1st International Symposium
Pathophysiology in Cardiometabolic Diseases

Valencia, Spain

25 - 26 June, 2026

ABSTRACTS BOOK

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25–26 June, 2026 · Valencia, Spain

Directors

Víctor M. Víctor, PhD
Milagros Rocha, PhD

MITOMETs
Grupo de Investigación Traslacional en Función Mitocondrial, Salud Cardiometabólica y Nutrición

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Welcome

Dear colleagues,

On behalf of the organizing and scientific committees, it is our great pleasure to welcome you to the 1st International Symposium on Pathophysiology in Cardiometabolic Diseases. Cardiometabolic disorders represent one of the greatest global health challenges of our time, driven by complex interactions between metabolism, inflammation, and mitochondrial dysfunction.

This symposium has been conceived as a multidisciplinary forum to integrate cutting-edge research spanning basic, translational, and clinical science. Particular emphasis has been placed on mitochondrial biology, immunometabolism, lifestyle interventions, and emerging therapeutic strategies targeting obesity, diabetes, and cardiovascular disease.

The abstracts presented in this book reflect the scientific excellence and diversity of the field, covering novel biomarkers, mechanistic insights, and intervention studies. We are especially proud to promote early-career researchers and foster collaboration across institutions and disciplines.

We warmly thank all speakers, participants, sponsors, and collaborators whose contributions have made this meeting possible. We hope that this symposium will stimulate discussion, inspire new ideas, and strengthen scientific networks.

Sincerely,

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Programme

Day 1, 25th June

09:00–09:30	Registration and Inauguration
Session 1	**Mitochondria, Oxidative Stress and Cardiometabolic Disease** Chair: Victor M. Victor / Milagros Rocha
09:30–09:55	Susana Rovira (FISABIO–University Hospital Doctor Peset) ***Immunometabolism at the Crossroads of Type 2 Diabetes and Diabetic Kidney Disease***
09:55–10:20	Marcello Pinti (University of Modena and Reggio Emilia) ***Mitochondrial DAMPs, immune system and cardiometabolic diseases***
10:20–10:45	Ruben Quintana (Cajal Institute-CSIC) ***Mitochondrial transfer: rewiring beyond the cellular edges***
10:45–11:15	**1 Selected Oral Presentations (3 × 8' + 2') – Young Investigators** O1. Julia Cacace *Circadian Disruption in Rotating Healthcare Workers Is Associated with Reduced Mitochondrial Function and Cardiorespiratory Fitness* O2. María Cuesta-Corral *Impact of mitochondrial transplantation on the cardiometabolic alterations associated with obesity: sex-comparative approach* O3. Remus Iulian Lupu *Effect of Rosmarinic Acid in Mitochondrias at Low Doses in Muscle Cells*
11:15–11:45	Coffee Break – Poster Session
Session 2	**Inflammation and Cardiometabolic Diseases** Chair: Milagros Rocha / Sandra López
11:45–12:10	Antonio Vidal-Puig (University of Cambridge) ***Adipose tissue expandability, lipotoxicity and the metabolic syndrome***
12:10–12:35	Juan Sastre (University of Valencia) ***Redox signaling in the pancreas in acute inflammation and obesity***
12:35–13:00	María Pelechá (FISABIO–University Hospital Doctor Peset) ***PCOS, periodontal disease and cardiovascular risk***

13:00–13:30	**2 Selected Oral Presentations (3 × 8’ + 2’) – Young Investigators** O4. Yara Cuesta Valero *Metabolic Control of Macrophage Activation by the Mitochondrial Enzyme SIRT4* O5. Sara Jimenez-Gonzalez *Contribution of mitochondrial oxidative stress to myocardial infarction-associated cardiac damage in the context of obesity* O6. Laura Perea Galera *Cambios Inflamatorios, Oxidativos e Inmunometabólicos asociados a la Terapia Hormonal de Afirmación de Género en Mujeres Trans: Implicaciones Cardiovasculares*
13:30–14:00	Poster Session
14:00–15:30	Lunch
15:30–16:30	**Plenary Lecture Lisardo Boscá (CSIC–Instituto de Investigaciones Biomédicas Sols-Morreale)** ***Tackling immunometabolism to assess atherogenic risks***

Session 3	**Microbiota and Cardiometabolic Diseases** Chair: Celia Bañuls / María Pelechá
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16:55–17:20	Neus Bosch-Sierra (FISABIO–University Hospital Doctor Peset) ***Impact of weight loss on gut microbiota and metabolomics in obesity***
17:20–17:50	**3 Selected Oral Presentations (3 × 8’ + 2’) – Young Investigators** O7. Jorge Álvarez Luis *Impaired Metabolic Plasticity in Epididymal Adipose Tissue Following High-Fat Diet: Phenotypic Divergence and Cardiometabolic Implications in a Murine Model* O8. Jaime López Bueno *Biomarcadores intestinales asociados a la fuerza y resistencia física en ratones G6PD de edad avanzada* O9. Mercedes Pardo-Tendero *NMR Metabolomics reveals early host–microbiota co-metabolism shifts in Cardiometabolic disease development*
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09:55–10:20	Omar Hernández-López (FISABIO-University of Valencia) ***Cardiorespiratory fitness as a predictor of metabolic, inflammatory and oxidative stress biomarkers***
10:20–10:45	Mari Carmen Gómez (University of Valencia) ***Mitochondrial remodelling in skeletal muscle underlies exercise-induced reversal of age-associated functional decline***
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LECTURES

Day 1, Session 1

L1

Immunometabolism at the Crossroads of Type 2 Diabetes and Diabetic Kidney Disase

Susana Rovira-Llopis (FISABIO–University Hospital Doctor Peset)

Diabetic kidney disease (DKD), the most common form of chronic kidney disease in type 2 diabetes (T2D), affects up to 50% of patients globally and markedly increases the risk of complications, including cardiovascular disease, heart failure, infections, reduced quality of life, and premature mortality. Immunometabolism—defined as the interplay between metabolic reprogramming and immune cell function—is increasingly recognized in T2D due to its role in glycaemic control, insulin resistance, and inflammation; however, its contribution to DKD onset and progression remains poorly understood.

Mitochondrial dysfunction in immune cells, including peripheral blood mononuclear cells (PBMCs), is a recognized hallmark of T2D and is particularly pronounced in subjects with DKD. We have recently studied PBMC immunometabolic profiles in T2D and DKD and found distinct metabolism-related transcriptomic signatures associated with systemic inflammation and mitochondrial dysfunction, reflecting coordinated alterations in key energy-regulating pathways alongside immune activation. Notably, CPT1A was consistently upregulated in DKD—validated by RT qPCR and external datasets—supporting its role as a feature of PBMC metabolic reprogramming, although with limited diagnostic discriminatory power. Our findings align with previous reports indicating that in T2D, immune cell inflammation is driven by impaired fatty acid oxidation and altered mitochondrial lipid handling—rather than by increased glycolysis—leading to enhanced Th17 -mediated inflammation.

Collectively, these findings support a model in which mitochondrial dysfunction and dysregulated fatty acid handling in PBMCs contribute to immunometabolic reprogramming, promoting a pro-inflammatory state that is intensified in the progression from T2D to DKD.

L2

Mitochondrial DAMPs, immune system and cardiometabolic diseases

Marcello Pinti (University of Modena and Reggio Emilia)

Mitochondria are key regulators of innate immunity beyond their roles in metabolism and apoptosis. Upon cellular stress or damage, mitochondrial damage-associated molecular patterns (mtDAMPs), including mitochondrial DNA (mtDNA), N-formyl peptides, ATP, and cardiolipin, are released into the cytoplasm or extracellular space, where they activate inflammatory pathways via receptors such as TLR9, NLRP3, and formyl peptide receptors.

In cardiometabolic diseases, chronic low-grade inflammation is a hallmark feature. Metabolic stressors impair mitochondrial integrity, promoting mtDAMP accumulation and release, which in turn exacerbates insulin resistance, endothelial dysfunction, and cardiac remodeling, creating a self-amplifying inflammatory loop.

We analyzed monocytes from 37 individuals with differing cardiovascular risk given their central role in innate immunity and atherosclerosis. mtDNA acted as a functional immunometabolic trigger: combined mtDNA and LPS stimulation increased TNF-α and IL-1β production and enhanced NF-κB activation. LPS stimulation also induced up to ~10-fold increases in cellular respiration, indicating tight coupling between inflammation and metabolic reprogramming. ddPCR confirmed increased mtDNA release under inflammatory conditions. Reanalysis of publicly available single-cell data from human atherosclerotic plaques identified distinct monocyte immunometabolic states. Monocytes from stable plaques showed higher oxidative phosphorylation, whereas those from vulnerable plaques exhibited increased inflammatory cytokine expression and alternative metabolic programs.

Overall, mtDAMP release contributes to immunometabolic dysregulation in cardiometabolic disease, suggesting that targeting mitochondrial homeostasis and mtDAMP signaling may offer therapeutic potential.

L3

Mitochondrial transfer: rewiring beyond the cellular edges

Ruben Quintana-Cabrera (Cajal Institute-CSIC)

The intercellular exchange of mitochondria has emerged as a mechanism capable of influencing mitochondrial composition and function, yet its physiological relevance and contribution to metabolic remodeling remain incompletely understood.

Here, we show that physiological mitochondrial exchange occurs between distinct cellular populations and is differentially regulated across cell types. This process depends on mitochondrial dynamics and transport, enabling recipient cells to internalize mitochondria. Once internalized, these organelles are selectively integrated or targeted for degradation, in parallel with coordinated changes in cellular morphology and function. Importantly, mitochondrial uptake reshapes the metabolic and respiratory activity of recipient cells. Unexpectedly, in certain contexts, the acquisition of exogenous mitochondria is associated with reduced respiratory performance despite increased mitochondrial content. The consequent metabolic rewiring is accompanied by transcriptional responses that drive extensive cellular reprogramming.

Collectively, our findings reveal the multifaceted impact of intercellular mitochondrial transfer, whereby distinct modes of organelle integration and remodeling shape cellular metabolism and physiology through previously underappreciated mechanisms.

Day 1, Session 2

L4

Adipose tissue expandability, lipotoxicity and the metabolic syndrome

Antonio Vidal-Puig University of Cambridge, Metabolic Research Laboratories, Wellcome-MRC Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, CB2 0QQ

The link between obesity and type 2 diabetes is clear on an epidemiological level, however the mechanism linking these two common disorders is not well defined. One hypothesis linking obesity to type 2 diabetes is the adipose tissue expandability hypothesis. The adipose tissue expandability hypothesis states that a failure in the capacity for adipose tissue expansion, rather than obesity per se is the key factor linking positive energy balance and type 2 diabetes. All individuals possess a maximum capacity for adipose expansion which is determined by both genetic and environmental factors. Once the adipose tissue expansion limit is reached, adipose tissue ceases to store energy efficiently and lipids begin to accumulate in other tissues. Ectopic lipid accumulation in non-adipocyte cells causes lipotoxic insults including insulin resistance, apoptosis and inflammation. In this lecture, we will address the mechanisms of adipose tissue expandability and briefly address the antilipotoxic role of BAT and the relevance of qualitative aspects of lipotoxicity in MASLD

L5

Redox signaling in the pancreas in acute inflammation and obesity

Juan Sastre (Department of Physiology, Faculty of Pharmacy & Food Sciences, University of Valencia, Spain)

Acute pancreatitis (AP) is an inflammatory process of the pancreatic gland that eventually may lead to a systemic inflammatory response, and in severe cases to death by multiple organ failure. Obesity is a well-established risk factor for increased severity and mortality in AP. However, the mechanisms by which obesity promotes severe AP are not elucidated yet.

We have found that the inflammatory cascade in AP is regulated by PGC-1α, which forms a complex with the NF-κB subunit p65. This inhibitory complex markedly restrains specifically the up-regulation of interleukin 6 that triggers pulmonary inflammatory infiltrate and damage.

Notably, obesity causes marked PGC-1α deficiency in the pancreas promoting pulmonary damage. Furthermore, over the course of AP p53 drives necroptosis of acinar cells via downregulation of sulfiredoxin, PGC-1α, and peroxiredoxin 3. In addition, we have identified a neutrophil-driven immune–metabolic pathway related to itaconate that protects against ferroptosis during pancreatic inflammation. Through paracrine transfer via the SLC13A3 transporter, myeloid-derived itaconate protects pancreatic acinar cells from ferroptosis by sustaining NRF2-dependent antioxidant responses. Obesity disrupts this protective axis by suppressing ACOD1 expression in infiltrating neutrophils, which limits itaconate production and weakens NRF2-driven redox defenses, leading to xCT–GPX4 downregulation and increased lipid peroxidation in the pancreas of obese mice with pancreatitis.

In conclusion, PGC-1α deficiency, and p53-driven necroptosis decisively contribute to a severe outcome in AP, particularly in obesity. Furthermore, neutrophil-derived itaconate is a key modulator of ferroptosis susceptibility, and its related immune cell metabolism may be a critical determinant of obesity-associated severity in acute pancreatitis.

L6

PCOS, periodontal disease and cardiovascular risk

María Pelechá Salvador (Grupo de Investigación MITOMETs, Fundación Fisabio (Valencia, España))

Polycystic ovary syndrome (PCOS) is a complex multisystem disorder characterized by chronic low-grade inflammation, oxidative stress, insulin resistance, and increased cardiovascular risk. Emerging evidence suggests an association between PCOS and periodontal disease (PD); however, the biological mechanisms linking periodontal inflammation to cardiometabolic dysfunction remain poorly understood, particularly during early, reversible stages like gingivitis. Thus, the impact of periodontal inflammation on cardiovascular risk in women with PCOS must be evaluated.

Peripheral blood leukocytes act as an integrative cellular model, serving as metabolic sensors that continuously integrate inflammatory, hormonal, and oxidative signals while actively contributing to vascular dysfunction and atherogenesis. By evaluating circulating immune cells, inflammatory mediators, oxidative stress, endoplasmic reticulum (ER) stress, inflammasome activation, and leukocyte–endothelial interactions, we explored the molecular pathways linking gingival inflammation to cardiometabolic dysfunction.

Women with PCOS exhibited a pro-inflammatory and pro-oxidative phenotype associated with early signs of endothelial dysfunction and subclinical atherosclerosis. The presence of gingival inflammation further amplified these alterations, promoting inflammasome activation, pro-apoptotic ER stress signalling, and enhanced leukocyte recruitment and adhesion to the vascular endothelium. Gingival inflammation was consistently associated with markers of systemic inflammation, cellular stress, and vascular dysfunction.

Collectively, these findings support the concept that PD acts as a systemic modulator of immune and vascular homeostasis in PCOS, exacerbating pathways involved in cardiometabolic risk. Oral health should therefore be considered an integral component of cardiovascular risk assessment and management in women with PCOS.

L7 Plenary Lecture

Tackling immunometabolism to assess atherogenic risks

Lisardo Boscá, Adrián Povo-Retana, Carlota Álvarez-Lucena Rodrigo Landauro
Instituto de Investigaciones Biomédicas Alberto Sols (CSIC-UAM), Madrid
Centro de Investigación Biomédica en Red en Enfermedades Cardiovasculares (CIBERcv)

Resident and organ-infiltrating macrophages under pathological conditions exhibit metabolic signatures that can be used to evaluate the inflammatory response associated with a given condition, ranging from cardiovascular diseases to cancer. Due to their immune and metabolic plasticity, macrophage function can be specifically modified by various extracellular factors. This includes cytokines, chemokines, and metabolic substrates, some of which are highly specific, such as itaconate derivatives and prostanoids. These interventions, in addition to altering macrophage function, constitute a complementary strategy for regulating their participation in inflammation and in the recruitment of other myeloid and lymphoid cells in an injured organ.

In this context, we have investigated the role of macrophages in the progression of atherogenesis, the control of plaque stability, and the assessment of their polarization phenotype within the atheroma. To do this, we used trimodal PET/CT molecular imaging and constructed metabolomic and fluxomic maps that provide a comprehensive view of macrophage and plaque fate.

By using different radiotracers, these studies have allowed us to develop new strategies to evaluate the activation status of atheromas, as well as to stabilize atherogenic lesions using specific metabolic approaches for activated macrophages and, in this way, to prevent plaque destabilization and the occurrence of adverse cardiovascular lesions, from infarction (tissue necrosis in the heart), ictus (cerebrovascular stroke in the brain), or claudication (ischemic arterial leg obstruction by athero-thrombi).

Day 1, Session 3

L8

Targeting gut microbiota dysbiosis and inflammation: nutraceutical strategies in metabolic syndrome

Teresa Vezza (University of Granada)

Metabolic syndrome is a major global health challenge characterized by obesity, insulin resistance, dyslipidemia, chronic low-grade inflammation, endothelial dysfunction, and impaired intestinal barrier function. Increasing evidence identifies the gut microbiota as a key player in the pathogenesis of these interconnected disorders, highlighting its potential as a therapeutic target.

Olive leaf extract (OLE), a rich source of bioactive phenolic compounds, has emerged as a promising nutritional strategy for improving cardiometabolic health. Evidence from experimental models of diet-induced obesity demonstrates that OLE attenuates weight gain, improves glucose and lipid homeostasis, reduces inflammatory responses, and restores endothelial function. These effects are accompanied by enhanced intestinal barrier integrity and significant modulation of gut microbial communities, including the enrichment of bacterial taxa associated with metabolic health.

Mechanistic studies further reveal a central role for the gut microbiota in mediating these benefits. Fecal microbiota transplantation experiments show that microbiota shaped by OLE partially transfers metabolic and vascular protection to recipient animals. Complementary studies in germ-free mice provide additional evidence supporting the contribution of host–microbiota interactions to the observed effects.

Emerging clinical data also support the beneficial impact of olive-derived phenolic compounds on metabolic and inflammatory parameters in individuals with cardiometabolic alterations.

Collectively, these findings provide novel insights into the microbiota-dependent mechanisms underlying the health-promoting effects of olive phenolics and position OLE as a promising nutritional approach for the prevention and management of metabolic syndrome.

L9

Impact of weight loss on gut microbiota and metabolomics in obesity

Neus Bosch-Sierra (FISABIO–University Hospital Doctor Peset)

Obesity is a chronic condition linked to gut microbiota dysbiosis and widespread metabolic disruption. Weight loss interventions — including dietary modification, intermittent fasting, and bariatric surgery — differentially reshape both the gut microbial ecosystem and the host metabolomic profile, with effects that depend on the nature and intensity of the intervention rather than on the magnitude of weight loss alone.

At the metabolomic level, weight loss consistently reduces circulating branched-chain amino acids (BCAAs) and aromatic amino acids, both established markers of insulin resistance. Lipid metabolism is also markedly altered, with reductions in sphingomyelins, ceramides, and saturated free fatty acids, alongside changes in lysophosphatidylcholines and acylcarnitines reflecting improved mitochondrial fatty acid oxidation. TCA cycle intermediates such as succinate, typically elevated in obesity, tend to decline following effective interventions.

Regarding microbiota-derived metabolites, non-surgical strategies consistently reduce trimethylamine N-oxide (TMAO) and, in certain approaches such as intermittent fasting, lower lipopolysaccharide (LPS) levels. Evidence on short-chain fatty acids (SCFAs) remains heterogeneous, modulated by dietary fiber content and individual microbiota composition. Bariatric surgery induces the most sustained changes, including marked reductions in LPS and increases in secondary bile acids.

Nevertheless, critical gaps remain. The extent to which observed microbial shifts translate into clinically meaningful outcomes, and how changes across microbial taxa functionally interact with one another, are still poorly understood. Furthermore, other questions remain to be addressed, for instance, how the integration of metagenomics and metabolomics may help disentangle the specific contribution of the gut microbiota to the metabolomic landscape observed after weight loss interventions.

Day 2, Session 4

L10

Innovations in Mitochondrial Research: Exploring Exercise-Induced Mitochondrial Adaptations in Skeletal Muscle

Pablo M. García-Roves (Department Physiological Sciences, University of Barcelona, Barcelona, Spain
Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain
CIBER-OBN, Spain)

Skeletal muscle mitochondrial respiratory capacity is a key determinant of athletic performance and is enhanced by diverse exercise modalities, with intensity and training load acting as critical modulators. High-resolution respirometry (HRR), combined with the substrate–uncoupler–inhibitor titration (SUIT) protocol, enables detailed characterization of mitochondrial states, including LEAK, oxidative phosphorylation (OXPHOS), and electron transfer (ET). Recent advancements integrating HRR with fluorescence and potentiometric sensors allow simultaneous real-time assessment of mitochondrial membrane potential, hydrogen peroxide (H_2O_2) production, ATP synthesis, and coenzyme Q (CoQ) redox dynamics.

Building on prior validation that CoQ2 can be used as a Q-mimetic without interfering with measurements in permeabilized fibers, this study integrates or first time HRR, membrane potential, and CoQ redox state analyses to investigate exercise-induced mitochondrial adaptations. Results show that both acute and chronic aerobic exercise produce modest increases in mitochondrial respiration in mouse extensor digitorum longus muscle. However, mitochondrial membrane potential and ETS-reactive CoQ redox state remain stable across respiratory conditions after chronic aerobic exercise training. These findings suggest that mitochondrial redox control is tightly regulated despite functional adaptations in respiration. However, we do observe some differences after and acute bout of exercise. We will be presenting the potential contribution of mitochondrial dynamics and supercomplex organization to further elucidate exercise-induced bioenergetic remodelling.

L11

Cardiorespiratory fitness as a predictor of metabolic, inflammatory and oxidative stress biomarkers

Omar A.Hernández-López (FISABIO-University of Valencia)

A sedentary lifestyle is associated with low cardiorespiratory fitness (CRF), a condition that increases the risk of cardiometabolic disease and all-cause mortality regardless of sex, age or ethnicity. Since the 1950s, the central role of physical exercise in the prevention and management of these conditions has been well established. However, changes associated with modern lifestyles have contributed to a progressive decline in physical activity levels worldwide.

Our findings show that even in apparently healthy young adults without established cardiometabolic disease, low CRF is associated with greater insulin resistance, systemic inflammation and oxidative stress, whereas individuals with good CRF exhibit a more favourable metabolic profile.

In type 2 diabetes (T2D), our research further indicates that, despite adequate glycaemic control and treatment with contemporary glucose-lowering therapies, including GLP-1/GIP-based therapies, low CRF is associated with impaired mitochondrial bioenergetics, increased oxidative stress, reduced metabolic flexibility and a more adverse cardiometabolic profile, including greater atherogenic risk, compared with individuals with T2D who exhibit adequate CRF levels.

Taken together, these findings support CRF as a key clinical and functional biomarker for the prevention and prognosis of chronic non-communicable diseases and highlight the value of investigating its associations with biochemical, metabolic and molecular biomarkers.

L12

Mitochondrial remodelling in skeletal muscle underlies exercise-induced reversal of age-associated functional decline

Mari Carmen Gómez (University of Valencia)

Loss of skeletal muscle mass and strength are common manifestations of frailty in older people and are linked to reduced quality of life. However, whether mitochondria are mechanistically linked to frailty and how physical activity, or lack thereof, is involved in age-related functional decline are still unknown. We report that exercise-induced improvements in functional capacity, including reduced frailty in old mice, are dependent on mitochondrial adaptations in skeletal muscle at structural, enzymatic, and functional levels. Our preclinical study included a healthy aging mouse line, a transgenic model of robustness, and a muscle-specific mitochondrial-deficient mutant mice, allowing us to assess both mitochondrial plasticity with aging and the necessity of intact mitochondrial function for exercise-induced adaptations. These findings were corroborated by a cross-sectional human study examining the relationship between skeletal muscle mitochondrial function, age, and physical capacity. We analyzed biopsies from 30 donors (men and women, aged 17-99 years) stratified into young and older adults with varying functional statuses.

Our results indicate that mitochondrial dysfunction in skeletal muscle is associated with the decline in locomotor muscle function in the elderly, highlighting the potential role of exercise or habitual physical activity in mitigating this phenotype.

Notably, we demonstrate that skeletal muscle mitochondria maintain plasticity during aging in mice and humans, and that this preserved adaptability can be leveraged to improve muscle performance and overall functional capacity.

Day 2, Session 5

L13

Dietary measures that reduce cardiovascular risk

Katherine García Malpartida (Valencia Clinical University Hospital)

Dietary interventions represent one of the most effective strategies for cardiovascular disease prevention. Evidence accumulated over the last decades indicates that cardiovascular risk depends more on the quality of foods and nutrients consumed than on total fat intake alone. Large prospective studies, including the Nurses' Health Study, have demonstrated that higher consumption of polyunsaturated fatty acids is associated with a lower risk of coronary heart disease, whereas trans-fat intake significantly increases cardiovascular risk.

Among dietary patterns, the Mediterranean diet has the strongest scientific support. It is characterized by a high intake of fruits, vegetables, legumes, whole grains, nuts, and extra-virgin olive oil, together with moderate consumption of fish and limited intake of processed meats and ultra-processed foods. Randomized clinical trials such as PREDIMED have shown an approximately 30% reduction in major cardiovascular events among individuals adhering to this dietary pattern.

Key dietary interventions include replacing saturated and trans fats with unsaturated fats derived from vegetable oils, nuts, seeds, and fatty fish; increasing dietary fiber intake through fruits, vegetables, legumes, and whole grains; reducing the consumption of sugar-sweetened beverages and ultra-processed foods; and limiting sodium intake to improve blood pressure control.

From a pathophysiological perspective, these interventions improve lipid profiles, reduce chronic low-grade inflammation, enhance insulin sensitivity, preserve endothelial function, and slow the progression of atherosclerosis. Collectively, adherence to healthy dietary patterns constitutes a cost-effective intervention with a cardiovascular benefit comparable to that achieved by several established pharmacological preventive strategies.

L14

PRESENTE Y FUTURO DE LOS ANÁLOGOS DE INCRETINAS EN DIABETES Y OBESIDAD

Rosa Casañ (University Hospital Doctor Peset)

Las terapias basadas en incretinas han transformado el manejo de la diabetes tipo 2 y la obesidad, logrando un control glucémico superior y una pérdida de peso significativa.
Además de sus efectos metabólicos, reducen drásticamente el riesgo de eventos cardiovasculares graves y protegen la función renal en pacientes crónicos. También producen beneficios en condiciones asociadas como la apnea del sueño y la enfermedad hepática.

Los mecanismos de acción van siendo más complejos cada vez, incluyendo agonistas selectivos del receptor de GLP-1 (mono-agonistas), como Dulaglutide, Semaglutide u Orfoglipron, así como agonistas duales GLP-1 y GIP como Tirzepatide o GLP-1 y glucagón como Survodutide y triples agonistas, como Retatrutide.

El agonismo de GIP aporta un efecto sinérgico en el peso, ya que la señalización del receptor de GIP en las neuronas GABAérgicas del sistema nervioso central media una supresión adicional de la ingesta de energía y una mayor pérdida de peso, independiente de los receptores de GLP-1.
El agonismo del Receptor de Glucagón puede elevar el gasto energético, estimular la lipólisis (quema de grasas) y aumentar la oxidación de ácidos grasos hepáticos. De ahí su especial efecto sobre la enfermedad metabólica hepática.

La amilina se co-secreta con la insulina y se utiliza en combinaciones (como CagriSema). Inhibe la secreción de glucagón y retrasa el vaciamiento gástrico. Hay nuevos mecanismos de acción como el Agonismo sesgado (Biased Agonism), y los antagonistas del receptor de GIP. Estos fármacos han sido clásicamente inyectables, pero cada vez más los tendremos en formulaciones para vía oral.

L15

Exercise, Mitochondria and Redox Signaling

Felipe Isidro (IICEFS)

La ponencia “Exercise, Mitochondria and Redox Signaling” plantea el ejercicio físico como una intervención biológica dosificable, capaz de modular funciones mitocondriales concretas en el contexto de la diabesidad y el envejecimiento.

El punto de partida es diferenciar entre el estrés oxidativo crónico, persistente y desregulado, característico de muchas enfermedades cardiometabólicas, y la señalización redox aguda, transitoria y adaptativa inducida por una dosis adecuada de ejercicio. El ejercicio no evita todo estrés biológico; lo convierte en información útil para la célula.

La mitocondria se presenta no solo como una “batería energética”, sino como un sensor e integrador metabólico implicado en la señalización redox, la inflamación, la sensibilidad a la insulina, el uso de sustratos, la respiración mitocondrial y la resiliencia celular.
Desde esta perspectiva, no todas las dosis entrenan la misma mitocondria. El ejercicio cardiorrespiratorio favorece especialmente la biogénesis mitocondrial y la capacidad oxidativa; los estímulos de alta intensidad pueden potenciar la señalización metabólica, la respiración mitocondrial y el remodelado funcional; y el entrenamiento de fuerza preserva masa muscular, superficie metabólica, captación de glucosa, calidad muscular y reserva funcional.

El bloque final traslada esta biología a la prescripción clínica: definir el objetivo, seleccionar ejercicios, organizar estímulos, ajustar frecuencia, intensidad, volumen, recuperación, progresión, tolerancia y carácter del esfuerzo. La idea central es que la mitocondria no responde al nombre del ejercicio, sino a la señal que genera una dosis concreta en un paciente concreto.

ORAL PRESENTATIONS

Day 1, Session 1 at 10:45h

O1

Circadian Disruption in Rotating Healthcare Workers Is Associated with Reduced Mitochondrial Function and Cardiorespiratory Fitness

Cacace Julia[1], Hermo-Argibay Alberto[1], García-García Inmaculada[1], Luna-Marco Clara[2], Hernández-López Omar[1], Víctor Víctor M[1,2], Rovira-Llopis Susana[1]

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Introduction: Rotating night-shift work is associated with increased cardiometabolic risk, including obesity, diabetes, and cardiovascular disease. The mechanisms linking circadian disruption to alterations in systemic metabolism and mitochondrial function remain unclear. This study compared fixed- and rotating-shift female healthcare workers to evaluate the impact of shift schedules on energy metabolism, cardiorespiratory fitness and cellular bioenergetics.

Methods: Nine hospital workers working fixed daytime shifts and 11 working rotating shifts that included night schedules were recruited. After an overnight fast, blood samples were collected at 8:00 AM and participants underwent anthropometric and bioimpedance measurements, indirect calorimetry and cycle ergometer VO_2max testing. Physical activity levels were evaluated using the International Physical Activity Questionnaire (IPAQ). Peripheral blood mononuclear cells were isolated to assess oxygen consumption rates by Seahorse and mitochondrial function and redox-related parameters by flow cytometry. Blood biochemical and antioxidant parameters were also analysed.

Results: No differences were observed in body composition between groups. Rotating-shift workers showed a trend toward lower phase angle ($p=0.09$). Slow-acting antioxidants were significantly reduced in rotating vs fixed shift workers ($p<0.01$). Despite comparable physical activity levels (IPAQ), the rotating-shift group had lower daily energy expenditure ($p<0.05$). Cardiorespiratory fitness parameters (VO2max and ventilator thresholds 1 and 2) were also reduced in rotating-shift workers (all $p<0.05$). Mitochondrial respiratory capacity and mitochondrial mass were significantly decreased in rotating-shift workers (all $p<0.05$).

Conclusion: Rotating night-shift work is associated with reduced systemic energy expenditure, impaired cardiorespiratory fitness, and decreased mitochondrial bioenergetic capacity in female healthcare workers, suggesting that chronic circadian disruption may compromise metabolic efficiency.

O2

Impact of mitochondrial transplantation on the cardiometabolic alterations associated with obesity: sex-comparative approach

Cuesta-Corral, María[1]; Montoro-Garrido, Alejandro[1]; Romero-Miranda, Ana[1]; Islas, Fabián[2]; Jiménez-González, Sara[1]; Cachofeiro, Victoria[1,3]; Martínez-Martínez, Ernesto[1,3]

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Obesity is characterized by excessive fat accumulation that impairs mitochondrial function, promoting cellular stress and contributing to metabolic and cardiovascular alterations associated with obesity. Mitochondrial transplantation (MT) has emerged as a promising strategy to restore mitochondrial function and attenuate obesity-related damage.

This study aimed to evaluate the potential beneficial effects of MT on obesity-associated cardiometabolic damage and to determine whether these effects differ between sexes.

Male (n=40) and female (n=40) Wistar rats were fed either a high fat diet (HFD group, 35% fat) or standard diet (CT group, 3.5% fat) for 10 weeks. Half of the animals of each group received weekly tail-vein injections of mitochondria (300µg of mitochondrial proteins in 125µl of PBS) or vehicle (125µl of PBS). Mitochondria were isolated from the hearts of healthy animals, their purity and functionality were confirmed.

HFD-fed rats exhibited an increased in body weight and inflammatory markers in white adipose tissue (osteopontin, CCL2 and TLR4 in males while TNFα, CCL2 and TLR4 in females). Interestingly, only male animals that received MT exhibited a smaller increase in body weight, without changes in caloric intake. However, MT improved in both sexes the increased inflammatory markers. At the cardiac level, MT was able to ameliorate alterations in both systolic and diastolic function. After 10 weeks, MT reduced collagen-I increased levels, endoplasmic reticulum stress activation (BiP, ATF6 and CHOP) and ROS accumulation in both sexes.

MT, thus, emerges as a potential therapeutic strategy against the cardiometabolic alterations associated with obesity in males and females.

O3

Effect of Rosmarinic Acid in Mitochondrias at Low Doses in Muscle Cells

LUPU, R.I., MARTÍNEZ-CANTÓ, M., OLASO-GONZÁLEZ, G., LÓPEZ-BUENO, J., RAZZAQ, N., GOMEZ-CABRERA, M.C., GAMBINI, J.

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BACKGROUND: Rosmarinic acid (RA) is a polyphenol found in various plants, especially in the Lamiaceae family, such as rosemary, sage, lemon balm, and basil, and especially in papermint. Mitochondria have cell-type-specific phenotypes, perform dozens of interconnected functions, and undergo dynamic and often reversible physiological recalibrations. One of the main current goals is to enhance mitochondrial function through various strategies, including nutritional ones.

METHODOLOGY: Mouse muscle cells (C2C12) were differentiated and treated with RA. Mitochondrial genes were measured by RT-qPCR, and proteins by Western blotting. Mitochondrial respiration was measured using Seahorse XF and Oroboros O2k. Mitochondrial biogenesis was analyzed by citrate synthase activity, MitoTrackerTM and electronic microscopy, finally the antioxidant role was observed by hydrogen peroxide production, catalase activity, and malondialdehyde (MDA) levels using HPLC. The potencial membrane of the mitochondria was measured by TMRM fluorochrome.

RESULTS: Mitochondrial genes were overexpressed compared to the control group using AR. Maximal respiration, complex 2 and 4, including ATP production, were higher with AR exposure. There was increased activity of the citrate synthase enzyme and intensity of fluorescence of MitoTracker and proteins such as PGC-1α and TFAM related to mitochondrial biogenesis. There was increased catalase activity, lower hydrogen peroxide levels, and lower MDA levels.

CONCLUSIONS: AR at nutritionally relevant doses (100 nM) increases mitochondrial function, mitochondrial biogenesis and acts as an antioxidant in differentiated mouse muscle cells.

Day 1, Session 2 at 13:00h

O4

Metabolic Control of Macrophage Activation by the Mitochondrial Enzyme SIRT4

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Mitochondria are central regulators of immunity through their roles in immunometabolism and inflammatory signaling. Sirtuins are NAD^+-dependent lysine deacylases that remove post-translational modifications from target proteins, thereby regulating their activity, stability, localization, and interactions. Because their enzymatic activity strictly depends on NAD^+ availability, sirtuins act as key metabolic sensors linking cellular energy status to adaptive gene expression and protein function. Among them, mitochondrial SIRT4 is unique in its ability to remove complex lysine acylations, including 3-hydroxy-3-methylglutarylation (HMG) and 3-methylglutaconylation (MGc), which originate from reactive intermediates of leucine catabolism.

The methylcrotonyl-CoA carboxylase complex (MCCC), a key enzyme in leucine degradation responsible for generating MGc-CoA, is itself modified by these acyl groups, suggesting a feedback mechanism coupling leucine catabolism to protein acylation and regulation via SIRT4. Loss of SIRT4 results in MCCC hyperacylation, impaired leucine catabolism and mitochondrial dysfunction. Because intracellular leucine is a potent activator of mTORC1 signaling, we hypothesized that SIRT4 regulates macrophage activation through modulation of leucine metabolism and mTORC1 activity.

To test this hypothesis, we generated SIRT4-deficient RAW264.7 murine macrophages using CRISPR/Cas9. SIRT4 knockout macrophages displayed a marked shift toward M1 polarization and enhanced secretion of proinflammatory cytokines. This effect was further enhanced under leucine-rich conditions, consistent with the established role of mTORC1 in promoting proinflammatory macrophage activation.

Together, our findings identify SIRT4 as a critical metabolic regulator linking leucine catabolism to macrophage activation via mTORC1 signaling. These results highlight SIRT4 as a potential therapeutic target for controlling metabolic inflammation and modulating innate immune responses in disorders characterized by altered nutrient sensing or mitochondrial dysfunction.

O5

Contribution of mitochondrial oxidative stress to myocardial infarction-associated cardiac damage in the context of obesity

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Obesity is a major risk factor for myocardial infarction (MI), one of the leading cardiovascular morbidity and mortality worldwide. Mitochondrial oxidative stress has been identified as a key mediator of cardiac damage in both obesity and MI. However, its contribution to cardiac injury in the coexistence of both conditions remains poorly understood.

Male Wistar rats were fed a high-fat diet (HFD; 35% fat) for 10 weeks. At week 6, MI was induced by ligation of the left anterior descending coronary artery (HFD-MI). During the following 4 weeks, the animals received either vehicle or the mitochondrial-targeted antioxidant MitoQ (MQ; 200 µM/kg/day). Rats fed a standard diet (3.5% fat) and subjected to sham surgery were used as controls (CT).

Obese-infarcted rats showed increased body weight and adiposity, accompanied by cardiac hypertrophy and impaired cardiac function. MitoQ treatment attenuated mitochondrial oxidative stress and improved cardiac function despite persistent obesity or cardiac hypertrophy. This improvement was associated with reduced cardiac fibrosis and the prevention of increased levels of collagen I and profibrotic mediators observed in HFD-MI animals. In addition, MitoQ preserved mitochondrial homeostasis by improving mitochondrial respiratory complexes, mitochondrial dynamics, and calcium-handling proteins dysregulation. These effects were further accompanied by attenuation of cardiac endoplasmic reticulum stress activation and prevention of increased galectin-3 levels.

These findings identify mitochondrial oxidative stress as a key driver of cardiac damage associated with the coexistence of MI and obesity. Thus, targeting mitochondrial oxidative stress may represent a promising therapeutic strategy to attenuate cardiac injury in this high-risk clinical setting.

O6

Cambios Inflamatorios, Oxidativos e Inmunometabólicos asociados a la Terapia Hormonal de Afirmación de Género en Mujeres Trans: Implicaciones Cardiovasculares

Perea Galera, Laura[1]; Hermenejildo Bello, Jonathan[1]; Fernández Collazo, Pablo[1]; Cacace, Julia[1]; Ferrer Martínez, Juan Emilio[1]; Flores Troncoso, Paola[1]; Rubio Puchol, Olalla[1]; Morillas Ariño, Carlos[1]; Pelechá Salvador, María[1]; López Domènech, Sandra[1]; Rocha Barajas, Milagros[1]

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INTRODUCCIÓN: La terapia hormonal de afirmación de género (THAG) en mujeres trans (MT) se asocia a modificaciones metabólicas e inflamatorias que podrían favorecer el desarrollo de aterosclerosis. Sin embargo, los procesos moleculares que subyacen a estas alteraciones permanecen poco caracterizados. En este contexto, la activación y adhesión de los leucocitos al endotelio vascular desempeñan un papel fundamental.

OBJETIVO: Evaluar el impacto de la THAG sobre la interacción leucocito-endotelio y los mecanismos inflamatorios, oxidativos y metabólicos implicados en la aterogénesis.

MATERIALES Y MÉTODOS: Estudio observacional en MT al inicio y tras 3 meses de THAG con estradiol y antiandrógenos según guías clínicas. Se evaluaron parámetros clínicos y bioquímicos, y se aislaron neutrófilos para estudiar la interacción leucocito-endotelio, producción de especies reactivas de oxígeno (ROS), función mitocondrial y la expresión génica de marcadores proinflamatorios, además de niveles de antioxidantes sistémicos.

RESULTADOS: Se incluyeron 12 MT (27,8 ± 10,2 años). A los 3 meses no se observaron cambios en el perfil bioquímico, excepto un aumento de linfocitos circulantes. A nivel intracelular, se evidenció un incremento de la masa mitocondrial y de ROS mitocondriales en neutrófilos. No se observaron diferencias significativas en la adhesión leucocito-endotelio, la expresión de marcadores proinflamatorios ni los niveles de antioxidantes sistémicos.

CONCLUSIÓN: La exposición temprana a THAG en MT no altera significativamente el perfil metabólico ni la interacción leucocito-endotelio. Sin embargo, el aumento de linfocitos circulantes y los cambios mitocondriales en neutrófilos sugieren una reprogramación inmunometabólica precoz que podría preceder a la aparición de alteraciones inflamatorias y vasculares.

AGRADECIMIENTOS: Este estudio ha sido financiado por PI25/01841, FI23/00141, CD23/0006, CM24/00261 del ISCIII; CIPROM/2022/32, CIGRIS/2021/112, CIGRIS/2022/172, CIGRIS/2024/070, Beca Investigación Senior 2025 y EU-Horizonte Europa (HORUS-nº101136516).

Day 1, Session 3 at 17:20h

O7

Impaired Metabolic Plasticity in Epididymal Adipose Tissue Following High-Fat Diet: Phenotypic Divergence and Cardiometabolic Implications in a Murine Model

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Obesity is a chronic disease associated with comorbidities such as type 2 diabetes and cardiovascular dysfunction. Despite therapeutic advances, its global prevalence continues to rise, underscoring the need for lifestyle-based strategies capable of restoring metabolic plasticity. The Lifestyle Matters (LiMa) project investigates how non-pharmacological interventions—such as exercise and fasting—reshape metabolic homeostasis in a murine model. A central observation is the marked susceptibility of visceral white adipose tissue (vWAT) to persistent mitochondrial dysfunction following high-fat diet (HFD) exposure, even after overt phenotypic recovery. Using the vWAT-to-liver weight ratio, two divergent phenotypes—High vWAT (H-vWAT) and Low vWAT (L-vWAT)—were defined, reflecting different degrees of adipose tissue exhaustion and systemic adaptation.

To dissect the cellular mechanisms underlying these phenotypes, single-nucleus RNA sequencing (snRNA-seq) was employed to resolve the heterogeneity of adipose cell populations and transcriptional states. This analysis revealed coordinated alterations in adipocyte identity, immune–stromal communication, and mitochondrial gene programs that segregate H-vWAT and L-vWAT, suggesting distinct trajectories of tissue remodeling and metabolic resilience. Given the systemic nature of metabolic stress, these transcriptional signatures will next be integrated with forthcoming echocardiographic assessments to explore potential associations between adipose-derived molecular programs and early changes in cardiac structure or function. Together, this combined approach aims to establish mechanistic links between adipose tissue plasticity, whole-body metabolic homeostasis, and cardiometabolic health.

O8

Biomarcadores intestinales asociados a la fuerza y resistencia física en ratones G6PD de edad avanzada

J. López-Bueno[1], A. Gorgori-González[1], N. Razzaq[1], J. Gambini-Buchón, E. Tamayo-Torres[1], M. Martinez-Cantón[1], S.J. Soto-Rodríguez[1], R. I. Lupu[1], M.C. Gómez-Cabrera[1] y G. Olaso-González[1].

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OBJETIVO: Aunque el envejecimiento reduce la función neuromuscular, el microbioma intestinal modula activamente la capacidad física. Investigaciones previas identifican cepas específicas, como Veillonella atypica, que mejoran la resistencia, o Roseburia inulinivorans, que induce hipertrofia y aumenta la fuerza. El propósito de este estudio fue identificar nuevas firmas bacterianas predictoras de fuerza y resistencia en un modelo murino de robustez.

MÉTODOS: Se evaluaron ratones transgénicos viejos (22-24 meses) que sobreexpresan glucosa-6-fosfato deshidrogenasa (G6PD). Se registró la fuerza de agarre máxima (normalizada por peso, N) y la capacidad aeróbica en tapiz rodante (s). La taxonomía del ADN fecal se determinó por secuenciación masiva (ARNr 16S). Tras aplicar la transformación CLR, se jerarquizaron las correlaciones de Spearman positivas vinculadas al rendimiento.

RESULTADOS: El ecosistema intestinal reveló firmas específicas fuertemente asociadas a cada cualidad física. Para la fuerza, las mayores correlaciones correspondieron a un taxón de la familia Ruminococcaceae (r=0.818, p=0.004) y al género Monoglobus (r=0.770, p=0.013). En resistencia, los taxones más positivos fueron Erysipelotrichaceae (r=0.758, p=0.015), Lachnoclostridium (r=0.721, p=0.024) y Anaeroplasma (r=0.709, p=0.026). Una mayor abundancia de estos biomarcadores correlacionó sistemáticamente con un fenotipo neuromuscular superior.

CONCLUSIONES: El rendimiento físico en la vejez se asocia a nichos taxonómicos específicos. Aunque no establecen causalidad directa, estas correlaciones sientan bases metodológicas para futuras investigaciones dirigidas a aislar y administrar estas cepas, permitiendo evaluar su potencial terapéutico real sobre la función neuromuscular.

O9

NMR Metabolomics reveals early host–microbiota co-metabolism shifts in Cardiometabolic disease development

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Introduction
Cardiometabolic disease is considered a comorbidities-related disease, associated with hypertension, dyslipidemia, or type 2 diabetes. These comorbidities can coexist, increasing the risk of developing disorders associated with high mortality. This pattern involves host–microbiota co-metabolism and is often exacerbated by high-fat diets. Studying the metabolism involved and identifying specific biomarkers for early detection may be essential for patient management. The aim of this study is to identify potential subclinical early biomarkers through the analysis of metabolic changes during cardiometabolic disease development using NMR-metabolomics.

Methods
Thirty-two male and female Wistar rats (16 weeks old) were fed a high-fat and high-sucrose diet for 12 weeks to induce metabolic disorders and were randomly divided into four groups based on diet and sex. For clinical characterization of disease were included measurements of blood pressure, body weight, blood glucose, serum insulin, cholesterol, and triglycerides. In addition, ^{1}H-NMR was used to determine metabolomic profiles in blood and fecal samples, and statistical analyses were performed with SPSS and Matlab.

Results
High-fat feeding induced increases in body weight, arterial pressure, and glycaemia, indicating early stages of related cardiometabolic disease factors. Cholesterol alterations were observed in males, whereas females showed fewer biochemical changes. Metabolomics showed differences in metabolites related to different metabolic pathways, revealing host–microbiota co-metabolites disruptions.

Conclusion
This study indicates that gut-microbiota co-metabolism could modulate early cardiometabolic disease development and NMR-based metabolomics offers a non-invasive approach for sub-clinical detection.

Day 2, Session 4 at 10:45h

O10

Resistance Training Sustains Functional Ability in Aged Mice: Combined Effects of Harmol and Piceid

Gorgori-González A. [1], Soto-Rodríguez S. [1], Serna-de Prádenas J. [1], Lupu R. [1], Stromsnes K. [1], Tamayo-Torres E. [1], Martínez-Cantón M. [1], Razzaq N. [1], López J. [1], Carretero A. [1], Gambini J. [1], Olaso-Gonzalez G. [1], Gómez-Cabrera M.C. [1]*

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Mitochondrial dysfunction is closely linked to sarcopenia and frailty, making it a potential target for mitohormetic interventions aimed at preserving physical function during aging. Mitohormetic agents induce mild reversible stress that activates adaptive responses, improving mitochondrial resilience and function. This study evaluated whether resistance training and/or supplementation with the mitohormetic compounds harmol (H) or piceid (P) could attenuate age-related functional and mitochondrial decline in old mice.

Old male C57BL/6 mice (n = 63; 20.3 ± 0.1 months) underwent a 6-week intervention including resistance training and/or oral supplementation with harmol or piceid (100 mg/kg body weight). Animals were divided into six groups: sedentary-water (SW), trained-water (TW), sedentary-piceid (SP), trained-piceid (TP), sedentary-harmol (SH), and trained-harmol (TH). Functional performance was assessed before and after the intervention. Mitochondrial analyses included respiration in permeabilized muscle fibres and isolated mitochondria, mitochondrial membrane potential (ΔΨm), peroxide production, citrate synthase activity, and plasma oxidative stress markers (8-OHdG and MDA).

VO_2max declined with age in all groups, but this reduction was attenuated in trained mice, demonstrating a protective effect of resistance training and, to a lesser extent, harmol and piceid supplementation. No significant differences were detected in mitochondrial respiration, citrate synthase activity, ΔΨm, peroxide production, or MDA levels. However, plasma 8-OHdG levels were significantly lower in TH mice. Additionally, complex IV activity differed among trained groups in isolated mitochondria.

Resistance training was the main contributor to functional preservation in aged mice, while harmol showed modest effects on oxidative DNA damage and mitochondrial complex IV activity.

O11

Exercise Snacks Program Impact on Metabolic, Muscular and Endothelial Biomarkers in Sedentary Women

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Introduction: Sedentarism is a leading modifiable risk factor for cardiometabolic disease, affecting young sedentary women. Exercise snacks are brief structured sets of physical activity distributed throughout the day that emerged as a feasible strategy to interrupt prolonged sedentary periods. However, their molecular and vascular effects remain poorly studied.

Methods: Twenty-two women (11 physically active [PA], 11 sedentary; IPAQ-classified) were enrolled in the study. Sedentary participants completed g a daily exercise snack program (3 × 5 mins functional aerobic and resistance exercise) for 8 weeks. Anthropometric and biochemical variables (BMI, insulin, HOMA-IR, antioxidant capacity, 25-OH vitamin D), estimated VO2max (Åstrand-Ryhming step test), handgrip strength, and microvascular function (NIRS O2 resaturation) were assessed. Mitochondrial dynamics (MFN1, MFN2, OPA1, FIS1), mitophagy (PINK1, PARKIN), and autophagy (LC3B, BECLIN, p62) gene expression was quantified by qPCR in peripheral blood mononuclear cells (PBMCs). Leukocyte–endothelium interactions (velocity, rolling, adhesion) were evaluated under physiological and TNF-α-stimulated conditions.

Results: Post-intervention, women showed significant improvements in VO2max, handgrip strength, insulin sensitivity (HOMA-IR), antioxidant capacity, 25-OH vitamin D, and faster O2 re-saturation speed. MFN1, MFN2, OPA1, FIS1, and LC3B expression increased significantly, approaching the PA group values. Leukocyte–endothelium interactions improved, showing greater leukocyte rolling velocity and reduced adhesion under both physiological and pro-inflammatory (TNF-α) conditions.

Conclusion: Eight weeks of daily exercise snacks induced significant metabolic, microvascular, mitochondrial, and endothelial improvements in sedentary women, progressively aligning their functional and molecular profiles with those of trained athletes. These findings support exercise snacks as an effective, accessible preventive strategy for cardiometabolic health promotion.

O12

Impact of a multidomain community-based intervention on functional capacity and cardiometabolic health in vulnerable urban populations: preliminary results from the EU HORUS project

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Introduction
Lifestyle interventions based on nutrition and physical activity are known to improve cardiometabolic health. However, evidence regarding their effectiveness in socially vulnerable populations under real-world community settings remains limited. This study evaluated the impact of a multidomain community-based intervention on functional capacity, anthropometric, and cardiometabolic parameters in vulnerable neighbourhoods of Valencia, Spain.

Methods
A longitudinal study was conducted in participants from structurally vulnerable neighbourhoods included in the HORUS-Valencia pilot. The intervention combined rotating group workshops on physical activity, nutrition, and healthy lifestyles, together with community engagement activities, motivational interviewing, and digital support through the Wakamola App. Health assessments performed at baseline and after 9 months included fasting glucose, blood pressure, anthropometric measurements, body composition by bioimpedance, advanced anthropometry (circumferences and skinfolds), isometric knee extension strength and hand grip.

Results
After 9 months, systolic blood pressure, waist circumference, waist-to-height ratio (WHtR) and cervical and submandibular skinfolds decreased significantly, while fat mass showed a decreasing trend. However, no changes were found in BMI, fasting glucose, visceral fat or muscle mass. In addition, the isometric knee extension increased after the intervention, while hand grip remained constant.

Conclusions
The HORUS multidomain community-based intervention was associated with improvements in functional capacity and cardiometabolic parameters in vulnerable urban populations. These findings support the potential of integrated community lifestyle interventions to improve health outcomes in socially vulnerable settings.

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POSTER PRESENTATIONS

Poster Session

P1

Mitochondrial Dysfunction and Extracellular Vesicle Signaling in the Progression of Obesity-Related Metabolic Disease

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Obesity has become a global epidemic, significantly reducing quality of life and life expectancy while increasing the risk of cardiometabolic diseases. It is characterized by chronic inflammation and dysfunction in visceral white adipose tissue (vWAT), a key regulator of systemic metabolic homeostasis.

Our research demonstrates that, although lifestyle interventions can partially reverse metabolic alterations, obesity induces persistent mitochondrial dysfunction in vWAT, leading to a marked loss of tissue metabolic plasticity. This dysfunction contributes to systemic metabolic impairment by altering adipokine secretion, immune responses, and cellular stress pathways, ultimately impacting multiple organs involved in cardiometabolic regulation, including the liver, vasculature, and potentially the heart.

A central aspect of this process is the alteration in the composition and signaling capacity of extracellular vesicles (EVs), which act as critical mediators of inter-organ communication. EVs derived from vWAT may carry molecular signals that propagate metabolic dysfunction and inflammation to distal tissues, thereby contributing to the progression of cardiometabolic disease. Following their isolation from WAT, EVs are subjected to proteomic analysis to characterize the molecular signatures associated with impaired tissue plasticity and to assess their systemic impact. EVs are analyzed at distinct stages of obesity in mice: an early phase characterized by vWAT expansion, and a later stage marked by ectopic lipid accumulation, increased liver mass, and reduced vWAT, reflecting advanced metabolic deterioration.

This integrative approach aims to elucidate the dynamic crosstalk between insulin-resistant tissues and the endocrine mechanisms driving the progression of obesity toward cardiometabolic disease, highlighting EVs as potential biomarkers and therapeutic targets.

P2

Asociación entre trastornos psicológicos, alteraciones metabólicas y función mitocondrial en personas con obesidad

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Introducción
La obesidad y los trastornos psicológicos comparten mecanismos inflamatorios y metabólicos, aunque su impacto sobre la homeostasis celular sigue poco caracterizado. Este estudio evaluó si la ansiedad/depresión modula la relación entre metabolismo, función mitocondrial y calidad del sueño en personas con obesidad.

Métodos
Estudio transversal en 64 adultos con obesidad, divididos según la presencia (n=27) o ausencia (n=37) de trastorno psicológico mediante la Escala DASS-21. Se analizaron composición corporal, parámetros bioquímicos, respiración y función mitocondrial en PBMCs, calidad del sueño y adherencia a dieta mediterránea.

Resultados
El grupo con trastorno psicológico presentó mayores niveles de insulina y menor potencial de membrana mitocondrial, sin diferencias en composición corporal, perfil lipídico ni respiración mitocondrial. En este grupo, la serotonina se correlacionó inversamente con glucosa (r=−0,419; p=0,033) y con proteína C-reactiva (r=−0,447; p=0,022), y el potencial de membrana se asoció con el índice triglicéridos/glucosa (r=−0,900; p=0,037). En el grupo sin trastorno, la serotonina se asoció con la calidad del sueño (r=0,47; p=0,005) y la adherencia dietética con el cLDL (r=-0,378, p=0,036). La regresión logística mostró que mejor calidad del sueño (OR=0,713; IC95%: 0,554-0,918; p=0,002) y sexo masculino (OR=0,061; IC95%: 0,006-0,623; p=0,006) se asociaron con menor probabilidad de presentar trastorno, mientras que mayor adherencia a la dieta mostró la asociación contraria (OR=1,555; IC95%: 1,044-2,315; p=0,020).

Conclusiones
La presencia de trastorno psicológico en obesidad se asocia con un perfil metabólico menos favorable y alteraciones mitocondriales, junto con diferencias en las asociaciones entre variables metabólicas, inflamatorias y conductuales.

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P3

Efecto de los flavonoides polimetoxilados en el perfil metabolómico de mujeres con obesidad bajo dieta hipocalórica

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Introducción: Recientemente, los flavonoides polimetoxilados han despertado un creciente interés por sus efectos beneficiosos. Este estudio tuvo como objetivo analizar el impacto del consumo diario de 200 mL de zumo de naranja enriquecido con tangeretina, sinensetina y nobiletina, combinado con una dieta hipocalórica, sobre el perfil metabólico de mujeres con obesidad.

Materiales y métodos: Se realizó un estudio de intervención aleatorizado, doble ciego, en 36 mujeres con obesidad tipo I y II remitidas al Servicio de Endocrinología y Nutrición del Hospital Dr Peset. Las participantes se distribuyeron aleatoriamente en 2 grupos: uno recibió el zumo enriquecido (n=16) y el otro un zumo placebo (n= 20); y ambos siguieron una dieta con restricción calórica de 500 kcal/día. Se realizaron análisis bioquímicos y metabolómicos en suero, al inicio y final de la intervención. Asimismo, se evaluó la influencia del estado menopáusico (edad ≥ 45 años).

Resultados: Se observaron mejoras significativas en el peso corporal (-3%), la grasa visceral y el perfil lipídico en ambos grupos. A nivel metabolómico, el grupo que consumió el zumo enriquecido presentó una reducción en los niveles de ácido succínico, DMA, leucina e isoleucina, frente al placebo. En mujeres menopáusicas, únicamente se redujeron DMA e isoleucina. Estos metabolitos se correlacionaron positivamente con niveles de IMC, insulina, glucosa, HOMA-IR y triglicéridos al inicio del estudio.

Conclusión: La ingesta de flavonoides, junto con una dieta hipocalórica, mejoró el perfil metabólico de mujeres con obesidad, independientemente del estado menopáusico, mediante la modulación de metabolitos asociados a la regulación glucémica y lipídica.

Agradecimientos: PI24/01010, FI25/00110, CD23/0029 (ISCIII), CIGRIS/2024/070 (GV).

Palabras clave: Flavonoides polimetoxilados; obesidad; análisis metabolómico; mujeres; menopausia; riesgo cardiovascular

P4

Role of the Aryl Hydrocarbon Receptor in Blood Glucose and Lipid Levels

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Introduction
The Aryl Hydrocarbon Receptor (AhR) is a ligand-dependent transcription factor initially identified for its role in xenobiotic metabolism in response to environmental toxins. Beyond detoxification, AhR regulates multiple physiological processes, including neuronal and cardiac development, skin differentiation, and maintenance of pulmonary and gastrointestinal barrier integrity. In pathological contexts, AhR deficiency has been linked to protection against obesity and insulin resistance, as well as modulation of inflammatory responses. This study investigates the systemic role of AhR, focusing on glucose metabolism, lipid profile, and hematological homeostasis.

Methods
Glucose tolerance tests (GTT) were conducted, and glycated hemoglobin (HbA1c) and blood lipid levels were measured. Hematological parameters were also analyzed. Experiments included young and adult mice of both sexes.

Results
AhR-deficient mice showed improved glucose tolerance, with lower GTT curves, reduced AUC, and decreased HbA1c levels ($P < 0.05$). In males, AhR deficiency increased HDL cholesterol and triglycerides ($P < 0.05$; $P < 0.01$). In females, total cholesterol decreased while triglycerides increased ($P < 0.05$). Hematological analysis revealed sex-dependent differences: males had reduced neutrophils, monocytes, and eosinophils, with increased erythroid indices, whereas females showed higher white blood cell counts, lymphocytes, and monocytes, along with reduced neutrophil percentage and increased red blood cell parameters.

Conclusion
AhR plays a significant role in regulating glucose and lipid metabolism and influences hematological parameters in a sex-dependent manner, highlighting its potential as a therapeutic target in metabolic and immune disorders.

P5

ROS induced mitochondrial hormesis partially protects from SGAs mitochondrial toxicity and cardiovascular disease

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Introduction: The chronic intake of second-generation antipsychotic drugs (SGAs) has been shown to increase CVD risk. SGAs are lipophilic polar molecules that can accumulate in mitochondrial membranes and thus interfere with normal mitochondrial functions. Since mitochondrial dysfunction is a relevant event on CVD development, we evaluated the contribution of SGAs mitochondrial interference to the associated increased of CVD risk.

Methods: To that end, we tested the SGAs Olanzapine (Ola), that induces weight gain, and Aripiprazole (Ari), that does not, in Primary bovine aortic endothelial cells (BAEC) and in WT and PGC-1α knockout mice, a model of mitochondrial dysfunction.

Results: We found that both SGAs reduced mitochondrial respiration, but acutely, Ola triggered reactive oxygen species (ROS) production more significantly than Ari. This response to Ola led to the activation of adaptive responses, including increased antioxidant defenses, enhanced glycolytic flux and maintenance of mitochondrial volume, thus enabling redox and metabolic homeostasis. In contrast, Ari failed to activate these compensatory mechanisms. In fact, Ari long-term treatment suppressed stress responses and reduced metabolic plasticity, promoting more pronounced and sustained CV damage than Ola, particularly under conditions of mitochondrial dysfunction or dependence on oxidative metabolism.

Conclusion: These findings indicate that the interference with mitochondrial activity and oxidative stress, along with the capacity of the subject to activate hormetic responses, play a key role in the CVD risk associated with chronic SGA treatment.

P6

Cambios metabólicos y moleculares tras cirugía bariátrica: implicación de la función mitocondrial y el estrés oxidativo un año después de la intervención

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Introducción:
La cirugía bariátrica constituye una estrategia eficaz para inducir una pérdida de peso sostenida y mejorar el perfil metabólico en pacientes con obesidad refractaria a intervenciones conservadoras. Sin embargo, los mecanismos moleculares subyacentes, particularmente los relacionados con la función mitocondrial y el estrés oxidativo, aún no se conocen completamente

Metodología:
Se incluyeron pacientes con obesidad (IMC ≥35 kg/m²), de entre 18 y 65 años, sometidos a cirugía bariátrica. Antes de la intervención y a los 12 meses del seguimiento, se evaluaron parámetros antropométricos y bioquímicos, composición corporal (BIVA), marcadores inflamatorios, función mitocondrial y estrés oxidativo (SeaHorse, ELISA, citometría de flujo).

Resultados:
Se analizaron 51 pacientes, de los cuales el 76% eran mujeres, con una edad media de 48,8 ± 9,2 años e IMC basal de 38,3 ± 5,2 kg/m². Tras la cirugía se observó una pérdida ponderal del 26%, acompañada de una mejora significativa del perfil lipídico, con disminución de HbA1c, triglicéridos e insulino-resistencia, así como aumento del colesterol HDL. Además, se detectó una reducción significativa de marcadores inflamatorios (PCRu, C3 y homocisteína). La función mitocondrial mostró una mejora evidenciada por diferentes parámetros relacionados con la respiración basal, la capacidad de respuesta y la masa mitocondrial (MTG). A nivel oxidativo, se observó una disminución significativa del daño oxidativo en el RNA/DNA (8-OHdG).

Conclusiones:
Un año después de la cirugía bariátrica, los pacientes presentan una pérdida de peso sustancial acompañada de cambios metabólicos, observados en la mejora del estado mitocondrial, la reducción del estrés oxidativo y la inflamación sistémica.

Agradecimientos: PI24/01010 (ISCIII)

P7

Pomegranate Extract as a Nutritional Strategy to Mitigate Functional and Molecular Alterations Associated with Ageing

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Introduction: Ageing is a multifactorial biological process characterised by progressive functional decline, increased oxidative stress, chronic inflammation, and heightened vulnerability to frailty. In this context, natural bioactive compounds have gained increasing scientific attention due to their potential to modulate mechanisms involved in healthy ageing.

Objective: To evaluate the effects of pomegranate extract (PE; Pomanox® P30), rich in polyphenols and ellagitannins, on functional capacity, oxidative stress, apoptosis, reactive oxygen species production, and ageing-related molecular alterations in aged mice.

Methods: A multidimensional experimental study was conducted using male C57BL/6J mice. Animals were divided into three groups: young adult controls, aged controls, and aged mice supplemented with PE. The supplemented group received PE at a dose of 150 mg/kg/day for 12 weeks. Physical performance was assessed through tests evaluating motor coordination, strength, and endurance. Systemic and tissue oxidative stress, apoptosis-related markers and gene expression profiles were analysed in the cerebellum and cerebral cortex.

Results: PE supplementation reduced age-associated involuntary weight loss and preserved motor coordination in aged mice. Supplemented animals also showed improved performance in the inclined ladder test, suggesting enhanced neuromuscular function. At the molecular level, PE improved systemic redox balance, reduced lipid peroxidation and reactive oxygen species production, and downregulated cerebellar markers associated with inflammation, ageing, and apoptosis. These effects were more evident in the cerebellum than in the cerebral cortex.

Conclusions: PE supplementation showed geroprotective potential in aged mice, mainly by improving functional performance, enhancing resilience to oxidative stress, and contributing to cerebellar preservation during ageing.

P8

Skeletal Muscle Loss Induced by a Very-Low-Calorie Diet Is Associated with Early and Mid-Term Weight Regain

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INTRODUCTION: Very-low-calorie diets (VLCDs) induce substantial weight loss in obesity but are frequently followed by weight regain. This study investigated whether skeletal muscle loss during a VLCD is associated with early and mid-term weight regain.

MATERIALS AND METHODS: This prospective interventional study included 48 adults with obesity undergoing two 6-week VLCD cycles alternated with a 3-month hypocaloric diet. Body composition and rectus femoris muscle thickness (RFMT) were assessed by bioelectrical impedance analysis and ultrasound, respectively. Appendicular skeletal muscle mass index (ASMMI) and bilateral lower-limb muscle mass (BLMM) were calculated. Weight regain was defined as the increase in body weight at 3 and 6-months following diet completion.

RESULTS: VLCD induced marked weight loss and reductions in fat-free mass, skeletal muscle mass, ASMMI, BLMM, and RFMT (all $p < 0.001$). At 3 months, weight regain was positively associated with total skeletal muscle mass loss ($R^2 = 0.19$, $p = 0.002$), ASMMI loss ($R^2 = 0.30$, $p < 0.001$), and BLMM loss ($R^2 = 0.30–0.31$, $p < 0.001$). Similar but attenuated associations persisted at 6 months ($R^2 = 0.12–0.15$, $p < 0.05$). Hierarchical multiple regression models demonstrated that ASMMI independently explained 33.6% of early weight regain ($R^2 = 0.336$, $p < 0.001$) and 16.1% of mid-term weight regain at 6 months ($R^2 = 0.161$, $p = 0.016$), independent of age, sex, and baseline BMI.

CONCLUSIONS: Appendicular and lower-limb muscle mass loss during VLCD-induced weight loss emerged as major determinants of early and mid-term weight regain. These findings support muscle-preserving exercise and nutritional strategies during weight-loss interventions.

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P9

Urinary extracellular vesicles reveal immunometabolic signatures associated with chronic alcohol exposure

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Introduction: Chronic alcohol consumption induces metabolic, inflammatory and oxidative stress-related alterations associated with cardiometabolic dysfunction. Urinary extracellular vesicles (uEVs) represent a promising source of non-invasive biomarkers. This study evaluated the lipid and microRNA cargo of uEVs from patients with alcohol use disorder (AUD) to identify molecular signatures associated with immunometabolic dysfunction.

Methods: uEVs were isolated by ultracentrifugation from urine samples of clinically characterized AUD patients and healthy controls. Lipidomic profiling was performed using LC-MS/MS, while miRNA expression was analyzed by small RNA sequencing. Differential expression and pathway enrichment analyses identified metabolic and inflammatory alterations associated with chronic alcohol exposure.

Results: uEVs from AUD patients showed enrichment in fatty acyls and glycerophospholipids, together with reduced sphingolipid content. Increased levels of saturated and very long-chain fatty acids (22–24 carbons) were observed, suggesting lipid remodeling associated with inflammation and metabolic dysfunction. Network analysis revealed dysregulation of ceramide and sphingomyelin metabolism involving enzymes related to immune signaling and lipid homeostasis. miRNome analysis identified sex-dependent molecular signatures associated with IL6/STAT3, PI3K/AKT/mTOR signaling, autophagy, oxidative stress and immune-inflammatory pathways. Functional enrichment analyses showed overrepresentation of pathways related to kinase-mediated signaling, cellular stress response and inflammatory regulation.

Conclusions: uEVs reflect molecular signatures associated with alcohol-induced immunometabolic dysfunction, highlighting their potential as non-invasive biomarkers of systemic metabolic alterations linked to cardiometabolic risk.

P10

SLC25A51 Directs Macrophage Polarization by Regulating Mitochondrial NAD+ Homeostasis

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Macrophages are key players in innate immunity, and their polarization is tightly linked to metabolic rewiring. In vitro, macrophages primarily differentiate into two phenotypes: M1, pro-inflammatory cells that rely on glycolysis, and M2, anti-inflammatory cells that preferentially utilize oxidative phosphorylation (OxPhos). M1 activation is associated with depletion of nicotinamide adenine dinucleotide (NAD+), a cofactor essential for glycolysis, rendering these cells dependent on the NAD+ salvage pathway. In contrast, inhibition of de novo NAD+ synthesis from tryptophan impairs OxPhos, promotes glycolysis, and favors M1 polarization.

These findings suggest that NAD+ availability and intracellular compartmentalization are critical determinants of macrophage fate. Recently, SLC25A51 was identified as the mitochondrial NAD+ transporter, providing a direct link between mitochondrial NAD+ homeostasis and cellular metabolism. We observed reduced mitochondrial NAD+ levels during M1 differentiation, whereas M2 macrophages displayed increased mitochondrial NAD+ content. Manipulation of SLC25A51 expression confirmed its role in macrophage polarization. SLC25A51 silencing enhanced pro-inflammatory cytokine secretion and promoted M1 polarization, while its overexpression increased the expression of M2-associated markers, including arginase, and reduced inflammatory cytokine production. RNA-sequencing analysis of SLC25A51-overexpressing macrophages revealed a broad attenuation of the pro-inflammatory transcriptional program. Mechanistically, alterations in SLC25A51 expression modified the mitochondrial redox state, affecting the NADH/NAD+ ratio and mitochondrial reactive oxygen species (ROS) production, indicating that mitochondrial NAD+ transport regulates inflammatory responses through metabolic and redox remodeling.

Together, our results identify SLC25A51 as a key regulator of macrophage polarization and inflammatory activation, highlighting mitochondrial NAD+ transport as a potential therapeutic target in autoimmune, inflammatory, and cardiovascular diseases.

P11

microRNAs targeting PGC-1α in acute pancreatitis

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Introduction: Acute pancreatitis (AP) is an inflammatory disorder characterized by local and systemic complications, in which necroptosis has emerged as a key mechanism driving pancreatic acinar cell death and tissue injury. This caspaseindependent pathway, mediated by RIPK1, RIPK3, and MLKL, promotes inflammation through the release of damage-associated molecular patterns and is critically dependent on mitochondrial reactive oxygen species (ROS) generation. Mitochondrial antioxidant responses may counteract this process, with PGC-1α driving the expression of antioxidant genes such as Prx3 to limit mitochondrial ROS accumulation and protect acinar cells. In this context, microRNAs (miRs) have emerged as potential key regulators of cell death and inflammation in AP.

Methods: We investigated the role of miRNAs in necroptosis using a cerulein-induced AP mouse model. MicroRNA sequencing was performed at 7 and 24 hours after cerulein administration, and selected candidates were validated by RT–qPCR.

Results: MicroRNA sequencing at 7 and 24 hours after cerulein injection identified candidate miRNAs potentially involved in the regulation of PGC-1α and necroptosis. Among them, miR-128-3p showed a transient increase at 7 hours, displaying an inverse pattern with PGC-1α expression and suggesting a potential direct regulatory interaction.

Conclusions: Further studies are required to validate these findings and define the underlying mechanisms. Targeting miRNA-mediated pathways may offer novel therapeutic strategies to limit pancreatic injury in AP.

P12

Reprogramación inmunometabólica temprana inducida por terapia hormonal de afirmación de género en hombres trans: implicaciones proaterogénicas

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Introducción y objetivo: La terapia hormonal de afirmación de género (THAG) podría aumentar el riesgo cardiovascular en hombres trans (HT), aunque los mecanismos implicados siguen sin definirse completamente. La interacción leucocito-endotelio constituye un evento clave en las fases iniciales de la aterogénesis y está estrechamente regulada por inflamación, estrés oxidativo y metabolismo celular. El objetivo fue evaluar el impacto temprano de la THAG sobre la activación leucocitaria y el estado inmunometabólico en HT.

Métodos: Estudio observacional en HT que iniciaban THAG con testosterona transdérmica (2%). Se analizaron parámetros clínicos y bioquímicos antes y tras 3 meses de tratamiento. Se aislaron neutrófilos para ensayos de interacción leucocito-endotelio y se evaluó la producción de especies reactivas de oxígeno (ROS), función mitocondrial (potencial de membrana, masa y ROS mitocondriales) y expresión génica de marcadores proinflamatorios (NF-κB, JNK, TNF-α, IL-1β, IL-6, IL-18), junto con niveles sistémicos de antioxidantes.

Resultados: Se incluyeron 11 HT (20,3 ± 3,5 años). Tras 3 meses de THAG se observó un aumento significativo de insulina, HOMA-IR, PCRus, leucocitos y monocitos. A nivel funcional, se detectó un incremento de la masa mitocondrial y de la expresión de IL-1β en neutrófilos, asociado a menor velocidad de rodamiento y mayor adhesión leucocitaria.

Conclusiones: La exposición temprana a THAG induce un fenotipo proaterogénico caracterizado por activación leucocitaria, inflamación sistémica y resistencia a la insulina. Los cambios observados sugieren una reprogramación inmunometabólica y una alteración de la homeostasis mitocondrial que podría estar implicada en las etapas iniciales del proceso aterosclerótico.

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P13

Resveratrol Modulate Lipid Catabolism and Mitochondrial Function at Nutritionally Relevant Concentrations in C2C12 Cells

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Introduction: Polyphenols have attracted considerable interest due to their potential beneficial effects on metabolic health, mitochondrial function, and oxidative stress. However, many in vitro studies have investigated these compounds using high concentrations that are difficult to achieve through diet. Therefore, this study investigated whether nutritionally relevant concentrations of resveratrol could modulate lipid catabolism, mitochondrial respiration, and redox status in murine skeletal muscle C2C12 cells.

Methods: Differentiated C2C12 cells were treated with resveratrol at 1 nM, 10 nM, 50 nM, and 100 nM. Additionally, cells were treated with resveratrol or piceid alone or in combination with the androgen receptor inhibitor bicalutamide. Gene expression associated with fatty acid transport, β-oxidation, and antioxidant defense was evaluated using RT-qPCR, while mitochondrial respiration was assessed by Seahorse XF.

Results: Treatment with 10 nM resveratrol for 24 hours significantly increased the expression of genes related to lipid catabolism, including Ampk, Acsl, Cpt1, Cact, and Ech1, while Acc1 expression was reduced. Resveratrol also increased maximal respiration and spare respiratory capacity while decreasing proton leak. Furthermore, glutathione peroxidase expression increased and intracellular H2O2 levels decreased following resveratrol treatment. These effects were not observed in cells co-treated with bicalutamide, suggesting the involvement of intracellular androgen receptor-mediated pathways.

Conclusion: Resveratrol, at nutritionally relevant concentrations, increase lipid catabolism and mitochondrial respiration mediated by androgen receptor.

P14

El perfil de la microbiota intestinal en el modelo murino G6PD se asocia a la atenuación de la pérdida de función motora

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Objetivo
El estudio de la fragilidad y sarcopenia suele centrarse en el músculo esquelético, pero el eje intestino-músculo también influye. El ratón que sobreexpresa glucosa-6-fosfato deshidrogenasa (G6PD) es un modelo de robustez. El objetivo es evaluar el efecto de esta sobreexpresión sobre los cambios taxonómicos asociados a la edad y al estado funcional.

Material y métodos
Se extrajo ADN fecal de ratones Wild Type (WT) y G6PD jóvenes (WT=10, G6PD=14) y viejos (WT=14, G6PD=9). Su microbiota se analizó mediante secuenciación del ARNr 16S y transformación CLR. Funcionalmente, se cuantificó la fuerza de agarre (Grip strength) y la capacidad aeróbica (Treadmill).

Resultados
El análisis de componentes principales (PCA) reveló una trayectoria genotipo-dependiente: los WT mostraron distanciamiento espacial entre jóvenes y viejos, mientras los G6PD permanecieron agrupados independientemente de la edad, indicando una desviación del envejecimiento fisiológico. Taxonómicamente, los G6PD jóvenes presentaron una expansión prematura de Muribaculaceae y L. taiwanensis ($p<0.01$). Esta firma eudisbiótica correlacionó positivamente con la resistencia aeróbica ($R=0.589$; $p<0.001$), justificando su mejor rendimiento inicial. El envejecimiento en WT indujo colonización por Prevotellaceae NK3B31 (asociada a inflamación) y P. goldsteinii ($p<0.001$), lo cual no ocurrió en los G6PD. Como Prevotellaceae NK3B31 correlacionó negativamente con la fuerza ($R=-0.435$; $p=0.005$), su represión atenuó significativamente la pérdida de fuerza en G6PD viejos ($p=0.007$).

Conclusiones
La sobreexpresión de G6PD influye en el eje intestino-músculo induciendo una eudisbiosis temprana que aumenta la capacidad aeróbica y bloquea bacterias proinflamatorias, actuando como mecanismo protector que mitiga la pérdida de fuerza asociada a la edad.

P15

In Vitro Study of the AHR Pathway as a Molecular Target in Diabetic Retinopathy and Its Modulation by Ligands and Specific Inhibition

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Introduction
Diabetic retinopathy (DR) is a severe neurovascular complication driven by chronic hyperglycemia, oxidative stress, and hypoxia. The aryl hydrocarbon receptor (AHR) has emerged as a crucial metabolic regulator of redox homeostasis. Dietary AHR agonists, such as Pterostilbene (Pter) and Indole-3-carbinol (I3C), may exert cytoprotective effects by inducing detoxifying enzymes and modulating hypoxia-related pathways. This study aimed to evaluate the specificity of AHR pathway activation in retinal cells using these ligands and its reversal by selective inhibition.

Methods
Human retinal pericytes (HRP) and retinal pigment epithelial cells (ARPE-19) were cultured and seeded at $1.5x10^6$ in T75 flasks. Cells were treated with 10 µM of agonists (Pter or I3C), alone or in combination with the specific AHR antagonist CH-223191 (CH). Gene expression study of the AHR canonical pathway (AHR, ARNT, CYP1A1, CYP1B1) was quantified by RT-PCR to assess pathway activation.

Results
Both Pter and I3C significantly upregulated AHR, ARNT, and downstream xenobiotic enzymes such as CYP1A1 and CYP1B1 in both retinal cell lines. Co-treatment with the selective antagonist CH significantly reversed this effect. These findings demonstrate specific activation of the AHR pathway by both ligands.

Conclusion
Selective AHR activation by Pter and I3C induces a detoxifying response in retinal cells. AHR agonists may represent promising targeted therapies in early-stage DR.

P16

Empagliflozin Improves Vascular Function in Interlobar Renal Arteries in a Rabbit Model of Metabolic Syndrome

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Introduction
Cardiovascular disease remains the leading cause of mortality and is strongly associated with the increasing prevalence of metabolic syndrome (MetS), a condition that promotes vascular dysfunction. Our previous studies in a rabbit model of MetS have shown that nitric oxide (NO)–dependent vasodilation is preserved in the main renal arteries through compensatory mechanisms; however, it is still unclear whether similar adaptations occur in smaller intrarenal vessels such as interlobar arteries. Empagliflozin, an SGLT2 inhibitor, has been shown to rapidly reduce cardiovascular events, suggesting vascular benefits beyond glucose lowering. Therefore, this study evaluated the effects of empagliflozin on vascular function in interlobar arteries from a rabbit model of MetS.

Methods
Interlobar artery rings were isolated from New Zealand White rabbits, which were divided into three groups: Control, MetS induced by a high-fat, high-sucrose diet over 32 weeks and MetS + empagliflozin (25 mg/day orally for 8 weeks). Concentration–response curves to acetylcholine (ACh) and sodium nitroprusside (SNP) were performed to assess endothelium-dependent and independent vasodilation. In separate experiments, ACh response was evaluated in the presence of L-NAME.

Results
Empagliflozin improved endothelial and vascular dysfunction induced by MetS. Interestingly, L-NAME did not modify ACh response in Control and MetS arteries. However, L-NAME right-shifted the ACh concentration-response curve in MetS + empagliflozin. Furthermore, eNOS and p-eNOS expression in the endothelial layer were comparable across all experimental groups.

Conclusion
Empagliflozin improved vascular function in interlobar arteries from rabbits with MetS and restored NO contribution without changes in eNOS activation.

P17

Empagliflozin reverses vascular transcriptomic alterations associated with metabolic syndrome in rabbit carotid artery

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Introduction

Metabolic syndrome (SMet) is defined by the presence of multiple cardiometabolic risk factors and is associated with vascular dysfunction. Sodium–glucose cotransporter 2 inhibitors, such as empagliflozin (E), have demonstrated cardiovascular benefits. However, the molecular mechanisms underlying these effects in the carotid artery remain incompletely understood. Therefore, the aim of this study was to perform a transcriptomic analysis in this experimental model.

Methods

Carotid arteries were obtained from male New Zealand White rabbits assigned to three groups: control (C) (n = 4), MetS (M) (n = 5), and MetS treated with empagliflozin 25 mg/day orally for 8 weeks (E) (n = 5). Gene expression was analyzed using microarrays (GeneChip™ Rabbit Gene 1.0 ST Array), with RMA normalization and eBayes analysis ($p < 0.05$) using Transcriptome Analysis Console. Principal component analysis, functional enrichment using DAVID, and network analysis with ClueGO in Cytoscape were performed.

Results

83 genes were common between E vs. M and C vs. M comparisons, suggesting a reversal toward a control-like profile. Functional analysis revealed enrichment in MAPK signaling ($p = 0.0052$) and angiogenesis ($p = 0.0106$). Treatment with E reduced the expression of inflammatory genes (IRF7, PLCG2) and oxidative stress-related genes (NOX4), while increasing genes involved in mitochondrial function (MRPL11, TIMM8A). Collectively, these findings suggest a vasculoprotective effect mediated through modulation of inflammatory, oxidative, and metabolic pathways, consistent with mechanisms previously described for SGLT2 inhibitors.

Conclusion

Empagliflozin induces a phenotypic shift in the carotid artery toward a less pro-inflammatory and metabolically more efficient state.

P18

Efectos de la ranolazina sobre los receptores adrenérgicos vasculares en la aorta de conejo

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Introducción:
Se han propuesto diferentes mecanismos de acción para la ranolazina (Rn). En este estudio evaluamos la posible implicación de receptores adrenérgicos, específicamente α1, α_2, β_2 y β_3, como mediadores de los efectos vasculares de la Rn.

Métodos:
Se utilizaron segmentos de aorta de conejo. La estimulación eléctrica de campo (EFS; 2, 4 y 8 Hz) indujo contracciones dependientes de la frecuencia que fueron abolidas por tetrodotoxina, prazosina o guanetidina (10^{-6} M), confirmando el origen neural de las respuestas. Los efectos de la Rn se evaluaron incubando con concentraciones de 10^{-7}–10^{-4} M y estimulación de 4 Hz. La participación de los receptores α_1-, α_2-, β_2- o β_3-adrenérgicos se analizó utilizando antagonistas específicos (10^{-6} M): prazosina (α_1), yohimbina (α_2), butoxamina (β_2) y SR59230A (β_3). Posteriormente, se realizaron estimulaciones eléctricas en presencia de Rn. La expresión de los receptores α_1-, α_2-, β_2- y β_3-adrenérgicos se determinó mediante Western blot.

Resultados:
La Rn disminuyó el efecto contráctil inducido por la estimulación nerviosa adrenérgica. En presencia de prazosin o yohimbina, la respuesta se redujo significativamente. La incubación con butoxamina o SR59230A incrementó la respuesta contráctil a la estimulación nerviosa adrenérgica. La expresión de los receptores α_1 y α_2 disminuyó al incubar con Rn. La expresión de los receptores β_2 y β_3 aumentó a 10^{-7} M, concentración inferior a las dosis terapéuticas de Rn.

Conclusión:
La Rn inhibe la vasoconstricción nerviosa adrenérgica por antagonismo sobre los receptores α_1 y α_2, y potencia la vasodilatación mediada por los receptores adrenérgicos β_2 y β_3.

P19

Efectos de GS-967, GS-6615 y ranolazina sobre las respuestas de la aorta de conejo a la estimulación nerviosa adrenérgica

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Introducción
Se han determinado los efectos de diferentes inhibidores de la corriente tardía de sodio (INa,late) sobre las respuestas vasculares a estímulos adrenérgicos, tanto endógenos como exógenos.

Métodos
Se usaron inhibidores específicos de INa,late como GS-967, GS-6615 y ranolazina (RAN). La estimulación eléctrica de campo (EFS) (2, 4 y 8 Hz) indujo contracciones dependientes de la frecuencia que fueron abolidas por tetrodotoxina, prazosina o guanetidina (10^{-6} M). La intervención de INa,late se evaluó incubando con GS-967, GS-6615 o RAN. Se realizaron curvas concentración–respuesta para GS-967, GS-6615 o RAN en anillos precontraídos con noradrenalina, endotelina-1 o KCl, con o sin inhibidores específicos (L-NAME, nimesulida, SC-560, verapamilo, nifedipino, apamina o charybdotoxina).

Resultados
La EFS indujo contracciones dependientes de la frecuencia, mediadas por noradrenalina actuando sobre receptores α_1-adrenérgicos. Los bloqueadores de INa,late GS-967 y GS-6615 redujeron la vasoconstricción inducida por la estimulación nerviosa simpática, efecto revertido por la charybdotoxina, lo que implica la participación de canales de potasio activados por calcio de gran conductancia. RAN produjo una atenuación de la vasoconstricción simpática, con un 20% de este efecto mediado por dichos canales. El mecanismo predominante fue el antagonismo competitivo de RAN sobre los receptores α_1-adrenérgicos.

Conclusión
Los resultados sugieren mecanismos de acción distintos entre los inhibidores de INa,late. La implicación de canales de potasio activados por calcio en los efectos de GS-967 y GS-6615, y un antagonismo α_1-adrenérgico competitivo para RAN. El uso de estos compuestos podría ser de interés en procedimientos clínicos asociados a una hiperestimulación del sistema nervioso adrenérgico.

P20

Potential therapeutic effect of mitochondrial transplantation in cardiorenal syndrome

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Cardiorenal syndrome is characterized by a bidirectional interaction between cardiac and renal dysfunction, in which injury in one organ promotes progressive damage in the other. Mitochondrial dysfunction is considered a key driver of metabolic reprogramming and tissue injury in this context. Therefore, this study aimed to evaluate the therapeutic potential of exogenous mitochondrial transplantation (MTx) in models of cardiorenal syndrome.

Two in vivo male rat models were used. The first consisted of primary cardiac injury induced by myocardial infarction (MI) and evaluated after 30 days following a single cardiac administration of MTx (equivalent to 180 µg of mitochondrial protein). The second model involved primary renal injury induced by weekly cisplatin administration (5 mg/kg) for one month, combined with weekly administration of MTx (equivalent to 300 µg of mitochondrial protein; i.v.). In both models, the effects of MTx on cardiac and renal damage were assessed.

In infarcted rats, MTx restored cardiac function and prevented cardiac hypertrophy and fibrosis, as well as the activation of inflammatory markers and endoplasmic reticulum (ER) stress. At the renal level, fibrosis, upregulation of the renal injury biomarker NGAL, and ER stress were also prevented by MTx. In the chronic kidney disease model, MTx prevented the increase in serum creatinine and urea levels, indicating improved renal function. In addition, cardiac function was preserved, together with reduced ER stress activation and fibrosis markers.

These findings demonstrate the therapeutic potential of MTx in experimental cardiorenal syndrome, supporting its role as a promising strategy to simultaneously target cardiac and renal dysfunction.

P21

Efectos de un programa de ejercicio en la función física y calidad de vida de personas trasplantadas renales: una serie de casos

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Introducción
Las personas trasplantadas renales presentan limitaciones funcionales y reducción de la calidad de vida, consecuencias del trastorno metabólico y desacondicionamiento físico previo y posterior al trasplante. El ejercicio físico estructurado ha demostrado ser una intervención segura y beneficiosa en esta población, aunque la evidencia aun es escasa.

Objetivo
Evaluar los efectos de un programa de ejercicio físico supervisado sobre la función física y la calidad de vida en personas trasplantadas renales de la Región de Los Ríos, Chile.

Métodos
Se desarrolló una serie de casos con tres pacientes trasplantados renales, quienes participaron en un programa multicomponente de 8 semanas de duración, con tres sesiones semanales de 60 minutos. Se evaluó la función física mediante pruebas estandarizadas (Dinamometría, Sit to Stand 60'', Test de marcha de 6 minutos, Timed Up and Go, Sit and Reach), la calidad de vida a través del cuestionario KDQ-36 y el nivel de actividad física mediante el IPAQ, antes y después de la intervención.

Resultados
Todos los participantes completaron el programa sin eventos adversos. Se obtuvieron mejoras en todas las evaluaciones realizadas, incluyendo fuerza prensil, fuerza y resistencia de miembros inferiores, capacidad aeróbica, riesgo de caídas y flexibilidad, así como un incremento del nivel de actividad física. Los dominios del cuestionario KDQ-36 mostraron estabilidad o leves mejoras, reflejando una mejor percepción general de salud.

Conclusión
Un programa de ejercicio físico supervisado puede ser una estrategia efectiva y segura para mejorar la función física y la calidad de vida en personas trasplantadas renales.

P22

Topological and multivariate mapping of frailty reversal following supervised strength training in older adults with and without Type 2 Diabetes

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Background
Type 2 Diabetes Mellitus (T2DM) accelerates neuromuscular decline and frailty during aging. Although resistance exercise is a cornerstone intervention, integrated clinical-molecular characterized from an multivariate perspective.

Methods
Eighteen older women (T2DM; n=9, controls; n=9) completed a supervised strength training program for 6 weeks. Pre/post assessments included maximum strength, quadriceps ultrasound, frailty scales, high-resolution respirometry in muscle fibers, plasma oxidative stress markers (MDA, 8OHdG), and G6PD activity. Data were integrated using multivariated analysis.

Results
Baseline topology revealed a highly heterogeneous signature in older adults with T2DM, contrasting with the more compact clustering observed in controls. PCA identified an adaptation axis linking quadriceps structure and G6PD activity with reduced frailty burden (PC1: 25.6%), whereas a second specific axis was dominated by oxidative stress marker (MDA loading ≈ 0.75). Training abolished frailty prevalence. Functional clustering and UMAP demonstrated convergence in both groups toward a shared robust phenotype, despite molecular heterogeneity in T2DM group. Correlation analysis showed stronger inverse associations between quadriceps thickness and frailty (r = -0.51) and positive associations between NS-pathway_ETS and 8OHdG after training (r = 0.62 y p = 0.006). Random Forest identified quadriceps ultrasound and knee extension (scores ≈ 0.18 each) as the strongest predictors of robust clinical status, surpassing age and systemic molecular biomarkers.

Conclusion
A supervised strength training program promoted functional and structural improvements associated with frailty reversion in older adults with and without T2DM. Multivariate analyses identified distinct molecular adaptation patterns in diabetic muscle despite convergence toward a shared robust functional phenotype.

P23

Efecto de un programa de snacks de ejercicio físico sobre marcadores cardiometabólicos, antropométricos y celulares en adultos con DM2 y controles

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Introducción
La diabetes mellitus tipo 2 se asocia con mayor riesgo cardiometabólico, alteraciones redox y deterioro funcional [1]. Los “snacks” de ejercicio, breves estímulos distribuidos durante el día podrían mejorar la salud metabólica y cardiorrespiratoria [2,3].

Métodos
Estudio piloto longitudinal en 13 adultos con diabetes mellitus tipo 2 y 7 controles sanos. Ambos grupos realizaron un programa estructurado de “snacks” durante 12 semanas. Se evaluaron variables antropométricas, composición corporal, capacidad cardiorrespiratoria, parámetros bioquímicos y marcadores celulares redox-mitocondriales. El análisis se realizó mediante ANOVA mixta de medidas repetidas.

Resultados
Tras la intervención se observaron cambios significativos respecto a la medición basal en ambos grupos. Aumentaron el consumo máximo de oxígeno, el colesterol unido a lipoproteínas de alta densidad, los antioxidantes totales, la capacidad antioxidante Q1 y la masa muscular esquelética. Disminuyeron el perímetro de cintura, el pliegue tricipital, la grasa visceral y el perímetro de cuello. También se detectaron cambios significativos en marcadores redox-mitocondriales en células mononucleares de sangre periférica y neutrófilos, concretamente en la producción de especies reactivas de oxígeno y el potencial de membrana mitocondrial. La capacidad antioxidante Q2, el área muscular del brazo corregida, el índice de masa muscular apendicular y la fuerza muscular específica mostraron tendencia al aumento. En diabetes mellitus tipo 2, la proteína C reactiva mostró tendencia a la disminución.

Conclusión
El programa de “snacks” produjo mejoras funcionales, cardiometabólicas, antropométricas y celulares en adultos con diabetes mellitus tipo 2 y controles sanos, reforzando el potencial de intervenciones breves y accesibles.

P24

Effects of Piceid and Harmol on Longevity, Frailty, and Immune Gene Expression in Oregon R Drosophila melanogaster

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Introduction

Aging is associated with progressive declines in physiological function, increased frailty, and altered immune responses. Therefore, this study evaluated the effects of piceid and harmol on longevity, frailty parameters, and immune-related gene expression in Oregon R Drosophila melanogaster.

Methods

Flies were separated into robust and frail populations and treated with 10nM piceid and harmol, separately. Longevity curves were established, while frailty associated parameters adapted from those proposed by Linda Fried, including geotaxis, phototaxis and food ingestion were assessed at 90%, 50%, and 10% survival. Immune- related, antioxidant, and mitochondrial gene expression was analyzed using RT-qPCR.

Results

Piceid treatment did not affect longevity or improve geotaxis and phototaxis performance. However, piceid modulated immune-related gene expression during aging. At 50% survival, Attacin C and Diptericin were upregulated in frail flies treated as compared to frail controls, while Cecropin expression increased in robust treated flies. At 10% survival, all immune-related genes were significantly upregulated in frail treated flies, while Diptericin expression increased in robust treated flies. No differences were observed in cat or MnSOD expression, although p53 expression increased at 50% survival in both frail and robust flies treated with piceid. Harmol treatment significantly improved longevity in frail flies but did not improve geotaxis, phototaxis, or food ingestion. At 50% survival, harmol treatment activated Diptericin and 16s rRNA expression in frail flies, whereas Cecropin C and Attacin C expression decreased in robust treated flies.

Conclusion

These findings aim to demonstrate that piceid and harmol differentially increase aging-associated immune genes in Drosophila melanogaster.

P25

Metodología y criterios de fragilidad en Drosophila melanogaster

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Introducción
Debido a la inversión de la pirámide poblacional y al consecuente envejecimiento de la población, se ha incrementado la prevalencia del síndrome de fragilidad con importantes implicaciones económicas y sociales. Por ello, proponemos un modelo de investigación básica, en Drosophila melanogaster (Dm), que aporta una nueva herramienta para el estudio de la fragilidad basada en el desarrollo de un método de fenotipado capaz de detectar este síndrome y permitir la evaluación de potenciales intervenciones.

Metodología
El fenotipo de fragilidad descrito por Linda Fried y colaboradores constituye la base conceptual de este trabajo. Los criterios se aplicaron y validaron mediante el análisis de supervivencia de la Dm, evaluando en distintos momentos del ciclo vital correspondientes al 90 %, 50 % y 10 % de supervivencia poblacional. Los parámetros propuestos para la detección de fragilidad incluyen: geotaxia, fototaxia, velocidad de la marcha, peso corporal, resiliencia y fertilidad.

Rresultados
Las moscas robustas, tanto hembras como machos, presentan valores significativamente mayores de supervivencia, geotaxia, fototaxia, velocidad de la marcha, resiliencia y fertilidad en comparación con las moscas frágiles, además de mantener un mayor peso corporal.

Conclusiones
Las moscas clasificadas como frágiles mediante nuestro método se confirman como tales, mientras que las clasificadas como robustas mantienen dicho fenotipo según el sistema de evaluación propuesto.

P26

Nuevo modelo de entrenamiento en moscas Drosophila

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Introducción
Drosophila melanogaster (DM), es un organismo modelo muy estudiado y manejable para entender los mecanismos moleculares de los humanos. Muchas propiedades biológicas, fisiológicas y neurológicas básicas se conservan entre los humanos y DM, donde casi el 75% de los genes son compartidos.

Metodología
Moscas tanto machos como hembras fueron entrenadas durante 6 semanas de entrenamiento mediante una resistencia en forma de viento en la parte superior de un tubo de cristal. Se realizaron pruebas funcionales y una transcriptómica para análisis de expresión génico.

Resultados
Tras finalizar el entrenamiento, tanto los machos como las hembras presentaron mayor funcionalidad respecto a las moscas control. Mediante un análisis transcriptómico, se evidencia una expresión génica metabólica diferencial respecto a las moscas control.

Conclusiones
El modelo de entrenamiento se propone sobreexpresa genes relacionados con el ejercicio y el músculo esquelético y también mejoran la funcionalidad de las moscas tras el entrenamiento. Éste podría ser un modelo válido para investigar en el campo de la fisiología, bioquímica y campos afines usando un modelo ideal como las moscas Drosophila melanogaster.

Thank you for your attendance

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