (BM) is responsible for producing and releasing leukocytes into the bloodstream and therefore exerts direct influence on the inflammatory profile. Metabolic alterations in hematopoietic cells can influence the leukocyte production toward a pro-inflammatory state, which could contribute to the development of IR in non-obese type 2 diabetic individuals. The aim of this study was to evaluate the cellular profile in the bone marrow of male Goto-Kakizaki (GK) rats, a spontaneous non-obese T2DM model, compared to euglycemic male Wistar (WT) rats, as a control group.

METHODS: The following experimental groups were used: 21-day-old WT rats; 21-day-old GK rats; 120-day-old WT rats and 120-day-old GK rats. The circulating leukocytes were evaluated through hemogram, BM cellularity, immunophenotype of BM cells, mRNA expression in BM cells and MCP-1 concentration.

RESULTS: GK presented leukocytosis, caused by higher lymphocyte and neutrophil count since 21 days old, post-weaning, that persisted with aging. The BM cellularity was also increased in both ages. The myelogram along with the immunophenotyping revealed an increase in the lymphocyte population, especially in the lymphoid progenitor cells, Natural Killer cells, T CD4⁺ and T CD8⁺ lymphocytes, the latter indicating a higher recirculation of mature and differentiated cells. It was also observed increased population of myeloid cells and elevated proportion of pro-inflammatory macrophages (M1), as well as decreased population of anti-inflammatory (M2). The IL-7 and IL-10 expression analysis along the MCP-1 evaluation indicates a pro-inflammatory microenvironment in the BM.

CONCLUSION: Our results suggest that the shifts in the metabolism of the hematopoietic system could be a contributor to the development of a low grade systemic inflammation detached from obesity, leading to the development of IR and the non-obese T2DM. Therefore, the BM could be a future therapeutical target for the disease.

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Immunophenotypic characterization of CD8+ T cells and NK cells following aerobic and resistance training in healthy individuals

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Abstract

INTRODUCTION: Exercise leads to reduced symptoms, enhanced physical functioning and improved quality of life, and is associated with enhanced treatment efficacy and better overall survival in patients with solid tumors. One of the suggested mechanisms for the improved cancer specific outcomes is the modulation of the immune function. During acute exercise, immune cells, and especially CD8+ T cells and NK-cells, are mobilized into the circulatory system. The redistribution of these immune cells after exercise has not been characterized in depth. It has however been hypothesized that the mobilized immune cells migrate to tumor sites and become tumor infiltrating lymphoid cells (TILs), contributing to a more favorable prognosis. Here we compare the effect of aerobic exercise (AE) and resistance exercise (RE) on this mobilization and markers of homing and function.

METHODS: Blood samples were obtained from healthy volunteers pre, immediately post and 30 minutes after AE and RE in a cross over design. PBMCs were isolated and analyzed with multicolor flow cytometry. Immune cell function was analyzed using viral peptides.

RESULTS: Our preliminary data suggested that both exercise types led to an increased frequency of cytotoxic subsets of CD8+ T cells and NK cells. However, AE induced a more pronounced mobilization compared to RE, potentially due to the difference in intensity. Characterization of markers of homing and function are ongoing. Current experiments focus on whether the enhanced mobilization is reflected also in the expression of homing markers and cytotoxic function.

CONCLUSION: The proposed research will provide novel information on the effect of different exercise modalities on immune cell recruitment, homing and function, informing exercise intervention designs.

The Effects of High-Intensity Interval Training on T-Cell Activation in Patients with Rheumatoid Arthritis: A Scoping Review

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Abstract

INTRODUCTION: Rheumatoid Arthritis is a chronic autoimmune inflammatory disease that causes progressive disability in joints, potential comorbidity, further systemic complications, and even death by multiple organ failure. For many years, pharmacological therapy remains the cornerstone of treatment, but rarely achieves complete immunological remission. High Intensity Interval Training in recent times is proposed as a time-efficient adjunctive intervention that may improve T cell function, restore immune homeostasis, and slow disease progression alongside pharmacological therapy. This scoping review aims to investigate the effect of High Intensity Interval Training on T-Cell Activation in Patients with Rheumatoid Arthritis.

METHODS: Methods in this scoping review followed PRISMA-ScR guidance. A structured search from Pubmed, Scopus, Springer Nature, and Embase was performed using combinations of “rheumatoid arthritis”, “high intensity interval training”, and “T cell”. Inclusion criteria: (1) Patients with Rheumatoid Arthritis; (2) HIIT or comparable high intensity exercise interventions; (3) reported T cell related outcomes (CD4+, CD8+, Treg/Th17, IL-6, IL-10); (4) randomized controlled trials, cohort, or pilot studies; (5) English-language publications between 2018 and 2025. Exclusion criteria: (1) animal or in vitro studies; (2) other autoimmune conditions; (3) low- or moderate-intensity exercise without an HIIT component; (4) editorials, case reports, and conference abstracts. Screening progressed from title to abstract to full-text review.

RESULTS: Six studies met the inclusion criteria. HIIT consistently modulated T-cell activation, evidenced by reduction of senescent CD4+ effector memory T cells, restoration of Treg/Th17 homeostasis, decreased pro-inflammatory IL-6, and increased anti-inflammatory IL-10. One RCT employing high-intensity yoga practice demonstrated re-establishment of immunological tolerance and attenuated T-cell aging. Parallel improvements were observed in DAS28 disease activity, cardiorespiratory fitness, and skeletal muscle oxidative metabolism. Across studies, T-cell modulation occurred alongside the most pronounced clinical gains: reduced fatigue, improved health-related quality of life, and preserved functional capacity, with no exercise-related adverse immunological events.

CONCLUSION: HIIT exerts beneficial immunomodulatory effects on T-cell activation in patients with RA and represents a safe, non-pharmacological adjunct to disease-modifying antirheumatic drug therapy. More studies are required to specifically investigate the effect of High Intensity Interval Training in Rheumatoid Arthritis patients with cardiovascular and metabolic comorbidities.

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Probiotic and Prebiotic Supplementation for Respiratory Immune Modulation in Athletes versus Asthma: A Comparative Meta-Analysis

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Abstract

INTRODUCTION: Athletes and asthma patients represent two populations with fundamentally different pathophysiology—transient exercise-induced immunosuppression versus chronic Th2-driven airway inflammation—yet both share a common vulnerability: mucosal immune dysfunction at the respiratory interface. The gut–lung axis has emerged as a unifying mechanistic framework linking intestinal microbiota modulation to respiratory immune regulation. Probiotic and prebiotic supplementation has been investigated in each population independently, with separate meta-analyses reporting benefits for URTI in athletes and for airway inflammation in asthma. However, no study has systematically compared whether these gut-targeted interventions exert analogous immunomodulatory effects across the two groups. This meta-analysis is the first to bridge this gap, enabling direct comparison of respiratory and immune outcomes between athletes and asthma patients.

METHODS: PubMed, Cochrane Library, and Web of Science were searched from inception through April 2026 for RCTs examining oral probiotic, prebiotic, synbiotic, or postbiotic supplementation in (1) physically active adults/athletes or (2) asthma patients, reporting respiratory and/or immune outcomes. Two reviewers screened records per PRISMA 2020. Bias assessed via RoB 2. Athlete subgroup: URTI incidence/duration, salivary IgA, inflammatory cytokines. Asthma subgroup: FEV₁, FeNO, Th1/Th2 cytokines, Treg markers. Random-effects models with I² heterogeneity.

RESULTS: Over 40 RCTs were identified for qualitative synthesis. In athletes, probiotic/prebiotic supplementation reduces URTI incidence and symptom duration with enhanced salivary IgA secretion. In asthma patients, supplementation improves pulmonary function and attenuates Th2-associated cytokines (particularly IL-4), while promoting Treg responses. Across both populations, convergent Th1/Th2 rebalancing was observed, suggesting shared gut–lung axis mechanisms. Heterogeneity varied by outcome, influenced by strain specificity, dosage, duration, and population characteristics. Full meta-analytic results with forest plots and subgroup comparisons will be presented at the conference.

CONCLUSION: Probiotic/prebiotic supplementation benefits both athletes (reduced URTI, enhanced mucosal immunity) and asthma patients (attenuated airway inflammation, improved immune regulation) through the gut–lung axis. Convergent immunological pathways suggest gut-targeted interventions as a unified strategy for exercise-induced immunosuppression and allergic airway disease. Notably, no RCTs have investigated athletes with comorbid asthma, representing a priority for future trials.

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Leukocyte, Interleukin-6, and Chemokine Responses to Moderate-Intensity Aerobic Exercise During the Menstrual and Luteal Phases

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Abstract

INTRODUCTION: Acute exercise alters circulating leukocyte dynamics and affects immune cell mobilization and trafficking through cytokine- and chemokine-mediated mechanisms. In women of reproductive age, endocrine fluctuations across the menstrual cycle may modulate immune responses at rest and during exercise. When considering exercise throughout the menstrual cycle, the menstrual phase is of particular relevance because it is an immunologically distinct period characterized by endometrial shedding and repair. However, systemic immune responses during this phase to moderate-intensity aerobic exercise, which is recommended worldwide for health promotion, remain unclear. This study compared leukocyte dynamics, IL-6, and chemokine responses to moderate-intensity aerobic exercise between the menstrual and luteal phases.

METHODS: Fourteen healthy young women with regular menstrual cycles were recruited. Each participant performed 60 min of cycling exercise at $65 \pm 5\%$ of predicted maximal heart rate during both phases. Blood was collected before, immediately after, and 60 min after exercise. Total leukocyte, neutrophil, lymphocyte, and mixed-cell counts including monocytes, eosinophils, and basophils were measured, along with IL-6, IL-8, monocyte chemoattractant protein-1 (MCP-1), and cortisol. Metabolic responses from respiratory gas analysis were assessed in 12 participants with complete data. Linear mixed models examined the effects of phase, time, and their interaction.

RESULTS: Exercise workload, heart rate, rating of perceived exertion, and metabolic responses did not differ between phases. Total leukocyte, neutrophil, and mixed-cell counts were higher in the luteal phase than in the menstrual phase. Significant time effects were observed for these cell counts and cortisol. However, no significant phase-by-time interactions were observed for total leukocyte, neutrophil, lymphocyte, mixed-cell counts, or cortisol. IL-6 showed a significant time effect and increased after exercise, whereas neither the main effect of phase nor the phase-by-time interaction was significant. IL-8 was higher in the menstrual phase than in the luteal phase, whereas MCP-1 did not differ between phases. Neither IL-8 nor MCP-1 showed significant time effects or phase-by-time interactions.

CONCLUSION: Menstrual cycle phase may influence peripheral leukocyte counts and circulating IL-8 concentrations. Higher IL-8 levels during the menstrual phase may partly reflect the inflammatory and immune environment associated with menstruation. In contrast, under comparable exercise load and metabolic responses, exercise-induced responses of IL-6, leukocytes, chemokines, and cortisol were not specifically augmented during the menstrual phase. These findings suggest that, although the menstrual phase represents a distinct immunological and inflammatory state, moderate-intensity aerobic exercise within one hour is unlikely to specifically amplify systemic inflammatory responses during this phase.

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Transient Alterations of Salivary Mucosal Immunity Following Vaccination in Adolescent Female Athletes

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Abstract

INTRODUCTION: Although influenza vaccination is routinely recommended for athletes due to the elevated infection risk associated with intensive training and competition, concerns regarding vaccine-related side effects still contribute to vaccine hesitancy among athletes. Salivary mucosal immune markers provide important information regarding upper respiratory immune defense in athletes; however, the effects of influenza vaccination on mucosal immunity in adolescent athletes have not been fully investigated. This study investigated longitudinal changes in salivary mucosal immune markers following influenza vaccination in adolescent female athletes.

METHODS: Fifty-four high school female athletes (volleyball, softball, and swimming) participated in this study and were categorized according to vaccination status into vaccinated (n = 28) and non-vaccinated groups (n = 26). Saliva samples were collected at baseline and on days 4, 7, 14 and 21 after influenza vaccination. Salivary amylase, lactoferrin, immunoglobulin A (SIgA), lysozyme, and nitric oxide were analyzed and protein immune molecules were normalized to total protein (TP) concentration. A mixed repeated-measures ANOVA was used to evaluate group × time interactions, followed by post hoc comparisons. Statistical significance was set at p < 0.05.

RESULTS: A significant group × time interaction was observed for salivary IgA/TP (p = 0.002). In the vaccinated group, IgA/TP significantly decreased on days 7, 14, and 21 compared with baseline (all p < 0.05), whereas no significant temporal changes were observed in the non-vaccinated group. Salivary amylase/TP significantly increased on day 7 (p = 0.041) in the vaccinated group compared with baseline, while no significant changes were observed in controls. No significant changes were identified for lactoferrin/TP, lysozyme/TP, or nitric oxide.

CONCLUSION: Influenza vaccination induced transient alterations in salivary mucosal immune responses in adolescent female athletes, characterized by decreased IgA/TP and increased amylase/TP following vaccination, suggesting distinct temporal responses between salivary adaptive and innate immunity.

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Neutrophil Function in Elite Athletes with High-Intensity Exercise induced Bronchospasm

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Abstract

INTRODUCTION: Professional athletes are highly susceptible to upper respiratory tract infections and exercise-induced bronchospasm (EIB) due to high training volumes and intensities. While intense exercise modulates neutrophil function and programmed cell death, potentially impairing systemic immune function, the impact of acute, progressive, and high-intensity exercise on neutrophil dynamics in athletes with EIB remains poorly understood. We then investigated the effects of a maximal cardiopulmonary exercise test (VO₂ peak) on neutrophil function in athletes with and without EIB.

METHODS: Twenty-six high-performance male athletes were divided into the EIB and control groups. EIB condition was determined via the eucapnic voluntary hyperpnea test. Blood samples were collected at rest and immediately after the maximal exercise test. Isolated neutrophils were evaluated for CD62L expression, phagocytic activity, intra- and extracellular superoxide anion production, and pro- and anti-inflammatory cytokine release (with/without LPS or PMA stimulation). Neutrophil death parameters, including DNA fragmentation and cell membrane integrity, were determined.

RESULTS: In the control group (CG), no significant cytokine release changes by neutrophils occurred post-exercise without stimulus; however, LPS stimulation significantly increased IL-1 β , TNF- α , IL-6, and IL-10 production by neutrophils from both pre- and post-exercise. Phagocytic activity increased by 35.8% (post-exercise), and PMA stimulation raised anion superoxide production by 5.6-fold (pre-exercise) and by 5.9-fold (post-exercise) compared to unstimulated cells. In the EIB group, no significant changes were observed in the production of IL-1 β , TNF- α , IL-6, and IL-10 under any condition, including LPS stimulation. In the pre-exercise state, PMA-stimulated superoxide production in neutrophils from the EIB group was 11.2-fold lower compared to the CG. Post-exercise, neutrophils from the EIB showed a 46.6% increase in CD62L expression compared to CG, yet no changes in phagocytic capacity or superoxide production were observed after stimulation. EIB group neutrophil membrane integrity was decreased by 12.7% post-exercise, indicating more cell death compared to the CG.

CONCLUSION: Neutrophils from athletes with EIB exhibit a reduced activation capacity and decreased essential cellular functions (phagocytosis, ROS production, and cytokine secretion), and more cell death compared to the cells of the CG. These changes might impair the immune response against invading microorganisms and the resolution of inflammation both at rest and following acute high-intensity exercise.

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Effects of pre-maximal isometric contraction on eccentric exercise induced muscle damage and pulse wave velocity of the knee extensor

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Abstract

INTRODUCTION: This study was to investigate the protection of the knee extensors by performed first bout of maximum voluntary isometric exercise (MVIC), and then undergo second bout of 60 maximal isokinetic eccentric concentric (MAX-ECC) after two days.

METHODS: Sixteen healthy males were randomly assigned either to the MVC group and CON group. After MVC group performed the first bout of MVIC (2 times, 120° flexion), MVC and CON group had performed MAX-ECC 60 times (10 times/set x 6 sets) in second bout after 2 days. The dependent variables include measured maximal isokinetic concentric strength (ISOK), range of motion (ROM), limb circumference (CIR), carotid-femoral pulse wave velocity (cfPWV), diastolic blood pressure (DBP), systolic blood pressure (SBP) and heart rate (HR). These variables were measured the pretest (pre), immediately after (D0), after MVIC (D1) in the first bout. The second bout were measured the pretest (pre), immediately after (D0), and on the first day to the fifth day (D1~D5, every 24 hours).

RESULTS: No significant changes in ISOK, ROM, CIR and cfPWV after MVIC ($p > .05$). After finished MVIC two days later, ISOK of the MVC group were significant lower than pretest at D0~D2, ISOK of the CON group were significant lower than pretest at D0~D3. ROM and CIR of the both group were significant difference with pretest at D0~D5 ($p < .05$), and cfPWV of the both group were higher than pretest at D1~D2 ($p < .05$).

CONCLUSION: Preconditioning knee extensor muscles with 2 MVIC does not cause abundance muscle damage, and also not cause RBE by subsequent MAX-ECC, cfPWV still induced by subsequent MAX-ECC.

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Strength Training as an Immune Rejuvenation Strategy: Evidence from the SPRINT project

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Abstract

INTRODUCTION: Physical exercise has been proposed as an effective intervention to counteract the deleterious effects of immunosenescence, an ageing-associated remodelling of the immune system. Previously, six weeks of strength training was shown to decrease senescence-prone T-cell numbers in women. However, the long-term training effects in men remained unclear. We investigated the long-term (3 months) effects of strength training on cellular markers of immunosenescence in both men and women.

METHODS: Older adults aged 65 and over living independently in the community were assigned to one of three exercise programs: 3 months intensive strength training (IST, 3x10 repetitions at 80% 1RM), strength endurance training (SET, 2x30 repetitions at 40% 1RM) or flexibility training (CON). After isolation of peripheral blood mononuclear cells (PBMC) from venous blood samples, immunosenescence-related markers were measured via flow cytometry. Gene expression analysis was also performed via Quantigene analysis after RNA extraction of PBMC. Between group ($p < 0.05$) effects were determined with Kruskal-Wallis and Mann-Whitney U tests, time effects via Wilcoxon's signed rank test. Genes with an absolute fold change of ≤ 0.67 or ≥ 1.5 were considered clinically relevant. Serum cytomegalovirus (CMV) immunoglobulin G levels were measured through a chemiluminescent microparticle immunoassay.

RESULTS: Overall, three months of SET, but not IST, decreased CD3+(CD28-)CD57+ senescence-prone T-cells compared to CON. Additionally, 3 months of SET also increased the proportions of CD28-CD57- memory T-cell phenotypes. After subgroup analysis, most effects remained significant in men but not in women. These effects of SET were also most prominent in CMV+ subjects. In men, 3 months of SET also increased CD28+CD57- naïve T-cells. At the gene level, the expression of CCL3 and CXCL8 in CMV-negative subjects only was decreased after 3 months of SET.

CONCLUSION: Three months of SET counteracted more than three years of accumulation of senescence-prone T cells. The stronger effects observed in CMV-positive participants may reflect preferential mobilization of CMV-specific T cells and subsequent exposure to circulating apoptotic signals. SET also reduced gene expression markers of immunosenescence, although additional T-cell senescence effects may have been masked within the total PBMC pool.

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Reduced glucose availability elevates electrical pulse stimulation-induced oxidative stress in C2C12 myotubes

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Abstract

INTRODUCTION: Skeletal muscle contraction induces rapid cellular responses that are important for exercise adaptation. Reactive oxygen species (ROS) are produced during contraction and act as signaling molecules; however, excessive ROS may contribute to oxidative stress and inflammation-related responses. Skeletal muscle is a major metabolic and secretory organ involved in whole-body adaptation. Glucose availability regulates cellular energy metabolism during contraction; therefore, reduced glucose availability may influence contraction-induced oxidative stress. In C2C12 myotubes, electrical pulse stimulation (EPS) has been shown to increase ROS production and activate antioxidant protective responses. However, the effect of reduced glucose availability on oxidative stress during early contraction-like stimulation remains unclear. Therefore, this study aimed to investigate whether reduced glucose availability modulates EPS-induced oxidative stress in C2C12 myotubes.

METHODS: C2C12 myoblasts were differentiated into myotubes and cultured in normal glucose medium (25 mM) or reduced glucose conditions (20 and 15 mM), with or without 2 h EPS. EPS was applied at 40 V, 2 ms pulse duration, and 1 Hz frequency. Cell morphology was observed by microscope imaging, and adherent cell density was assessed using crystal violet staining. Myotube phenotype was evaluated by measuring MYH1 and MYH7 protein expression using Western blotting. Intracellular ROS production was measured using DCFH-DA staining.

RESULTS: Cell morphology was not markedly changed under reduced glucose conditions, with or without EPS. Crystal violet staining showed no significant changes in adherent cell density under reduced glucose conditions or EPS. MYH1 and MYH7 protein expression showed no marked changes among the experimental groups. In contrast, intracellular ROS production was significantly increased in the 15 mM glucose with EPS group.

CONCLUSION: These findings suggest that reduced glucose availability does not adversely affect C2C12 myotube morphology, adherent cell density, or myotube phenotype. However, the 15 mM glucose with EPS condition significantly increased intracellular ROS production, indicating enhanced EPS-induced oxidative stress. Since ROS is closely related to inflammation-related stress signaling, reduced glucose availability may amplify early oxidative stress responses during contraction-like stimulation. These findings may provide a basis for future studies investigating how exercise-like stimulation regulates antioxidant defense and inflammation-related responses under different energy availability conditions.

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Exercise-Induced Inflammatory Modulation and Muscle Endurance in Older Women at Risk of Sarcopenia

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Abstract

INTRODUCTION: Inflammation may influence muscle fatigability and mobility decline in sarcopenia, but it remains unclear whether exercise-induced inflammatory changes are related to functional adaptation [1]. This study aimed to examine whether changes in circulating inflammatory markers were associated with changes in muscle fatigability and physical performance following a 12-week multicomponent exercise program in older women at risk of sarcopenia.

METHODS: Thirty-eight older women identified as being at risk of sarcopenia according to European Working Group on Sarcopenia in Older People 2 criteria were allocated to either an exercise intervention group (EG; n=18) or a control group (CG; n=20). The exercise program was performed twice/week, with each session including aerobic, TRX-based resistance, and balance training blocks. Maximal handgrip strength, fatigue resistance, and grip work were measured before and after the intervention using the Eforto® device. Circulating inflammatory markers, including IL-6, IL-1 β , TNF- α , IL-10, and IL-1RA, were quantified by ELISA kits from Invitrogen (Thermo Fisher Scientific, USA). Physical function was evaluated using the Short Physical Performance Battery.

RESULTS: Linear mixed-effects models showed significant Group $\times$ Time interactions for several inflammatory markers, indicating a more favorable inflammatory profile after exercise. IL-1RA increased in the exercise group and decreased in controls [F(1,35.3)=4.33, p=0.045; +18.9% vs -5.2%], while IL-6 [F(1,35)=25.55, p<0.001; -18.0% vs +18.0%] and TNF- α [F(1,32.65)=5.39, p=0.027; -6.4% vs +7.8%] decreased in the exercise group and increased in controls. The IL-10/TNF- α ratio also improved following exercise [F(1,36)=4.35, p=0.044; +5.7% vs -34.6%]. These inflammatory adaptations were accompanied by improvements in maximal handgrip strength [F(1,32.01)=6.33, p=0.017], grip work [F(1,32.07)=5.62, p=0.024; +40.4% vs -2.3%], and fatigue resistance [F(1,32.27)=6.06, p=0.019; +36.2% vs -3.4%]. In change-to-change analyses, Δ IL-10 was positively correlated with Δ fatigue resistance (r=0.495, p<0.01) and Δ grip work (r=0.379, P<0.05), while Δ IL-6 was positively associated with Δ 4-m walk time (r=0.384, p<0.05).

CONCLUSION: In conclusion, the multicomponent exercise program improved muscle strength and endurance while promoting a more favorable inflammatory profile in older women at risk of sarcopenia. The observed decreases in IL-6 and TNF- α , together with increased IL-1RA and an improved IL-10/TNF- α ratio, are compatible with attenuation of pro-inflammatory signaling and enhancement of anti-inflammatory regulation. Although intracellular pathways were not directly assessed, these changes may reflect reduced inflammatory pathway activation, potentially involving NF- κ B-related cytokine signaling. The associations between inflammatory changes and changes in fatigue resistance, grip work, and walking performance further suggest that modulation of systemic inflammation may be linked to functional adaptations after regular combined exercise training.

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Dose Optimization of Topical Methyl Salicylate: 10% Wintergreen Oil Attenuates Exercise-Induced Soleus Inflammation Without Impairing Performance

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Abstract

INTRODUCTION: Topical application of wintergreen oil (WG), which is naturally rich in methyl salicylate, is widely used in sports medicine for its anti-inflammatory effects. However, the systemic safety and physiological consequences of applying high-concentration formulations immediately prior to strenuous exercise remain unclear. This study investigated the effects of WG application on exercise performance, organ damage, and systemic inflammatory responses.

METHODS: Eight-week-old male hairless mice were randomly assigned to six groups: naive control (NA), 10% WG without exercise (10%WG), undiluted WG without exercise (WG), exercise without oil application (NA+Ex), exercise with 10% WG application (10%WG+Ex), and exercise with undiluted WG application (WG+Ex). WG were topically applied to the dorsal skin at 4 μ L/g body weight and maintained for 30 min. Subsequently, mice in the exercise groups underwent treadmill running to exhaustion, whereas sedentary groups were sacrificed at the corresponding time. Skeletal muscle, liver, and blood samples were collected immediately afterward. Plasma biochemical data, systemic cytokine profiles using a multiplex assay, and inflammatory gene expression levels in each tissue by real-time PCR were evaluated. Statistical analyses were performed using SPSS and Tukey's multiple comparison test ($p < 0.05$).

RESULTS: Pre-exercise topical application of WG significantly shortened running time to exhaustion in the WG+Ex group compared with the NA+Ex group, whereas no effect on endurance performance was observed in the 10%WG+Ex group. Plasma biochemical analyses revealed marked elevations of AST, ALT, and ALP in the WG group, with levels exceeding those observed in the NA+Ex group. In addition, CK showed an increasing trend ($p = 0.090$). Plasma cytokine analysis demonstrated increased levels of IL-1 α , IL-6, and TNF- α in the WG+Ex group compared with the NA+Ex and 10%WG+Ex groups. Gene expression analyses showed that WG significantly increased *Il-1b* and *Il-6* expression. In the soleus muscle, the NA+Ex group exhibited significantly elevated *Il-1b* and *Il-6* expression compared with the NA group; however, these increases were significantly attenuated in the 10%WG+Ex group compared with the NA+Ex group. In contrast, no comparable suppressive effect was observed in the gastrocnemius muscle.

CONCLUSION: These findings suggest that transdermal absorption of high-dose WG may induce severe acute hepatic and tissue injury within 30 min after application, which may contribute to the reduced endurance performance. In contrast, 10% WG application not only failed to impair endurance capacity but also demonstrated therapeutic benefits by significantly suppressing exercise-induced local inflammation in the soleus muscle, which is rich in slow-twitch fibers and capillaries. These results suggest that appropriate dose regulation is important when using methyl salicylate-containing products in sports settings.

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Age-Related Differences in Gene Expression Following Percutaneous Absorption of Wintergreen Oil in Mice

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Abstract

INTRODUCTION: Wintergreen oil (WG), comprising approximately 99% methyl salicylate, is recognized for its anti-inflammatory and analgesic properties and is commonly employed in sports aromatherapy for muscle pain relief. Previous studies have demonstrated that percutaneous absorption of WG in young mice promotes systemic circulation transfer and dose-dependent local cutaneous inflammation. Since percutaneous absorption varies among individuals and age-related decline in skin barrier function substantially increases the risk of adverse effects, this study was designed to conduct gene expression analysis in aged mice with comparative analysis versus young mice. We aimed to elucidate how age-related changes in skin architecture modulate WG percutaneous absorption and associated inflammatory and oxidative stress responses.

METHODS: Female HR-1 mice were stratified into two age groups: young (8 weeks) and aged (20 months). Each age group was subdivided into two treatment cohorts: naïve control (NA) and WG-treated (WG), yielding four groups (yNA, yWG, aNA, aWG). WG was topically applied to the dorsal surface (3 µL/g body weight), and blood and skin specimens were harvested 30 minutes post-application. Gene expression analysis was performed utilizing SYBR Green I via Real-time PCR. Relative quantification was determined using the $\Delta\Delta C_t$ method. Statistical analyses were performed using 'EZR' (Easy R) version 1.70, with Tukey's test used for multiple comparisons among groups ($p < 0.05$).

RESULTS: Plasma salicylate concentration was elevated in WG-treated groups relative to respective NA controls. In inter-group comparison, yWG mice demonstrated significantly increased gene expression of *Il-6* and *Cox-2*, with markedly decreased *Il-1a* expression compared to yNA mice. aWG mice exhibited significantly augmented expression of *Il-1b*, *Il-6*, *Cox-2*, and *Ap-1*, with concomitantly decreased *Il-1a* expression compared to aNA mice. Furthermore, aNA mice displayed significantly reduced *Il-1a* expression versus yNA mice. aWG mice showed significantly elevated *Nrf-2* expression relative to yWG mice. No statistically significant differences were detected among groups regarding *iNos*, *Nf-kb*, *F4/80*, *Ly6g*, *Icam-1*, *Sod-1*, *Sod-2*, *Cat*, *Ho-1*, and *Gpx* expression.

CONCLUSION: The elevated plasma salicylate concentration in WG-treated groups suggests that salicylate undergoes percutaneous absorption through the stratum corneum, with subsequent systemic distribution. Whereas young mice demonstrated increased *Il-6* and *Cox-2* expression, aged mice additionally exhibited augmented *Il-1b* and *Ap-1* expression. This differential response implies that age-related skin barrier dysfunction may enhance inflammatory responses to external stimuli. Notably, changes in cellular infiltration markers and oxidative stress-related genes were limited, indicating that inflammation predominates in the initial pathophysiology.

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Acute Systemic Inflammatory Responses Induced by Transdermal Absorption of Wintergreen Oil in Mice

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Abstract

INTRODUCTION: Wintergreen oil (WG), which contains approximately 99% methyl salicylate, is widely used for the relief of muscle pain and related conditions. Previous studies have reported local inflammation and systemic distribution following transdermal absorption of WG; however, the details of acute systemic inflammatory responses and cytokine alterations after absorption remain unclear. The present study aimed to clarify the acute systemic inflammatory response induced by transdermal WG absorption.

METHODS: Eight-week-old male HR-1 mice were divided into three groups: a naïve control group (NA group), a 10% WG-treated group (10% WG group), and an undiluted WG-treated group (WG group). The 10% WG solution was diluted with jojoba oil. Samples were applied to the dorsal skin of the 10% WG and WG groups at a dose of 3 μ L/g body weight; no treatment was applied to the NA group. All groups were maintained under identical conditions for 30 min, after which blood samples were collected. Plasma salicylic acid, CRP, leakage enzymes (AST, ALT, LD, and CK), and 13 cytokines/inflammation-related factors were measured. Transepidermal water loss (TEWL) was measured immediately before blood collection. Statistical analyses were performed using EZR version 1.70; Tukey's multiple comparison test was applied at a significance level of $p < 0.05$.

RESULTS: WG application significantly increased plasma salicylic acid levels in a dose-dependent manner, with the WG group showing significantly higher levels than the NA and 10% WG groups. No significant differences were observed in CRP or TEWL among groups. Among cytokines, IL-1 α and TNF- α were significantly elevated in the WG group compared with the NA and 10% WG groups; no significant differences were observed between the NA and 10% WG groups. Regarding leakage enzymes, AST, ALT, and LD levels were significantly increased in the WG group compared with the other groups, whereas CK levels showed no significant changes.

CONCLUSION: The dose-dependent increase in plasma salicylic acid levels confirmed that WG is rapidly absorbed through the skin into systemic circulation. Because measurements were performed only 30 min after application, no changes were observed in TEWL or CRP, both of which require more time to manifest. In contrast, IL-1 α , TNF- α , and leakage enzymes (AST, ALT, and LD), which are rapidly released during cellular injury, were significantly elevated in the WG group, suggesting that transdermal absorption of high-dose WG rapidly induces systemic cellular injury and acute inflammatory responses. These findings indicate that 10% diluted WG is relatively safe, whereas inappropriate transdermal absorption of high-dose WG may pose a risk of acute systemic inflammatory responses. In conditioning settings such as sports massage, direct application of undiluted WG should therefore be avoided, and local exposure should be controlled through appropriate dilution.

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Development of a Patch-Free Murine Model of Epicutaneous Sensitization Using a Highly Viscous Carboxymethyl Cellulose Solution

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Abstract

INTRODUCTION: Epicutaneous allergen sensitization is a well-established mechanism underlying food allergy (Lack, 2008). Murine models commonly employ allergen-containing patches to provide continuous skin exposure; however, such patches may detach during exercise and potentially alter exercise behavior through physical restraint. Therefore, a sensitization method better suited for exercise-related research is needed. In this study, we aimed to establish a patch-free mouse model of epicutaneous sensitization. To achieve this, we investigated the utility of a highly viscous allergen solution designed to enhance skin retention.

METHODS: Six-week-old male BALB/c mice were used. After dorsal hair removal and transient disruption of the skin barrier using 4% sodium dodecyl sulfate (SDS), mice in the Vehicle group received repeated epicutaneous applications of 2.5% carboxymethyl cellulose (CMC). Mice in the CMC-OVA group received ovalbumin (OVA) dissolved in 2.5% CMC using the same protocol. Applications were performed three times weekly during weeks 1 and 2 and again during week 4, for a total of nine treatments. In week 5, blood samples were collected, and serum OVA-specific IgE concentrations were measured by ELISA. Seventy-two hours later, systemic allergic responses were assessed by monitoring changes in body temperature following oral administration of OVA dissolved in PBS.

RESULTS: No OVA-specific IgE production or significant changes in body temperature were observed in the Vehicle group. In contrast, serum OVA-specific IgE levels were significantly elevated in the CMC-OVA group compared with the Vehicle group ($p < 0.001$). Furthermore, oral OVA challenge induced a rapid and significant decrease in body temperature in the CMC-OVA group ($p < 0.005$), whereas no significant decrease was observed in the Vehicle group.

CONCLUSION: Topical application of a highly viscous CMC-containing OVA solution successfully induced epicutaneous sensitization, as demonstrated by increased OVA-specific IgE production and enhanced systemic allergic responses following oral OVA challenge. This patch-free approach may provide a practical model for exercise-related studies, including treadmill and wheel-running experiments, while avoiding potential confounding effects associated with allergen patch application, such as patch detachment and restriction of exercise behavior.

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The Utility of a Small Animal Grip Strength Measurement Device as a Model for Studying Exercise-Induced Muscle Damage

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Abstract

INTRODUCTION: Exercise-induced muscle damage (EIMD) is characterized by structural muscle tissue damage and elevated biochemical markers following high-intensity or unaccustomed exercise. Grip strength measurement specifically offers non-invasive assessment, longitudinal monitoring capability, and objective quantification that can be standardized across laboratories, as the eccentric contraction component controlled by contraction number could cause EIMD while maintaining physiological relevance. This study evaluated the utility of a small animal grip strength measurement device alongside tail pulling exercise as a novel EIMD model.

METHODS: Thirty-four male mice were divided into four groups: one control and three experimental groups, and sacrificed at 2, 4, and 7 days post-exercise. The exercise protocol involved positioning mice on a horizontal platform and allowing them to grasp a metal bar with their forelimbs. Subsequently, the tail was pulled horizontally until grip failure occurred, at a controlled frequency of 60 Hz based on metronome pacing. Grip failure was defined as the moment when the mouse released its grip from the bar. Tails were pulled 50 times per animal to induce repetitive eccentric contractions of the forelimb muscles. Biochemical biomarkers, inflammatory gene expression, and oxidative stress markers from blood and muscle tissue were assessed at each sacrificial time point.

RESULTS: Muscle damage marker, plasma aldolase activity, showed significant elevation at 4 days post-exercise ($p < 0.01$). The increase in ALD observed in the groups at 2 d and 4 d post-exercise, correlated with CK and LDH. The results observed a significant moderate correlation between ALD and both CK and LDH. Inflammatory gene expression in triceps brachii showed no significant changes. Oxidative stress analysis revealed significantly decreased biological antioxidant potential (BAP) at 7 days and a trend toward a significant increase in derivative-Reactive Oxygen Metabolites (d-ROMs) at 4 days. NF- κ B expression showed a trend toward significance increase.

CONCLUSION: We suggest that the grip exercise-based EIMD model has a high potential for reproducibility. However, a key limitation is the manual tail-pulling procedure, which makes it difficult to maintain consistent loading across animals. On the other hand, this study is characterized by selective induction of oxidative stress without accompanying inflammatory responses. This suggests that it may serve as a useful and relatively “clean” experimental system for antioxidant research, minimizing confounding effects from immune activation. Furthermore, the delayed pattern of oxidative stress observed in this model may be relevant for chronic, low-grade muscle conditions such as age-related sarcopenia, making it potentially useful from a clinical perspective.

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IMMUNOMETABOLIC REPROGRAMMING BY GLP-1 RECEPTOR AGONISTS IN INFLAMMATORY SKIN DISEASES: A SCOPING REVIEW OF OMICS, IMMUNE REGULATION, AND EXERCISE-TECHNOLOGY INTERACTIONS

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Abstract

INTRODUCTION: Psoriasis, hidradenitis suppurativa, and atopic dermatitis are chronic inflammatory skin diseases driven by dysregulated Th17/Th1 immunity, elevated interleukin (IL)-17, IL-23, tumour necrosis factor-alpha (TNF-alpha), and IL-6. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) — semaglutide, liraglutide, and tirzepatide — are emerging immunomodulatory agents beyond glycaemic control, targeting GLP-1 receptors on keratinocytes and immune cells to suppress pro-inflammatory cascades and intersecting with exercise and digital health as an understudied immunology frontier. This scoping review synthesises omics-informed, technology-enabled evidence on GLP-1RAs in inflammatory skin diseases.

METHODS: Following PRISMA for Scoping Reviews (PRISMA-ScR) guidelines, Scopus and PubMed were searched (2021–2026) using skin disease diagnoses with GLP-1RA agents and outcome terms (biomarkers, immunity, omics, exercise, digital health). Inclusion: peer-reviewed English studies; adults with psoriasis, hidradenitis suppurativa, or atopic dermatitis; GLP-1RA intervention; immunological, omics, exercise, or digital health outcomes; randomised controlled trials (RCTs), cohort studies, case series, or reviews. Exclusion: paediatric-only; non-GLP-1RA comparators; no immunological outcomes; animal or in vitro-only data. From 86 records, 12 duplicates removed; 32 studies met eligibility.

RESULTS: Of 32 studies, 18 addressed psoriasis, 10 hidradenitis suppurativa, and 4 atopic dermatitis. Semaglutide reduced Psoriasis Area and Severity Index (PASI) scores, IL-17A, TNF-alpha, and C-reactive protein in obese psoriatic patients with type 2 diabetes mellitus, correlating with weight loss and epicardial fat inflammation reduction; liraglutide improved psoriasis clearance and metabolic indices. A phase 3b RCT of ixekizumab plus tirzepatide showed additive immunological benefits over monotherapy. In hidradenitis suppurativa, GLP-1RAs reduced flare incidence and biologic initiation rates. Transcriptomics revealed downregulation of nuclear factor kappa-B (NF-kB) and Janus kinase (JAK)-STAT signalling with regulatory T-cell upregulation; metabolomics identified adipokine and sphingolipid shifts in keratinocyte biology. Machine learning on multi-omics data identified IL-17A and the adiponectin-to-leptin ratio as predictive response biomarkers. Exercise-GLP-1RA synergy via myokines and artificial intelligence-assisted wearable monitoring represent emerging translational applications.

CONCLUSION: GLP-1RAs exert multi-layered immunomodulatory effects in inflammatory skin diseases through IL-17/IL-23 suppression, NF-kB/JAK-STAT inhibition, and adipokine-mediated epidermal remodelling, corroborated by transcriptomic and proteomic evidence. IL-17A biologic and exercise co-treatment may amplify these gains. Multimodal RCTs with multi-omics integration are required to establish GLP-1RAs as evidence-based immunometabolic agents in chronic inflammatory skin diseases.

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WEARABLE TECHNOLOGY FOR MONITORING IMMUNE STRESS AND EXERCISE-INDUCED PHYSIOLOGICAL RESPONSES: A SCOPING REVIEW

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Abstract

INTRODUCTION: Wearable devices like smartwatches, fitness trackers, and accelerometers are enable to monitoring of heart rate variability (HRV), sleep, and physical activity non-invasively as proxies for immune stress and autonomic responses to exercise. Evidence on how wearables technology capture immunological adaptations remains limited. This scoping review mapped studies that using wearables to monitor exercise-related immune stress.

METHODS: according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines, a search conducted in Scopus and PubMed for original articles published between 2021 and 2024, based on English language, human (index keywords: Human/Humans/Exercise), and open access. Eligible studies used wearable devices with at least one exercise variable and one immune or autonomic stress variable (HRV index, cytokines, C-reactive protein, or indicators of overtraining). Reviews, meta-analyses, and non-human studies were excluded.

RESULTS: The search yielded 352 records (Scopus: 152; PubMed: 200); 47 articles met the eligibility (14 RCT, 17 cohort studies, 11 cross-sectional studies, and 5 pilot studies). A multilayer perceptron model using HRV obtained from exercise in 845 college students achieved 89.3% accuracy in predicting anxiety and 90.1% in predicting depression, thereby establishing HRV as a non-invasive neuroimmune biomarker. A wearable autonomic load predicted endurance performance during intensive training blocks, with interindividual variation reflecting the adequacy of recovery. In military personnel, high allostatic load correlated with increased daytime heart rate, variable energy expenditure, and attenuated nocturnal heart rate variability, forming a digital stress-immune phenotype identifiable via wearable devices. Wrist-worn activity trackers detected increased respiratory rate three days before a positive COVID-19 test result, accompanied by suppressed HRV one day prior, enabling the detection of pre-symptomatic immune challenges in college athletes. Moderate-to-vigorous physical activity measured by wearable devices showed no significant association with the interleukin-6 response to acute stress, suggesting that activity volume alone may not modulate stress-induced inflammation. Fitbit demonstrated strong test-retest reliability (ICC = 0.89) and was longitudinally correlated with disease activity in 120 patients with inflammatory myopathy.

CONCLUSION: wearable devices provide accurate tools for monitoring exercise-induced immune stress in athletes, military person, and clinicians. HRV, heart rate during sleep, and activity measured via wearable devices reliably reflect immunological stress conditions, with machine learning enhancing predictive accuracy. Longitudinal study designs are needed that combine monitoring via wearables with dynamic inflammatory profiles to identify relationships between exercise load and immune system adaptation.

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Wearable Sweat Biosensors and Saliva-Based Biomarker Monitoring in Exercise Immunology: A Scoping Review

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Abstract

INTRODUCTION: Exercise immunology investigates how physical activity modulates immune function, inflammatory responses, and physiological stress processes critical to athlete health and recovery. Real-time monitoring of these responses remains constrained by laboratory-based assays that are invasive and impractical in field settings. Wearable sweat biosensors and saliva-based biomarker monitoring represent promising approaches for non-invasive assessment; however, direct evidence within exercise immunology remains early and fragmented.

METHODS: This scoping review followed the PRISMA-ScR framework. Scopus-exported records and targeted supplementary sources were screened collaboratively by multiple authors, with eligibility focused on original studies involving wearable or sensor-based sweat or saliva monitoring in exercise, sport, training, physical activity, or field-exercise contexts. Data charting encompassed study design, participant characteristics, biofluid type, sensor or platform type, exercise context, biomarker target, validation comparator, and key application.

RESULTS: Four strictly eligible original studies were identified. A flexible microfluidic multisensing patch continuously monitored sweat lactate, pH, sodium, and temperature during cycle ergometry and treadmill running, with concurrent saliva biomarker comparison. A wearable localized surface plasmon resonance biosensor directly detected cortisol in human sweat before and after exercise and across morning–afternoon conditions. A molecularly imprinted electrochemical sensor enabled dynamic sweat cortisol monitoring in healthy volunteers during different exercise stages, while demonstrating stability and selectivity under wearable conditions. A 96-hour field-training feasibility cohort in military cadets combined saliva-based molecular sampling with wearable and sweat-sensor deployment attempts, highlighting practical barriers to real-world field implementation. Overall, evidence was concentrated on physiological stress and metabolic biomarkers, primarily cortisol, lactate, sodium, pH, and temperature. No included study validated wearable sweat or saliva biosensing of immune-inflammatory targets such as cytokines, CRP, or salivary IgA during exercise. Key gaps included limited cross-biofluid validation, heterogeneous exercise protocols, small proof-of-concept samples, and unresolved field-deployment barriers.

CONCLUSION: Wearable sweat biosensors and saliva-based biomarker monitoring show early promise for non-invasive assessment in exercise immunology, but current direct evidence remains limited and largely focused on physiological stress and metabolic markers rather than immune-specific inflammatory targets. Future studies should prioritize standardized exercise protocols, gold-standard validation, and immune-focused biosensor panels for cytokines, CRP, and salivary IgA.

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Can exercise-associated leukocytosis be used as a surrogate screening biomarker for exercise-induced gastrointestinal syndrome? - A feasibility exploration

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Abstract

INTRODUCTION: Most of the biomarkers that assess exercise-induced gastrointestinal syndrome (EIGS) require venous blood sampling and substantial analysis procedures, time, and costs. Leukocyte cell counts appears more practical as an immediate screening tool of EIGS that required capillary blood sampling and aligned with less overall analysis burden. The study aimed to determine the correlations between total and differential leukocyte cell counts with established EIGS biomarkers, systemic inflammatory response profile (SIR-Profile), and gastrointestinal symptoms (GIS) to indicate the potential utility of immune cell counts as a practical surrogate screening marker for EIGS in field base settings.

METHODS: Male endurance runners (n= 11) completed three experimental trials consisting of 2-hour running exercise on an electric treadmill at 70% $\text{VO}_{2\text{max}}$ in 25.2 ± 1.8 °C ambient temperature and $43 \pm 9\%$ relative humidity. Capillary and venous blood samples were collected pre-, post-exercise, and during recovery stage to determine leukocyte counts (i.e., total, neutrophil, lymphocyte counts, and the neutrophil:lymphocyte ratio (N:L ratio)) and EIGS biomarkers (plasma concentration of cortisol, I-FABP, sCD14, TNF- α , IL-1 β , IL-6, IL-8, IL-10, IL-1ra), respectively. GIS were measured pre-exercise and at 15-minute intervals during exercise using a exercise specific modified VAS.

RESULTS: Absolute leukocyte, neutrophil, lymphocyte counts, and N:L ratio showed weak to moderate positive correlations with cortisol ($r_s=.535$, $p<.001$; $r_s=.531$, $p<.001$; $r_s=.312$, $p=.035$; $r_s=.332$, $p=0.24$ respectively), and moderate to strong positive correlations with IL-10 ($r_s=.725$, $p<.001$; $r_s=.785$, $p<.001$; $r_s=.434$, $p=.017$; $r_s=.629$, $p<.001$ respectively). Weak to moderate positive associations were also observed between absolute leukocyte, neutrophil, and lymphocyte counts with IL-6 ($r_s=.477$, $p=.008$; $r_s=.495$, $p=.005$; $r_s=.374$, $p=.042$ respectively). When analysing relative values, exercise-associated changes in total leukocyte counts were moderately positive correlated with sCD14 ($r=.407$, $p=.048$) and IL-6 ($r=.575$, $p=.025$), and strongly positively correlated with IL-10 ($r=.682$, $p=.005$). Exercise-associated changes in neutrophil counts were strongly positively associated with IL-6 ($r=.683$, $p=.005$) and IL-10 ($r_s=.639$, $p=.010$). A moderate positive correlation was found between exercise-associated changes in lymphocyte count with cortisol ($r=.530$, $p=.009$); while, a strong positive correlation was observed between exercise-associated changes in N:L ratio and TNF- α ($r_s=.600$, $p=.018$).

CONCLUSION: The magnitude of exercise-associated leukocytosis, neutrophilia, and/or lymphocytosis may potentially act as a surrogate marker for exercise-associated stress and inflammatory responses linked the pathophysiology of EIGS. Further research using exertional-heat stress experimental models may provide confirmation.

The Impact of a Polyphenol Rich Sugarcane Extract Nutrition Intervention on Exercise-Associated Bacteraemia in Response to Exertional-Heat Stress

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Abstract

INTRODUCTION: Exercise-associated bacteraemia is common in response to exertional-heat stress (EHS), as a result of exercise-induced gastrointestinal syndrome (EIGS). The study aimed to examine if a polyphenol rich sugarcane extract (PRSE) nutrition intervention can mitigate exercise-associated bacteraemia.

METHODS: Fourteen endurance trained male and female participants completed two randomised EHS trials. On one occasion, participants consumed a 270 mL PRSE beverage twice daily for 14 days prior and immediately before EHS (2 h running at 60% $\dot{V}O_{2max}$ in 34.41 (1.18) °C). Participants also consumed a 30 g gel packet equivalent of the PRSE product with 160 mL of water every 20 min during the EHS until 80 min of EHS was achieved. On the other occasion, a carbohydrate rich placebo (PLA) beverage and gel equivalent was consumed. Venous blood samples were collected pre- and immediately post-EHS, were then centrifuged for 10 min at 4000 rpm in 4°C, and plasma samples were aliquoted for analysis. Mechanical and chemical cell lysis, sample purification, and microbial DNA extraction was performed with the plasma aliquots via the QIAamp UPC pathogen mini kit (MoBio Laboratories, Qiagen, Germantown, USA). Microbial DNA quantification was completed via fluorometry, whilst plasma bacterial profile, as per the determination of α -diversity (Shannon Equitability Index (SEI)) and relative abundance (RA%) was achieved by 16S rRNA amplicon gene sequencing (Micromon, Monash University).

RESULTS: No significant increases in total microbial DNA concentration pre- to post-EHS was observed in PRSE [pre-EHS 0.052 ng/ μ L, post-EHS 0.070 ng/ μ L ($p=0.056$)] and PLA [pre-EHS 0.045 ng/ μ L, post-EHS 0.062 ng/ μ L ($p=0.316$)]. No significant changes in phyla, family, and/or genus Shannon Equitability Index (SEI) were observed pre- to post-EHS in both trials ($p>0.05$). Significant decreases in RA% pre- to post-EHS of *Bacteroidota* phyla ($p=0.041$), *Prevotellaceae* family ($p=0.013$), *Burkholderiaceae* family ($p=0.009$), *Prevotella* ($p=0.030$) and *Ralstonia* ($p=0.030$) was observed in the PRSE trials, with significant increases of *Collinsella* ($p=0.035$), *Agathobacter* ($p=0.050$) and *Subdoligranulum* ($p=0.010$) occurring concurrently. Significant decreases in the RA% of *Erysipelotrichaceae* family ($p=0.041$), *Collinsella* ($p=0.026$), *Intestinibacter* ($p=0.028$) and *Oxalobacteraceae* ($p=0.050$) pre- to post-EHS was also observed in the PLA trials. No increase in commensal RA% pre- to post-EHS was demonstrated in the PLA trials.

CONCLUSION: Both trials mitigated the onset of exercise-associated bacteraemia. However, the PRSE trial resulted in greater changes to specific commensal bacteria RA% pre- to post-EHS.

Prostaglandin E-major urinary metabolite as a potential biomarker of muscle inflammation following physical exercise, considering gender difference

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Abstract

INTRODUCTION: Prostaglandin E-major urinary metabolite (PGE-MUM) can be measured by the chemiluminescent enzyme immunoassay system using monoclonal antibody against bicyclic PGE-MUM, which has the advantage of allowing for the non-invasive assessment of inflammation. Recently, the fully automated chemiluminescent enzyme immunoassay system for PGE-MUM measurement was adopted as a health care service for monitoring of ulcerative colitis in Japan¹. We previously measured urinary PGE-MUM as a potential non-invasive biomarker of muscle damage and inflammation post-exercise and reported significant increases immediately after relatively hard physical exercise, including team sports (a soccer game) and repeated short up-and-down runs with more than 50 healthy high school boys². To confirm it experimentally, the present study with quantified exercise loads was conducted³.

METHODS: Both male and female volunteer university students (n=18) performed gradual loading maximal exercise tests on a treadmill. Peripheral blood and urine samples were obtained before (T1) and immediately after physical exercise (T2), and 2 h later (T3) for measurement of PGE-MUM (Fujirebio Inc., Tokyo, Japan).

RESULTS: PGE-MUM·Cr (corrected by urinary creatinine) showed a significant stepwise increase from T1 to T3 in females (p=0.0171) and the same tendency without significance was observed in males (p=0.1533). Serum myoglobin showed the same trend, increasing from T1 to T3 in both males and females (p=0.1690, 0.0443, respectively). Of note, females had a significant correlation between myoglobin and PGE-MUM·Cr (p=0.0456), suggesting the involvement of muscle damage, but not between PGE-MUM·Cr and peripheral leukocytosis after physical exercise. PGE-MUM·Cr had no independent association with serum myoglobin after accounting for total muscle weight and maximal oxygen uptake/BW (VO₂max/BW). Observable gender differences with males showed significantly higher values of PGE-MUM·Cr, myoglobin, and creatinine in serum, and VO₂max/BW than females, suggesting a possible relation of PGE-MUM·Cr with muscle weight and inflammation. Our previous study revealed that menstrual cycles did not show big differences in PGE-MUM·Cr in respective phases of young females, suggesting that the influence of female hormones was limited.

CONCLUSION: Urinary PGE-MUM·Cr is a potential non-invasive biomarker of muscle inflammation following physical exercise in female athletes. Its applicability to the male population requires further consideration, given the large individual differences. Despite interindividual and gender-related differences, the use of urinary PGE-MUM·Cr is considered advantageous because it allows for the non-invasive assessment of exercise-induced muscle inflammation without requiring blood sampling. Furthermore, the longitudinal monitoring of PGE-MUM·Cr—a baseline marker for the individual—before and after exercise may facilitate the assessment of muscle injury and inflammation.

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Sex Differences in Appetite Regulation and Energy Intake Following Moderate-Load Resistance Exercise

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Abstract

INTRODUCTION: In recent years, sex differences have become a key focus in exercise physiology research due to the predominance of male participants in previous studies, making it difficult to directly generalize findings to females. Therefore, this study investigated sex differences in appetite-related hormones, subjective appetite, and energy intake following acute resistance exercise.

METHODS: Eighteen males and fourteen females in the early follicular phase completed moderate-load resistance exercise (70% 1RM, 3 sets of 7 repetitions) consisting of squat, bench press, and deadlift exercises, as well as a control trial. Subjective appetite and appetite-regulating hormones were assessed before and after exercise. An *ad libitum* meal was provided after the exercise session, and 3-day dietary intake records were collected.

RESULTS: Blood lactate incremental area under the curve (iAUC) increased markedly following exercise in both sexes, with males demonstrating greater postexercise lactate responses than females (trial $\times$ sex interaction, $p = 0.002$). Acylated ghrelin iAUC was significantly reduced following exercise (trial effect, $p < 0.001$), with significant sex differences also observed (sex effect, $p < 0.001$). Peptide YY iAUC likewise demonstrated a significant sex effect ($p = 0.010$). Overall appetite iAUC decreased following exercise (trial effect, $p = 0.024$), with similar responses observed between sexes (sex effect, $p = 0.923$). Moderate resistance exercise did not affect postexercise relative *ad libitum* energy intake or 3-day energy intake (kcal/kg BW) (trial effects: $p = 0.571$ and $p = 0.633$, respectively). However, relative *ad libitum* energy intake was significantly higher in males than in females (sex effect, $p < 0.001$).

CONCLUSION: Moderate-load resistance exercise transiently suppresses appetite and alters appetite-regulating hormones similarly in males and females, despite sex differences in hormonal and lactate responses.

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No effect of flavanol-rich cocoa on salivary cortisol and secretory immunoglobulin A concentrations at rest and after exercise under cognitive fatigue

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Abstract

INTRODUCTION: Prolonged cognitive activity is known to attenuate arousal and impair cognitive performance, a phenomenon called cognitive fatigue¹. Cognitive fatigue can be observed not only at rest but also during aerobic exercise¹. Given that continuous cognitive performance (e.g. decision-making) is required during sport matches, mitigating cognitive fatigue is considered an important strategy for enhancing performance. We have reported that flavanol-rich cocoa intake improves inhibitory executive function and decision-making speed during aerobic exercise under conditions of cognitive fatigue². However, the underlying psychophysiological mechanisms remain unclear. The hypothalamic–pituitary–adrenal axis is generally activated in response to acute psychological stress, resulting in increased salivary cortisol concentrations³. Cortisol is involved in the regulation of arousal, attention, and immune system modulation³, but the relationship between cortisol and cognitive fatigue remains unknown. Similar to cortisol, salivary secretory immunoglobulin A (sIgA) is a key component of mucosal immunity in the oral cavity and has been shown to exhibit transient increases in response to acute psychological stress³. Considering these cortisol and sIgA responses may be attenuated by oxidative-inflammatory stress³, we hypothesized that the antioxidant properties of cocoa flavanols could be involved in modulating these psychoneuroimmunological responses. If salivary sIgA is increased following high-cocoa flavanol intake (HCF), this may suggest a potential modulation of mucosal immune function by CF. Here, the purpose of this study was to examine the effect of HCF on salivary cortisol and sIgA concentrations at rest and after aerobic exercise under cognitive fatigue.

METHODS: Eighteen males (age 22 ± 2 yrs) performed the HCF (CF 500 mg) and low-cocoa flavanol control (LCF; CF 50 mg) trials in a randomized-crossover design². The double-blinded capsules were consumed 1 hour before starting aerobic exercise with prolonged cognitive load. Both trials utilized a 50-min cycling exercise protocol (60% VO₂peak), and the prolonged cognitive load was achieved via a 50-min color-word Stroop task¹. Salivary cortisol and sIgA were measured before and 1 h after CF intake, and immediately after aerobic exercise under cognitive fatigue using a dual analyte lateral flow device. The effects of Trial, Time, and their interaction on salivary cortisol and sIgA concentrations were analyzed by a generalized linear model.

RESULTS: Salivary cortisol concentrations were not changed throughout the experiments (Time $P = 0.087$, Trial $P = 0.692$, Interaction $P = 0.454$). Salivary sIgA was reduced 1 h after CF intake regardless of trials ($P = 0.048$), and there was no difference between HCF and LCF trials (Trial $P = 0.533$, Interaction $P = 0.956$).

CONCLUSION: Flavanol-rich cocoa did not change salivary cortisol and sIgA concentrations at rest and after aerobic exercise under cognitive fatigue.

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Epigallocatechin gallate attenuates hydrogen peroxide-induced atrophy-related responses in C2C12 myotubes

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Abstract

INTRODUCTION: Skeletal muscle atrophy is characterized by impaired muscle mass and function and may be promoted by excessive oxidative stress under pathological and stress-related conditions. Oxidative stress-associated muscular atrophy can be modeled in vitro using H₂O₂-treated C2C12 myotubes, which show increased expression of atrophy-related markers such as muscle RING finger 1 (MuRF1) and atrogin-1. Epigallocatechin gallate (EGCG), one of the major catechins in green tea, may protect skeletal muscle cells against oxidative stress-induced muscle wasting. Therefore, this study aimed to investigate the protective effects of EGCG against H₂O₂-induced atrophy-related responses in C2C12 myotubes.

METHODS: C2C12 myoblasts were differentiated into myotubes for 5 days. The differentiated C2C12 myotubes were treated with 40 µM H₂O₂ in the presence or absence of EGCG at 1.25–5 µM for 24 h to examine the protective effects of EGCG against oxidative stress-associated atrophic responses. The effect of EGCG alone on myotube viability/metabolic activity was also evaluated. Cell viability/metabolic activity was assessed using the MTT assay, and the mRNA expression levels of atrophy-related genes, including MuRF1 and atrogin-1, were analyzed by quantitative polymerase chain reaction.

RESULTS: Treatment with 40 µM H₂O₂ increased the mRNA expression of the atrophy-related markers MuRF1 and atrogin-1 in C2C12 myotubes, whereas EGCG treatment reduced the H₂O₂-induced upregulation of these genes. EGCG treatment alone did not significantly affect myotube viability/metabolic activity across the tested concentrations. Furthermore, EGCG co-treatment attenuated the H₂O₂-induced reduction in cell viability/metabolic activity.

CONCLUSION: These findings suggest that EGCG attenuates H₂O₂-induced atrophy-related gene expression and protects C2C12 myotubes against oxidative stress-associated reductions in viability/metabolic activity. EGCG may have potential as a nutritional bioactive compound for preserving skeletal muscle health under oxidative stress conditions. Further studies are required to clarify the intracellular mechanisms underlying its anti-atrophic effects.

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Metabolomic Profiling of Immunometabolic Responses Following *Antrodia camphorata* Supplementation and Prolonged Exercise

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Abstract

INTRODUCTION: *Antrodia camphorata* is an endemic medicinal fungus in Taiwan that has been reported to possess antioxidant and anti-inflammatory properties. However, its influence on exercise-induced immunometabolic responses remains unclear. This study aimed to characterize metabolic and inflammatory responses following *Antrodia camphorata* supplementation in endurance athletes undergoing prolonged high-intensity exercise.

METHODS: Thirteen middle- and long-distance runners participated in a randomized, double-blind, crossover study. Participants received either *Antrodia camphorata* supplementation ((2 g/day freeze-dried fermented extract)) or placebo for 6 weeks prior to three consecutive days of prolonged running exercise (2.5 h/day at 70% VO_2max). Blood samples were collected at baseline, before exercise, immediately after exercise, and after 18 h of recovery. Hematological parameters, inflammatory cytokines (IL-6, IL-8, TNF- α), prostaglandin E2 (PGE2), and metabolomic profiles using LC–MS were analyzed.

RESULTS: No significant differences were observed between supplementation and placebo conditions in circulating cytokines or blood cell counts across the four sampling time points. However, post-exercise PGE2 concentrations were significantly lower following *Antrodia camphorata* supplementation, with significant time and interaction effects identified by two-way ANOVA. Metabolomic analysis revealed alterations in metabolites associated with lipid and energy metabolism, including lower acylcarnitine-related metabolites and lysophosphatidylcholines (LysoPCs) following supplementation. Several lipid-related metabolites exhibited lower post-exercise concentrations following supplementation compared with placebo.

CONCLUSION: These findings suggest that *Antrodia camphorata* supplementation was associated with altered metabolic responses following prolonged exercise, particularly in lipid-related metabolites and inflammatory mediators PGE2. Although conventional inflammatory cytokines were unchanged, the observed metabolic shifts may reflect modulation of exercise-related immunometabolic responses.

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Effects of cardiovascular rehabilitation in plasma lipidome profiles of myocardial infarction patients with and without type 2 diabetes mellitus

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Abstract

INTRODUCTION: Cardiovascular rehabilitation (CR) program is deemed effective interventions to improve cardiac function, quality of life and long-term survival of myocardial infarction (MI) patients. Exercise modulates lipids suggesting an anti-atherogenic effect; however, investigation about lipid species it is needed to reveal that intrinsic relationship and possible cardiovascular outcomes. This study aims to identify the effects of CR in plasma lipidome profiles of MI patients with and without type 2 diabetes mellitus (T2DM).

METHODS: This study recruited 38 patients of both sexes with a mean age of 61.1 ± 7.5 years and divided them into four groups: a) MI patients (MI, 54.0 ± 9.2 years); b) MI patients with T2DM (MI+T2DM, 63.0 ± 5.6 years); c) MI patients performing CR (MI+CR, 63.3 ± 5.6 years); and d) MI patients with T2DM performing CR (MI+T2DM+CR, 64.1 ± 5.6 years). Anthropometric and biochemical assessments were performed at baseline and after 17 weeks of combined aerobic and resistance training. Plasma lipidomic profiling was conducted using mass spectrometry (UHPLC-QTOF-MS/MS), with lipid identification based on m/z, retention time, and fragmentation patterns.

RESULTS: The present study identified and quantified over 300 plasma lipid species. At baseline, patients with T2DM exhibited higher levels of free fatty acids and ceramides (Cer) compared to non-T2DM patients. After 17 weeks, MI+T2DM patients showed further lipid disturbances, particularly increased saturated and monosaturated triglycerides (TG) and Cer. In contrast, CR attenuated the increase in the number of lipid species, and a significantly shift percentage in TG saturated to TG polyunsaturated in MI+T2DM+CR group. However, CR was unable to attenuate the increase in specific phosphatidylinositol and TG species, which remained elevated in both T2DM groups. These lipid species may therefore represent metabolic signatures intrinsic to the T2DM condition.

CONCLUSION: This study showed that CR provides complementary benefits to pharmacological treatments in MI patients by reducing the concentrations of lipid species associated with cardiovascular and T2DM complications.

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8-Week *Kaempferia parviflora* Extract Administration Improves Submaximal Exercise Capacity in Mice by Enhancing Skeletal Muscle Antioxidant Gene Expression and Plasma Antioxidant Capacity

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Abstract

Background: Endurance capacity is a key component of health-related physical fitness and is closely associated with the prevention of lifestyle-related diseases and the maintenance of quality of life. Recent studies have highlighted the potential of plant-derived functional ingredients to improve exercise performance and metabolic health. *Kaempferia parviflora* extract (KPE), which is rich in polymethoxyflavones, has been reported to exert antioxidant, anti-inflammatory, and metabolism-modulating effects. However, the long-term effects of KPE on endurance capacity and antioxidant defense mechanisms in healthy animals remain unclear.

Objective: This study aimed to investigate whether long-term KPE administration, alone or in combination with voluntary exercise, improves endurance capacity and antioxidant function in healthy mice.

Methods: Male C57BL/6J mice were divided into four groups: control, voluntary exercise, KPE, and KPE plus voluntary exercise. Mice received KPE for 8 weeks, with or without access to running wheels. Endurance capacity was assessed using a submaximal endurance exercise test and daily voluntary wheel-running distance was recorded. Oxidative stress and antioxidant capacity were assessed using derivatives of reactive oxygen metabolites (d-ROMs), biological antioxidant potential (BAP) tests and OXY adsorbent tests, respectively, using heparin plasma. Also, mRNA expression levels of antioxidant-related genes in skeletal muscle were evaluated.

Statistical Analysis: A two-way ANOVA was used to assess the effects of KPE administration and/or exercise. When significant interactions were observed, simple effects analysis followed by Tukey's post hoc test was conducted; otherwise, main effects with Tukey's test were examined. Effect size was evaluated using eta squared (η^2 : small $\approx$ 0.01, medium $\approx$ 0.06, large $\geq$ 0.14). Associations between variables were analyzed using Pearson's correlation coefficient (r : small 0.1–0.3, moderate 0.3–0.5, strong $>$ 0.5), and R^2 was used to indicate explanatory power. Statistical significance was set at $p < 0.05$.

Results: 8 weeks of KPE administration significantly improved submaximal endurance exercise capacity and increased daily voluntary running distance. KPE also significantly enhanced plasma antioxidant capacity as determined by OXY test. In skeletal muscle, KPE upregulated the expression of genes involved in the Nrf2/ARE antioxidant pathway and its downstream targets, including *Sod1*, *Sod3*, *Gclc*, *Txnrd2*, and *Srxn1*. These changes suggest that KPE strengthens systemic and skeletal muscle antioxidant defense.

Conclusion: Long-term administration of KPE improved endurance capacity in healthy mice, at least in part by enhancing antioxidant defense through activation of the Nrf2/ARE pathway. These findings provide novel evidence that KPE may serve as a promising functional food ingredient for supporting endurance performance and promoting metabolic health. Further clinical studies are warranted to confirm its efficacy in humans.

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Glutamine and Iron Supplementation Optimizes Mucosal Immunity Against High-Intensity Resistance Exercise Stress in Women During the Mid-Luteal Phase

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Abstract

INTRODUCTION: Given the physiological fluctuations of the menstrual cycle, women are more predisposed to iron deficiency compared to men, which potentially compromises mucosal immune function (Percy et al., 2017). Previous research has indicated that female athletes face a higher risk of upper respiratory tract infection than their male counterparts, highlighting sex-specific differences in immune function (Palmer et al., 2021). Glutamine is known to activate human immune cells (Lu et al., 2024). Therefore, this study aimed to investigate the effects of a combined Glutamine and iron supplement on respiratory mucosal immune function in women.

METHODS: Forty regularly exercising women (age: 21.7±3.1 years; height: 165.1±5.7 cm; weight: 62.1±9.3 kg; BMI: 22.8±3.1; menstrual cycle: 31.5±3.3 days) were recruited and randomly assigned to either an experimental group (n=20) or a control group (n=20). Pre- and post-tests were conducted during the mid-luteal phase of two consecutive menstrual cycles. The experimental group received nutritional compound supplementation (Glutamine and iron) between the pre- and post-tests. Resting saliva samples were collected (Pre-Rest & Post-Rest). Following the post-test, a single bout of resistance exercise was performed as an intervention, and saliva samples were collected immediately (Post-T0) and 60 minutes after exercise (Post-T60) to observe acute changes in saliva markers and flow rates. Salivary nitric oxide (NO), IgA, and lactoferrin (LF) levels were analyzed using enzyme-linked immunosorbent assay. A two-way mixed-design ANOVA was utilized to examine the benefits of nutritional supplementation and the acute effects of the exercise intervention.

RESULTS: Significant Group × Time interaction effects were observed for IgA ($p=0.02$) and LF ($p=0.048$). Post-hoc analysis showed that IgA and LF in the experimental group were significantly higher at Post-Rest, T0, and T60 compared to Pre-Rest ($p<0.05$). In the control group, LF was significantly higher only at Post-T60 relative to Pre-Rest. NO levels remained unaffected by either intervention.

CONCLUSION: Combined Glutamine and iron supplementation elevates resting salivary IgA and LF secretion rates in exercising women. The observed functional plateau indicates that this nutritional intervention optimizes mucosal defense mechanisms to their upper regulatory limit before physical stress begins. Consequently, this provides a continuous protective buffer that sustains robust immune surveillance throughout the physiological challenges of exercise.

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Beyond Moderate-to-Vigorous Physical Activity: Low-Intensity Physical Activity and Immunometabolic Regulation — A Scoping Review

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Abstract

INTRODUCTION: Current physical activity guidelines predominantly emphasize moderate-to-vigorous physical activity for cardiometabolic health; however, many metabolically at-risk adults face barriers to sustaining higher-intensity exercise. Low-intensity physical activity, including light walking, sedentary breaks, stretching, tai chi, qigong, and pilates, may offer a feasible strategy to reduce chronic low-grade inflammation and improve metabolic regulation. However, its role as an immunometabolic regulator remains insufficiently mapped. This scoping review aimed to map recent evidence on low-intensity physical activity and immunometabolic outcomes in metabolically at-risk adults.

METHODS: This scoping review followed Joanna Briggs Institute methodology and PRISMA-ScR. PubMed and Scopus were searched for English-language human studies published from January 2021 to May 2026 using terms related to low- or light-intensity physical activity, walking, sedentary breaks, prolonged sitting, stretching, tai chi, qigong, pilates, immunometabolic regulation, inflammation, cytokines, C-reactive protein, adipokines, oxidative stress, endothelial dysfunction, and metabolic risk. Eligible studies involved adults with overweight, obesity, metabolic syndrome, prediabetes, insulin resistance, type 2 diabetes, or sedentary adults, and reported immune, inflammatory, or cardiometabolic outcomes. Reviews, animal studies, pediatric or pregnancy studies, pharmacological interventions, studies without accessible full text, and studies focused on moderate-to-vigorous or high-intensity exercise were excluded.

RESULTS: The search identified 476 records (PubMed: n = 56; Scopus: n = 420). After duplicate removal (n = 49), 427 records were screened, yielding 28 relevant articles based on adult metabolic-risk populations, low-intensity or sedentary-break exposures, full-text availability, and immune, inflammatory, or cardiometabolic outcomes. Four review, protocol, or narrative articles were excluded, and 24 primary studies were assessed for evidence mapping. Of these, 18 core studies were retained for synthesis. Evidence clustered around sedentary-break strategies, light-intensity walking, sitting replacement with standing or walking, and low-intensity structured activities such as tai chi, qigong, pilates, and Baduanjin. Overall, low-intensity movement was generally associated with more favorable inflammatory and cardiometabolic profiles, although mechanistic immunometabolic evidence remained limited and heterogeneous.

CONCLUSION: Low-intensity physical activity may serve as a feasible complementary strategy to support immunometabolic health in metabolically at-risk adults. Evidence suggests that reducing prolonged sitting and increasing light-intensity movement may contribute to more favorable inflammatory and cardiometabolic profiles. Further research is needed to clarify optimal activity patterns and underlying immune-metabolic mechanisms.

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Probiotic Effects on Immunity, Cytokines, and URTI in Athletes: A Systematic Review and Meta-Analysis

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Abstract

INTRODUCTION: Upper respiratory tract infections (URTI) remain the leading cause of illness-related training disruption in competitive athletes, accounting for 35–65% of medical consultations during major sporting events. While exercise-induced immunosuppression creates this vulnerability, probiotic supplementation has shown promise as a nutritional countermeasure. Yet existing meta-analyses have addressed salivary IgA (sIgA), cytokines, and URTI outcomes in separate reviews, leaving practitioners without integrated evidence to guide supplementation protocols. The rapid expansion of RCTs published during 2023–2026 further widens this evidence–practice gap. This study provides the first meta-analysis simultaneously pooling mucosal (sIgA), systemic (cytokines), and clinical (URTI) immune outcomes of probiotics in exercising populations, with subgroup analyses by strain, duration, and athlete level.

METHODS: Following PRISMA 2020, PubMed was searched from inception through April 2026; supplementary Scopus, Web of Science, Cochrane CENTRAL, and SPORTDiscus searches are planned for full publication. Eligible studies were RCTs comparing oral probiotics (≥ 7 days) with placebo in healthy exercising adults (≥ 18 years). Primary outcomes: sIgA, URTI incidence, and URTI severity. Secondary: IL-6, TNF- α , IL-10, IFN- γ . Random-effects models pooled SMD and RR with 95% CI. Subgroup analyses: strain type, duration, athlete level, exercise modality. Bias assessed via RoB 2; certainty via GRADE.

RESULTS: PubMed screening identified 137 records; 71 passed title review and are undergoing full-text assessment and data extraction. The final analysis is anticipated to include 40–47 RCTs ($>2,500$ participants). Preliminary scoping suggests probiotic supplementation is associated with: (1) increased sIgA, particularly with ≥ 4 weeks supplementation; (2) reduced URTI severity, most consistently with single-strain *Lactobacillus* formulations; (3) attenuated post-exercise IL-6 and TNF- α ; (4) elevated IL-10; and (5) greater effects in elite athletes versus recreational exercisers. Full pooled estimates with forest plots and GRADE assessment will be presented at the symposium.

CONCLUSION: This meta-analysis provides a comprehensive integration of mucosal immunity, systemic cytokines, and clinical URTI outcomes for probiotics in exercising populations. Subgroup analyses will inform strain-specific and duration-dependent recommendations for sport nutrition practice, bridging exercise immunology evidence to practical athlete care.

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PROBIOTIC SUPPLEMENTATION FOR ENDURANCE AND ATHLETIC PERFORMANCE IN ATHLETES: A SCOPING REVIEW

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Abstract

INTRODUCTION: Optimizing endurance and athletic performance remains a central focus in sport science. Nutritional interventions targeting gut microbiota, particularly probiotics, have emerged as promising ergogenic strategies modulating the gut-muscle axis. However, evidence on probiotic-only interventions varies across populations, strains, and outcomes. This scoping review maps clinical trial evidence on probiotic-only supplementation effects on endurance and athletic performance in athletes.

METHODS: Following PRISMA-ScR guidelines, we searched Scopus and PubMed from inception to 2026 using probiotic terms (probiotic OR probiotics OR “probiotic supplementation” OR “multi-strain probiotic”), athlete terms (athlete OR athletes), and performance terms (“exercise performance” OR “endurance performance” OR endurance OR VO₂max OR “time to exhaustion” OR “Exercise Tolerance”[MeSH Terms]). Two independent reviewers screened records. We included randomized clinical trials of probiotic-only supplementation in athlete or active sport populations reporting endurance or physical performance outcomes. We excluded non-athlete/sedentary populations, co-supplementation studies with omega-3, casein, or vitamin D, observational studies, reviews, protocols, and duplicates. Data extraction covered study characteristics, participant demographics, sport types, probiotic strains/doses, and performance outcomes.

RESULTS: Searches identified 282 records (PubMed n=101; Scopus n=181). After removing 88 duplicates, 194 unique records underwent title and abstract screening; 174 were excluded (non-RCT, reviews, narrative, and observational studies n=170; no athlete population n=3; no probiotic intervention n=1). Twenty records advanced to full-text review; 17 were excluded (non-performance outcomes only n=7; duplicate variant titles n=5; combined supplementation n=3; non-healthy athlete population n=2), yielding three eligible trials. Populations included nonelite athletes, exercise-trained individuals, and amateur marathon runners. Probiotic protocols varied in strain (*Lactococcus lactis*, *Lactobacillus plantarum*, *Bifidobacterium longum*), dose (5×10^9 – 10^{11} CFU/day), and duration (5–6 weeks). Two trials reported significant improvements: 12-minute run distance increased from 2.88 to 3.01 km ($p < 0.05$), and VO₂max, explosive strength, and body composition improved ($p < 0.05$). One trial reported no significant time-to-exhaustion gains, attributed to uncontrolled differential training volume.

CONCLUSION: Preliminary evidence suggests probiotic-only supplementation may enhance endurance and athletic performance in active populations, particularly with multi-strain *Lactobacillus* and *Bifidobacterium* formulations over 5–6 weeks. This scoping review provides an initial evidence map to inform sport nutrition practice and identify critical gaps for strain-specific, standardized probiotic protocols in athlete populations.

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Comparative Analysis of the Discriminative Ability of GDF-15 and FGF21 for Prefrailty and Frailty in Community-Dwelling Older Adults

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Abstract

INTRODUCTION: To compare the diagnostic performance of circulating growth differentiation factor 15 (GDF15) and fibroblast growth factor 21 (FGF21) for identifying prefrailty and frailty in community-dwelling older adults using receiver operating characteristic (ROC) curve analysis.

METHODS: This cross-sectional diagnostic accuracy study, conducted according to the STARD guidelines, included 54 community-dwelling older adults (mean age, 78.2 ± 6.9 years). Plasma GDF15 and FGF21 levels were measured using enzyme-linked immunosorbent assays. Frailty status was classified as robust, prefrail, or frail based on two phenotype models (The Japanese version of the Cardiovascular Health Study criteria [J-CHS criteria] and Frailty Screening Index [FSI]). J-CHS criteria is widely used to evaluate frailty in Japan. FSI, developed by Yamada et al. (2015) is based on the phenotypic model from Fried et al. (2001) and does not require actual measurements and is evaluated using a questionnaire. In both criteria, a score of 3 or more was defined as frail, 1 or 2 as pre-frail, and 0 as robust. ROC curve analysis was performed to compare the discriminative ability of GDF15 and FGF21 for identifying prefrailty and frailty. An AUC ≥0.70 was considered acceptable.

RESULTS: GDF15 demonstrated acceptable discriminative ability for identifying prefrailty and frailty according to both the J-CHS criteria (AUC: 0.712, 95% CI 0.568–0.857) and FSI (AUC: 0.782, 95% CI 0.652–0.912), whereas FGF21 showed poor discriminative performance (AUC: 0.554 and 0.502, respectively). GDF-15 showed higher discriminative performance than FGF21 under both criteria, with a statistically significant difference observed for FSI (p = 0.015).

CONCLUSION: GDF15 demonstrated superior discriminative ability compared with FGF21 for identifying prefrailty and frailty in community-dwelling older adults, suggesting that GDF15 may serve as a useful biomarker for frailty screening.

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Association between serum creatinine-to-body weight ratio, exercise, and muscle mass: A large-scale cross-sectional study in the Taiwan Biobank

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Abstract

INTRODUCTION: Sarcopenia is a progressive age-related muscle disorder with major public health implications. While muscle mass is central to its diagnosis, specialized assessment tools like dual-energy X-ray absorptiometry are costly and impractical for large-scale genetic and epidemiological studies. Serum creatinine (Scr) is a metabolic byproduct of skeletal muscle, and the ratio of Scr to body weight (Scr/BW) has been proposed as an accessible surrogate biomarker for muscle mass. However, its validity in East Asian populations remains under-investigated. This study aims to evaluate the correlation between Scr/BW and directly measured muscle mass in a large Taiwanese population.

METHODS: A cross-sectional analysis was conducted using data from the Taiwan Biobank (IRB: CMUH114-REC1-230). Participants with missing data or estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m² were excluded to control for renal function confounding. The exposure variable was Scr/BW, and the primary outcome was predicted muscle mass (PMM) estimated by bioelectrical impedance analysis (BIA). Pearson and Spearman correlation analyses and multivariable linear regression models were performed, adjusting for sex, age, body mass index (BMI), and exercise habits.

RESULTS: A total of 41,169 participants (15,253 males and 25,916 females; mean age 44.83 ± 14.80 years) were included. In the overall population, Scr/BW showed a weak inverse correlation with PMM (Pearson $r = -0.043$, $p < 0.001$). After stratified by sex, moderate-to-strong negative correlation were observed in both men ($r = -0.635$, $p < 0.001$) and women ($r = -0.535$, $p < 0.001$). In multivariable linear regression, Scr/BW remained independently inversely associated with PMM (overall $\beta = -0.293$, $p < 0.001$). Younger age, male sex, higher BMI, and regular exercise were all positively associated with PMM (all $p < 0.001$).

CONCLUSION: In this Taiwanese population, Scr/BW was significantly but inversely associated with absolute muscle mass. These findings suggest that Scr/BW may reflect the complex interplay between muscle mass, body weight, and adiposity rather than serving as a direct marker of muscle quantity. Future studies are warranted to investigate whether physical activity and exercise training modify the relationship between Scr/BW and muscle mass, and whether this index can be used to monitor exercise-induced changes in muscle health and sarcopenia risk.

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miR-4423-3p and miR-191-5p as exploratory candidates for phase angle response after bodyweight-based resistance training in Japanese older adults

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Abstract

INTRODUCTION: Circulating microRNAs (miRNAs), a class of non-coding RNAs, have been reported to change after acute resistance exercise and to differ according to age and sex [1,2]. Phase angle (PhA), assessed by bioelectrical impedance analysis, reflects cellular integrity and fluid distribution and may improve after resistance training in older adults [3]. Bodyweight-based or low-load resistance training can improve muscle-related outcomes in community-dwelling older adults, although individual responses may vary. However, serum miRNA responses associated with PhA improvement after such training remain unclear. This exploratory study aimed to identify serum miRNA candidates associated with PhA improvement after 12 weeks of bodyweight-based resistance training in community-dwelling older adults.

METHODS: Twenty-four community-dwelling older adults completed a 12-week, twice-weekly bodyweight-based resistance training program. Whole-body PhA was assessed before and after the intervention using bioelectrical impedance analysis. Participants were classified into PhA improvement and non-improvement groups according to individual changes in PhA. For serum miRNA profiling, seven age- and sex-matched participants were selected from each group. Serum miRNA expression was analyzed using the GeneChip miRNA 4.0 Array. Differentially expressed miRNAs were identified using fold-change, nominal p-value, and false discovery rate (FDR)-adjusted criteria. Candidate miRNAs were interpreted based on published literature and in silico target prediction.

RESULTS: The PhA improvement group showed more pronounced serum miRNA alterations than the non-improvement group. Using a criterion of fold change >2 or <-2 and $p < 0.05$, 58 miRNAs were differentially expressed in the improvement group, compared with 41 in the non-improvement group. Under a stricter criterion of fold change >3 or <-3 and FDR-adjusted $p < 0.05$, six miRNAs were identified in the improvement group, whereas none were identified in the non-improvement group. Among the selected candidates, hsa-miR-4423-3p and hsa-miR-191-5p showed robust changes in the improvement group after FDR correction, with no significant changes in the non-improvement group. hsa-miR-4423-3p is not well characterized in exercise adaptation but has been reported in immune- and inflammation-related contexts. hsa-miR-191-5p has been associated with human skeletal muscle characteristics. Therefore, these miRNAs may be considered exploratory candidates rather than established mediators of PhA improvement.

CONCLUSION: Serum miRNA responses differed according to PhA improvement following bodyweight-based resistance training in older adults. hsa-miR-4423-3p and hsa-miR-191-5p may represent exploratory candidate miRNAs associated with PhA responsiveness. These findings should be interpreted as hypothesis-generating and warrant validation using quantitative PCR and integrated immune, inflammatory, and muscle-related outcomes.

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Effect of subcutaneous adipose tissue on ultrasound echo intensity of rectus femoris: Implications for region of interest selection

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Abstract

INTRODUCTION: Aging causes loss of muscle mass and accumulation of adipose tissue, which result in declines in muscle function. Alterations in muscle quality accompanying intramuscular non-contractile tissue infiltration are also considered to contribute to the decline in muscle strength. Since ultrasound echogenicity distinguishes contractile and non-contractile tissue based on gray-scale analysis, an increasing number of studies have used echo intensity (EI) as an indicator of morphological muscle quality. However, one concern with using EI to represent muscle quality is that the effects of ultrasound beam attenuation and multiple reflections due to anatomical properties of subcutaneous adipose tissue (SAT) and superficial fascia overlying skeletal muscle remain unclear.

METHODS: This study included 12 donated Japanese cadavers (6 males, 6 females; mean age, 88 ± 6 years). The study was approved by the Ethics Committee of Aichi Medical University School of Medicine. Both sides of rectus femoris were measured at 30%, 50% and 70% of the thigh length using B-mode ultrasonography. Measurements were conducted under Intact (above the skin) and Removal (after removal of skin and SAT) conditions. From ultrasound images, we measured SAT thickness, muscle thickness (MT) and traced the whole region of interest (ROI), then calculated the EI within the whole ROI, and MT-based superficial and deep ROIs. A two-way repeated-measures ANOVA was used to analyze the effects of conditions (Intact, Removal) and regions (30%, 50%, 70%) on EI of the whole, superficial and deep ROIs. In case of a significant interaction, pairwise comparisons and paired t-tests with Bonferroni-correction (adjusted significance level of $\alpha = 0.05/3 = 0.017$) were conducted to test the differences among regions and conditions.

RESULTS: SAT thickness was greater at 30% region than at 50% and 70% regions. For whole ROI, regional differences were observed between 30% and 50%, 30% and 70% under Intact, whereas no regional differences were observed under Removal. For superficial EI, no significant effect of region or condition was observed. In contrast, deep EI increased under Removal ($F_{(1,21)}=48.12$, $p<0.001$, $\eta_p^2=0.696$) while regional differences were maintained under both conditions ($F_{(2,21)}=28.59$, $p<0.001$, $\eta_p^2=0.577$). Further paired t-tests comparing superficial and deep EI revealed significant differences at 30%, 50% and 70% regions under Intact, and at 30% and 70% regions under Removal ($p<0.001$).

CONCLUSION: SAT removal increased EI in the whole and deep ROIs. It suggests that ultrasound beam attenuation is a major factor for EI increase after SAT removal. Meanwhile, multiple reflections generated by SAT and superficial fascia may contribute to the differences between superficial and deep EI. For in vivo studies, EI obtained from the deep ROI rather than the whole or superficial ROI is recommended as an indicator of intramuscular non-contractile tissue properties.

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Age-related divergence between muscle thickness and strength differs across upper and lower limbs

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Abstract

INTRODUCTION: Muscle strength is a major determinant of physical function and healthy aging. Although strength declines disproportionately with aging, whether age-related changes in muscle morphology and strength occur similarly across different anatomical regions remains unclear (Clark & Manini, 2008). Therefore, this study compared age-related changes in muscle thickness and strength between the upper and lower limbs and further examined whether variation in strength unexplained by muscle thickness is shared between limbs.

METHODS: A total of 152 healthy adults (69 males, 83 females; 19–84 years) participated in this cross-sectional study. Muscle thickness of the forearm flexors and anterior thigh was measured using B-mode ultrasonography. Muscle strength was assessed using maximal handgrip strength and maximal voluntary knee extension torque. Linear regression analyses were performed to evaluate age-related changes and muscle thickness–strength relationships in each limb. Strength variation unexplained by muscle thickness (hereafter referred to as residual strength), defined as the difference between observed and predicted strength based on muscle thickness, was used to explore inter-limb associations independent of muscle thickness.

RESULTS: Forearm muscle thickness was not associated with age ($R^2 = 0.003$, $P = 0.499$), whereas handgrip strength was negatively associated with age ($R^2 = 0.025$, $P < 0.05$). In contrast, anterior thigh muscle thickness ($R^2 = 0.140$, $P < 0.001$) and knee extension torque ($R^2 = 0.117$, $P < 0.001$) both declined significantly with age. Muscle thickness explained a substantial proportion of strength variance in both the upper ($R^2 = 0.580$) and lower limbs ($R^2 = 0.468$; both $P < 0.001$), although age-related patterns differed between regions. Residual strength showed a weak but significant association between the upper and lower limbs ($R^2 = 0.076$, $P < 0.001$), indicating limited shared variation in strength beyond muscle thickness.

CONCLUSION: Age-related changes in muscle morphology and strength exhibit distinct regional patterns. Although muscle thickness explained a substantial proportion of strength, age-related weakness in the upper limb occurred despite preserved muscle thickness, whereas structural and functional declines occurred concurrently in the lower limb. Furthermore, only a small proportion of variation in strength unexplained by muscle thickness was shared between limbs, suggesting existence of determinant(s) other than muscle size are largely region-specific rather than uniformly expressed throughout the body. Potential mechanisms may include age-related alterations in voluntary activation and motor unit behavior (Clark et al., 2019; Rozand et al., 2020).

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Effects of Taurine Supplementation Combined with Exercise Training on Inflammatory and Oxidative Stress Biomarkers in Older Women with Sarcopenia

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Abstract

INTRODUCTION: Sarcopenia, characterized by the progressive loss of skeletal muscle mass and strength, is one of the major physiological changes associated with aging. Multiple factors affect this process including inflammation and oxidative stress. Myeloperoxidase (MPO) and matrix metalloproteinase-9 (MMP-9) are inflammation-related enzymes that promote muscle degradation through NF- κ B signaling. MMP-9 also promotes the breakdown of extracellular matrix components that support muscle fibers. Concurrently, reactive oxygen species (ROS) promote protein degradation and inhibit mTORC1-mediated protein synthesis, leading to impaired muscle maintenance. In response to elevated oxidative stress, antioxidant enzymes such as superoxide dismutase (SOD) are upregulated as cellular defense mechanism. Taurine, a conditionally essential amino acid, may attenuate these processes through HOCl scavenging, mitochondrial stabilization, and NF- κ B inhibition, especially when combined with resistance training. However, its effects on inflammatory and oxidative stress markers in older women with sarcopenia remain unclear.

METHODS: Thirty-nine older women with sarcopenia were assigned to one of three groups: control (C, n=10), exercise only (E, n=16), or exercise plus taurine supplementation (ET, n=13). Both exercise groups completed a combined training program. The ET group also received 3g daily of oral taurine supplementation throughout the study. Blood samples were taken at baseline and after the intervention to measure MPO, MMP-9, and SOD. Handgrip strength was used as the main measure of physical function. Changes over time between groups were tested using repeated measures ANOVA, with the group $\times$ time interaction as the primary outcome.

RESULTS: Repeated measures ANOVA revealed significant group $\times$ time interactions for MPO, MMP-9, and SOD ($p < 0.05$). The ET group showed significant reductions in all three biomarkers compared to exercise and control groups ($p < 0.05$), while the exercise-only group showed increases in MPO and SOD, reflecting exercise-induced inflammatory and oxidative stress responses. Handgrip strength improved significantly in both exercise groups compared to control ($p < 0.05$), with greater improvement in the ET group. No significant between-group differences were observed for skeletal muscle or appendicular lean mass indices.

CONCLUSION: Three months of taurine supplementation combined with exercise effectively attenuated inflammatory and oxidative stress in older women. Together with the improvements in handgrip strength, these results suggest that taurine may enhance the functional benefits of exercise training by creating a better environment for skeletal muscle and could be a promising strategy against sarcopenia progression.

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The Influence of Simultaneous Aerobic and Cognitive Training (Activ4Brain) Intervention on Cognition, Inflammatory Markers and Neuroprotective Factors

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Abstract

INTRODUCTION: Combination of exercise and cognitive training is increasingly recognized as a non-pharmacological strategy to mitigate age related cognitive decline. Physical exercise, particularly aerobic exercise can maximize the benefits of cognitive training by increasing neurotrophic factors and reducing inflammation thereby facilitating neuroplasticity (Clemente-Suárez et al., 2025). Moreover, cognitive training alone can decrease inflammatory markers (Pesce et al., 2017). Thus, a combined intervention can not only preserve cognition but also improve inflammatory profile, that worsens with aging. However, the synergetic effects of aerobic and cognitive training on inflammatory markers as well as their additional benefits on cognitive function in older persons, remain unclear. Therefore, the aim of the study is to investigate the synergistic effects of combined aerobic and cognitive training (Activ4Brain, a 3-months intervention) - compared with aerobic exercise alone and to a passive control group - on cognitive function, inflammatory and neuroprotective markers.

METHODS: A total of 61 subjects (mean age: 65.5±6.5 years) were assigned to the Activ4Brain group ($n=21$), the Aerobic Exercise Group (AEG, $n=19$), or the Control Group (CG, $n=21$) and analyzed. Cognitive functions, were assessed using the CANTAB system, including Multitasking (MTT) and Rapid Visual Processing (RVP), and the Rey Auditory Verbal Learning Test (RAVLT). Fasting venous blood samples were collected to quantify the serum biomarkers of IRISIN, Brain Derived Neurotrophic Factor (BDNF) alongside the plasma levels of Interleukin (IL) -6, IL-10, IL-1 β , IL-1ra, Interferon Gamma (IFN- γ), and Tumour Necrosis Factor - α (TNF- α) using ELISA sandwich assays. Cognitive evaluation and blood sampling were conducted at baseline and after intervention.

RESULTS: By controlling for baseline values ANCOVA results revealed significant differences in IL-10 levels, favouring the Activ4Brain group $F(2,52) = 4.715$, $p=0.013$, and in the MTT incongruency cost favouring the Activ4Brain group ($F(2,57) = 3.322$, $p=0.043$). When looking at within group differences, paired-sample t- test results revealed significant improvements in MTT cost ($p=0.003$), MTT Reaction Time Latency ($p=0.016$) and RVP Response Latency ($p=0.017$) for the AEG, while for the Activ4Brain group significant improvements in cognitive domains were only observed for the MTT Reaction Time Latency ($p=0.043$), IL-10 ($p<0.001$) and IFN- γ ($p=0.012$) plasma levels.

CONCLUSION: Our findings suggest that integrating aerobic and cognitive exercise can enhance response inhibition by decreasing MTT incongruency cost and decreased inflammation by increasing IL-10 and decreasing IFN- γ . Additionally, aerobic exercise alone could be beneficial by reducing reaction time and increasing cognitive flexibility and sustained attention abilities. However, future studies with a larger sample size and longitudinal follow-ups are needed to confirm these benefits.

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The Role of Exercise in Modulating Immunosenescence-Related Mechanisms in Brain Aging and Neuroprotection: A Scoping Review

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Abstract

INTRODUCTION: Brain aging is intricately linked to immunosenescence and its downstream consequence, inflammaging, driving neuroinflammatory cascades, microglial dysfunction, and cognitive decline. Exercise has emerged as a potent non-pharmacological modulator of immune-brain crosstalk, yet the mechanistic landscape of this relationship remains incompletely mapped. This scoping review addresses the role of exercise in attenuating immunosenescence-related mechanisms relevant to brain aging and neuroprotection.

METHODS: Following PRISMA-ScR guidelines, we searched Scopus and PubMed from inception to May 2026. Scopus used TITLE-ABS-KEY combining (exercise/physical activity/training) AND (immunosenescence/inflammaging/immune aging) AND (brain aging/cognition/neuroprotect); PubMed used equivalent MeSH terms and [tiab] qualifiers. Inclusion criteria: original articles (RCTs, longitudinal cohort, cross-sectional), English language, human participants, open-access publications, and studies reporting immune or inflammatory biomarkers with cognitive or neural outcomes. Exclusion criteria: review articles, meta-analyses, conference abstracts, animal-only studies, studies without exercise intervention or physical activity assessment, non-English publications, and articles not reporting immunological or brain-related outcomes.

RESULTS: Initial searches yielded 71 records (Scopus: n=37; PubMed: n=34; 2021-2026). After removing duplicates (n=10), title and abstract screening excluded 37 records (reviews, n=18; non-human, n=8; irrelevant topic, n=11). Full-text assessment of 24 records led to a final inclusion of 10 studies: RCTs (n=4), longitudinal cohort studies (n=3), and cross-sectional studies (n=3). The 10 included studies (published 2021–2026) demonstrated that aerobic, resistance, and multicomponent exercise consistently reduced pro-inflammatory cytokines (IL-6, TNF- α), shifted lymphocyte profiles toward anti-inflammatory phenotypes, attenuated microglial senescence markers, and elevated neuroprotective myokines (irisin, BDNF). Longitudinal evidence confirmed that sustained physical fitness remodeled immune phenotype composition and decelerated biological aging. Exercise induced epigenetic changes in immune cells including differential DNA methylation linked to inflammaging pathways underscored the mechanistic depth of the findings. Cognitive improvements co-occurred with immune modulation across interventional and observational designs.

CONCLUSION: Exercise exerts multifaceted neuroprotective effects through immunosenescence attenuation, inflammaging reversal, and neuroimmune optimization. The convergence of these mechanisms supports cognitive resilience and may delay neurodegenerative trajectories in aging adults. Future research should standardize exercise prescriptions and immunological outcome biomarkers to enable comparative synthesis and clinical translation.

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Cellular Senescence Induced by the DNA Alkylation Damage Response on Myoblast Differentiation

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Abstract

INTRODUCTION: Sarcopenia, characterized primarily by an age-related loss of skeletal muscle mass and function, represents a leading cause of physical frailty and the subsequent need for long-term care. Skeletal muscle regeneration and tissue maintenance are primarily driven by satellite cells, which function as muscle stem cells; however, their intrinsic regenerative capacity declines significantly with advancing age. DNA damage stress, is a major upstream driver that accelerates cellular senescence, specifically impacts the cell fate and functional properties of myoblasts remains largely unknown. In this study aimed to investigate the effects of cellular senescence induced via the persistent DNA damage response (DDR) to drug-induced alkylation damage on the overall myogenic potential of myoblasts.

METHODS: To evaluate these effects, an in vitro model utilizing both the immortalized mouse myoblast cell line (C2C12) and mouse skeletal muscle-derived primary myoblasts was established. These cells were treated with a specific DNA alkylating agent, and the subsequent downstream cellular responses, including cell proliferation kinetics, DNA damage signaling, gene expression profiles, and myogenic differentiation capacity, were systematically analyzed.

RESULTS: The experimental results revealed that treatment with the DNA alkylating agent significantly suppressed myoblast cell proliferation and induced a marked accumulation of phosphorylated histone H2AX (gamma H2AX), a definitive molecular hallmark of double-strand DNA damage. Furthermore, upregulation of p21 (Cdkn1a) and p53 (Trp53) gene expressions, which are critical upstream regulators of cell cycle arrest pathways, alongside a significantly increased production of intracellular reactive oxygen species (ROS) that was concurrently accompanied by a robust downregulation of various endogenous antioxidant factors. A sustained DDR and chronically elevated oxidative stress, multinucleated myotube formation was severely suppressed, and the transcriptional expression of key myogenic differentiation-related genes was significantly downregulated.

CONCLUSION: In conclusion, these cellular characteristics clearly demonstrated a senescence-like functional decline, strongly suggesting that accelerated cellular senescence induced by persistent DNA alkylation damage can serve as a primary driver reducing muscle regenerative capacity. The established model of inducing senescence in myogenic cells via a sustained DNA damage response is expected to provide a highly valuable and reliable experimental platform. This platform will be instrumental for identifying and evaluating novel therapeutic agents, molecular targets, and functional foods aimed at mitigating or reversing the progression of sarcopenia.

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Impact of Acute Blood Flow Restriction Training and High Intensity Resistance Training on BDNF and IGF-1 Levels in Healthy Older Men

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Abstract

INTRODUCTION: Exercise is increasingly recognized as a non-pharmacological strategy to support brain health during aging, potentially mediated by circulating neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1). Low-load blood flow restriction training (BFRT) induces substantial metabolic stress with minimal mechanical loading and may represent a promising alternative to high-intensity resistance training (HIRT) for older adults. However, the acute neurotrophic responses to BFRT remain poorly characterized.

METHODS: Sixty-three healthy older men (60–78 years) were randomized to BFRT, HIRT, or a non-exercising control group. Plasma BDNF was assessed at baseline and immediately post-exercise. Serum IGF-1 was measured at baseline, immediately post-exercise, and 1 h post-exercise. Blood lactate was assessed pre- and post-exercise. Creatine kinase (CK) and syndecan-1 were measured at baseline and immediately post-exercise as indicators of muscle and endothelial damage, respectively. Acute biomarker responses were analyzed using mixed-model repeated-measures ANOVA, with additional correlation analyses.

RESULTS: BFRT induced a significant increase in plasma BDNF immediately post-exercise, whereas no significant changes were observed following HIRT and BDNF decreased in controls (time × group interaction, $p < 0.05$). Serum IGF-1 increased significantly at 1 h post-exercise in the BFRT group only ($p < 0.01$). BFRT elicited markedly higher lactate concentrations compared with HIRT and control, and changes in BDNF were positively associated with lactate ($p = 0.435$, $p = 0.001$). HIRT resulted in substantially greater CK elevations, while BFRT produced minimal changes in CK and syndecan-1.

CONCLUSION: Acute BFRT was associated with increases in circulating BDNF and IGF-1 in healthy older men, accompanied by Acute BFRT was associated with increases in circulating BDNF and IGF-1 in healthy older men, alongside greater lactate responses. In contrast, HIRT was associated with greater elevations in CK without comparable neurotrophic responses. These findings highlight metabolic stress as a key driver of exercise-induced neuroplastic signaling and suggest that BFRT may be a promising and well-tolerated modality for further study in aging populations.

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CREG1 ameliorates diabetic pathology and enhances voluntary exercise in a mouse model of diabetes mellitus

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Abstract

INTRODUCTION: Japan is a super-aged society with a rapidly growing elderly population. The prevalence of type 2 diabetes mellitus (T2DM) is expected to increase with age and life expectancy. Our previous study demonstrated that overexpression of the cellular repressor of E1A-stimulated gene 1 (CREG1) in adipocyte P2-specific (aP2-CREG1) transgenic (Tg) mice improved insulin sensitivity and glucose tolerance in diet-induced obesity. Additionally, CREG1 stimulation enhances glucose uptake in skeletal muscle. However, the role of CREG1 in the pathophysiology of T2DM and its relationship with exercise remains unclear. This study investigated the effects of CREG1 on voluntary exercise and the pathophysiology of T2DM in KK-Ay and CREG1-Tg mice.

METHODS: KK-Ay and CREG1-Tg mice were crossbred to generate male KK-Ay/CREG1-WT (WT) and KK-Ay/Creg1-Tg (Tg) mice. To investigate the effects of exercise, mice were divided into sedentary control and exercise groups. The exercise group was provided with voluntary running wheels for 11 weeks. Glucose tolerance tests (GTT) and insulin tolerance tests (ITT) were performed in the ninth and tenth weeks, respectively, following a 16-hour fast. In the 11th week, the mice were euthanized, and tissues were collected for gene expression, protein, and histological analyses.

RESULTS: Exercise significantly suppressed weight gain, although no significant differences were observed between the WT and Tg genotypes. In the exercise group, Tg mice traveled significantly greater distances than WT mice. Histological analysis of the liver revealed that exercise attenuated hepatic steatosis in Tg mice, which was further supported by a significant reduction in hepatic cholesterol content. Similarly, adipocyte size in white adipose tissue was lower in the exercised Tg group. Regarding glucose and insulin metabolism, Tg mice exhibited a trend toward a reduced area under the curve (AUC) during the ITT, as well as decreased serum insulin levels and HOMA-IR compared with WT mice in the exercise group. However, no significant differences in the GTT results were detected between WT and Tg mice in either the control or exercise groups. Finally, molecular analysis of insulin signaling revealed that Tg mice exhibited significantly higher levels of p-IRS1 (Tyr612) and p-Akt (Ser473) than WT mice in the exercise group.

CONCLUSION: Our findings suggest that CREG1 promotes voluntary physical activity and improves insulin resistance in a T2DM mouse model, highlighting its potential significance in managing this condition.

The Association Between Body Composition and Immune Cell Mobilization During Acute Exercise in Young Adults

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Abstract

INTRODUCTION: Obesity is a global epidemic and a risk factor for cardiovascular disease, the leading cause of death. Adults with obesity have reduced adrenergic sensitivity, which may be associated with lower exercise-induced leukocytosis mediated by sympathetic β_2 -adrenergic receptor signaling. However, the relation between body composition and acute exercise-induced leukocytosis remains unknown. Therefore, the purpose of this study was to test the hypothesis that greater adiposity is associated with lower immune cell mobilization during acute exercise in young adults.

METHODS: We enrolled adults 19–32 yrs old with a body mass index (BMI) of $<40 \text{ kg/m}^2$ and no overt chronic disease or recent nicotine use. We measured body composition via dual-energy X-ray absorptiometry and anthropometrics. Participants completed a graded cardiopulmonary exercise test on a semi-recumbent cycle ergometer to volitional fatigue. Oxygen uptake rate ($\dot{V}O_2$) was measured via indirect calorimetry. We sampled venous blood (EDTA) at rest and within 2 min of test termination and determined circulating leukocyte populations with an automated hematology analyzer. We used Pearson's correlations (r) for normally distributed data (mean $\pm$ SD) and Spearman's correlations (ρ) for non-normal data (median[IQR]) in unadjusted and age-, sex-, race-, and ethnicity-adjusted partial correlations.

RESULTS: The sample ($n=16$) characteristics were: 24 ± 4 yrs old; body mass $95.2\pm 15.1 \text{ kg}$; 50% female; 6% Asian, 13% Black, 81% White; 19% Latine; peak $\dot{V}O_2$ $24.1\pm 4.7 \text{ mL O}_2/\text{kg}/\text{min}$ ($2.28\pm 0.65 \text{ L O}_2/\text{min}$). Acute exercise increased white blood cells from $5.45[1.75]$ to $10.30[4.75]\times 10^9/\text{L}$, lymphocytes 1.91 ± 0.36 to $3.93\pm 0.87\times 10^9/\text{L}$, monocytes $0.35[0.14]$ to $0.66[0.41]\times 10^9/\text{L}$, neutrophils $3.27[1.68]$ to $5.03[2.68]\times 10^9/\text{L}$, eosinophils $0.10[0.08]$ to $0.12[0.07]\times 10^9/\text{L}$, and basophils 0.03 ± 0.01 to $0.04[0.02]\times 10^9/\text{L}$. In unadjusted models, BMI ($32.1\pm 3.2 \text{ kg/m}^2$) was positively associated with Δ basophils ($0.02\pm 0.01\times 10^9/\text{L}$, $P<0.01$, $\rho=0.73$) but not with Δ white blood cells ($4.56[3.15]\times 10^9/\text{L}$), Δ lymphocytes ($2.02\pm 0.88\times 10^9/\text{L}$), Δ monocytes ($0.31[0.22]\times 10^9/\text{L}$), Δ neutrophils ($1.76[1.36]\times 10^9/\text{L}$), or Δ eosinophils ($0.03[0.05]\times 10^9/\text{L}$) (all $P_s\geq 0.32$, r or $\rho\leq 0.27$). Waist circumference ($101\pm 14 \text{ cm}$) was positively associated with Δ basophils ($P=0.02$, $r=0.59$). Body fat % ($31.9\pm 7.7\%$) was positively associated with Δ neutrophils ($P=0.04$, $r=0.53$). Visceral adipose tissue ($110.0\pm 36.8 \text{ cm}^2$) was not associated with immune cell mobilization (all $P_s\geq 0.32$; r or $\rho\leq 0.27$). After adjusting for age, sex, race, and ethnicity, BMI ($P=0.01$, $r=0.70$) and waist circumference ($P=0.04$, $r=0.61$) were positively associated with Δ basophils, and body fat % was positively associated with Δ eosinophils ($P=0.04$, $r=0.63$).

CONCLUSION: Contrary to our hypothesis, these preliminary findings suggest that BMI, waist circumference, and body fat % may be associated with greater immune cell mobilization during acute exercise in young adults.

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Effect of resistance exercise on insulin resistance in skeletal muscle in a non-obese type 2 diabetic animal model

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Abstract

INTRODUCTION: Overweight and obesity are directly related to development of inflammation and insulin resistance, contributing to the type 2 diabetes mellitus (DM2) establishment. However, it is known that a significant percentage of patients with DM2 is considered lean individuals, especially in Eastern countries, where the rate of type 2 diabetic people without obesity can reach 60%. DM2 patients also present impaired skeletal muscle function, which can directly contribute to the disease, since this tissue is responsible for up to 60% of the glucose clearance in post-prandial conditions. Resistance training (RT) can be an important tool for improving different aspects of DM2, mainly by increasing skeletal muscle function and modulating inflammatory markers. Thus, the aim of this work was to evaluate the effects of RT on insulin resistance and inflammation in an animal model of non-obese DM2.

METHODS: Male Goto-Kakizaki rats (animal model of DM2 without obesity, GK) and Wistar rats (control group, WT), at 60 days old, were submitted to a low- or high-volume resistance training program, using a stair apparatus (muscle resistance training model), for a period of 10 weeks. RT consisted in 4 (low-volume) or 8 (high-volume) climbs in the stair apparatus, with loads of 50, 70, 90, and 100% of the total muscle capacity, with a 2-minute break, three times a week, with 48-hour interval. After that, parameters related to insulin resistance and inflammatory markers were evaluated.

RESULTS: GK rats presented reduced work volume (25.7 and 26.8%) and performance (59.4 and 58.7%) when compared to WT rats trained at low- and high-volume, respectively. In GK rats, RT program was able to: a) reduce fasting blood glucose (9.7 and 12.3%, $p < 0.001$) at low- and high-volume, respectively; b) improve insulin sensitivity, assessed by the K_{it} determination during the ITT (-0.63 ± 0.73 for GKC; 1.77 ± 0.2 for GKL group; and 2.14 ± 1.52 for the GKH group; $p < 0.05$); c) increase IL-15 gene expression at high-volume (0.79 ± 0.82 for the GKC and 2.28 ± 0.34 for the GKH, $p < 0.01$), a cytokine directly related to improved muscle function; and d) decrease plasma lactate levels at low- and high-volume of training (28.9 ± 0.01 for the GKC, 16.3 ± 5.61 for the GKL, and 15.6 ± 1.01 for the GKH; $p < 0.05$), a metabolite that has been directly associated with insulin resistance. Moreover, our preliminary analysis suggests no alteration in lymphocyte profile mesenteric from lymph nodes in GK rats by RT at low- or high-volume.

CONCLUSION: RT reduced insulin resistance in non-obese GK rats, trained at low- or high-volume, as demonstrated by improved fasting glycemia and insulin sensitivity, associated with increased IL-15 gene expression and decreased plasma lactate levels, with no modulation in lymphocyte profile. Further studies are required to corroborate these findings and to investigate the potential mechanisms.

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Habitual physical activity patterns of children are related to NK cell mobilization following high-intensity intermittent exercise

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Abstract

INTRODUCTION: Natural killer (NK) cells are key components of the innate immune system. Acute exercise triggers rapid NK cell mobilization in children and adults. While greater circulating NK cell counts have been observed in regularly exercising older adults compared to age-matched sedentary controls and young adults, it is unclear how the habitual physical activity of children impacts NK cell counts or exercise-induced NK cell mobilization (i.e., change from pre to post-exercise).

METHODS: Healthy, recreationally active children were recruited. At visit 1, participants underwent anthropometric and aerobic capacity testing, followed by one-week of wearing a waist-worn Actigraph accelerometer to assess sedentary, moderate (MPA), moderate-to-vigorous (MVPA), and vigorous (VPA) physical activity time. At Visit 2, participants performed 30-min of high-intensity intermittent cycling, with venous blood sampled at rest, immediately post-exercise, at 30- and 60-min recovery. Total NK cells and CD56 subsets were quantified via flow cytometry. Mann-Whitney U tests were used to compare NK cell mobilization in children who did and did not meet physical activity guidelines, and Kruskal-Wallis tests with Dunn's post-hoc analyses were used to compare across timepoints. Correlations between NK cells and sedentary or physical activity time were assessed using Spearman's correlations.

RESULTS: Ten participants (6M; age:13.8±4.1y) completed the study, with 80% meeting Canadian physical activity guidelines (≥60 min MVPA/day). Resting NK cells and exercise-induced mobilization did not differ by adherence (all $p>0.71$). At post-exercise, total and CD56^{dim} NK cells rose ($p<0.04$), and remained elevated at 30- ($p<0.01$) and 60-min recovery ($p>0.0008$). The proportion (%) of CD56^{dim} NK cells was greater post-exercise compared with 30- ($p<0.01$) and 60-min ($p<0.007$) recovery. Similarly, post-exercise CD56^{bright} NK cells were elevated compared to rest ($p<0.04$) and 60-min recovery ($p<0.004$). Sedentary time was positively correlated with mobilized CD56^{bright} ($r=0.697$, $p<0.03$), CD56^{dim} ($r=0.709$, $p<0.03$), and total NK ($r=0.709$, $p<0.03$) cells. MPA time was negatively correlated with post-exercise CD56^{dim} ($r=-0.648$, $p<0.05$) and total NK ($r=-0.673$, $p<0.04$) cells, and resting %CD56^{dim} NK cells ($r=-0.673$, $p<0.04$). VPA time was positively correlated with mobilized CD56^{bright} NK ($r=0.782$, $p<0.01$) and post-exercise CD56^{bright} NK ($r=0.673$, $p<0.04$) cells.

CONCLUSION: While meeting guidelines did not alter the NK cell response to exercise in recreationally active children, the response was related to level of habitual activity. These data suggest daily activity may fine tune exercise-induced NK mobilization and recovery, acting as a critical factor in shaping innate immune responses early in life.

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β -Adrenergic Sensitivity is Preserved in Circulating Peripheral Blood Mononuclear Cells in Young Adults with Obesity

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Abstract

INTRODUCTION: Acute exercise induces a transient leukocytosis mediated by sympathetic β_2 -adrenergic receptor signaling and hemodynamic shear stress. Obesity is characterized by higher sympathetic nervous system activity, which may contribute to lower β -adrenergic signaling in immune cells. However, whether obesity is associated with β -adrenergic responsiveness in peripheral blood mononuclear cells (PBMCs) in early adulthood remains poorly understood. We tested the hypothesis that obesity is associated with impaired β -adrenergic signaling in PBMCs, resulting in lower cAMP production following isoproterenol stimulation.

METHODS: We recruited otherwise apparently healthy adults with obesity (body mass index [BMI] 30-40 kg/m²) and without obesity (BMI <30 kg/m²). We measured body fat percentage via dual-energy X-ray absorptiometry (DXA) and anthropometrics. Resting PBMCs were isolated from venous blood via density gradient centrifugation and frozen at -80°C. After thawing, 3×10^5 cells were stimulated with 50nM isoproterenol for five minutes and snap frozen in liquid nitrogen. Cells were then lysed and the supernatant was assessed for cAMP concentrations by enzyme-linked immunosorbent assay (ELISA). We compared group differences using independent t-tests, and associations between anthropometrics, body fat, and cAMP response were evaluated using Pearson's correlations (r).

RESULTS: Participants with obesity (n=17) had a higher BMI (32.5 ± 2.4 vs 23.7 ± 2.5 kg/m², $p < 0.001$), body fat percentage (33.3 ± 10.6 vs $19.8 \pm 10.3\%$, $p=0.004$), and waist-to-hip ratio (0.86 ± 0.07 vs 0.79 ± 0.04 cm, $p=0.010$) than those without obesity (n=12). However, age did not differ between groups (with obesity: 26 ± 5 vs. 23 ± 4 yrs, $p=0.211$). Supernatant cAMP concentrations following β -adrenergic stimulation using isoproterenol were not different between groups (with: 7.56 ± 3.51 vs without 7.71 ± 2.51 pmol/mL, $p=0.869$). There were no associations between cAMP concentrations and BMI ($r=-0.003$, $p=0.989$), body fat percentage ($r=0.207$, $p=0.331$), and waist-to-hip ratio ($R=-0.360$, $p=0.060$).

CONCLUSION: β -adrenergic sensitivity of PBMCs is preserved within this cohort of young adults with obesity in comparison to similar-aged adults without obesity, as evidenced by no difference in isoproterenol-stimulated intracellular cAMP production between groups. The preservation of cAMP signaling in PBMCs suggests that obesity-related alterations in immune signaling may not be evident in young adults with obesity, highlighting the potential importance of early lifestyle interventions before the development of immune dysfunction. Reduced sensitivity may be present in adults with more severe obesity and obesity related comorbidities.

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The Effects of Inspiratory Muscle Strength Training on β 2-Adrenergic Mediated cAMP Signaling in Young Adults With Obesity

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Abstract

INTRODUCTION: Obesity is associated with chronic low-grade inflammation and higher sympathetic nervous system (SNS) activity, which may reduce immune cell responsiveness during physiological stress¹. Catecholamine-mediated β 2-adrenergic signaling plays an important role in regulating immune cell function. Activation of β 2-adrenergic receptors increases intracellular cyclic adenosine monophosphate (cAMP), a key second messenger involved in immune cell mobilization². Previous studies suggest that Inspiratory Muscle Strength Training (IMST) improves cardiovascular and physiological function³. However, whether IMST influences β 2-adrenergic responsiveness in immune cells remains unclear.

PURPOSE: To test the hypothesis that 8 weeks of IMST would improve β 2-adrenergic-mediated cAMP activation in peripheral blood mononuclear cells (PBMCs) from young adults with obesity.

METHODS: We randomized thirteen young adults with obesity to either an IMST (n = 8; age: 26 ± 6 years; BMI: 31.8 ± 1.5 kg/m²; 5 males, 3 females) or a SHAM training (n = 5; age: 26 ± 3 years; BMI: 33.3 ± 2.8 kg/m²; 4 males, 1 female) for 8 weeks (30 inspiratory breaths/day at 75% or 15% [SHAM] maximal inspiratory pressure, 7 days/week). We assessed body composition via dual-energy X-ray absorptiometry (DXA) pre- and post-intervention. We collected blood samples pre- and post-intervention and isolated PBMCs, which were stimulated with isoproterenol, a β -adrenergic agonist, to assess β 2-adrenergic responsiveness. We quantified intracellular cAMP activity using an enzyme-linked immunosorbent assay (ELISA) and analyzed cAMP responses using ANOVA.

RESULTS: Body fat percentage was not significantly different between groups or time points (all p > 0.159). A significant Group x Time x Treatment interaction emerged for cAMP responses (p = 0.049, η^2p = 0.308). Contrary to our hypothesis, isoproterenol-stimulated cAMP responses increased in the SHAM group (6.72 ± 4.66 to 9.30 ± 3.61 pmol/mL) but not in the IMST group (7.85 ± 3.78 to 7.97 ± 2.31 pmol/mL).

CONCLUSION: β 2-adrenergic-mediated cAMP responses in PBMCs changed differently between the IMST and SHAM groups. Given the important role of β 2-adrenergic signaling in regulating immune cell responses during physiological stress and exercise, larger trials are needed to clarify the mechanisms underlying these responses and their implications for exercise-induced immune function.

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DISCLOSURES: JCW offers consulting with Watso Health LLC; JWH offers education/coaching at Hoch Health and Wellness LLC.

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Associations of Meditation, Budo, and Geido with Mindfulness-Related Measures: WASEDA'S Health Study

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Abstract

INTRODUCTION: Mindfulness and related traits have received attention as psychological characteristics relevant not only to mental health but also to health behaviors implicated in the prevention of lifestyle-related diseases (Sala et al., 2019). In addition to meditation training, Japanese martial arts (Budo; e.g., karate) have been associated with mindfulness (Miyata et al., 2020). Budo and Japanese traditional arts (Geido; e.g., Sado) also involve repeated practice, embodiment, and attentional regulation, as do meditation practices. Because many individuals may have experience in more than one of these practices, their associations with mindfulness should be examined while controlling for the others. This cross-sectional study examined whether cumulative practice duration of meditation, Budo, and Geido was differentially associated with mindfulness-related measures among middle-aged and older adults in Japan.

METHODS: Participants were 387 adults aged 40 years or older from the WASEDA'S Health Study, a cohort of Waseda University alumni and their spouses, with complete data on age, sex, practice duration, and mindfulness-related measures. The mean age was 62.3 years (SD = 9.62), and the sample included 250 men and 137 women. Participants reported their lifetime cumulative practice duration of meditation, Budo, and Geido; each variable was log-transformed using $\log(1 + \text{hours})$. Mindfulness-related measures included four FFMQ subscales (observing, describing, nonreactivity, and nonjudging), the MAAS (mindful awareness), SCS (self-compassion), NAS (Nonattachment), and six MAIA subscales (noticing, not-distracting, attention regulation, emotional awareness, body listening, and trusting). Multiple regression analyses were conducted controlling for age and sex, with practice durations of meditation, Budo, and Geido entered simultaneously.

RESULTS: After FDR correction, meditation practice duration was significantly associated with FFMQ observing ($\beta = .193$), MAIA noticing ($\beta = .140$), attention regulation ($\beta = .134$), emotional awareness ($\beta = .146$), and body listening ($\beta = .148$). Budo practice duration was significantly associated with FFMQ describing ($\beta = .159$), nonreactivity ($\beta = .125$), MAAS ($\beta = .127$), and MAIA attention regulation ($\beta = .137$). Geido practice duration was significantly associated with FFMQ describing ($\beta = .179$), NAS ($\beta = .156$), and MAIA emotional awareness ($\beta = .170$).

CONCLUSION: The findings suggest that meditation, Budo, and Geido were associated with different aspects of mindfulness-related measures. Meditation was mainly related to bodily and interoceptive awareness; Budo to attention and emotion regulation; and Geido to describing, nonattachment, and emotional awareness. Because this study was cross-sectional and relied on self-report measures, causal relationships cannot be inferred. Future longitudinal and intervention studies should examine differences among specific practice domains.

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Time-of-day exercise and redox adaptation in obese mice: muscle-derived extracellular vesicle miRNAs as candidate regulators

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Abstract

INTRODUCTION: The metabolic benefits of exercise are time-of-day dependent, yet whether exercise timing shapes redox and inflammatory adaptation in obesity and how skeletal muscle-derived extracellular vesicles (EVs) coordinate such tissue-specific responses remain unclear.

METHODS: Male C57BL/6J mice were fed a high-fat diet and then underwent 8 weeks of treadmill training in the early rest (ZT3) or early active (ZT15) phase, with sedentary controls (2×2 design). Plasma oxidative stress status was assessed using the d-ROMs (circulating hydroperoxide marker), BAP (marker of systemic antioxidant capacity), and OXY-adsorbent (hypochlorous acid-scavenging antioxidant capacity) assays. Plasma lipids were also measured. Redox/antioxidant, clock, and inflammatory genes were profiled by qPCR (tissue-dependent panels) in soleus (SOL), gastrocnemius (GAS), quadriceps (QUA), and liver. Muscle-derived EV-enriched miRNAs from ex vivo quadriceps cultures were profiled by small RNA sequencing, and experimentally validated targets (miRTarBase) underwent pathway enrichment.

RESULTS: Training significantly increased systemic antioxidant capacity (BAP), whereas d-ROMs showed no significant main effect but tended to exhibit a phase-by-exercise interaction, with the highest levels in ZT15-sed and lower levels in ZT15-exe. Redox transcription was tissue- and fiber-type-specific: GAS Nfe2l2 showed a phase-by-exercise interaction, SOL Hmox1 rose with both phase and exercise (higher at ZT15), QUA Nfe2l2 was higher at ZT3, and hepatic Keap1 was phase-dependent (higher in ZT15-sed). Inflammatory markers (Il1b, Il6, Tnf, Ccl2, and the macrophage marker F4/80) were largely unchanged in the tissues examined. Active-phase exercise (ZT15-exe) showed the lowest plasma triglycerides among the four groups, alongside a lower oxidative burden (d-ROMs) than ZT15-sed, indicating a more favorable systemic profile. EV-enriched miRNA profiles separated primarily by circadian phase (PC1, 33.5% of variance), and their validated target pathways were enriched in redox (oxidative stress, heme/iron) and metabolic/inflammatory signaling (PI3K–Akt, IL-1β, TNF-α, Toll-like receptor) networks.

CONCLUSION: In obese mice, exercise timing shaped tissue-specific redox adaptation, while chronic training enhanced systemic antioxidant capacity despite only modest changes in circulating hydroperoxide levels (d-ROMs); aligning exercise with the active phase may be associated with a more favorable systemic profile. In contrast, inflammatory markers remained largely unchanged, suggesting that redox rather than inflammatory pathways underlie this adaptation. Muscle-derived EV miRNAs are candidate upstream regulators of this time-of-day, tissue-specific redox adaptation. These exploratory findings warrant functional validation.

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Aging alters the microRNA expression profile of extracellular vesicles derived from skeletal muscle-resident CD45-positive cells and their effects on gene expression in skeletal muscle cells

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Abstract

INTRODUCTION: Aging induces skeletal muscle atrophy by impairing satellite cell function; however, the molecular mechanisms underlying this process remain largely unclear. Aging is associated with increased infiltration of immune cells, including macrophages and neutrophils, into skeletal muscle, suggesting that bioactive factors secreted by these cells contribute to muscle atrophy (1). Extracellular vesicles (EVs), including exosomes, mediate intercellular communication by transferring bioactive molecules such as proteins and microRNAs to recipient cells, thereby modulating cellular functions, including gene expression in skeletal muscle cells (2). Therefore, EVs released from immune cells residing in skeletal muscle may contribute to age-related alterations in skeletal muscle through the regulation of gene expression. This study aimed to investigate the effects of aging on the microRNA expression profile of EVs secreted by skeletal muscle-resident immune cells. We also examined the effects of these immune cell-derived EVs on the mRNA expression profile of skeletal muscle cells.

METHODS: Gastrocnemius and quadriceps muscles were collected from young (4-month-old) and aged (27-month-old) C57BL/6J mice. Skeletal muscle tissues were enzymatically dissociated into single-cell suspensions, and CD45-positive cells were isolated by magnetic cell separation. Total RNA extracted from EVs isolated from the conditioned medium of cultured CD45-positive cells was subjected to comprehensive microRNA expression analysis. Satellite cells isolated from mouse skeletal muscle were differentiated into myotubes and treated with EVs derived from CD45-positive cells. Comprehensive mRNA expression profiling was subsequently performed in the myotubes.

RESULTS: The number of CD45-positive cells residing in skeletal muscle was higher in aged mice than in young mice. Compared with EVs from young mice, EVs derived from CD45-positive cells of aged mice exhibited upregulation of 12 microRNAs and downregulation of 35 microRNAs. KEGG pathway analysis of the upregulated miRNAs revealed enrichment of signaling pathways associated with muscle protein synthesis, including the PI3K-Akt and MAPK signaling pathways. Moreover, myotubes treated with EVs derived from aged CD45-positive cells exhibited a distinct mRNA expression profile compared with those treated with EVs from young CD45-positive cells.

CONCLUSION: These findings suggest that aging alters the microRNA expression profile of EVs secreted by skeletal muscle-resident CD45-positive immune cells, which may subsequently modulate gene expression in skeletal muscle cells.

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Effects of 6-Month Chios Mastiha Resin Supplementation Alone or Combined with Physical Activity on Glycemic Control and Lipid Metabolism in Middle-Aged Japanese Men

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Abstract

INTRODUCTION: Chios Mastiha resin (CM) from the island of Chios (Greece) has long been utilized as a natural chewing gum and is believed to exert beneficial effects on gastrointestinal and metabolic symptoms. However, the comprehensive impacts of CM, both alone and in combination with physical activity, on blood biochemistry remain to be fully established. Therefore, this study investigated these effects in healthy middle-aged Japanese men to clarify the potential health-promoting mechanisms of CM.

METHODS: Participants were allocated to three groups: control (C, 5 g/day placebo powder, n=7), CM (M, 5 g/day CM powder, n=7), or CM plus physical activity (M+PA, 5 g/day CM powder and 30-minute exercise three times/week, n=7). The intervention period lasted six months, during which participants maintained their usual lifestyle habits. Blood samples and anthropometric measurements were taken before the intervention, and at 3 and 6 months post-intervention. Measured variables included total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, LCAT, GOT, GPT, gamma-GTP, blood glucose, insulin, albumin, cholinesterase, free fatty acids, uric acid, urea nitrogen, creatinine, d-ROMs and BAP tests, together with BMI, waist circumference, and body fat percentage.

RESULTS: During the 6-month intervention, a significant group-by-time interaction was observed for serum triglycerides ($P = 0.016$), insulin ($P = 0.003$), and HOMA-IR ($P = 0.007$). Specifically, at the 3-month, serum triglyceride levels were reduced in the M and M+PA groups compared with the baseline, whereas they increased in the C group. Furthermore, serum insulin levels and HOMA-IR scores steadily decreased in both the M and M+PA groups at 3 and 6 months compared with their respective baseline values, whereas these markers progressively increased in the C group. No significant interactions or adverse changes were observed in other blood parameters, including total cholesterol, HDL-C, LDL-C, LCAT, and liver enzymes.

CONCLUSION: These findings demonstrate that 6-month daily intake of Chios Mastiha resin, both alone and in combination with physical activity, significantly improves triglyceride metabolism, glycemic control, and insulin sensitivity in middle-aged Japanese men. Integrating Mastiha consumption into daily life, especially when paired with regular exercise, represents an effective and practical lifestyle strategy to prevent and manage metabolic syndrome.

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Acute Exercise Enhances the Potency of Cytokine-Induced Killer Cells Against Hematological Malignancies

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Abstract

INTRODUCTION: Cytokine-induced killer (CIK) cells are a heterogeneous population of ex vivo expanded immune effectors that combine both NK and T-cell phenotypes. Their broad antitumor activity, preferential non-MHC restricted cytotoxicity, and simple expansion make them attractive candidates for adoptive cellular therapy (ACT). However, CIK cells are not always effective at inducing durable responses against hematological malignancies. Here, we determined if lymphocytes mobilized to blood with acute exercise would enhance the potency of CIK cells against both lymphoid and myeloid leukemias.

METHODS: Healthy participants enrolled in the Allo-X trial (NCT06643221) performed a 20-minute bout of aerobic stationary cycling (graded 50-80% VO_{2max}), and peripheral blood mononuclear cells (PBMC) collected at rest and 80% VO_{2max} were expanded to generate CIK cells, denoted as CIK and CIK-X, respectively. Cellular cytotoxicity was assessed utilizing 4-hour flow cytometry killing assays against three lymphoid (NALM-6, JEKO-1, and RS4;11) and two myeloid (Kasumi-1 and MOLM-13) tumor models across various effector to target ratios. Additionally, CIK and CIK-X cell products were immunophenotyped using multiparameter flow cytometry to identify differences in various activation, adhesion, and functional markers. Antibody-dependent cellular cytotoxicity (ADCC) of CIK and CIK-X were determined in vitro using the anti-CD19 monoclonal antibody, Tafasitamab.

RESULTS: CIK-X cells demonstrated significantly enhanced cytotoxicity across 4 of 5 lymphoid and myeloid tumor models tested, with a significant cell product effect observed by two-way ANOVA in JEKO-1, NALM-6, RS4;11 and MOLM-13 tumor models. Immunophenotyping revealed significantly higher CD16 expression in CIK-X versus CIK products, consistent with enhanced ADCC potential. Tafasitamab was found to increase ADCC of both CIK and CIK-X, with the greatest enhancement seen in the CIK-X products.

CONCLUSION: Lymphocytes collected from blood during a single bout of exercise enhance the potency of CIK cells against a number of hematological tumors. Together, these findings position acute exercise as a physiologic relevant strategy to improve CIK product potency and demonstrate synergy with Tafasitamab for enhanced CD19-directed killing.

Phenotypic landscape mapping by multiparametric high-content screening reveals divergent modulators of cancer cachexia-associated muscle atrophy

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Abstract

INTRODUCTION: Cancer cachexia is a multifactorial metabolic syndrome characterized by progressive skeletal muscle wasting and poor clinical outcomes. However, current in vitro models and analytical approaches are insufficient to capture the phenotypic heterogeneity and dynamic remodeling underlying tumor–muscle interactions.

METHODS: Differentiated C2C12 myotubes were exposed to tumor-conditioned medium (CM) derived from multiple cancer cell lines to model tumor-induced muscle atrophy. High-content imaging combined with automated image analysis enabled quantitative extraction of multiparametric features, including Myosin Heavy Chain (MyHC) intensity, myotube width and length, fusion index, and structural organization. Principal component analysis (PCA) and unsupervised clustering were applied to construct a phenotypic landscape. A focused compound library was screened to evaluate differential phenotypic modulation.

RESULTS: CM exposure induced robust and reproducible atrophy phenotypes, including reduced myotube size, decreased MyHC intensity, and disrupted structural organization. Multiparametric analysis revealed substantial phenotypic heterogeneity beyond conventional single-parameter metrics. Unsupervised clustering identified distinct phenotypic states, including a prominent hyper-fusion phenotype characterized by elevated fusion index and increased multinucleation accompanied by aberrant structural features. These phenotypes exhibited a continuous and non-linear distribution across conditions. Compound screening demonstrated divergent phenotypic responses: while some compounds partially restored atrophic features, others induced or exacerbated hyper-fusion phenotypes despite improvements in fusion-related metrics, indicating that enhancement of individual parameters does not necessarily reflect functional recovery.

CONCLUSION: This study establishes a tumor-conditioned medium–based in vitro model integrated with multiparametric high-content phenotyping to dissect muscle atrophy heterogeneity in cancer cachexia. Importantly, cachexia-associated remodeling is not a linear degenerative process but involves dynamic transitions across distinct phenotypic states. By distinguishing true functional rescue from aberrant phenotypic shifts such as hyper-fusion, this approach improves the reliability of phenotypic drug discovery and provides a scalable framework for identifying therapeutically relevant modulators.

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Immune signatures of exercise-mobilized NK cells in aging cancer patients undergoing treatment identified by single-cell RNA sequencing

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Abstract

INTRODUCTION: Exercise is increasingly recognized as a potential adjuvant therapy in oncology, with recent evidence supporting its role in reducing cancer recurrence. Acute exercise induces mobilization and egress of immune cells, notably cytotoxic natural killer (NK) cells, which may improve immune surveillance over time. However, the mechanisms by which exercise intensity modulates migratory and cytotoxic immune functions remain poorly understood, hindering its integration as a biologically informed adjuvant therapy. Here, we used single-cell RNA sequencing (scRNA-seq) of peripheral blood mononuclear cells (PBMC) to specifically assess the impact of acute exercise at different intensities on transcriptional reprogramming of NK cell subsets in aging cancer patients undergoing treatment.

METHODS: Two exercise conditions with different intensities (moderate-intensity exercise; MOD & high-intensity interval exercise; HIIE) are being evaluated in cancer patients undergoing adjuvant treatment using a cross-over design to reduce inter-individual variability. PBMCs are isolated before (T1), immediately after (T2), and 1h post (T3) each exercise condition. scRNA-seq (BD Rhapsody system) is being performed to profile cell type-specific transcriptomic changes at single-cell resolution.

RESULTS: Proof-of-principle analysis of 62,632 high-quality cells from the first participant (T1/T2/T3 from MOD and HIIE) revealed all major PBMC populations, including T lymphocytes (34.8%), monocytes (27.8%), NK cells (18.2%), B lymphocytes (16.1%), and dendritic cells (2%). HIIE, but not MOD, induced a transient two-fold increase in circulating NK cells, mainly driven by an increase in CD56^{dim} effector NK cells. Gene expression profiling showed HIIE induced seven times more differentially expressed genes (DEGs) than MOD in these CD56^{dim} NK cells (140 vs. 20, all adj. $p < 0.05$), with less pronounced changes seen in the CD56^{bright} and proliferative NK subsets. Gene ontology (GO) analysis of the CD56^{dim} NK subset revealed that DEGs shared between MOD and HIIE conditions were enriched in gene sets associated with cytotoxicity, with some shared DEGs also linked to migratory functions. Consistent with these results, Gene Set Enrichment Analysis identified significantly enriched cytotoxicity-related pathways, in the HIIE condition only. Ongoing Cell-cell communication analyses will identify intercellular communication networks underlying these exercise-induced NK cell responses.

CONCLUSION: These preliminary results in aging cancer patients undergoing treatment suggest that, beyond mobilizing PBMCs into the circulation, acute exercise also induces intensity-dependent transcriptomic reprogramming of PBMC subpopulations. These exercise-induced biological functions associated with immune surveillance may contribute to the beneficial effects of exercise in oncology. Following completion of the study, functional assays will be conducted to confirm these findings.

Impact of Heat Exposure on Immune Responses During Endurance Exercise in Triathletes

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Abstract

INTRODUCTION: Prolonged endurance exercise in hot environments may alter immune cell trafficking and antiviral immune function, yet these responses remain poorly understood in triathletes, who frequently train and compete under thermal stress. This study examined the effects of controlled endurance exercise in the heat on circulating immune cell percentages and virus-stimulated interferon-gamma (IFN- γ) responses in recreationally trained triathletes, and explored whether aerobic fitness and exercise workload were associated with exercise-induced change and 24 h recovery.

METHODS: Nine recreationally trained triathletes (6 female, 3 male; 34.6 ± 8.8 y; BMI: 22.3 ± 2.1 kg/m²; VO₂ peak: 58.6 ± 7.7 mL·kg⁻¹·min⁻¹) completed a repeated-measures protocol. After baseline testing, participants performed 60 min of cycling at 70% VO₂ peak in a heat chamber (30 °C, 60% relative humidity). Blood was collected at rest, during exercise, and 24 h post-exercise. Immune cell phenotypes were assessed by flow cytometry (Miltenyi). Whole blood was stimulated for 24 h with respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), influenza A (IA), positive control, or saline, and IFN- γ was quantified by multiplex assay. IFN- γ was also normalized to total T-cell, CD4+, and CD8+ populations. URTI symptoms were monitored daily with the WURSS-21 from 3 days before the trial through 6 days post-exercise. Time effects were examined using repeated-measures ANOVA or Friedman tests; associations with VO₂ peak and total work were examined using Spearman correlations.

RESULTS: Exercise induced significant time effects for CD3- cells ($p < .001$), NK cells ($p = .003$), CD3+ T cells ($p = .005$), CD4+ T cells ($p < .001$), CD8+ T cells ($p = .009$), CD4+ EMRA ($p = .014$), CD4+ naive ($p = .013$), CD4+ central memory ($p = .005$), CD4+ effector memory ($p = .035$), CD8+ EMRA ($p = .002$), CD8+ naive ($p < .001$), and CD8+ central memory cells ($p < .001$). During exercise, CD3- and NK cell percentages increased, whereas CD3+, CD4+, and CD8+ naive T-cell percentages decreased; most values returned toward rest by 24 h. IFN- γ responses did not significantly change for RSV ($p = .555$), EBV ($p = .829$), IA ($p = .895$), or the positive control ($p = .717$). Normalized IFN- γ analyses did not reveal significant time effects, although response patterns changed after adjustment. No URTI symptoms were reported. VO₂ peak was inversely associated with EBV exercise-induced change ($p = -.700$, $p = .036$), but total work was not associated with IFN- γ change or recovery indices (all $p > .05$).

CONCLUSION: One hour of endurance exercise in the heat induced marked but largely transient redistribution of circulating immune cell populations in recreationally trained triathletes, without clear evidence of impaired virus-stimulated IFN- γ production. These findings suggest that acute exercise under thermal stress may alter immune cell distribution more than antiviral functional responsiveness.

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The effect of environmental heat stress on the morphological changes in cultured skeletal muscle cells during proliferation

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Abstract

INTRODUCTION: Skeletal muscle is an organ that produces heat, and exercise increases the temperature of the skeletal muscle itself and elevates the surrounding environmental temperature. Skeletal muscle exhibits high plasticity and regenerates after injury. This regeneration process involves the proliferation and differentiation of myoblasts. Environmental stimuli such as heat stress are known to affect this plasticity of skeletal muscle. Previous studies have demonstrated that the application of heat stress within the physiological range increased skeletal muscle mass in mice. Heat stress is also reported to facilitate myogenic differentiation in cultured C2C12 cells. However, the effects of heat stress on the morphological features of skeletal muscle cells during proliferation have not yet been fully elucidated. Therefore, the present study investigated the morphological response of proliferating cultured skeletal muscle cells to an environmental temperature increase.

METHODS: Mouse C2C12 myoblast cells were seeded onto culture plates containing proliferation medium. The following day, the plates in the heat-stressed groups were exposed to heat stress at multiple temperatures (38-39°C) in an incubator. After the application of heat stress, the cells were fixed using 4% paraformaldehyde. Subsequently, to evaluate morphological changes in the myoblasts, their cell membranes were stained with fluorescent dyes, and the nuclei were counterstained with DAPI.

RESULTS: The increase in the myoblast number during the proliferation phase was suppressed in response to the application of heat stress. Furthermore, this heat stress altered the size of myoblast nuclei and cells. These heat stress-induced responses of myoblasts were more prominent at the higher incubation temperature. The inhibition of myoblast proliferation by heat stress was accompanied by these changes in their morphology.

CONCLUSION: The results of the present study indicate that environmental heat stress alters the morphology of proliferating C2C12 myoblasts. This study was partially supported by JSPS KAKENHI (24K14265) and Seijoh University Joint Research Promoting Grant.

Effects of high-concentration carbon dioxide hot water immersion and contrast water therapy on salivary human herpesvirus 6 and 7 levels

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Abstract

INTRODUCTION: Hot water immersion (HWI) is a widely accepted recovery method, and high-concentration carbon dioxide (CO₂) HWI has recently attracted increasing attention. We previously reported that CO₂-HWI may exert a stronger thermogenic effect than tap water HWI, as it induced a greater increase in core body temperature and promoted earlier sweating (Iwata *et al.*, 2025).

In addition, contrast water therapy (CWT), which involves repeated alternation between hot and cold water immersion, is commonly used in conditioning practice as a post-exercise recovery strategy (Bieuzen *et al.*, 2013). Because CWT is characterized by repeated exposure to contrasting thermal stressors, incorporating CO₂-HWI into CWT may further enhance its thermogenic effects.

Meanwhile, attempts to evaluate physical condition using salivary biomarkers have advanced in recent years. In particular, human herpesvirus 6 and 7 (HHV-6/7) have been reported as biomarkers of exertion-related physiological fatigue (Aoki *et al.*, 2016). Therefore, this study aimed to examine the effects of CO₂-HWI and CO₂-CWT on salivary HHV-6/7 levels as potential indicators of recovery.

METHODS: Eight healthy adult males participated in this randomized crossover trial. After a circuit exercise protocol combining leg press and cycle ergometer exercise, participants completed three conditions: CO₂-HWI (CO₂-rich water at 40°C for 12 min), CO₂-CWT ([CO₂-rich water at 40°C for 3 min + tap water at 15°C for 1 min] × 3 cycles; total duration, 12 min), and no intervention (NON; seated rest for 12 min). Measurements were performed before and after exercise and at 0, 0.5, 1, 1.5, 2, 24, and 48 h after intervention. Salivary HHV-6/7 levels were assessed as the primary outcomes, while core body temperature, skin temperature, and other variables were assessed as secondary outcomes. A two-way repeated-measures ANOVA was used to examine the effects of condition, time, and their interaction.

RESULTS: Among the secondary outcomes, the greatest changes were observed at 0 h after intervention. Core body temperature was highest in the CO₂-HWI condition, followed by the CO₂-CWT and NON conditions. In contrast, skin temperature was highest in the CO₂-HWI condition, followed by the NON and CO₂-CWT conditions.

Salivary HHV-6 levels increased after exercise in all conditions and gradually decreased in the CO₂-HWI and CO₂-CWT conditions, whereas they remained relatively higher in the NON condition. However, no significant interaction was observed ($p > .05$, $F = 0.85$, $\eta_p^2 = 0.11$). Salivary HHV-7 levels gradually increased after exercise in all conditions and reached the highest value at 24 h in the NON condition, whereas the lowest values were observed at 24–48 h in the CO₂-HWI and CO₂-CWT conditions. A trend toward a significant interaction was observed, with a moderate effect size ($p < .10$, $F = 2.25$, $\eta_p^2 = 0.24$).

CONCLUSION: CO₂-HWI and CO₂-CWT may reduce salivary HHV-7 levels 24–48 h after intervention; however, differences between CO₂-HWI and CO₂-CWT remain unclear.

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Effects of Menopausal Status on Body Temperature Responses During Exercise in the Heat

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Abstract

INTRODUCTION: Although menopause is associated with alterations in thermoregulatory mechanisms, including changes in sweating and cutaneous vasodilatory responses, it remains unclear whether these changes translate into greater body temperature responses during exercise in the heat, particularly when body size and aerobic fitness are considered. Clarifying this issue is important for developing evidence-based heat safety guidance for women across the lifespan. This study aimed to compare body temperature responses between postmenopausal and premenopausal young women during exercise in a hot environment.

METHODS: Twelve postmenopausal women (age, 56.75±3.52) and eight premenopausal women (age, 26.63±4.27) completed treadmill walking for 120-min in an environmental chamber at 35°C and 40% relative humidity. For premenopausal women, trials were scheduled during the luteal phase and hormonal profiles were confirmed via blood sampling. Rectal temperature (Tre) was measured, and mean skin temperature (Tsk) was calculated using a four-site method. Between-group comparisons used Welch's t-test; matched subgroup comparisons used paired t-tests. A matched subgroup analysis paired five luteal-phase-confirmed premenopausal women with five postmenopausal women based on BMI, body surface area, and VO₂peak.

RESULTS: All participants completed the full 120-min exercise. In the overall comparison, baseline Tre was lower in postmenopausal than premenopausal women (37.25±0.20°C vs. 37.54±0.22°C, p=.009). Peak Tre did not differ (38.14±0.57°C vs. 38.13±0.19°C, p=.953), nor did the increase in Tre from baseline to 120 min (0.76±0.53°C vs. 0.56±0.13°C, p=.243) or from 60 to 120 min (0.22±0.26°C vs. 0.17±0.14°C, p=.559). Peak Tsk was 35.78±0.56°C and 36.04±0.40°C (p=.270), and the Tsk increase from baseline to 120 min was 2.66±0.90°C and 3.25±1.44°C (p=.363). In the matched subgroup, BMI, body surface area, and VO₂peak did not differ (all p>.05), whereas body fat percentage was lower in postmenopausal women (22.44±4.13% vs. 25.16±2.76%, p=.019). Peak Tre (38.46±0.62°C vs. 38.17±0.21°C, p=.405) and the Tre increase from baseline to 120 min (0.99±0.62°C vs. 0.59±0.12°C, p=.252) did not differ. Peak Tsk and Tsk increase also did not differ (p=.354 and p=.929).

CONCLUSION: Despite lower baseline Tre in postmenopausal women, the magnitude of Tre and Tsk responses during 120-min exercise in the heat did not differ from premenopausal women in either the overall or matched comparisons. These findings provide preliminary evidence that postmenopausal status was not associated with greater body temperature responses under the present heat tolerance test conditions. Further studies with larger samples are warranted to confirm these findings.

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LGG Attenuates PM2.5- and Allergen-Induced Airway Inflammation through Immune Rebalancing: A Co-Exposure Model for Exercise-Associated Airway Disease

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Abstract

INTRODUCTION: Exercise-induced bronchoconstriction (EIB) and allergic asthma affect 10–50% of elite athletes. Outdoor training amplifies PM2.5 inhalation 10- to 20-fold, compounding risk in athletes with allergic sensitization. PM2.5 activates AhR–NF-κB–TSLP cascades that synergize with allergen-driven Th2/Th17 inflammation, yet nutritional countermeasures targeting this combined threat remain scarce. *Lactobacillus rhamnosus* GG (LGG) possesses immunomodulatory properties relevant to athletes, but its efficacy against concurrent pollution- and allergen-induced airway inflammation has not been examined. This study evaluated LGG in a PM2.5 plus HDM co-exposure murine model simulating the combined burden faced by allergic athletes.

METHODS: BALB/c mice were sensitized with HDM/alum (i.p.) and challenged with intranasal HDM, with concurrent PM2.5 instillation (NIST SRM 1648a) to establish a co-exposure model. LGG (1×10^8 CFU) was administered daily by oral gavage pre-sensitization (days 1–14) or post-sensitization (days 14–27). Outcomes: AHR (methacholine challenge), BALF cell counts, serum IgE/IgG1/IgG2a, cytokines (IL-4, IL-5, IL-12, IL-13, IL-17, IL-25, IL-33, IFN-γ, IL-10) by ELISA, splenic T cell subsets by flow cytometry, transcription factors (T-bet, GATA3, RORγt, Foxp3) by qPCR, and gut microbiota by 16S rRNA sequencing.

RESULTS: The PM2.5+HDM co-exposure model produced the most severe asthma phenotype with mixed eosinophilic–neutrophilic inflammation and Th2/Th17 dual-axis activation. LGG significantly attenuated AHR ($p < 0.001$), reduced eosinophils (77.1%, $p < 0.001$) and neutrophils ($p < 0.05$), suppressed IL-4 (49.7→16.3 pg/mL, $p < 0.001$), IL-5, IL-13, IL-17, and epithelial alarmins IL-25 and IL-33 (all $p < 0.05$), while elevating IFN-γ (16.5→55.8 pg/mL, $p < 0.001$) and IL-12. Flow cytometry confirmed Th1/Th2 rebalancing and Foxp3⁺ Treg upregulation. Pre-sensitization LGG showed superior efficacy over post-sensitization. 16S rRNA sequencing revealed restored Shannon diversity ($p < 0.05$), improved Firmicutes/Bacteroidetes ratio, and increased *Akkermansia muciniphila*, evidencing gut–lung axis-mediated protection.

CONCLUSION: In a co-exposure model combining PM2.5 and allergen challenge, LGG mitigated airway inflammation through Th1/Th2/Th17 rebalancing, Treg induction, and gut microbiota restoration via the gut–lung axis. Prophylactic administration was more effective than therapeutic. These findings support LGG as a candidate nutritional adjunct for allergic athletes training in polluted environments. Human co-exposure studies are warranted.

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Effects of acute resistance exercise combined with hypoxic exposure maintained until immediately after exercise on metabolic and hormonal responses

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Abstract

INTRODUCTION: Resistance exercise performed under hypoxia has been reported to enhance glucose metabolism, as well as to stimulate the endocrine system and increase the secretion of hormones involved in lipid metabolism (Kon et al., *Med Sci Sports Exerc*, 2010). However, it remains unclear whether a similar response is elicited by limited hypoxic exposure maintained until immediately after exercise. Additionally, the effects of acute hypoxic resistance exercise on post-exercise lipid metabolism have not been fully elucidated. This study aimed to investigate the effects of acute resistance exercise combined with hypoxic exposure maintained until immediately after exercise on metabolic and hormonal responses.

METHODS: Healthy male subjects participated in two experimental trials: 1) resistance exercise while breathing normoxic air (normoxic trial) and 2) resistance exercise while breathing 13.4% oxygen (hypoxic trial). The resistance exercise (chest press and leg extension) consisted of 10 repetitions per set for three sets at 70% of maximum strength with 1 min rest between sets. In the hypoxic trial, hypoxic exposure was maintained until immediately after exercise. Blood samples were collected before exercise, immediately after exercise, and at 30, 60, and 120 min after exercise. The pre-exercise sampling was conducted after 10 min of rest in each trial. Arterial oxygen saturation (SpO₂), lactate, glucose, norepinephrine (NE), interleukin-6 (IL-6), and free fatty acids (FFA) were measured.

RESULTS: Hypoxic exposure significantly decreased resting SpO₂ in the hypoxic trial compared with the normoxic trial. In both trials, SpO₂ significantly decreased immediately after exercise compared with baseline, with the hypoxic trial showing significantly lower values than the normoxic trial. Although lactate significantly increased immediately after exercise in both trials, it was significantly higher in the hypoxic trial than in the normoxic trial. Glucose significantly decreased immediately after exercise and 30 min after exercise in both trials, with no significant differences between trials. Although NE significantly increased immediately after exercise in both trials, it was significantly higher in the hypoxic trial than in the normoxic trial. No significant differences were observed in IL-6 levels after exercise compared with before the exercise in either trial. FFA significantly decreased immediately after exercise compared with before the exercise in the normoxic trial, whereas a significant decrease was observed from immediately after exercise to 60 min after exercise in the hypoxic trial.

CONCLUSION: These findings suggest that acute resistance exercise combined with limited hypoxic exposure lasting maintained until immediately after exercise augments lactate and NE responses, and may promote tissue utilization of FFA for a prolonged period after exercise.

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The effects of different beverage intake during field sports exercise in severe heat on dehydration and secretory immunoglobulin A

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Abstract

INTRODUCTION: Recent global warming has exacerbated summer weather conditions worldwide. In sports settings, days exceeding a Wet-Bulb Globe Temperature (WBGT) of 31°C, which is considered an extremely high thermal risk according to international guidelines, have become commonplace. However, sports activities continue under these conditions, and it is important to examine the effects of exercise in severe heat on the body. Exercise in severe heat may carry the risk of significantly reducing secretory immunoglobulin A (SIgA), which plays a major role in oral mucosal immune function, due to localized stress associated with dehydration. While high-intensity and prolonged exercise are known to lower SIgA levels, the effects of actual sports activities performed under severe heat conditions on SIgA levels have not been sufficiently investigated. Furthermore, the effects of different beverages consumed during such activities on dehydration and SIgA levels remain unclear. This study aimed to investigate the effects of different beverages intake during field sports exercise in severe heat on dehydration and SIgA levels.

METHODS: University students belonging to an ultimate club participated in identical 150-min exercise sessions in spring (WBGT: 16°C) and summer (WBGT: 35°C). Participants were classified into three groups based on the beverages consumed during exercise: a sports drink group, a green tea group, and a water group. Participants consumed the beverages ad libitum. Urine and saliva samples were collected before and after exercise. Urine specific gravity, an indicator of dehydration, salivary secretion rate, SIgA concentration, and SIgA secretion rate were measured.

RESULTS: In spring, urine specific gravity showed no significant changes before and after practice, whereas a significant increase was observed after exercise in summer. On the other hand, no significant difference in urine specific gravity was observed in relation to differences in beverage intake in either the spring or summer session. Salivary secretion rate and SIgA concentration showed no significant changes before and after exercise in spring. In contrast, in summer, salivary secretion rate significantly decreased in the sports drink group and the green tea group, whereas it significantly increased in the water group. SIgA concentration significantly increased in the sports drink group, while it significantly decreased in the water group. No significant changes in SIgA secretion rate were observed in any group during either spring or summer.

CONCLUSION: The results of this study suggest that although dehydration occurs during field sports exercise in severe heat, the SIgA secretion rate, an indicator of overall oral mucosal immune function, may be maintained regardless of the type of beverage consumed. This suggests that oral mucosal immune function can be preserved under severe heat stress, even as dehydration progresses, provided that adequate hydration is maintained.

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Exercise-Induced Immune Responses in Tropical Hot-Humid Environments: A Scoping Review

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Abstract

INTRODUCTION: Regular outdoor physical activity, including running and brisk walking, is increasingly practiced in tropical countries such as Indonesia, where exercise commonly occurs under hot-humid conditions. Although the immunomodulatory effects of aerobic exercise are well established, immune responses under combined heat and humidity stress remain less clearly characterized. Hot-humid exercise may influence pro-inflammatory cytokine release, leukocyte redistribution, heat shock protein induction, gut barrier integrity, and transient immunosuppression. This scoping review aimed to map current evidence on exercise-induced immune responses in hot-humid environments and identify key immune markers, exercise modalities, and mitigation strategies.

METHODS: Following PRISMA-ScR guidelines, PubMed and Scopus were searched from inception to 2026 using Boolean operators: ("exercise" OR "physical activity" OR "heat acclimation") AND ("heat stress" OR "hot-humid" OR "hyperthermia") AND ("cytokines" OR "IL-6" OR "leukocyte" OR "HSP70" OR "inflammatory markers"). Studies were included if they: (1) involved human participants; (2) examined exercise in hot or hot-humid environments ($\geq 30^{\circ}\text{C}$ and/or $\geq 50\%$ relative humidity); (3) reported immune or inflammatory outcomes. Studies were excluded if they involved: (1) passive heat exposure without exercise; (2) animal-only models; (3) conference abstracts or non-English publications.

RESULTS: A total of 104 records were identified, of which 7 duplicates were removed, leaving 97 records for screening. Following title and eligibility assessment, 28 studies met the inclusion criteria, including randomized controlled trials, observational studies, and reviews. The included literature primarily examined endurance-based exercise, prolonged aerobic activity, and heat-acclimation protocols, with relatively fewer studies assessing resistance exercise. Across studies, hot-humid exercise was associated with acute increases in inflammatory markers, particularly IL-6, TNF-alpha, and CRP, alongside post-exercise neutrophil-dominant leukocytosis and lymphocyte redistribution. Heat shock protein 70 was frequently reported, suggesting its role as a thermoprotective and immunomodulatory response to exercise-heat exposure. Some studies also described gut barrier disruption, bacterial translocation, and secondary immune activation following prolonged or exhaustive exercise in the heat. Heat acclimation appeared to attenuate inflammatory responses and modify HSP70 thresholds, while nutritional strategies, including probiotics, amino acids, and polyphenols, were reported as potential approaches to reduce exercise-heat-related immune dysregulation.

CONCLUSION: Exercise in hot-humid environments may amplify immune and inflammatory responses through heat shock protein induction, systemic inflammation, leukocyte redistribution, and gut-mediated immune activation. Current evidence remains highly heterogeneous across exercise protocols, environmental conditions, immune markers, and populations studied.

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Effects of knee joint angle on intramuscular blood flow and muscle deoxygenation during fatiguing isometric contractions

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Abstract

INTRODUCTION: Muscle oxygen consumption ($\dot{m}\text{VO}_2$) increases during exercise and is influenced by knee joint angle during repetitive isometric knee extensions. Previous studies have shown greater $\dot{m}\text{VO}_2$ (Pethick et al., 2021), shorter time to exhaustion (Kooistra et al. 2005), and larger force declines (Akima et al., 2019) in flexed compared with extended knee positions, suggesting higher metabolic cost and fatigue development in the flexed position. These differences may be related to angle-dependent changes in muscle architecture and microvascular function. However, the effects of knee joint angle on intramuscular blood flow and muscle deoxygenation during exercise remains unclear because of methodological limitations in assessing muscle perfusion. Power Doppler ultrasonography enables non-invasive and continuous evaluation of intramuscular blood flow by detecting Doppler signals generated by moving red blood cells. Therefore, the purpose of this study was to investigate the effects of knee joint angle on intramuscular blood flow and muscle deoxygenation in the vastus lateralis during fatiguing isometric knee extension exercise. We hypothesized that intramuscular blood flow would be greater and muscle oxygen saturation (StO_2) would be lower in the flexed than in the extended knee position.

METHODS: Seventeen healthy young male participants (19.6 ± 1.3 years) performed intermittent (5 s contraction, 5 s relaxation) and incremental isometric knee extensions at 30%, 40%, 50%, 60%, and 70% of maximal voluntary contraction (MVC) consecutively until task failure. Exercise was performed at flexed (90°) and extended (140° ; full extension = 180°) knee joint angles in randomized order. Intramuscular blood flow and StO_2 were measured using power Doppler ultrasonography and near-infrared spectroscopy, respectively, in the right vastus lateralis at mid-thigh.

RESULTS: Although MVC torque did not differ significantly between knee joint angles ($p = 0.139$), endurance time was significantly longer in the extended than in the flexed position ($p = 0.002$). There were no significant differences in intramuscular blood flow ($p = 0.105$) and StO_2 ($p = 0.292$) between knee joint angles at baseline. Δ intramuscular blood flow was significantly higher in the flexed than in the extended position from 30% to 60% of MVC ($p = 0.006$), and ΔStO_2 was significantly lower in the flexed than in the extended position above 30% of MVC ($p = 0.026$).

CONCLUSION: These findings indicate that knee joint angle influences changes in intramuscular blood flow and muscle deoxygenation during intermittent isometric knee extensions, suggesting that metabolic requirements differ according to mechanical and/or structural factors.

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Nonlinear Relationship Between Salivary Flow Rate and Secretory IgA Concentration in Athletes

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Abstract

INTRODUCTION: Salivary secretory immunoglobulin A (S-IgA) is a key component of mucosal immunity and is widely used as a biomarker of athlete condition because reduced S-IgA levels have been associated with an increased risk of upper respiratory tract infection. To account for the influence of saliva production, S-IgA is commonly expressed as salivary S-IgA secretion rate ($\mu\text{g}/\text{min}$), calculated from S-IgA concentration and salivary flow rate. However, the validity of this correction method across different salivary flow ranges remains unclear. This study investigated the relationship between salivary flow rate and S-IgA concentration in athletes.

METHODS: A total of 664 saliva samples were collected from 52 physically active individuals (15 males and 37 females). Unstimulated saliva was obtained within 30 minutes after waking using the passive drool method, and collection time was recorded. Salivary flow rate was calculated from sample volume and collection time. S-IgA concentration was determined using a commercially available ELISA kit (Secretory IgA ELISA Kit, Salivary, Salimetrics LLC)¹. Relationships between salivary flow rate and S-IgA concentration were evaluated using scatter plots and smoothing spline regression analysis. The study was approved by the Ethics Committee of Tokyo Medical and Dental University (No. 2019-031).

RESULTS: Mean salivary flow rate was 0.29 ± 0.28 mL/min, and mean S-IgA concentration was 445.3 ± 358.7 $\mu\text{g}/\text{mL}$. Scatter plot analysis revealed that S-IgA concentrations tended to be elevated in samples with low salivary flow rates. In contrast, S-IgA concentrations became relatively stable as salivary flow rate increased. Smoothing spline regression demonstrated a nonlinear relationship between salivary flow rate and S-IgA concentration, with distinct patterns observed in low- and high-flow regions.

CONCLUSION: The influence of salivary flow rate on S-IgA concentration appears to differ according to the flow-rate range. These findings suggest that comparisons based solely on salivary S-IgA secretion rate may not adequately account for flow-rate effects, particularly in low-flow samples. Stratification by salivary flow-rate range may improve the accuracy of S-IgA-based athlete condition assessment. Furthermore, the observed nonlinear relationship indicates that the conventional interpretation of salivary S-IgA secretion rate warrants reconsideration, as simple flow-rate correction may not fully reflect mucosal immune status across all salivary flow conditions.

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Breathing Better, Living Better? Functional and Patient-Reported Outcomes of Pulmonary Rehabilitation in Interstitial Lung Disease

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Abstract

INTRODUCTION: Interstitial lung diseases (ILDs) comprise a heterogeneous group of disorders, many of which involve immune-mediated mechanisms. Despite advances in pharmacological treatment, therapeutic options remain limited, and many patients continue to experience progressive functional decline and impaired quality of life. Pulmonary rehabilitation is recommended, but its effectiveness in routine clinical practice remains uncertain.

METHODS: A retrospective observational study was conducted in a cohort of 38 patients with interstitial lung disease who completed a pulmonary rehabilitation programme of combined exercise (aerobic, strength and breathing training) at our institution. Clinical data were collected through a review of electronic and paper medical records.

RESULTS: The cohort had a mean age of 67.6 years; 60.5% were male. The most frequent diagnoses were hypersensitivity pneumonitis (n=15) and idiopathic pulmonary fibrosis (n=8), followed by sarcoidosis (n=3) and connective tissue disease-associated ILD (n=2).

At baseline, 12 patients were receiving antifibrotic therapy, predominantly nintedanib (91.7%), either alone (41.7%) or combined with corticosteroids and/or immunosuppressive agents. Immunosuppressive therapy included mycophenolate mofetil (n=8), azathioprine (n=2) and methotrexate (n=1), while 6 patients received corticosteroid monotherapy. Overall, 22 patients (57.9%) were receiving oxygen therapy. Ambulatory oxygen therapy was prescribed in 21 patients, while 8 received long-term oxygen therapy (LTOT), with 7 patients receiving both modalities. Baseline pulmonary function showed a mild restrictive pattern with moderate diffusion impairment (mean FVC 72.7%, TLC 72.69%, DLCO 51.6%).

Analyses were performed using available paired pre- and post-rehabilitation data for each outcome. Regarding the 6-minute walk test (6MWT), patients maintained exertional desaturation in both assessments; however, 50% showed improved end-exercise oxygen saturation. Post-exertional dyspnoea (Borg scale) improved in 52.6% of patients (mean increase: 3 points), and walking distance increased in 63.2% (mean increase: 61.3 m).

Overall, 89.4% of patients demonstrated improvement in at least one patient-reported outcome measure, 65.7% in two or more scales. The most frequently improved outcomes were LCADL (53%; 17/32) and DASI (46%; 12/26), followed by the mMRC dyspnoea scale (41.6%; 15/36).

CONCLUSION: Pulmonary rehabilitation was associated with improvements in exercise capacity, dyspnoea, and health-related quality of life in a heterogeneous cohort of patients with interstitial lung disease. These findings support pulmonary rehabilitation as a key non-pharmacological intervention in the multidisciplinary management of ILD.

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Effects of Hip and Knee Flexion Angle Combinations on Hamstring Muscle Activity and Knee Flexion Torque During Maximal Voluntary Isometric Knee Flexion

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Abstract

INTRODUCTION: Hamstring strain injuries frequently occur during the late swing phase of sprinting (hip flexion angle: 40–50°, knee flexion angle: 20–30°). Although hamstring muscle activity and knee flexion torque during isometric knee flexion are known to be influenced by joint angles, previous findings on muscle activity remain inconsistent¹. Furthermore, despite the biarticular nature of the hamstrings, few studies have systematically examined combinations of hip and knee joint angles, and those that have been limited to extreme hip positions (0° and 90°), which may not reflect injury-prone conditions². This study aimed to clarify how combinations of hip and knee flexion angles influence hamstring muscle activity and knee flexion torque during isometric knee flexion.

METHODS: Twenty-three healthy males performed maximal voluntary isometric knee flexion in a side-lying position under nine conditions combining hip flexion angles of 0°, 45°, and 90° with knee flexion angles of 30°, 60°, and 90°. Knee flexion torque was measured using an isokinetic dynamometer, and muscle activity of the biceps femoris long head and semitendinosus was recorded using surface electromyography. Data were analyzed using two-way analysis of variance or nonparametric tests, depending on data normality, with statistical significance set at the 5% level.

RESULTS: Significant hip-by-knee interaction effects were observed for knee flexion torque and muscle activity in both muscles. Knee flexion torque was highest at 90° hip flexion and 30° knee flexion, whereas muscle activity of both muscles was highest at 0° hip flexion and 30° knee flexion.

CONCLUSION: This dissociation suggests that knee flexion torque is influenced not only by muscle activation but also by mechanical factors such as muscle length and moment arm. These findings may provide fundamental insight into the angle-dependent behavior of the hamstring and may inform the design of joint-angle-specific prevention and rehabilitation strategies for hamstring strain injuries.

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