CNR IRIB
Consiglio Nazionale delle Ricerche
ISTITUTO PER LA RICERCA E L'INNOVAZIONE BIOMEDICA

Con il patrocinio della
Città Metropolitana di Palermo

21 – 23 OTTOBRE 2026

Formazione e Innovazione nella Ricerca Biomedica Traslazionale

Atti di Congresso

COMITATO SCIENTIFICO

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Area Territoriale di Ricerca di Palermo del CNR

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Prefazione

Questo volume raccoglie i contributi presentati al congresso “Formazione e Innovazione nella Ricerca Biomedica Traslazionale”, organizzato dall’Istituto per la Ricerca e l’Innovazione Biomedica del CNR e svoltosi a Palermo dal 21 al 23 ottobre 2026, presso l’Area Territoriale di Ricerca del CNR.

Un istituto articolato in sedi e gruppi diversi, impegnati su linee di ricerca differenti che vanno dalla biologia molecolare all’epidemiologia, dalle neuroscienze alle nanotecnologie, ha bisogno di momenti in cui i protagonisti si incontrino, raccontino e discutano criticamente le loro attività. Tre giornate di formazione e confronto in presenza ci sono sembrate il modo più concreto per farlo.

Il programma ha riunito tematiche, come la progressione tumorale e la resistenza alle terapie, i disturbi del neurosviluppo e la neurodegenerazione, l’immunità e la senescenza, il rapporto tra ambiente e salute, che hanno basi biologiche comuni e che nella pratica clinica spesso procedono in parallelo. Accanto agli interventi scientifici, abbiamo voluto dare spazio alla formazione, come l’etica della pubblicazione e dell’authorship, la progettazione, il rapporto con i finanziamenti locali ed europei e la gestione delle infrastrutture. L’aggettivo traslazionale, presente nel titolo, indica proprio questo.

Le due lectio magistralis hanno offerto uno sguardo ampio sulla biologia cellulare e sull’invecchiamento. Il prof. Andrea De Gaetano ha affrontato la dinamica della mitofagia e dell’autofagia, il prof. Calogero Caruso ha presentato i risultati dello studio sui semisupercentenari e sui supercentenari italiani. Le due relazioni hanno offerto due prospettive diverse, pur accomunate da una domanda centrale per la biomedicina di oggi, ovvero cosa permetta all’organismo di mantenersi in equilibrio omeostatico nel tempo.

Un’attenzione particolare è stata riservata ai ricercatori più giovani, protagonisti degli interventi e della sessione poster, e coinvolti nella riflessione sulla costruzione di una rete che renda l’istituto più coeso. Gli atti restituiscono questo lavoro nella sua varietà, e speriamo che possano essere utili sia a chi era presente sia a chi desidera conoscere dove sta andando la ricerca dell’istituto.

Ringraziamo il Direttore f.f. dell’Istituto, dott. Pasquale Picone, le autorità e gli ospiti che hanno portato il loro saluto e il loro contributo, i relatori e i chair delle sessioni, i colleghi del Comitato Organizzatore e della segreteria, senza il cui impegno il congresso non si sarebbe potuto realizzare.

Palermo, ottobre 2026

Il Comitato Scientifico

Maria Vincenza Catania, Maria Lucibello, Domenico Nuzzo, Patrizia Spadafora, Gennaro Tartarisco

GIORNO 1

21 OTTOBRE 2026

14:00 – 14:30 — **Registrazione dei partecipanti**

14:30 – 15:00 — **Saluti istituzionali e apertura dei lavori**

Prof. Francesco Dotta – Direttore Dipartimento di Scienze Bio-Mediche del CNR
Ing. Maurizio Urso – Presidente Area Territoriale di Ricerca del CNR di Palermo
Dott. Pasquale Picone – Direttore f.f. Istituto per la Ricerca e l'Innovazione Biomedica

15:00 – 15:30 — ***Lectio magistralis***

Prof. Andrea De Gaetano
Modeling the dynamics of mitophagy and autophagy

15:30 – 16:20 — **L'authorship scientifica sotto la lente**

Chair: Dott.ssa Silvia Ruggieri

15:30 - 15:50
Dott.ssa Roberta Martina Zagarella – CNR-CID Ethics
The unwritten rules of publication ethics

15:50 - 16:20
Prof.ssa Silvia Scalzini – Università degli Studi di Parma
Scientific authorship: issues and perspectives

16:20 – 16:45 — ***Coffee break***

16:45 – 18:15 — **Progressione tumorale e resistenza alle terapie**

Chair: Dott. Melchiorre Cervello, Dott.ssa Maria Lucibello

16:45 - 17:00
Dott. Ciro Caldiero
Study of tumor microenvironment in pancreatic adenocarcinoma progression through the modulation of neutrophil activity

17:00 - 17:15
Dott.ssa Emanuela Peri
Exploiting the formation of stress granules as therapeutic strategy for hepatocellular carcinoma

17:15 - 17:30
Dott. Daniele Guglielmini
Study of the immune-metabolic axis for the maintenance of the immunosuppressive tumor microenvironment in patients with pancreatic cancer

17:30 - 17:45
Dott.ssa Sabrina Picciotto
Microalgal-Derived Extracellular Vesicles as Engineered Bio-Based Nanocarriers for Drug and siRNA Delivery in Cancer

17:45 - 18:00
Dott.ssa Giovanna Barbieri
Targeting Melanoma Immune Escape and Detection: MHC Class II-Driven Extracellular Vesicle Remodelling and Magneto-Plasmonic Nanoassemblies for Liquid Biopsy Detection

18:00 - 18:15
Dott.ssa Selene Sammataro
Study of the effects of the bisphosphonates on pancreatic cancer cells for potential immunotherapeutic applications

20:30 — ***Social dinner - Palazzo Comitini*** ***Informazioni utili***

GIORNO 2
22 OTTOBRE 2026

09:30 – 11:00

Progettualità @IRIB2023

Chair: Prof. Andrea De Gaetano, Prof.ssa Giuseppa Mudò

09:30 - 09:45
Dott.ssa Elena Lo Presti
Study on oxidative stress machinery to activate immune response against multiple myeloma

09:45 - 10:00
Dott. Walter Arancio
Genome-wide analysis of Chromatin Associated RNAs retained in metaphase chromosomes (Meta-CAR)

10:00 - 10:15
Dott.ssa Monica Salamone
Enhancing Beta Pancreatic Functionality with 4MU for Cell Therapy Applications

10:15 - 10:30
Dott. Gaspare Drago
Modeling trophoblast–macrophage interactions at the maternal–fetal interface

10:30 - 10:45
Dott.ssa Giuseppa Augello
Role of Thioredoxin reductase 1 and NRH:quinone oxidoreducatse 2 as potential prognostic and therapeutic targets in breast cancer

10:45 - 11:00
Dott.ssa Giorgia Adamo
DetectEV: a Novel Diagnostic Tool for Cancer Detection Based on the Evaluation of Extracellular Vesicle Bioactivity

11:00 – 12:00

Poster, Networking & *Coffee break*

Dott. Luigi Citrigno
The Mitochondrial Genome Instability Index (MGII): an integrative biomarker of mitochondrial genetic integrity in human disease

Dott.ssa Simona D'Antoni
Age-dependent changes in metabotropic glutamate receptor expression in synapses and astrocytes in a mouse model of Fragile X Syndrome

Dott.ssa Paola Dell'Albani
Multitarget effects of 3-o-decanoylquercetin in u373-mg human glioma cells

Dott.ssa Valentina La Cognata
An integrative systems biology approach to neurological diseases: from experimental models to precision medicine

Dott.ssa Nadia Lampiasi
Early Molecular Responses of Primary Human Monocytes during the Initial Phase of Acclimatization to Simulated Hypobaric Hypoxia

Dott.ssa Marzia Franzò
Targeting osteosarcoma cell lines with vietnamese ginseng extracts: from bioactive compound to prospective therapeutic approach

Dott.ssa Alessia Li Vigni
Molecular characterization of natural populations of glycyrrhiza glabra l. In sicily within the ambrosia project

Dott.ssa Nicoletta Polerà
Oleacein Modulates the Epigenetically Relevant lncRNA MEG3 in Astrocytic Models of Alzheimer's Disease

Dott.ssa Margherita Stefania Rodolico
Study for Identification of Early Multiorgan Markers in Anderson-Fabry Disease

Dott. Antonio Qualtieri
Cytoprotective effect of Gentiana Lutea L. leaf extract and development of nanostructured delivery systems

Dott.ssa Roberta Russo
Sea urchin as a pilot model for studies on autism spectrum disorder (asd)

Dott.ssa Monica Salamone
4-Methylumbelliferone Modulates β-Cell Function: Implications for Type 1 Diabetes

12:00 – 12:30 ***Lectio magistralis***

Prof. Calogero Caruso - Dipartimento di Biomedicina, Neuroscienze e Diagnostica Avanzata, Università degli Studi di Palermo
A Life Beyond Time: Insights from Italian Semi- and Supercentenarians

12:30 – 13:20 **Neurodegenerazione e neurosviluppo: dai meccanismi alle prospettive di cura**

Chair: Dott. Domenico Nuzzo, Dott.ssa Patrizia Spadafora

12:30 - 12:45
Dott.ssa Rosalia Maria Cristina Pellitteri
Olfactory Ensheathing Cells: characteristics and their applications

12:45 - 13:00
Dott.ssa Giorgia Serena Gullotta
Metabotropic glutamate receptors modulate senescence-associated response in etoposide-induced human microglia

13:00 - 13:15
Dott.ssa Liliana Ruta
From developmental cascades to precision implementation translational esdm research in the first three years of life

13:15 - 13:30
Dott.ssa Laura Palumbo
Microfluidic Myelin Nanovesicles: A Brain-Targeted Strategy Against Multiple Sclerosis

13:30 – 14:30 ***Lunch***

14:30 – 16:30 **Dai circuiti cerebrali ai disturbi del neurosviluppo**

Chair: Dott.ssa Maria Vincenza Catania, Ing. Giovanni Pioggia

14:30 - 14:45
Dott.ssa Chiara Failla
Quantitative Characterization of Static Postural Control in Autistic Children Using the Virtual Reality Rehabilitation System: An Exploratory Observational Study

14:45 - 15:00
Dott.ssa Rosa Musotto
Granger Causality Reveals Directed and Spatially Organized Astrocyte Networks

15:00 - 15:15
Dott. Francesco Bedogni
Proliferation, differentiation and neuronal network maturation in the cerebral cortex of mouse models of neurodevelopmental disorders

15:15 - 15:30
Dott.ssa Michela Spatuzza
Cellular response to oxidative stress and senescence in Fragile X syndrome: an explorative in vitro and ex vivo study

15:30 - 15:45
Dott.ssa Gaia Roccaforte
Variability as Phenotype: A Multiscale Neuroengineering Framework for Autism

15:45 - 16:00
Dott.ssa Simona Campisi
From Movement to Mutual Gaze: A Multimodal Computational Approach to Study Adult-Child Interaction

16:00 - 16:15
Dott.ssa Ileana Scarcella
Spatial Kinematic Signatures of Manual Gesture Imitation in Autism Spectrum Disorder: A Video-Based Computer Vision Analysis

16:15 - 16:30
Dott.ssa Silvia Ruggieri
Eating Disorders risk among adolescents: a multidimensional epidemiological approach

16:30 – 17:00 ***Coffee break***

17:00 – 18:15 **Immunità e infiammazione: nuove prospettive di ricerca**

Chair: Dott.ssa Antonella Bongiovanni, Dott.ssa Antonella Cusimano

17:00 - 17:15
Dott. Fabrizio Chiodo
Carbohydrates at the Host-Microbe Interface: From Vaccine-Design to Microbiota-Immune Interactions

17:15 - 17:30
Dott. Gaetano Spinelli
p65 iso5 and its splice variants p65 iso5 Δ6/7 and p65 iso5 Δ10: novel modulators of inflammatory and glucocorticoid responses

17:30 - 17:45
Dott.ssa Giuseppa Biddeci
NF-κB p65 isoforms remodeling reveals a new dimension of Fabry Disease heterogeneity

17:45 - 18:00
Dott.ssa Laura Trombetta
Immunological implications of psychoactive drugs in patients with inflammatory bowel disease

18:00 - 18:15
Dott.ssa Valeria Longo
BDE-47-Exposed Macrophages Induce Indirect Hepatic Responses through Secreted Factors in a HepG2 3D Spheroid Model

18:15 - 21.00 **Poster, Networking &** ***Light dinner***

GIORNO 3

23 OTTOBRE 2026

09:30 – 11:30

Presentazione di progettualità di successo e aspetti amministrativi

Chair: Dott.ssa Sara Genovese

09:30 - 09:50
Dott. Giuseppe Magnifico – Ufficio Grant e Infrastrutture di Ricerca CNR
La gestione delle infrastrutture di ricerca del CNR

09:50 - 10:10
Dott.ssa Anna Pelagotti – Liaison Office Bruxelles CNR
Esperienze e prospettive del Liaison Office CNR a Bruxelles

10:10 - 10:25
Dott. Giosuè Zurzolo
Programmazione e progettazione: un approccio win-win

10:25 - 10:45
Dott.ssa Mariacristina Morsellino – Europrogettista
Progettualità e finanziamenti in ambito locale e europeo

10:45 - 11:00
Dott. Fabio D'Elia – Food Hub
Navigare la ricerca con l'AI

11:00 - 11:15
Dott.ssa Antonella Girgenti e Dott.ssa Sabrina Picciotto
Making Connections: una rete di giovani ricercatori per IRIB

11:15 - 11:30
Dott.ssa Rossella Lucà
URT CNR-IRIB di Roma, attività e progettualità

11:30 – 11:45 — ***Coffee break***

11:45 – 12:45

Ambiente e Salute

Chair: Dott. Paolo Colombo, Dott.ssa Roberta Russo

11:45 - 12:00
Dott.ssa Ilaria Cosentini
Prenatal environmental exposure: linking the maternal–foetal interface to early-Life development

12:00 - 12:15
Dott.ssa Irene Deidda
Radial glia-like cell populations across the sea urchin life cycle: from development to environmental stress

12:15 - 12:30
Dott.ssa Antonella Girgenti
Nanoplatforms for Innovative Brain Delivery Strategies

12:30 - 12:45
Dott.ssa Francesca Zito
Native pl-nectin from paracentrotus lividus and Recombinant domains as potential tissue bioadhesives

12:45 - 13:15 — **Direttore f.f. IRIB & Comitato Scientifico**

Tavola rotonda, conclusioni e ringraziamenti

13:15 — ***Lunch***

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4-Methylumbelliferone Modulates β-Cell Function: Implications for Type 1 Diabetes

Giorgia Adamo [1], Daniele Romancino [1], Paola Gargano [4], Marta Sarullo[1], Aldo Nicosia [1,2], Sabrina Picciotto [1-2], Antonella Bongiovanni [1], Monica Salamone [1] *

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Recent studies have demonstrated that the coumarin derivative 4-methylumbelliferone (4MU) exerts antidiabetic effects in rodent models. 4MU is known to decrease the availability of hyaluronan (HA) substrates and inhibit the activity of different HA synthases. Nevertheless, it has also been observed that 4MU may affect cellular metabolism.

In this study, we used the rat insulinoma beta-cell line INS-1E cultured under both two-dimensional and three-dimensional experimental conditions (pseudo-islets) co-cultured with stromal vascular fraction of adipose tissue as an in vitro model to investigate beta-cell functionality. For the first time, we observed that treatment of INS-1E cells with 4MU resulted in enhanced insulin secretion. Additionally, we found that 4MU treatment induced morphological changes from multilayered to monolayer conditions, together with alterations in the distribution of insulin granules and cell adhesion properties.

To better understand the mechanism of action of 4MU, we transfected the cells with Hyaluronan Synthase 3 (HAS3), an enzyme involved in inflammation and directly inhibited by 4MU. These experiments aim to investigate the mechanism of action of 4MU in the context of its potential application in the early stages of type 1 diabetes and in improving islet transplantation outcomes.

Keywords: 4-methylumbelliferone, Type 1 Diabetes, insulin secretion, Hyaluronan, pseudo-islets

Age-dependent changes in metabotropic glutamate receptor expression in synapses and astrocytes in a mouse model of Fragile X Syndrome

Simona D'Antoni[1], Andrea Giuseppe Cristaldi[2], Lucia Di Pietro[2], Giorgia Serena Gullotta[3], Michela Spatuzza[1], Rossana Di Martino[1], Maria Vincenza Catania[1]

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Fragile X syndrome (FXS) is a major genetic cause of intellectual disability and autism, resulting from loss of fragile X messenger ribonucleoprotein 1 (FMRP) and consequent alterations in synaptic plasticity and cellular homeostasis. Metabotropic glutamate (mGlu) receptors regulate excitatory neurotransmission and contribute to the pathophysiology of FXS. While mGlu5 receptor signalling has been extensively investigated, the involvement of other mGlu receptor subtypes remains poorly understood.

This study aimed to investigate age-dependent changes in mGlu receptor expression in synaptic and astrocytic compartments in the *Fmr1* knockout (KO) mouse model.

mGlu5, mGlu3, and mGlu7 receptor expression was analysed in cortical synaptosomes and magnetic-activated cell sorting (MACS)-isolated astrocytes from young adult and aged *Fmr1* KO and wild-type mice. The functional role of mGlu3 receptors was examined in cultured mouse astrocytes.

mGlu5 and mGlu3 receptors showed age- and compartment-dependent alterations in *Fmr1* KO mice, whereas mGlu7 receptor levels were unchanged compared with wild-type mice. mGlu3 receptor activation modulated stress granule formation in *Fmr1* KO astrocytes, supporting a role in cellular stress responses.

These findings identify mGlu3 as a potentially relevant component of the altered glutamatergic signalling associated with FXS and suggest a role for mGlu3 receptors in astrocytic responses to cellular stress.

Keywords: mGlu3 receptors, mGlu5 receptors, astrocytes, synapses, stress granules

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An integrative systems biology approach to neurological diseases: from experimental models to precision medicine

La Cognata V.; Morello G.; Gentile G.; Guarnaccia M.; Cavallaro S.

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Advances in high-throughput technologies have transformed our ability to investigate the molecular complexity of neurological diseases, by integrating large-scale genomic and transcriptomic data with clinical and experimental information. Our research group employs an integrative systems biology approach, that combines experimental models, patient-derived samples, multi-omics profiling, bioinformatics and artificial intelligence (AI) to elucidate underlying disease mechanisms and uncover clinically relevant signatures. By combining in vitro cell cultures and in vivo disease models with molecular profiling and imaging-based analyses, we investigate the transcriptional programs regulating neuronal death and survival and their involvement in disease pathogenesis. In neurodegenerative diseases, including amyotrophic lateral sclerosis, and neuro-oncological disorders, such as adult diffuse gliomas, multi-omic strategies enable the identification of distinct molecular subtypes and disease associated signatures with direct applications in diagnosis, prognosis and patient stratification. Network-based and machine learning algorithms further support the discovery of key master regulators and early predictive markers, providing a rational foundation for therapeutic targets and drugs repurposing. Overall, our research aims to build a translational *continuum* from experimental models to patients, laying the groundwork for precision medicine in neurological diseases.

Keywords: Systems biology, Multi-omics, Cell models, Imaging, Artificial intelligence, Neurological diseases, Precision medicine

BDE-47-Exposed Macrophages Induce Indirect Hepatic Responses through Secreted Factors in a HepG2 3D Spheroid Model

Giulia Smeraldi[2,1], Federica Affranchi[1], Alessia Maria Sampino[1], Noemi Aloi[3,1], Natalia Rigoglioso[1], Giuseppa Augello[1], Paolo Colombo[1] and Valeria Longo[1].

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Polybrominated diphenyl ethers (PBDEs) are persistent environmental contaminants associated with adverse metabolic, endocrine, and immune effects. Among them, 2,2′,4,4′-Tetrabromodiphenyl ether (BDE-47), a major human-exposure congener, has been implicated in hepatotoxicity, but the contribution of immune-mediated mechanisms remains poorly understood. Here, we investigated whether macrophage-derived soluble factors modulate hepatic responses to BDE-47. THP-1 macrophage-like cells were exposed to BDE-47, and conditioned media were subsequently applied to HepG2 3D spheroids. Spheroid growth, cell death, and transcriptional markers of inflammation, oxidative/nitrosative stress, senescence, xenobiotic metabolism, extracellular matrix remodeling, and lipid metabolism were assessed. Although conditioned media did not significantly affect spheroid growth, they increased cell death and induced a pronounced inflammatory response, with upregulation of IL-6, IL-8, and TNF-α. Markers of oxidative/nitrosative stress and senescence, including NOS2, HMOX1, and p16, were also increased. Furthermore, xenobiotic metabolism, lipid metabolism, and extracellular matrix-related pathways were altered. These findings suggest that BDE-47-exposed macrophages may indirectly disrupt hepatic homeostasis through secreted mediators, highlighting immune–liver crosstalk as a relevant mechanism in environmental toxicology.

Keywords: BDE-47, macrophage secretome, HepG2 3D spheroids, immune-liver crosstalk

Carbohydrates at the Host-Microbe Interface: From Vaccine-Design to Microbiota-Immune Interactions

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Carbohydrates are central players at the host-bacteria interface, contributing both structural functions and immunological signals. Understanding these interactions is therefore relevant for vaccines design as well as to study host-microbiota interactions.

In conjugate-vaccines, bacterial capsular polysaccharides may have a dual function: besides acting as antigens that induce protective anti-carbohydrate antibodies, they may directly modulate innate immune responses. By investigating the recently approved pneumococcal conjugate vaccine QuimiVio®, we observed that selected *Streptococcus pneumoniae* capsular polysaccharides actively influence multiple *in vitro* innate immune pathways.

A rational glycans-based strategy was also applied to the development of SARS-CoV-2 Soberana vaccines. Mammalian-cell-expressed the viral receptor-binding domain, formulated either as a dimer or conjugated to tetanus toxoid, generated robust immunological and clinical results across phase 1-3 studies in adults and children, including heterologous booster regimens.

Finally, we investigated how bacterial glycoconjugates derived from the microbiota modulate immune responses via pattern-recognition receptors, including TLR and lectins.

Together, these findings highlight carbohydrate-mediated mechanisms as relevant determinants of both vaccine-induced immunity and host-bacteria interactions.

Keywords: glycobiology, translational research, conjugate-vaccines, vaccinology, microbiota.

Cellular response to oxidative stress and senescence in Fragile X syndrome: an explorative *in vitro* and *ex vivo* study

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Fragile X syndrome (FXS) is the most frequent form of inherited intellectual disability and a leading genetic cause of autism. It is caused by mutations in the fragile X mental retardation 1 (FMR1) gene which results in the reduction or lack of the fragile X mental retardation protein (FMRP). FMRP binds mRNAs and regulates mRNA transport and protein synthesis. Its absence in the brain may cause an altered expression of proteins at synapses and consequently brain dysfunction. Evidence in the mouse model of FXS suggests an excess of oxidizing agents in the brain, which are harmful to DNA, lipids, and proteins, and can cause increased susceptibility to cell damage and death. Oxidative stress can cause cellular senescence, which is characterized by the arrest of growth and secretion of senescence-associated proteins, which can have a neurotoxic effect. We are currently studying the susceptibility of FXS neurons and astrocytes to cellular stress and their tendency to undergo senescence in both cultures and brain slices from the Fmr1 knockout mouse model of the disease. This study is relevant because FXS patients exhibit accelerated cognitive aging, suggesting an increased susceptibility of FXS brain to cumulative stress occurring in aging. The obtained results may open a new therapeutic perspective to the use of drugs that eliminate senescent cells and that exert a neuroprotective effect in FXS.

Keywords: Developmental disorders, intellectual disability, Fmr1 knockout mouse, stress granules, cell viability.

Sponsorship: Project # GRT-2022A-2142 Foundation Lejeune Paris.

Cytoprotective effect of Gentiana lutea L. leaf extract and development of nanostructured delivery systems

Antonio Qualtieri[1], Selene de Benedittis[1], Rosa Pittelli[2], Rita Muzzalupo[2], Federica Scalzo[1,2], Francesca Cavalcanti[1], Patrizia Spadafora[1].

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Oxidative stress is one of the main mechanisms involved in the pathogenesis of neurodegenerative diseases. In this context, natural compounds with antioxidant activity have attracted increasing interest for the development of novel neuroprotective strategies.

Gentiana lutea L. root extracts have now been well studied from both a phytochemical and pharmacological perspective due to their beneficial medicinal properties, particularly their antioxidant activity. However, the availability of roots is limited by the plant's slow growth rate; it takes at least 5–10 years for the plant to reach maturity. Conversely, the use of extracts from aerial parts, such as the leaves, would therefore represent a viable alternative. To this end, both the phytochemical profile using HPLC, UV absorbition, MALDI-TOF MS and the in vitro cytoprotective activity against neurodegeneration in SH-SY5Y pseudoneuronal cells subjected to oxidative stress have been studied. Furthermore, the extracts were also delivered via a nanostructured system consisting of niosomes, which demonstrated a significant potentiation of activity, protecting cells from oxidative stress at concentrations 16 times lower than those of the crude extract. These results suggest a promising intervention strategy for counteract neurodegeneration .

Early Molecular Responses of Primary Human Monocytes during the Initial Phase of Acclimatization to Simulated Hypobaric Hypoxia.

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Hypoxia is a common physiological and pathological stressor that profoundly influences cellular metabolism and immune homeostasis. The mechanisms distinguishing beneficial, reversible immune adaptation to acute physiological hypoxia from the maladaptive responses observed in chronic or pathological hypoxia remain incompletely understood. This preliminary study investigated the molecular effects of acute hypobaric hypoxia (AHH) on the short-term kinetics (1-6 and 24 hours) of purified primary human monocytes in healthy male volunteers exposed to a simulated altitude of 3,800 m in the terraXcube climate chamber. Molecular analysis revealed distinct response profiles, suggesting that subjects could be classified as pro-inflammatory "responders" or hyporesponsive "non-responders". In non-responders, an absence of early induction of *IL1B*, *TNF*, and *TGFB1* was observed; conversely, in responders, their levels increased early during hypoxia and subsequently normalized within 24 hours, except for one participant. This heterogeneity was also reflected in *VEGFA* expression, which significantly increased only in responders (except for one subject). Intriguingly, despite the hypoxic stimulus, *HIF1A* expression was uniformly downregulated across all subjects and time points, paralleled by a decline in caspase-1 activity by 24 hours. In conclusion, our findings indicate an interindividual heterogeneity in the innate immune response within the first 24 hours of AHH and reveals a counterintuitive, uniform downregulation of *HIF1A*, uncovering a shared intrinsic bias toward early hypoxic homeostasis.

Keywords: Monocyte, *HIF1A*, *IL1B*, caspase1, climate chamber, acute hypobaric hypoxia.

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Eating Disorders risk among adolescents: a multidimensional epidemiological approach

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Background: Eating disorders (EDs) frequently emerge during adolescence, a key period for behavioral and lifestyle changes. Our epidemiological research focuses on EDs prevention, investigating individual, familial, and social factors, behaviors and particularly modifiable psychosocial factors.

Methods: A previous cross-sectional study evaluated 1,740 students aged 14–16 years from 15 Sicilian secondary schools, assessing EDs risk, body appreciation, BMI, social media use and bullying. Building on these findings, a new multicenter cross-sectional study of adolescents aged 12–16 years across Sicily investigated EDs risk factors, with particular attention to family context and parental recognition.

Results: Among 11,498 adolescents (mean age 13.7±1.32 years; 55.2% females), 5.5% were at high risk of EDs, predominantly females. A major finding was the marked gap between adolescents self-report and parental recognition: approximately two-thirds of high-risk adolescents were considered not at risk by their parents. High-risk adolescents were characterized by multiple vulnerability factors, including self-harm, substance use, bullying, and intensive social-media use. Among males, muscularity concerns were relevant.

Conclusions: Findings highlight a substantial burden of EDs risk, marked sex differences and considerable parental underestimation. This discrepancy underscores the need for school-based screening, parent education, awareness campaigns and responsible social-media use to facilitate EDs early identification and prevention.

Keywords: Eating disorders; Epidemiology; Risk factors; Prevention

From developmental cascades to precision implementation translational esdm research in the first three years of life

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Developmental cascades during the first three years provide a framework for translating early autism research into clinical and educational services. This contribution connects evidence on the Early Start Denver Model (ESDM) with precision implementation, focusing on parent coaching through video feedback and synchronous telehealth. In an observational community study of 112 autistic children, ESDM delivered for three hours weekly was associated with steeper six-month trajectories in language, personal-social skills, performance and general development than usual care delivered for six hours. A second observational study involving 248 children examined hybrid ESDM combining therapist intervention with remote parent coaching. Compared with usual care, the hybrid pathway showed greater six-month increases in Total and Personal-Social Developmental Quotients, by 7.9 and 13.1 points, respectively. They inform a translational research agenda extending ESDM strategies into everyday routines in infant-toddler childcare settings. Precision implementation will examine how training, coaching and contextual adaptations can be matched to child profiles, family resources and service characteristics. Linking developmental outcomes with feasibility, acceptability, fidelity and sustainability aims to guide accessible, individualized pathways connecting families, clinical services and early childhood education.

Keywords: developmental cascades, ESDM, precision implementation, telehealth, early childhood education

From Movement to Mutual Gaze: A Multimodal Computational Approach to Study Adult-Child Interaction

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Introduction. Social development in early childhood unfolds through interaction, yet behavioral assessment still relies largely on observing the individual child. This limitation is particularly relevant in autism, where social behavior may depend on the exchange with a partner. Noninvasive sensing and computational methods can complement clinical observation by quantifying adult-child interaction directly.

Methods. We present MIND-Play, a semi-structured play paradigm for studying social behavior in ecologically relevant conditions. Ninety preschool children (55 with autism spectrum condition, 35 typically developing) were recruited, together with an adult facilitator, while wrist movement, cardiac activity and video were recorded synchronously.

Results. Dyadic motor coupling captured dynamics emerging from the adult-child pair rather than the individual child and was associated with adaptive functioning in the autistic group. Cardiac responses to play events revealed group differences in orienting responses that persisted after accounting for motor activity. Finally, we developed and validated a deep learning algorithm for mutual face gaze detection, and evaluate its application to MIND-Play, testing its generalization to a new context.

Conclusion. MIND-Play illustrates how movement, physiology, and visual behavior offer complementary, quantitative measures of adult-child interaction, opening new opportunities for studying interaction dynamics in autism.

Keywords: Autism, Adult-Child Interaction, Wearable Sensors, Interaction Dynamics, Computer Vision.

Granger causality reveals directed and spatially organised astrocyte networks

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Astrocytes contribute actively to the regulation of neuronal activity through intracellular Ca^{2+} dynamics, although the spatial and temporal organization of functional interactions within astroglial networks is still not fully understood. In this study, time-lapse Ca^{2+} fluorescence recordings are analyzed to characterize the relationship between network structure, signal dynamics, and functional organization. Granger causality analysis is applied to normalized Ca^{2+} time series to identify directed functional interactions among astrocytes and reconstruct the resulting network topology. The analysis reveals a non-random and hierarchical organization, characterized by “pivot” astrocytes with high outgoing connectivity and “hub” astrocytes receiving inputs from multiple cells. Examination of directed pathways further identifies sequential chains of activity consistent with structured propagation of Ca^{2+} signals across the network. Moreover, the spatial distribution of functional connections is strongly distance-dependent, with connectivity probability decreasing exponentially as intercellular distance increases, suggesting a characteristic spatial scale for astrocytic Ca^{2+} communication. Taken together, these findings provide a quantitative characterization of the functional and spatial organization of astroglial networks and support the view of astrocytes as coordinated components of brain information processing.

Harnessing the potential value of TCTP in advance in TNBC

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Triple-negative breast cancer (TNBC) is a heterogeneous and complex disease. Patients with metastatic TNBC have a poorer prognosis than patients with other breast cancer subtypes due to the inherently aggressive clinical behavior of the disease and the lack of molecular targets for therapy.

Translationally controlled tumor protein (TCTP) is an intriguing protein, involved in stress response and resistance to radio- and/or chemotherapy. Clinical evidence has shown that elevated TCTP levels correlated with poor survival outcomes in several cancers. We recently demonstrated that phosphorylated TCTP (p-TCTP) is an independent, negative prognostic marker in breast cancer. We also showed that high levels of p-TCTP levels were associated with a poor response to anti-HER2 agents, suggesting its potentially predictive value. Consistent with these findings, our preliminary RNA-Seq analysis revealed higher expression of TPT1/TCTP in metastatic vs. primary TNBC samples and higher expression of phospho-TCTP-positive cells in metastatic lesions than in the corresponding primary TNBC samples and in TNBC patients unresponsive to first-line chemotherapy.

Collectively, these data suggest that genetic profiling of high p-TCTP populations may provide important biomarker signatures for patient stratification with respect to therapy resistance that may otherwise escape analysis of the tumor as a whole.

Keywords: Breast cancer, TCTP, therapy resistance, biomarker

Immunological implications of psychoactive drugs in patients with Inflammatory Bowel Disease

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Inflammatory bowel diseases (IBDs) are a group of chronic disorders whose pathogenesis typically involve the gut–brain axis; they are characterized by persistent inflammation of the gastrointestinal tract which can exacerbate under stress exposure with the most common forms being Crohn's disease and ulcerative colitis. The introduction of immunotherapies, particularly monoclonal antibodies targeting pro-inflammatory cytokines, such as Infliximab and Adalimumab, has significantly improved the clinical management of the disease. Psychiatric comorbidities, particularly anxiety and depression, are frequent among patients with IBD and may negatively affect disease course and quality of life. Psychoactive drugs are therefore commonly prescribed in this population. However, their potential effects on immune responses and intestinal inflammation remain incompletely understood. This study aimed to investigate the potential immunological implications of psychoactive drug use in patients with IBD, focusing on the relationship between pharmacological treatment and systemic inflammatory and immune profiles. Our findings support the hypothesis that psychoactive medications may have immunological effects beyond their primary activity on the central nervous system. Understanding the interaction between psychoactive treatment and immune regulation may provide new insights into the complex gut–brain–immune axis in IBD and may contribute to a more comprehensive evaluation of pharmacological treatment in patients with chronic intestinal inflammation.

Keywords: Inflammatory Bowel Disease (IBD); Psychoactive drugs; gut–brain axis; cytokines

Metabotropic glutamate receptors modulate senescence-associated response in etoposide-induced human microglia

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Microglia senescence is linked to neuroinflammation, brain aging and cognitive decline. Here, we generated human senescent microglia by exposing HMC3 cells to etoposide (ETO) and investigated whether modulation of metabotropic glutamate receptors (mGluRs)2, 3 and 5 could modulate the senescence-related microglia phenotype.

Viability, morphology, cell cycle and ROS production were analyzed by imaging flow cytometry. Expression of senescence markers and mGluRs was analyzed by immunocytochemistry, Western Blot and qRT-PCR. Activity of mGluRs was modulated using mGluR2/3 and mGluR3 agonists and the mGluR5 antagonist MTEP, alone or in combination. Computational analysis of available datasets was carried out to validate results.

Exposure to ETO induced cell cycle blockade and enhancement of senescence-related markers. Elevated ROS production and over-expression of the SASP-related genes *IL1B*, *IL6*, *CCL2*, *IL8, VEGFA* and *MMP9* were observed, together with an increase of *GRM2* and mGluR5. mGluR3 stimulation reduced ROS production, DNA damage and the expression of *IL1B* and *CCL2*, while antagonism of mGluR5 decreased ROS production and *IL1B* expression. Computational analysis revealed similar pathways of senescence associated genes in human microglia.

Our data suggest that modulation of mGluR3 and mGluR5 might represent a pharmacological intervention to reduce the detrimental effects of microglia senescence.

Keywords: microglia, senescence, neuroinflammation, metabotropic glutamate receptors.

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Microalgal-Derived Extracellular Vesicles as Engineered Bio-Based Nanocarriers for Drug and siRNA Delivery in Cancer

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Extracellular vesicles (EVs) have emerged as promising bio-nanovehicles for the delivery of bioactive compounds. To address challenges related to the scalability, sustainability, and engineering of EV-based delivery systems, our research group developed a sustainable and cost-effective platform for the production and engineering of microalgal-derived EVs, referred to as nanoalgosomes. Our previous studies established their biochemical and biophysical properties, non-cytotoxic profile, and efficient cellular uptake *in vitro*, their intrinsic antioxidant and anti-inflammatory activities and *in vivo* biocompatibility and biodistribution, revealing preferential bone tropism and supporting their potential for osteosarcoma-targeted delivery. We also developed and patented DetectEV, a new approach to evaluate the EV-bioactivity. We further explored nanoalgosomes as engineered carriers for anticancer drugs and nucleic acids. Nanoalgosomes loaded with doxorubicin showed enhanced anticancer activity against breast cancer cells compared with free doxorubicin, as demonstrated by a lower IC50. In parallel, nanoalgosomes were engineered for siRNA delivery in osteosarcoma models. Efficient loading of siRNAs targeting β-catenin was achieved, resulting in effective gene silencing and associated biological responses. Overall, these findings demonstrate the versatility of nanoalgosomes as naturally derived and engineerable nanocarriers for the delivery of both chemotherapeutic drugs and nucleic acids, highlighting their potential as a sustainable platform for next-generation cancer therapy.

Keywords: Nanoalgosomes, Microalgal extracellular vesicles, DetectEV-enzymatic assay, Doxorubicin, siRNA delivery

Microfluidic Myelin Nanovesicles: A Brain-Targeted Strategy Against Multiple Sclerosis

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Multiple sclerosis is a chronic neurodegenerative disease of the CNS in which myelin loss and neuronal damage are driven by persistent inflammation and an autoimmune response directed against myelin antigens. Unfortunately, effectively treating such neurodegenerative conditions remains challenging, as the blood-brain barrier (BBB) prevents most drugs from reaching brain tissue. Consequently, there is growing interest in delivery systems capable of interacting with and crossing the BBB without compromising its integrity, thereby enabling targeted delivery to damaged areas. In this context, we propose a microfluidic method to produce myelin vesicles (MyVes) for use as a therapeutic tool. Following production, the vesicles were characterized to verify reproducibility and the presence of myelin components. To validate the ability of the MyVes to reach their cellular target, an organ-on-chip system was used as a drug screening platform. We evaluated their toxicological profile to ensure safety and tolerability. Finally, efficacy was subsequently tested in a MS rat model via intranasal administration to determine whether MyVes reach the brain and modulate the disease course. The results indicate that the method yields reproducible and well-tolerated vesicles that are effective in the *in vivo* model, supporting the potential of MyVes as a therapeutic strategy for MS.

Keywords: Multiple sclerosis, Nanomedicine, Myelin nanovesicles, Blood-brain barrier, drug-delivery system

Modeling trophoblast–macrophage interactions at the maternal–fetal interface

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The placenta is a dynamic interface between mother and fetus, where trophoblast and immune cells interact to support pregnancy and regulate processes essential for placental function. However, experimental models that reproduce this cellular interplay remain limited. We developed a versatile in vitro system based on commercially available BeWo trophoblast cells and THP-1 monocytes/macrophages to investigate interactions between trophoblast and immune cells at the maternal–fetal interface. The model allows different cellular configurations and trophoblast phenotypes, including undifferentiated cells and syncytiotrophoblast-like cells, in combination with different macrophage states or undifferentiated monocytes. Functional characterization showed that conditioned medium (CM) derived from THP-1 macrophages modifies the phenotype of BeWo cells, demonstrating that soluble factors released by immune cells can influence trophoblast characteristics. This interaction provides a flexible experimental framework in which different cellular states can be combined to reproduce biological processes occurring at the maternal–fetal interface. The model may therefore be used to investigate cellular communication and to reproduce different events relevant to placental physiology, including trophoblast differentiation and functional changes associated with immune–trophoblast interactions. Its modular design also provides a platform for subsequent studies investigating how external factors may interfere with these physiological interactions.

Keywords: Placental physiology, Trophoblast cells, Macrophages, Cell–cell communication, In vitro model.

Molecular characterization of natural populations of *glycyrrhiza glabra* l. In sicily within the ambrosia project

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Glycyrrhiza glabra (liquorice) is a medicinal plant traditionally used for its anti-inflammatory and anticancer properties. Within the AMBROSIA project framework, this study investigates the genetic and therapeutic potential of wild Sicilian *G. glabra* populations. Spontaneous samples were collected from small meadows in Agrigento (Cardo/Valley of the Temples, Casteltermini) and Trapani (Marsala) provinces. Genetic diversity and evolutionary relationships were evaluated using rDNA-ITS sequencing and ISSR-PCR profiling. Molecular results revealed the complete sequence identity among all Sicilian specimens as well as a high similarity with sequences from other countries in the world. Moreover, genetic analysis showed that the Sicilian sequences are very similar to *G. inflata*. Additionally, ongoing biological assays are being conducted to screen the functional effects of these native liquorice extracts using RAW264.7 macrophage cells and sea urchin embryos as responsive experimental models. Preliminary bioactivity assays suggest promising cell-responsive modulations, highlighting the extract's functional potential. Furthermore, integrating molecular and cyto-toxicological analyses of Sicilian liquorice supports the conservation of sustainable genotypes with health-related applications. We thank AMBROSIA project ("Attività di monitoraggio in agricoltura biologica per coltivazioni sostenibili di liquirizia"), funded by Italian Ministry of Agricultural, Food and Forestry Policies (MIPAAF), D.M.8/10/2020, CUP:B53C20040660001.

Keywords: Mediterranean liquorice, genetic conservation, RAW264.7, sea urchin embryos.

MOSAIC: an automated RNA-seq platform integrating transposable element, RNA editing and splicing dynamics across cellular senescence and mitosis

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Comprehensive interpretation of RNA-seq data requires many specialised tools spanning differential expression, transposable element (TE) quantification, alternative splicing, RNA editing and metatranscriptomics. These analyses are usually run separately and selectively, so what a study finds is bounded by what it set out to look for. We developed MOSAIC, a modular pipeline that orchestrates more than twenty analytical modules from raw reads to interactive reports through a single configuration file, executing all core analytical layers by default. Applied unchanged to a public senescence dataset, MOSAIC recovered the canonical senescence programme and the late-specific derepression of L1 elements described in the original study, and in the same run surfaced layers that the original analysis did not examine: genome-wide satellite-repeat transcription, a progressive increase in A-to-I RNA editing and extensive splicing remodelling. Applied to chromatin-associated RNA newly generated from mitotic fibroblasts, it revealed the opposite repeat behaviour, chromatin-specific eviction, together with a marked depletion of circular RNA from the chromatin fraction; representative changes were confirmed by RT-qPCR. Default classification of host-unmapped reads additionally identified a contamination confined to the late-senescence libraries of the public dataset.

Keywords: RNA-seq; transposable elements; cellular senescence; chromatin-associated RNA; reproducible pipelines

Multitarget Effects of 3-*O*-Decanoylquercetin in U373-MG Human Glioma Cells

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Background: Gliomas are highly heterogeneous brain tumors characterized by aberrant signaling pathways, therapeutic resistance, and poor clinical outcomes. Quercetin and its derivatives have demonstrated promising anticancer properties. In earlier work, we synthesized and evaluated a series of quercetin derivatives and identified the acylated compound 3-*O*-decanoylquercetin (Q-3-Dec) as particularly effective in reducing glioma cell viability.

Objectives: This study investigated the activity of 3-*O*-decanoylquercetin (Q-3-Dec) on U373-MG glioma cell line, focusing on its effects on NF-κB/STAT3 signaling, mitochondrial function, apoptotic regulators, and O6-methylguanine-DNA methyltransferase (MGMT) expression in glioma cells.

Results: In U373-MG glioma cells, treatment with 50 μM Q-3-Dec triggered pronounced, time-dependent morphological changes and an early loss of mitochondrial membrane potential after 3 h. With prolonged exposure, Q-3-Dec markedly decreased NF-κB and STAT3 phosphorylation and reduced the expression of the anti-apoptotic proteins Bcl-2 and survivin, alongside a significant decrease in MGMT levels. All these effects culminated in a progressive increase in cell death of U373-MG, reaching approximately 30% after 48 h.

Conclusions: Q-3-Dec exerts multifaceted anti-glioma activity by concurrently disrupting survival signaling pathways, impairing mitochondrial function, and reducing MGMT expression. These findings support its further preclinical evaluation as a potential therapeutic agent for improving glioma treatment strategies.

Keywords: Glioma, quercetin, signal transduction, survivin, MGMT.

Nanoplatforms for Innovative Brain Delivery Strategies

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Nanotechnology-based platforms has been identified as a potentially effective approach for the development of innovative therapeutic strategies for central nervous system (CNS) disorders. However, the complexity of the CNS and the restrictive properties of the blood-brain barrier (BBB) represent significant challenges to the effective delivery of therapeutic compounds to the brain. The present research is focused on the development and biological evaluation of innovative nanoplatforms inspired by biological systems, including plant-derived vesicles, nanoemulsions, and mitochondrial vesicles, for disorders of CNS. An investigation was conducted into plant-derived vesicles (NatureVes), which were obtained through a standardised biofabrication approach. The nanoscale vesicles exhibited favourable stability, neuronal biocompatibility, and efficient uptake by SH-SY5Y cells. The enrichment of these samples in plant-derived bioactive compounds, including polyphenols, carotenoids, and chlorophyll, was associated with antioxidant properties, highlighting their potential as natural nanocarriers for neuroprotective applications. In addition, physcion-loaded nanoemulsions were investigated as a strategy to enhance the dispersion and biological availability of this naturally occurring compound, which is poorly soluble. Preliminary studies demonstrated a concentration- and time-dependent effect in neuronal cells, while greater tolerance was observed in barrier models. Furthermore, a novel strategy has been developed as an innovative approach to mitochondrial transplantation (MT), based on the nanostructuring of mitochondrial components into vesicular nanoplatforms (MTves), with the aim of transforming mitochondrial material into stable delivery systems at the nanometre scale. It has been demonstrated that MTves can enhance mitochondrial delivery across the BBB and integration into neuronal models.

In conclusion, these studies highlight the potential of nanotechnology as a versatile strategy to overcome CNS delivery barriers, enhance cellular targeting, and support the development of innovative therapeutic approaches for neurological disorders.

Keywords: Nanotechnology, Plant-derived vesicles, Mitochondrial transplantation, Blood-brain barrier, CNS drug delivery

Native pl-nectin from *paracentrotus lividus* and recombinant domains as potential tissue bioadhesives

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Marine invertebrates exhibit impressive abilities to attach underwater to a wide variety of surfaces. Sea urchins rely on temporary adhesion to move across various environments. Through a repetitive attachment/detachment mechanism, they can firmly adhere and subsequently release themselves via chemical secretions produced by numerous sensory-secretory tube feet. Pl-nectin is an adhesive protein highly expressed in *Paracentrotus lividus* tube feet and deposited in the footprint left on surfaces during locomotion. Pl-nectin is also present in eggs and is secreted into extracellular matrix after fertilization. It consists of six tandem discoidin-like domains (D1-D6, 151-156aa each). Within the PRIN 2022-PAWS project framework, native Pl-nectin was purified from unfertilized eggs, while recombinant domains D1-D2 and D2 were produced in *E. coli* and characterized. The adhesive properties of the three proteins were investigated using NIH-3T3 cells through *in vitro* cell-adhesion assays and their effects on gene expression were evaluated by qPCR. Preliminary results showed that native and recombinant proteins supported cell-adhesion, at different concentrations and with diverse strength, and stimulated the expression of the immediate-early genes *Egr1* and *Jun*. Our findings indicate that all three proteins possess adhesive properties and may represent promising surface-coating materials for biomedical applications, such as regenerative medicine and tissue engineering.

Keywords: adhesion, gene expression, cell morphology, cytoskeleton organization, biomaterial

NF-κB p65 isoforms remodeling reveals a new dimension of Fabry Disease heterogeneity

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Fabry disease (FD) is an X-linked lysosomal storage disorder caused by pathogenic variants in the *GLA* gene and characterized by marked molecular and clinical heterogeneity. Beyond α-galactosidase A (α-Gal A) deficiency and glycosphingolipid accumulation, chronic immune-inflammatory mechanisms may contribute to disease progression. Here, we investigated whether alternative NF-κB p65/RelA isoforms are associated with immune-inflammatory remodeling in FD and may provide molecular insights into disease heterogeneity. Analysis at the transcript and protein levels revealed a distinct shift in p65 isoform expression in FD, characterized by reduced p65 iso5 and concomitant upregulation of p65 iso5 Δ6/7 and p65 iso5 Δ10. Notably, p65 iso5 Δ6/7 upregulation was also evident at the protein level. Strikingly, both alternative isoforms were increased in individuals carrying *GLA* variants of uncertain significance, despite preserved α-galactosidase A activity and normal lyso-Gb3 levels. These findings reveal an isoform-specific redistribution of NF-κB p65 associated with FD and support the presence of immune-inflammatory remodeling extending beyond conventional biochemical abnormalities. Integrating such molecular profiles with clinical and genetic information through computational and artificial intelligence approaches may provide a multidimensional framework for better capturing FD heterogeneity and advancing precision medicine.

Keywords: Fabry disease, NF-κB, p65 isoforms, immune-inflammatory remodeling, precision medicine.

Oleacein Modulates the Epigenetically Relevant lncRNA MEG3 in Astrocytic Models of Alzheimer's Disease

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by amyloid-β deposition, tau pathology, mitochondrial dysfunction, oxidative stress and epigenetic alterations. Long non-coding RNAs (lncRNAs) play key roles in neuronal survival and neurodegenerative pathways. Among them, MEG3 is an epigenetic regulator involved in inflammation, apoptosis, mitochondrial homeostasis and neuronal integrity. Bioactive compounds from extra virgin olive oil, including oleacein, exhibit neuroprotective and anti-inflammatory properties, although the epigenetic mechanisms underlying their activity remain poorly understood.

Here, we investigated the effects of oleacein on MEG3 expression in immortalized hippocampal astrocytes from wild-type and triple-transgenic AD mice (WT-iAstro and 3Tg-iAstro). Basal MEG3 expression was normalized to 1.0 in both groups. In WT-iAstro cells, DMSO induced MEG3 expression (3.0-fold), while oleacein partially normalized this response at 5 µM (1.2-fold) and moderately increased expression at 10 µM (2.5-fold). In 3Tg-iAstro cells, DMSO reduced MEG3 expression (0.7-fold), whereas 10 µM oleacein restored it to near-physiological levels (1.2-fold).

Overall, these findings identify MEG3 as an epigenetically relevant target of oleacein and suggest that its modulation may contribute to neuroprotective effects in AD cellular models. The differential response between WT-iAstro and 3Tg-iAstro cells further supports a disease-context-dependent regulation of MEG3 by oleacein.

Keywords: Alzheimer's disease (AD), Oleacein, MEG3, Long non-coding RNA (lncRNA), Epigenetic regulation

Olfactory Ensheathing Cells: characteristics and their applications

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The olfactory mucosa is considered a promising source of neural stem cells due to the presence of specialized glial cells, Olfactory Ensheathing Cells (OECs). They secrete a variety of growth factors playing a crucial role in neuroregeneration. Consequently, OECs have attracted considerable interest in their remarkable neural plasticity.

We employed OECs as an experimental model in several studies investigating on the protective effects of natural compounds against amyloid-β (Aβ)-induced toxicity; on the potential of nanostructured lipid carriers as drug delivery systems and their cellular uptake in OECs; on the biocompatibility of silicon (Si) and silicon carbide (SiC) surfaces for OEC growth and adhesion.

Primary OECs were prepared from neonatal mouse olfactory bulbs. Cell viability by MTT assay, marker expression by immunofluorescence and SEM analysis were assessed.

Our findings demonstrated that: (1) natural compounds exert protective effects against Aβ-induced toxicity in OECs; (2) OECs efficiently internalize drug-loaded nanoparticles, showing enhanced uptake compared with the free drug and suggesting improved drug permeability; (3) OECs exhibit excellent biocompatibility with both Si and SiC substrates, supporting their potential use in implantable devices.

These results highlight the relevance of OECs for neuroregenerative applications, underscoring their potential as valuable tools for neural tissue repair and regeneration.

Keywords: olfactory ensheathing cells, natural compounds, neuroregeneration, biocompatibility, drug-loaded nanoparticles

p65 iso5 and its splice variants p65 iso5 Δ6/7 and p65 iso5 Δ10: novel modulators of inflammatory and glucocorticoid responses

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NF-κB (Nuclear Factor-κB) is a central regulator of inflammation, controlling immune responses and cellular processes whose dysregulation contributes to inflammatory diseases. We identified and characterized p65 iso5 as a novel p65 isoform with distinct transcriptional properties and the ability to bind dexamethasone. We subsequently characterized two additional splice variants, p65 iso5 Δ6/7 and p65 iso5 Δ10, in human peripheral blood mononuclear cells (PBMCs). Both p65 iso5 Δ6/7 and p65 iso5 Δ10 displayed distinct expression patterns in response to inflammatory and anti-inflammatory stimuli and in disease contexts. Strikingly, both isoforms bound dexamethasone and formed novel nuclear complexes with activated glucocorticoid receptor (GR), uncovering a previously unrecognized molecular connection between NF-κB and glucocorticoid signaling and suggesting a role in the modulation of GR-dependent responses. To further investigate p65 iso5 function, transcriptomic profiling was performed in HeLa cells expressing GFP-fused canonical p65 or p65 iso5, with or without dexamethasone. GFP-positive cells were sorted before treatment. Transcriptomic analysis revealed distinct isoform-dependent transcriptional programs and marked modulation of glucocorticoid-responsive gene expression by p65 iso5. Collectively, these findings identify p65 iso5, p65 iso5 Δ6/7 and p65 iso5 Δ10 as possible modulators of inflammatory and glucocorticoid responses, highlighting their potential as therapeutic targets.

Keywords: NF-κB, p65 isoforms, Alternative splicing, Glucocorticoid signaling, Inflammation.

Prenatal environmental exposure: linking the maternal–foetal interface to early-Life development

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Pregnancy represents a critical window of susceptibility during which chronic exposure to environmental chemicals, even at relatively low levels, may influence biological processes with consequences extending beyond birth.

Within the Neonatal Environment and Health Outcomes (NEHO) birth cohort, we investigated prenatal exposure to persistent organic pollutants and essential elements across maternal and foetal compartments, integrating molecular responses with early-life developmental outcomes. Our findings indicate that environmental exposures are associated with multiple, interconnected levels of biological response. Maternal and cord blood concentrations were associated with distinct miRNA signatures, revealing compartment-specific molecular responses and supporting the placenta as an active interface capable of modulating environmental signals between mother and foetus. These exposures were also associated with postnatal phenotypes, including sex-specific growth trajectories during the first year of life and neurodevelopmental outcomes at four years of age. Differences between maternal and cord associations further highlight the importance of considering the maternal–placental–foetal unit as an integrated system.

Overall, these studies suggest that chronic prenatal exposure to low levels of environmental chemicals may produce detectable effects from molecular regulation to child development, emphasizing the placenta as a potential mediator of early-life environmental programming.

Keywords: birth cohort, prenatal exposome, placenta, infant growth trajectories, neurodevelopment

Proliferation, differentiation and neuronal network maturation in the cerebral cortex of mouse models of neurodevelopmental disorders

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Excitatory neurons of the cerebral cortex are generated during embryonic life, when proliferating cortical progenitors either self-renew and proliferate or exit the cell cycle to become postmitotic cells. The importance of these early events is illustrated by the fact that cell-cycle progression is often affected in neurodevelopmental disorders (NDDs). Accordingly, NDD symptoms often overlap and arise from impaired neuronal differentiation and poor maturation of cortical neuronal networks. This suggests that common developmental processes may be disrupted across a range of NDDs.

Altered cell-cycle dynamics and differentiation defects are also observed in models carrying Copy Number Variations of the 16p11.2 locus, a major risk factor for NDDs. Although 16p11.2 duplication carriers show greater cognitive impairments and increased risk of psychosis than deletion carriers, individuals with either deletion or duplication display increased risk of intellectual disability and autistic traits, suggesting symptoms overlaps. Accordingly, we show that deletion and duplication of the 16p11.2 locus oppositely affect progenitor proliferation but similarly impair postmitotic differentiation. These findings suggest that similar differentiation deficits can emerge through opposite regulation of proliferation timing associated with deletion or duplication of the 16p11.2 locus. Collectively, this evidence supports the existence of shared pathogenic mechanisms common to multiple NDDs.

Keywords: Neurodevelopment, Cerebral cortex, proliferation, differentiation, activity

Quantitative Characterization of Static Postural Control in Autistic Children Using the Virtual Reality Rehabilitation System: An Exploratory Observational Study

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Background and Purpose: Quantitative assessment of postural control may contribute to characterizing motor heterogeneity in autistic children. Objectives: This study investigated static postural control and its relationship with age and cognitive functioning. Methods: Fifty autistic children aged 6–10 years completed a static balance assessment using the Virtual Reality Rehabilitation System (VRRS) stabilometric platform. Thirteen center-of-pressure (COP) parameters describing displacement, variability, excursion, velocity, and sway area were examined. Cognitive functioning was assessed using Full Scale Intelligence Quotient (FSIQ). Main Results: Age-related differences in postural parameters were limited and were not robust after correction for multiple comparisons. Conversely, higher FSIQ was associated with reduced COP displacement and variability, particularly across global, anteroposterior, and mediolateral measures. Exploratory analysis further indicated a modest association between higher FSIQ and reduced mediolateral displacement, independently of age. Conclusions: Cognitive functioning emerged as a relevant factor associated with static postural control, whereas chronological age showed limited relationships with balance performance. These findings suggest that cognitive heterogeneity should be considered when characterizing motor and postural profiles in autistic children.

Radial glia-like cell populations across the sea urchin life cycle: from development to environmental stress

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Radial glial cells are key regulators of vertebrate nervous system, contributing to its development, homeostasis, and regeneration. Although radial glia-like cells have recently been characterized in adult nervous system of some echinoderms, their presence and molecular identity during embryonic development remain largely unknown. Here, we investigated radial glia-like populations across the life cycle of the sea urchin *Paracentrotus lividus,* highlighting its potential as a comparative model for studying the evolution of glial cell programs. Through phylogenetic analyses, developmental gene expression profiling, and high-resolution immunolocalization, we identified conserved radial glial-associated markers, including glutamine synthetase (GS), GLAST and Sox2. These markers display distinct spatial and temporal expression patterns from larval stages to adulthood, revealing molecularly heterogeneous radial glia-like populations with morphologies characteristic of vertebrate radial glial-like, including elongated processes and close association with neuronal structures. Additional preliminary studies, aimed at investigating the response of these markers to environmental stressors in embryos and adult nervous structures, revealed changes in the expression of radial glial-associated markers following environmental stress. Together, our findings support *P. lividus* as a promising deuterostome model for investigating conserved glial mechanisms and their responses to cellular stress, providing an *in vivo* model for studies of neurotoxicity, neuroprotection and potentially regeneration.

Keywords: Glial evolution, Lengsin, radial nerve, tube feet, neurotoxicity.

Sea urchin as a pilot model for studies on autism spectrum disorder (asd)

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In this study, we evaluated the effects of chemicals, such as metals, on *Paracentrotus lividus* sea urchin embryos, through morphological, biochemical and molecular analyses. We analyzed the sea urchin homologs of vertebrate genes implicated in the onset of ASD, and *in silico* analysis showed a complex network among the investigated genes, also compared with vertebrate homologs. We studied the differential expression of the genes *glast, glutamine synthetase, shank, sox2, sox6* and *ube2a* after treatment with Lithium (Li), Nickel (Ni) and Zinc (Zn), chemical compounds associated in various ways with ASD, as dietary nutrients or pollutants or therapeutics. Interestingly, results demonstrated that these metals modulated the expression of several ASD-related genes. Li, used as a therapeutic agent against neurological disorders, downregulated most of the above-mentioned genes. Zn caused the upregulation of *gs, shank, sox2* and *ube2a*, whereas Ni upregulated *gs, sox2, sox6* and *ube2a*. Consistent with these findings, immunofluorescence analyses using glial and neuronal markers revealed their altered distribution in treated embryos. These findings support the *P. lividus* embryo as *in vivo* model for investigating molecular responses associated with ASD-related genes, exposed to environmental/pharmacological agents. We thank the Project "READS-Reading Early Autism Disorders Signs", MISE Accordo per l'innovazione DM 5.3.2018, n.867, 2022-25.

Keywords: transcriptional expression, chemical compounds, health, gene network.

Spatial Kinematic Signatures of Manual Gesture Imitation in Autism Spectrum Disorder: A Video-Based Computer Vision Analysis

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Motor difficulties are a clinically relevant but under-assessed dimension of autism spectrum disorder (ASD). This study characterized the manual motor profile of children with ASD versus typically developing (TD) peers using video-based kinematic feature extraction. Thirty-eight children (20 ASD, 18 TD; 7–13 years) were video-recorded imitating manual sequences from the NEPSY-II imitation subtest; seven sequences suitable for automated tracking were analyzed via a customized MediaPipe HandLandmarker pipeline. Spatial, dynamic, rhythmic and bimanual kinematic features were compared between groups (Mann–Whitney U, Cliff's delta, Benjamini–Hochberg FDR correction), with correlations against WISC-IV, Movement ABC-2 and BRIEF-2 scores. Group differences were concentrated in the spatial domain: lateral trajectory amplitude (rom_x_norm) was consistently greater in ASD across five of seven sequences, surviving FDR correction and sensitivity analyses ($p < .001$, $\delta = 0.53$). In the most demanding bimanual sequence, inter-hand velocity correlation (lr_corr_v3D) was the strongest discriminator ($p < .001$, $\delta = 0.74$), indicating reduced bimanual organization in ASD. Dynamic and rhythmic features were less consistently discriminative. Video-based kinematic analysis detects replicable, spatially specific differences in manual imitation in ASD, chiefly reduced spatial containment of the gesture, supporting kinematic markers as candidate complements to standardized clinical assessment, pending replication in larger samples.

Keywords: autism spectrum disorder; kinematic analysis; digital motor markers; computer vision; gesture imitation; motor phenotyping.

Study for Identification of Early Multiorgan Markers in Anderson-Fabry Disease

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Background: Anderson-Fabry disease (AFD) is an X-linked multisystem lysosomal disorder characterized by phenotypic variability. Early detection of organ involvement is crucial for intervention before irreversible damage occurs.

Objective: To identify and characterize early multidimensional markers of organ involvement in AFD using an integrated approach, with emphasis on the inflammatory mechanisms underlying Fabry cardiomyopathy.

Methods: The diagnostic and monitoring pathway includes family history, genetic analysis, measurement of α-galactosidase A activity and Lyso-Gb3 levels, cascade family screening, and evaluation of target organs. Cardiovascular assessment includes electrocardiography, echocardiography with speckle-tracking analysis, Global Longitudinal Strain and Myocardial Work, cardiac magnetic resonance with T1 mapping, capillaroscopy, and color Doppler ultrasonography. Neurological evaluation includes neuroimaging, transcranial Doppler, transcranial magnetic stimulation, neurocognitive assessment, and skin biopsy. The research program integrates tissue analyses, characterization of peripheral immune cells, and functional models to identify biomarkers and potential therapeutic targets.

Expected Results: The identification of early cardiovascular, neurological, renal, and peripheral abnormalities, together with the characterization of inflammatory pathways, might contribute to the identification of biomarkers and help define a therapeutic window.

Conclusions: Integrating clinical, instrumental and biological markers could improve risk stratification, facilitate monitoring of disease progression, support personalized diagnostic and therapeutic pathways and enable assessment of treatment response.

Keywords: Anderson-Fabry disease, Multiorgan involvement, Biomarkers, Fabry cardiomyopathy, Inflammation

Study of the Effects of the Bisphosphonates on Pancreatic Cancer Cells for Potential Immunotherapeutic Applications

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Pancreatic cancer is one of the most challenging solid tumors to treat, not only because of the difficulty of achieving an early diagnosis, but also because effective curative treatments are still lacking. Currently, surgical resection represents the first-line treatment for eligible patients, whereas combination chemotherapy regimens are available for patients who are not candidates for surgery. One of the major areas of interest in modern oncology is the understanding of the immune response to tumors.

Several drugs originally developed and commonly used for the treatment of one disease have subsequently been repurposed for therapeutic applications in other conditions, as in the case of bisphosphonates, which is now routinely used in oncology. Although extensive research has investigated the effects of this drug in cancer patients, little is currently known about the fine regulatory mechanisms induced by bisphosphonates in tumor cells following its uptake.

The aim of this study is to investigate the cytotoxic potential of γδ T cells following bisphosphonates treatment, with the ultimate goal of identifying novel therapeutic targets.

Keywords: bisphosphonate, T cells, immunotherapy, pancreatic cancer

Study of the immune-metabolic axis for the maintenance of the immunosuppressive tumor microenvironment in patients with pancreatic cancer

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Pancreatic ductal adenocarcinoma (PDAC) is characterized by an immunosuppressive tumor microenvironment (TME), which represents a major barrier to effective antitumor immunity and contributes to poor therapeutic response. Increasing evidence indicates that metabolic alterations within the TME actively regulate immune-cell function and may contribute to the persistence of immune suppression. This study aimed to investigate the immune-metabolic profile of patients with pancreatic cancer by evaluating circulating lipid metabolites and exploring their potential association with the mechanisms underlying tumor-associated immune suppression. Blood samples were collected from patients with pancreatic cancer, and selected lipid metabolites were quantified using targeted metabolic analyses. In the same way, soluble molecules were identified from serum' patients to evaluate new biomarkers. Our findings support a potential role for circulating lipid metabolites in the immune-metabolic axis associated with pancreatic cancer. Characterization of these metabolic alterations may contribute to a better understanding of the mechanisms sustaining tumor-associated immune suppression and may identify candidate circulating biomarkers for patient stratification and future therapeutic investigation.

Keywords: pancreatic cancer; immunotherapy; lipid metabolites; tumor microenvironment (TME)

Study of tumor microenvironment in pancreatic adenocarcinoma progression through the modulation of neutrophil activity

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Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy projected to become the second leading cause of cancer-related mortality within the next decade. Among solid tumors, PDAC is characterized by delayed diagnosis, largely due to nonspecific symptoms and the lack of reliable biomarkers for early detection. The pro-tumorigenic microenvironment of PDAC is sustained by a highly fibrotic stroma and extensive infiltration by immunosuppressive cell populations. The multifaceted and often opposing roles of neutrophils in cancer have increasingly been recognized.

Using spectral flow cytometry, we characterized the phenotype of circulating and tumor-infiltrating neutrophils in 25 treatment-naïve patients with pancreatic cancer at the time of initial diagnosis. Peripheral blood-derived neutrophils were further assessed for their functional properties using immunofluorescence assays and monitored over a time-course experimental setting. Our findings demonstrate that pancreatic tumor cells and cancer-associated fibroblasts differentially sustain neutrophil activation. Secretome analysis revealed distinct molecular mediators produced by each cell type that contribute to maintaining neutrophil functional competence, as well as the production of molecules associated with angiogenesis and metastatic dissemination. Collectively, these results may contribute to the development of novel immunotherapeutic approaches targeting neutrophil activation pathways, with the potential to interfere with tumor-promoting processes within the pancreatic cancer microenvironment.

Keywords: immunotherapy, pancreatic cancer, neutrophils, fibroblast associated cancer (CAFs)

Targeting Melanoma Immune Escape and Detection: MHC Class II-Driven Extracellular Vesicle Remodelling and Magneto-Plasmonic Nanoassemblies for Liquid Biopsy Detection

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Melanoma progression is driven by tumour-derived extracellular vesicles (EVs) that reshape the tumour microenvironment and promote immune escape, frequently linked to constitutive Major Histocompatibility Complex (MHC) class II expression. MHC class II engagement activates signalling proteins, kinases, and adhesion receptors, shaping EV-mediated immune regulation and microenvironment remodelling. Melanoma cell lines constitutively expressing MHC class II molecules (A375, HT-144) were stimulated with the anti-HLA-DR mAb L243; secreted EVs were isolated by ultracentrifugation and characterised by Western blot and dynamic light scattering. MHC class II engagement enriched EVs with HLA-DRα, MCAM, ICAM, PD-L1, and STAT3, thereby enhancing EV-mediated PBMC apoptosis and driving autocrine/paracrine migration of melanoma cells and fibroblasts. Melanoma spreads via hematogenous dissemination, making early detection of circulating tumour cells (CTCs) and EVs a priority. To improve liquid biopsy detection, fluorescent magneto-plasmonic cationic amphiphilic cyclodextrin-based nanoassemblies (SC16NH3+/MHS-26/Ada-Rhod), with or without hyaluronic acid (HA) functionalization, were developed and characterized. The nanoassemblies showed selective uptake by melanoma cells, magnetic capture from PBMC-spiked blood-simulating models, and EV recruitment. HA-mediated CD44-dependent uptake was confirmed by competitive inhibition. Together, these findings identify MHC class II signalling as a regulator of melanoma EV-mediated immune escape and support magneto-plasmonic nanoassemblies as multifunctional platforms for targeted liquid biopsy.

Keywords: Extracellular vesicles; MHC class II molecules; Melanoma; Liquid biopsy; Magneto-plasmonic nanoassemblies.

Targeting osteosarcoma cell lines with vietnamese ginseng extracts: from bioactive compound to prospective therapeutic approach

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Osteosarcoma (OS) is the most common primary bone tumor, mainly affecting adolescents and young adults. Despite MAP chemotherapy and surgery, survival remains poor in metastatic disease, and chemoresistance calls for new strategies. One promising direction is natural compounds, which often target multiple tumor processes, including cell death, cell cycle, and motility, with lower toxicity than chemotherapy. Among them, *Panax vietnamensis* (Vietnamese ginseng) has a distinctive ginsenoside-rich phytocomplex with reported antiproliferative activity but remains underexplored in OS. We investigated the antitumor effects of four *P. vietnamensis* extracts (BS, CS, RS, LS) in two OS cell lines differing in p53 status: SaOS-2 (p53-null) and MG-63 (mutated p53). BS, RS, and LS dose-dependently reduced viability at 24 and 48 h in both lines, whereas CS did not. The response was cell line-specific: SaOS-2 showed an increased sub-G0/G1 peak and late apoptosis, while MG-63 underwent G2/M arrest. In addition, RS and LS induced early, dose-dependent reactive oxygen species (ROS) production in both lines, suggesting oxidative stress as a possible shared trigger. The extracts also significantly impaired wound closure over 48 h. These findings support *P. vietnamensis* extracts as promising candidates for OS; future studies will clarify cell death mechanisms and use an osteosarcoma-on-chip model.

Keywords: Osteosarcoma, *Panax vietnamensis*, ginsenosides, reactive oxygen species, cell migration

The Mitochondrial Genome Instability Index (MGII): an integrative biomarker of mitochondrial genetic integrity in human disease

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ABSTRACT TEXT

Background: Mitochondrial dysfunction is a major pathogenic mechanism in inherited and acquired disorders, including primary mitochondrial diseases, neurodegeneration, cancer, metabolic syndrome, and aging. Although next-generation sequencing (NGS) enables detailed characterization of mitochondrial DNA (mtDNA) variation, current approaches typically evaluate individual parameters independently, limiting a comprehensive assessment of mitochondrial genome integrity. Objectives: To develop a quantitative framework that integrates multiple dimensions of mtDNA instability into a single metric reflecting overall mitochondrial genomic health. Methods: We developed the Mitochondrial Genome Instability Index (MGII), a composite score derived from high-depth NGS data. The index integrates mtDNA copy number variation, heteroplasmic mutational burden, rare variant accumulation, large-scale deletion load, and mtDNA sequence diversity into a standardized measure of genomic instability. Results: The MGII combines distinct genomic features into a unified score, enabling a global evaluation of mitochondrial genome integrity. This multidimensional approach may better distinguish physiological mitochondrial variability from pathological instability than analyses based on individual parameters alone. Conclusions: The MGII represents a novel systems-level biomarker of mitochondrial health with potential applications in mitochondrial diseases, neurodegenerative disorders, and aging-related conditions. By providing a comprehensive assessment of mtDNA instability, the index may support improved patient stratification, disease monitoring, and therapeutic evaluation in precision medicine.

Keywords: mitochondrial dysfunction, mtDNA heteroplasmy, mitochondrial copy number, genome instability, next-generation sequencing, mitochondrial diseases.

Thioredoxin Reductase-1 and NRH:Quinone Oxidoreductase-2 as Potential Prognostic and Therapeutic Targets in Breast Cancer

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Background: Redox-regulating enzymes such as thioredoxin reductase 1 (TrxR1) and NRH:quinone oxidoreductase 2 (NQO2) contribute to tumor survival and treatment resistance, but their interplay in breast cancer (BC) remains poorly characterized.
Objectives: To investigate the effects and mechanisms of combined TrxR1/NQO2 inhibition in BC.
Methods: TrxR1 and NQO2 expression was assessed in BC tissues and cell lines. Auranofin (TrxR1 inhibitor) and S29434 (NQO2 inhibitor), alone or combined, were evaluated in vitro, validated by dual siRNA knockdown, and assessed in MDA-MB-231 xenografts. Network and functional enrichment analyses were also performed.
Results: Both enzymes were overexpressed in BC, with high expression associated with poorer overall survival. Combined inhibition produced synergistic antiproliferative effects, increased ROS, and modulated apoptosis, autophagy, ferroptosis-associated signaling, and DNA damage markers. Dual knockdown recapitulated these effects, while combined treatment suppressed tumor growth in vivo. Network analyses highlighted oxidative stress and redox homeostasis, identified CRYZ as a connected node, and combined inhibition reduced BCL2 expression.
Conclusions: TrxR1 and NQO2 represent complementary redox-regulatory vulnerabilities in BC, supporting their combined pharmacological targeting.

Keywords: Breast cancer (BC), Thioredoxin reductase 1 (TrxR1), NAD(P)H:quinone oxidoreductase 2 (NQO2), Redox homeostasis, Drug combination, Crystallin Zeta (CRYZ).

Variability as Phenotype: A Multiscale Neuroengineering Framework for Autism

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Phenotypic heterogeneity remains a major obstacle to replicable biomarkers and personalised intervention in autism, as group-level profiles poorly capture individual developmental trajectories. We propose that such variability is not merely noise, but reflects structured, person-specific and temporally organised patterns. Neurodevelopment is modelled as an open, multiscale dynamical system in which variability becomes the object of measurement rather than its residual. At the cellular level, computational models of the tripartite synapse and astrocytic Ca^{2+} signalling formalise glial modulation of neuronal gain and dynamic range. At the neurophysiological level, electroencephalographic, autonomic, kinematic and oculomotor signals are treated as observations of person-specific latent states. At the interpersonal level, interaction is modelled as coupled agents, while social robots and immersive environments provide reproducible perturbations for closed-loop system identification. In a 12-week factorial randomised controlled trial involving 80 autistic children aged 4–8 years, a therapist-supervised social robot increased emotional-competence gains (ANCOVA $F(6,73)=16.53$; adjusted $R^2=0.58$; $\eta^2=0.12$, $p=0.002$). The framework yields three falsifiable predictions: within-person transition signatures, superior performance of individual generative models over group classifiers, and dyadic coupling mismatch as a marker of social difficulty. Together, these principles support a predictive, adaptive science of neurodevelopment centred on individual trajectories rather than population averages.

Keywords: autism; neuroengineering; dynamical systems; complex systems; digital phenotyping; social robotics