UNIVERSITÀ DEGLI STUDI FIRENZE

Da un secolo, oltre.

SOCIETÀ ITALIANA DI BIOCHIMICA E BIOLOGIA MOLECOLARE - 1951 -

Congresso SIB TUM – Toscana Umbria Marche
9 giugno 2025

Università degli Studi di Firenze

Centro Didattico Morgagni

Viale Giovanni Battista Morgagni 40
50134 Firenze

GiovenTUM 2025:
il futuro della biochimica
si incontra a Firenze

Responsabile scientifico
Prof. Niccolò Taddei

GiovenTUM 2025: il futuro della biochimica si incontra a Firenze

Responsabile scientifico

Prof. Niccolò Taddei

Comitato scientifico:

Prof. Andrea Bellelli (Presidente SIB)
Prof.ssa Paola Chiarugi (Past-president SIB)
Prof. Matteo Becatti (Firenze)
Prof.ssa Giulia Bernardini (Siena)
Prof.ssa Jlenia Brunetti (Siena)
Prof.ssa Valentina Cecarini (Camerino)
Prof.ssa Monica Emanuelli (Politecnica delle Marche)
Prof.ssa Arianna Vignini (Politecnica delle Marche)
Prof.ssa Carla Emiliani (Perugia)
Dott.ssa Francesca Felice (Pisa)
Prof.ssa Laura Bordoni (Camerino)
Prof. Michele Guescini (Urbino)
Prof.ssa Sabata Martino (Perugia)
Prof. Michele Menotta (Urbino)
Prof.ssa Luigia Pazzagli (Firenze)
Dott.ssa Rebecca Piccarducci (Pisa)

Comitato organizzatore:

Dott.ssa Roberta Cascella (Firenze)
Dott.ssa Anastasia Ricci (Urbino)
Dott. Leonardo Gatticchi (Perugia)
Dott.ssa Alessandra Bigi (Firenze)
Prof.ssa Francesca Cencetti (Firenze)
Dott. Luigi Ippolito (Firenze)
Dott.ssa Manuela Leri (Firenze)
Dott. Simone Luti (Firenze)
Dott.ssa Benedetta Mannini (Firenze)
Prof. Matteo Ramazzotti (Firenze)

Sito internet e gestione abstract:

Prof. Matteo Ramazzotti
Dott. Lorenzo Casbarra

Questo evento è sponsorizzato da

Per segnalazioni sul contenuto del libretto contattare matteo.ramazzotti@unifi.it

PROGRAMMA

- **Ore 8,30 - 9,45: Registrazione**

- **Ore 9,45 - 10,00: Apertura convegno**

- **Ore 10,00 - 11,15: Sessione I**

  Moderatori: Matteo Becatti (Firenze) e Giulia Bernardini (Siena)

  Matteo Prisinzano (Università di Firenze)
  Characterization of functionally relevant G protein-coupled receptors in endometriotic epithelial cells

  Emilia Maria Lombardi (Università di Perugia)
  Restoring defective Alanine:Glyoxylate Aminotransferase folding in primary hyperoxaluria type I by a new class of pharmacological chaperones

  Michela Bruschi (Università di Urbino)
  Cytotoxicity studies and cellular redox modulation through a synthetic thiol compound tuning the metabolic profiles

  Haidara Nadwa (Università di Siena)
  Computational study of the (un)folding mechanism of Serum Amyloid A (SAA) protein

  Roberto Campagna (Università Politecnica delle Marche)
  Paraoxonase-2 in osteosarcoma: potential for the development of a targeted anticancer therapy

  Gloria Basso (Università di Pisa)
  Adenosine role in myofibroblasts-lipofibroblast transition in an in vitro model of lung fibrosis

- **Ore 11,15 - 11,45: Coffee break**

- **Ore 11,45 - 13,00: Sessione II**

  Moderatori: Arianna Vignini (Università Politecnica delle Marche) e Michele Menotta (Urbino)

  Helena Juricic (Università di Camerino)
  Effect of probiotics and gamma-oryzanol on cytokines-induced alteration of intestinal epithelial cell monolayer permeability

  Francesco Mengarelli (Università Politecnica delle Marche)
  Role of Coenzyme Q10 in mitochondrial dysfunction and oxidative damage in RETT syndrome

Enxhi Shaba (Università di Siena)
Proteomics based evaluation of potential treatment for idiopathic pulmonary fibrosis: investigation of HDAC6i effects on lung fibrotic fibroblasts

Matteo Seccaroni (Università di Perugia)
Understanding the role of I-1β in tenocyte homeostasis: a proteomic and lipidomic perspective

Liliana Napolitano (Università di Firenze)
The rational engineering of a dimeric single-domain antibody enhances the detection of toxic Aβ42 oligomers

Fabiana Fanelli (Università di Urbino)
Characterization of the VPS13B splicing pattern in a Cohen syndrome patient harboring a large deletion in the VPS13B gene

- **Ore 13,00 - 14,45: Lunch e sessione poster**

- **Ore 14,45 - 15,45: Sessione III**

Moderatori: Francesca Felice (Pisa) e Laura Bordoni (Camerino)

Lorenzo Ceccarelli (Università di Pisa)
A hybrid computational approach to personalize neuroinflammation diagnosis: targeting TSPO mutations with quantum and machine learning

Elena Perla (Università di Urbino)
Red blood cells-derived extracellular vesicles as a novel RNA delivery system

Tiziana Di Crescenzo (Università Politecnica delle Marche)
Taste sensitivity and salivary antioxidants in feeding and eating disorders: the role of integrated therapy

Omar Francesco Biasco (Università di Siena)
Exploring the role of ZFHX2 in neuroinflammation: implications for microglia activation

Federica Carnemolla (Università di Firenze)
Fibrinogen-mediated neuroinflammation: how extra virgin olive oil polyphenols defend the brain

- **Ore 15,45 – 16,45: Sessione IV**

Moderatori: Luigia Pazzagli (Firenze) e Carla Emiliani (Perugia)

Alessandro Rencinai (Università di Siena)
Branched oncolytic peptides target HSPGs, inhibit metastasis, and trigger the release of immunogenic cell death-related DAMPs in pancreatic cancer

Federica Forte (Università di Urbino)
The mini recombinant protein ED-sRGN: a compact and versatile genome editing tool

Serena Borghi (Università di Firenze)
Short-chain fatty acid supplementation mitigates oxidative stress and thrombosis risk in Behçet's syndrome

Lorenzo Germelli (Università di Pisa)
Enhancing RNA delivery via extracellular vesicles: loading efficiency, cargo characterization, and functional uptake

Martina Guzzetti (Università di Perugia)
Exploring limbal stem cell aging: the role of extracellular vesicles in microenvironment modifications

- **Ore 16,45-17,30: Premiazioni e conclusione**

ABSTRACT SELEZIONATI

Characterization of functionally relevant G protein-coupled receptors in endometriotic epithelial cells

Prisinzano Matteo1,2, Seidita Isabelle1, Romeo Lucia1, Maryam Raeispour1, Bernacchioni Caterina1, Cencetti Francesca1, Bruni Paola1, Meyer zu Heringdorf Dagmar2, Donati Chiara1.

1. Dipartimento di Scienze Biomediche Sperimentali e Cliniche, Firenze
2. Institut für Allgemeine Pharmakologie und Toxikologie, Goethe-Universität Frankfurt, Universitätsklinikum, Frankfurt am Main, Germany

Endometriosis is a chronic inflammatory disease characterized by the invasion of endometrial cells outside the uterine cavity, pain and infertility. Current interventions for the disease are unsatisfactory, relying on the surgical removal of the lesions and hormonal therapies with high symptom relapse and collateral effects, respectively. Aim of the present study was to expand our knowledge on the molecular mechanisms responsible for endometriosis pathogenesis and to exploit the rationale for G protein-coupled receptors (GPCR) as non-hormonal therapeutic targets in this disease. For this, human endometriotic epithelial 12Z cells were employed to study GPCR-mediated increases in intracellular Ca2+ concentrations ([Ca2+]i) using fluo-4. Cell invasion assays (Boyden chamber) were used to study the potential of the identified GPCR to trigger endometriotic cell invasion. The results show that 12Z endometrial epithelial cells express a number of GPCR that are linked to [Ca2+]i increases, such as oxytocin, bradykinin, histamine, lysophosphatidic acid (LPA), and sphingosine 1-phosphate (S1P) receptors. Recently, we demonstrated that the signaling of the pleiotropic sphingolipid S1P is profoundly altered in endometriosis. In particular, S1P1, S1P3 and S1P5 receptors were highly expressed in endometriotic lesions as well as 12Z cells. We show here that pretreatment with pertussis toxin significantly reduced S1P-dependent [Ca2+]i increases in 12Z cells, highlighting the involvement of Gi-mediated signaling. Employing specific agonists and/or antagonists of S1P receptors isoforms, we demonstrate that S1P1, S1P3 and S1P5, but not S1P2 and S1P4 mediated the [Ca2+]i increase in these cells. Moreover, the aforementioned GPCR ligands were studied in cellular invasion assays. Interestingly, while bradykinin, histamine and oxytocin exerted a limited pro-migratory effect, the bioactive lipids LPA, and particularly S1P, acting via S1P1, S1P2 and S1P5, effectively stimulated cell invasion. The data illustrate the importance of the S1P-GPCR, compared to other GPCR that are functionally expressed, in triggering the invasive phenotype of endometriotic epithelial cells.

The project is financed within the PRIN 2022 PNRR D.D. 1409 14/9/2022 National Recovery and Resilience Plan, Mission 4 - Component 2, Investment 1.1 funded by the European Union - NextGenerationEU - CUP_ B53D23024590001.

contact : matteo.prisinzano@unifi.it

Restoring defective Alanine:Glyoxylate Aminotransferase Folding in Primary Hyperoxaluria Type I by a new class of Pharmacological Chaperones

Emilia Maria Lombardi1, Marco Pieroni2, Silvia Grottelli1, Giannamaria Annunziato2, Luana Ruta1, Gioena Pampalone1, Elisa Bianconi3, Antonio Macchiarulo3, Gabriele Costantino 2 and Barbara Cellini1",

1 Department of Medicine and Surgery, University of Perugia, Perugia Italy.
2 Department of Food and Drug, University of Parma, Parco Area delle Scienze, Parma, Italy.
3 Department of Pharmaceutical Sciences, University of Perugia, Perugia, Italy.

Rare diseases affect a small percentage of people worldwide. Among them, a large subgroup is represented by enzyme deficits, which often display a loss-of-function pathogenesis. A severe form of rare disease is Primary Hyperoxaluria Type 1 (PH1), caused by the deficit of Alanine:Glyoxylate aminotransferase 1 (AGT1). AGT1 is a Pyridoxal 5'-phosphate (PLP) dependent enzyme localized in liver peroxisomes, where it catalyzes the transamination of L-alanine and glyoxylate into pyruvate and glycine, respectively. Mutations in the AGXT gene encoding AGT1 lead to the AGT1 functional deficit of AGT1 and to the consequent accumulation of glyoxylate and oxalate, which culminate in nephrolithiasis, end-stage renal disease and systemic oxalosis. In humans are present two polymorphic non-pathogenic variants of the AGXT gene: the major allele (encoding AGT-Ma) and the minor allele (encoding AGT-Mi). More than 200 pathogenic mutations associated with PH1 have been identified, the majority of which lead to AGT1 deficit by causing protein misfolding (1). Therefore, pharmacological chaperones (PCs), i.e. small molecules acting that specifically bind a misfolded protein and promote the correct folding, could represent a promising therapeutic strategy. Previous data indicate that aminooxyacetic acid (AOA) is a PC for AGT1, although it is not specific (2). Here, to identify specific PCs, we tested synthetic molecules analogues of AOA as putative ligands on AGT-Ma, AGT-Mi and four pathogenic variants: G41R-Ma, G170R-Mi, F152I-Mi and I244T-Mi using a dual strategy approach on recombinant proteins and cellular models. Specifically, we determined the inhibition potency and evaluated the stabilizing effect through thermophoresis analyses and limited proteolysis assays. We then tested the chaperone effect of each compound in HepG2 AGXT-KO cells (a validated model of PH1) stably expressing the species under study upon lentiviral infection, and we found that two compounds significantly increase the expression of AGT1. These data represent a good starting point to further develop the active molecules as PCs, paving the way for further medicinal chemistry optimization strategies.

1 Cellini B, Curr. Opin. Nephrol. Hypertens. 2024
2 Grottelli S. et al., J Med Chem 2022

contact: emiliamaria.lombardi@collaboratori.unipg.it

Cytotoxicity studies and cellular redox modulation through a synthetic thiol compound tuning the metabolic profiles

Bruschi Michela, Masini Sofia, Biancucci Federica, Piersanti Giovanni, Canonico Barbara, Menotta Michele, Magnani Mauro, Fraternale Alessandra

Department of Biomolecular Sciences, University of Urbino Carlo Bo, 61029 Urbino (PU), Italy

Nowadays, cysteine pro-drugs are emerging as new potential therapies in cardiovascular and inflammatory diseases due to their cytoprotective effects. In this research, cytotoxicity studies of a synthetic thiol compound, i.e., I-152, a precursor of N-acetylcysteine (NAC) and cysteamine (MEA), were conducted on three different cell lines (A549, HaCat, and HEK293T). Then, considering that the vascular endothelium is the first interface exposed to circulating compounds and oxidative as well as pro-inflammatory stimuli, the effects of redox modulation on energy metabolism were examined in human umbilical cord endothelial cells (HUVECs) where toxicity studies had been already carried out. Regarding the first part of the study, toxic effects were not registered up to 1 mM I-152. Thiol analysis, performed in HUVECs via both HPLC and a mass spectrometry-based metabolomic approach, revealed higher cysteine and glutathione (GSH) content, in concomitance with I-152 derivatives, i.e., dithiol compound (NACMEAA) and triacetylated I-152 as well as NAC and MEA. Mass spectrometry revealed that I-152 boosted ATP production, specifically through the mitochondrial OXPHOS, as determined via Seahorse assay without inducing oxidative stress. Additionally, I-152 treatment of HUVECs before co-culture with LPS-stimulated macrophages provided GSH and cysteine sustainment and attenuated the transcription of adhesion molecules as well as iNOS expression. Identifying the impact of redox regulation in physiological conditions and the possible metabolic targets could aid the application of novel thiol-based therapeutics.

FUNDINGS: This work was supported by the European Union fundings: - NextGeneration EU under the Italian Ministry of University and Research (MUR) National Innovation Ecosystem grant ECS00000041 - VITALITY - CUP H33C2200043000 and by PRIN (Bando 2017; Prot. 2017Z5LR5Z)

contact: michela.bruschi@uniurb.it

Computational Study of the (un)Folding Mechanism of Serum Amyloid A (SAA) Protein

Nadwa Haidara1, Brotzakis Faidon2,3, Santucci Annalisa1, Braconi Daniela1, Vendruscolo Michele3

1 Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy.
2 Institute for Bioinnovation, Biomedical Sciences Research Center “Alexander Fleming”, Vari, Greece.
3 Centre for Misfolding Diseases, Department of Chemistry, University of Cambridge, Cambridge, United Kingdom

Serum amyloid A (SAA) is an inflammatory acute-phase apolipoprotein found as the major component of AA amyloid deposits characterizing AA amyloidosis, ensuing upon long-term complications of several chronic inflammatory disorders.The formation of amyloid fibrils in AA amyloidosis is due to the misfolding and aggregation of circulating SAA after a significant increment of its serum level.
In order to better understand the (un)folding mechanism of SAA, it is essential to characterize such a process in terms of structural ensembles, which are often represented through free energy landscapes providing information on the molecular structure of the metastable states, the pathways of interconversion, and the possible mechanism of the (un)folding process.
In this context, to characterize the thermodynamics of SAA, we ran a series of Parallel-tempering Metadynamics (PTMetaD) simulations as it allows for long-timescale phenomena to be simulated obtaining the free energy surface (FES).
Here, a 1-D collective variable (CV) was constructed through a supervised learning class classification paradigm (Harmonic Linear Discriminant Analysis) HLDA then used to bias the simulations in parallel tempering Metadynamics simulations.In the end, we obtained the FES along different sets of CVs, which enabled us to probe the structural features of the identified metastable states and suggest a possible SAA (un)folding path.
Our findings indicate that some secondary structures, predominantly loops, along with tertiary structures, are formed initially, establishing a folding nucleus. This process is subsequently followed by helix formation, consistent with the nucleation–condensation folding mechanism. The secondary structure analyses showed that SAA is not an intrinsically disordered protein (IDP) considering the idea that IDPs become more ordered at high temperatures. We found that at higher temperatures SAA is represented by highly unstructured conformations (almost completely loops). However, at lower temperatures structured conformations are present.
Our approach provides an atomic-level characterization and investigation of the structural properties for the identified metastable states of the system along the proposed (un)folding pathway. This approach leads to better understanding of the underlying (un)folding mechanism. Furthermore, we were able to define a set of structures that may be used as targets to design inhibitors capable of binding SAA to stabilize it and prevent the misfolding.

1 Sack Jr, G. H. (2018). Molecular medicine, 24(1), 46
2 Mendels, D.; Piccini, G.; Brotzakis, Z. F.; Yang, Y. I.; Parrinello, M. (2018). Folding a small protein using harmonic linear discriminant analysis. The Journal of chemical physics, 149
3 Nadwa, H., Brotzakis, Z. F., Santucci, A., Braconi, D., Vendruscolo, M. “Computational Study of the (un)Folding Mechanism of Serum Amyloid A (SAA) Protein” Manuscript in preparation",

contact: haidara.nadwa@student.unisi.it

Paraoxonase-2 in osteosarcoma: potential for the development of a targeted anticancer therapy

Campagna Roberto, Pompei Veronica, Gerini Eleonora, Pozzi Valentina, Salvolini Eleonora, Sartini Davide, Emanuelli Monica

Dipartimento di Scienze Cliniche Specialistiche ed Odontostomatologiche, Università Politecnica delle Marche, Ancona

Osteosarcoma (OS) is a rare and aggressive form of bone cancer that primarily affects children, adolescents, and young adults, although it can occur at any age. OS arises from mesenchymal stem cell as well as committed osteoblast precursors and it most commonly develops in the long bones, such as the arms and legs, and often affects the area around the knee. OS is a fast-growing cancer which tends to grow aggressively into nearby tissues and structures, such as muscles, blood vessels, and nerves. This local invasion can complicate surgical removal and contribute to the difficulty in treating the disease. Moreover, since bone is a dynamic tissue with a rich blood supply, it provides a fertile environment for tumor growth and spread, resulting in a marked tendency to early metastasize, most commonly to the lungs. Finally, OS often displays intrinsic or acquired chemoresistance, which complicates its management. Since OS is an extremely aggressive cancer often characterized by poor prognosis, the identification of novel biomarkers with a diagnostic and prognostic purpose, or for targeted therapies, are urgently required. In this study, we first focused on the expression of paraoxonase-2 (PON2), an enzyme associated with membranes of organelles such as endoplasmic reticulum and mitochondria, which has been demonstrated to exert anti-oxidative, anti-apoptotic and anti-atherosclerotic effects. Immunohistochemical analyses revealed that PON2 protein expression was significantly higher in OS compared with control bone tissue samples. Subsequently, we analyzed the impact of shRNA-mediated PON2 silencing on proliferative capacity, migration, chemoresistance, reactive oxygen species (ROS) levels and glucose uptake in U-2 OS and Saos-2 OS cell lines, which are well-established OS models. The shRNA-mediated downregulation of the enzyme resulted in a significant decrease of proliferative capacity, vitality, and migration ability of OS cells. Furthermore, PON2 silencing resulted in higher sensitivity of OS cells to the chemotherapeutic drugs cisplatin and doxorubicin, enhanced ROS levels, and triggered apoptosis activation, as demonstrated by increased caspase levels. Finally, PON2 downregulation weakened glucose uptake by OS cells due to lower GLUT1 glucose transporter levels. Taken together, our findings provide the first evidence of PON2 overexpression in OS, suggesting a possible application of the enzyme as diagnostic biomarker, highlighting its potential for targeted therapy in human OS.

contact: r.campagna@univpm.it

Adenosine role in myofibroblasts-lipofibroblast transition in an in vitro model of lung fibrosis

Gloria Basso1, Maria Sofia Bertilacchi1, Chiara Giacomelli1, Laura Marchetti1, Francesca Cencetti2, Maria Letizia Trincavelli1

1 Department of Pharmacy, University of Pisa, 56126, Pisa, Italy
2 Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Italy

Pulmonary fibrosis (PF) is a pathological condition common to many Interstitial Lung Diseases (ILDs), characterized by aberrant fibroblast activation and excessive extracellular matrix (ECM) deposition leading to lung remodeling and progressively respiratory failure. In this context, Transforming Growth Factor-β (TGF-β) plays a central role driving the phenotypic switching from fibroblasts to myo-fibroblasts, the pro-fibrotic phenotype. Moreover, myo-fibroblasts are able to trans-differentiate into lipo-fibroblasts after PPAR-γ signalling activation; this phenotypic switching could resolve the fibrotic state1. Recent evidence suggests that some extracellular factors, including adenosine (ADO), are involved in the pathogenesis of fibrosis-even if its role is not clear yet2. First, to investigate ADO effects on fibroblasts phenotypic switching, an in vitro model of IMR-90 (human lung fibroblasts) was developed to reproduce the myofibroblast-lipofibroblast transdifferentiation. Fibroblast treatment with TGF-β 5 ng/ml for 24h followed by Rosiglitazone treatment 100 uM for 24h highlighted a decrease in α-smooth muscle actin (α-SMA) expression, an increase in lipid droplet accumulation and elevated perilipin (PLIN2) levels, confirming the phenotypic switching. Afterwards, the adenosine receptors (A1AR A2AAR, A2BAR, A3AR) expression and of the purinome machinery enzymes (CD39, CD73, ADK) and the ADO transports, ENT1 and ENT2, were investigated during fibroblasts differentiation. Especially, the expression patterns of A2A, A2B and A3 receptors were modulated during fibroblast to lipofibroblast differentiation. Among the purine metabolism machinery, only an increase in the levels of CD39 and CD73 were detected in lipofibroblasts. In addition, ADO cell treatment was not able to counteract myo-to lipofibroblast switching favoring the fibrotic phenotype. Overall, these results pave the way for a better understanding of molecular mechanisms underlying the pathogenesis of PF and adenosine role in fibroblast differentiation, allowing the identification of new therapeutic targets.

This study received funding from European Union-Next-GenerationEU-National Recovery and Resilience Plan (PNRR)–MISSION 4 COMPONENT 2, INVESTIMENT N. 1.1, PRIN 2022–2022NAFK8C CUP I53D23004290006

1. El Agha, E. et al., Two -Way conversion between Lipogenic and myogenic fibroblastic phenotypes marks the progression and resolution of Lung Fibrosis, Cell Stem Cell, 2017 Feb 2; 20(2): 261–273.e3
2. Cash E, Goodwin AT, Tatler AL. Adenosine receptor signalling as a driver of pulmonary fibrosis. Pharmacol Ther. 2023 Sep;249:108504

contact: gloria.basso@phd.unipi.it

Effect of probiotics and gamma-oryzanol on cytokines-induced alteration of intestinal epithelial cell monolayer permeability

Helena Juricic1, Ziqi Liu1, Giulia Abate2, Daniela Uberti2, Laura Bonfili1, Massimiliano Cuccioloni1, Mauro Angeletti1, Anna Maria Eleuteri1 and Valentina Cecarini1

1 School of Biosciences and Veterinary Medicine, University of Camerino, Italy
2 Department of Molecular and Translational Medicine, University of Brescia, Italy

Many studies reported the positive impact of treatments based on the combination between natural bioactive compounds and probiotics. On such a basis, the aim of the present work was to explore the effects of two commercial probiotic strains, Lacticaseibacillus rhamnosus IMC 501 ® and Lacticaseibacillus paracasei IMC 502 ® , and gamma-oryzanol, a phytochemical present in large amounts in rice bran, on Caco-2 intestinal cells, properly differentiated to mimic the intestinal epithelium. The capacity of gamma-oryzanol to maintain the growth of the two strains was tested. No inhibition was observed in either case, but the growth of L. rhamnosus IMC 501 ® was enhanced by γ-oryzanol. In addition, the cell free supernatant (CFS) of 30 hours L. rhamnosus IMC 501 ® culture supplemented with γ-oryzanol had a significant visible effect against selected strains of potential pathogenic bacteria showing good antimicrobial activity. Then, the ability of probiotics and gamma- oryzanol, alone or in combination, to prevent cytokines-mediated damages to the epithelium was evaluated testing TEER values and permeability to 4-kDa fluorescein isothiocyanate (FITC)- dextran (FD4). To further explore the mechanism of action and the effects of treatments on intestinal integrity, the expression of tight junctions (TJs) proteins, such as occludin, ZO-1 and claudin, was monitored. Taken together, our results provide evidence on the ability of the two probiotics and gamma-oryzanol to counteract the alteration of monolayer permeability and loss of TJs proteins in Caco-2 cells supporting their combined use in the prevention or treatment of diseases characterized by intestinal permeability disorders."

contact: helena.juricic@unicam.it

Proteomics based evaluation of potential treatment for Idiopathic Pulmonary Fibrosis: investigation of HDAC6i effects on lung fibrotic fibroblasts

Shaba Enxhi1, Vantaggiato Lorenza1, Carullo Gabriele2, Ciccone Valerio2, Donnini Sandra3, Morbidelli Lucia3, Gemma Sandra2, Butini Stefania2, Campiani Giuseppe2, Bini Luca1, Landi Claudia1

1 Functional Proteomics Lab., Life Sciences Dept., University of Siena, Siena, Italy;
2 Dept. of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy;
3 Pharmacology of angiogenesis Lab., Life Sciences Dept., University of Siena, Siena, Italy;

Idiopathic pulmonary fibrosis (IPF) is a chronic fibrotic rare disease with few not resolutive-therapeutic options, and novel drugs as targeted therapeutic approaches are needed. Histone Deacetylases (HDACs) represent potential drug targets, due to their role in IPF pathogenesis. HDACs are enzymes that deacetylate lysine residues in histones and non-histone proteins. Interestingly, HDAC6 is involved in TGF-β1-induced epithelial-to-mesenchymal transition and SMAD3-signaling in IPF fibrogenesis, and its specific expression is demonstrated in IPF-type-II alveolar epithelial cells (AECII) of IPF lungs, but not in normal AECII. These evidences strongly support the potentiality of HDAC6 as druggable target.
Among recently designed selective HDAC6 inhibitors (HDAC6i), NF2376 proved to be effective in reversing the IPF phenotype in ex vivo experiments.
Given this, the aim of this study was to evaluate the proteomic changes of fibrotic lung fibroblasts after HDAC6i treatment, by using NF2376 and the new compound NF3126, developed starting from the solved crystal structure of NF2376 in zfHDAC6 (PDB: 6V79).
We performed a top-down differential proteomic analysis of human lung fibroblast cell line IMR-90 after treatment with 1 μM of NF2376 (C5) or NF3126 (C2) for 48 h in co-stimulation with TGF-β1 (5 ng/mL) as fibrosis-inducing stimulus.
Target validation of HDAC6i was confirmed, showing a specific HDAC6 inhibitory activity. Fibrosis markers, such as COL1A1 and FN1, were down-regulated after HDAC6i treatment and morphometric analysis of cell shape supported evidence of HDAC6i anti-fibrotic activity.
Proteomic analysis evidenced 122 differential spots with a distinct proteomic profile of healthy fibroblasts (CTRL) from that of TGF-β1-induced ones (TGFβ), further showing characteristic clusters of spots that well distinguish from TGFβ and that highlight different responses to the two HDAC6i. Results show that C2-related modulated proteins are associated with regulation of telomere maintenance, regulation of apoptotic process, alternative mRNA splicing, unfolded protein response, microtubule-associated processes, chaperone-mediated processes, regulation of TNF-mediated signaling. In addition, C5-related modulated proteins are associated with protein folding, ER-associated protein degradation, response to xenobiotic stimulus, PI3K/AKT pathway and extracellular matrix rearrangement. As further step, the current experimental design will be applied to human IPF fibrotic lung fibroblasts, the most similar scenario to IPF disease.

This work is part of the research project HIDE IPF “Epigenetic and proteomic approaches towards innovative targeted therapies for IPF” funded by Tuscany Region - Bando Ricerca Salute 2018.

contact: enxhi.shaba@unisi.it

Understanding the role of il-1β in tenocyte homeostasis: a proteomic and lipidomic perspective

Matteo Seccaroni1, Sandra Buratta2, Alessia Tognoloni1, Lorena Urbanelli2, Roberto M Pellegrino2, Husam BR Alabed2, Yalda Ashraf Kharaz3, Mandy Peffers3, Carla Emiliani2, Elisabetta Chiaradia1

1 Department of Veterinary Medicine, University of Perugia, Perugia, Italy
2 Department of Chemistry, Biology and Biotechnology, University of Perugia, Perugia, Italy
3 Department of Musculoskeletal and Ageing Science, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom.

Tendinopathy is a degenerative condition traditionally associated with overuse and mechanical stress, but growing evidence highlights the role of inflammation in its pathogenesis.
Specifically, cytokines such as interleukin-1β (IL-1β) have been implicated in both the onset and progression of tendon disorders, as well as in the modulation of tissue repair and regeneration.
This study investigates the effects of 48 hours of exposure to IL-1β (10 ng/mL) on the proteome and lipidome of tenocytes.
Label-free proteomic analysis revealed changes in the abundance of various proteins involved in molecular and metabolic pathways previously associated with tendinopathy.
Enrichment analysis demonstrated that the differentially abundant proteins are involved in extracellular matrix (ECM) organization and degradation, cytoskeletal dynamics, cell adhesion, metabolic pathways, hypoxia response, oxidative stress, ferroptosis, and apoptosis. Most of these findings were validated by qPCR, flow cytometry, Western blotting, and ELISA. Additionally, lipidomic analysis showed changes in the abundance of some lipid species in tenocytes exposed to IL-1β, suggesting potential alterations in lipid composition.
This study evidence a possible role of IL-1β in the alteration of tenocyte metabolism,highlighting molecular processes that might be involved in the etiopathogenesis of tendon disease.The cellular pathways in which deregulated proteins appear to be implicated could represent potential targets for novel therapeutic strategies

contact: seccaronimatteo@gmail.com

The rational engineering of a dimeric single-domain antibody enhances the detection of toxic Aβ42 oligomers

Napolitano Liliana1,2, Vadukul Devkee2, Bigi Alessandra1, Cecchi Cristina1, Chiti Fabrizio1, Cascella Roberta1, Aprile Francesco2

1 Dipartimento di Scienze Biomediche Sperimentali e Cliniche, Firenze.
2 Department of Chemistry, Molecular Sciences Research Hub, Imperial College London Londra

Soluble amyloid-β42 (Aβ42) oligomers, rather than insoluble amyloid fibrils, are the major neurotoxic agents in Alzheimer's disease (AD).
These small, transient and heterogeneous aggregates, formed during the early stages of the aggregation process of the peptide or release from mature fibrils make difficult their detection, quantification and isolation from biological fluids.
In a previous work, we rationally designed a single domain antibody (sdAb), called DesAbO, with high specificity for Aβ42 oligomeric conformers[1].
Recently, we showed the ability of DesAbO to selectively detect synthetic Aβ42 oligomers in cultured cells, neutralizing their associated neuronal dysfunction[2].
This sdAb can also identify Aβ42 oligomers in the cerebrospinal fluid samples (CSFs) of AD patients, compared to healthy individuals, preventing cell dysfunction induced by CSFs administration[2].
To further improve the binding properties of DesAb-O and obtain a refined tool for oligomer detection and neutralization, we engineered a dimeric DesAb-O variant hereafter referred to as DiDesAb-O. This dimeric sdAb was able to markedly interfere with the Aβ42 aggregation process in Thioflavin T (ThT) assays and can recognize Aβ42 oligomers with significantly higher specificity and selectivity than DesAb-O as revealed by ELISA assays.
Furthermore, with the application of Transmission Electron Microscopy (TEM), dot blot and proteinase K (PK) analyses, we monitored the morphological and structural changes in the Aβ42 fibrils obtained by co-incubating the Aβ42 monomer in the absence or presence of the sdAbs.
We found that fibrils obtained in the presence of DiDesAb-O showed jagged appearance with the presence of globular structures on their surface, and a reduced diameter as compared to those formed in the presence of DesAb-O or in the absence of sdAbs, resulting exceptionally thin and fragile. Notably, DiDesAb-O selectively identified Aβ42 oligomers present in the CSFs of AD patients as compared to control individuals and completely prevented the increase of intracellular Ca2+ levels induced by toxic oligomers present in the CSFs of AD patients at lower concentrations compared to DesAb-O.
In conclusion, DiDesAb-O appears to be a promising tool for the future development of sdAb based immunodiagnostic tests for the early diagnosis of AD as well as the starting point for the generation of novel therapeutic approaches.

References
1. Aprile et al, (2020) PNAS. 117(24), 13509–13518;
2. Bigi A, Napolitano L et al, (2024) Alzheimers Res Ther. 16,13

contact: l.napolitano@ifac.cnr.it

12

Characterization of the VPS13B splicing pattern in a Cohen Syndrome Patient harboring a large deletion in the VPS13B gene

Fanelli Fabiana1, Saltarelli Roberta1, Fichera Marco3,4, Romano Corrado3,4, Barbieri Elena1, Barone Rita2, Annibalini Giosuè1

1.University of Urbino Carlo Bo, Department of Biomolecular Sciences, Urbino, Italy;
2.University of Catania, Child Neurology and Psychiatry Unit, Department of Clinical and Experimental Medicine, Catania, Italy;
3.Oasi Research Institute-IRCCS, Unit of Rare Diseases and Neurodevelopmental Disorders, Catania, Italy;
4.University of Catania, Department of Biomedical and Biotechnological Sciences Section of Clinical Biochemistry and Medical Genetics, Catania, Italy.

The human VPS13B gene is localized on chromosome 8 (8q22.2) and comprises 62 exons. Alternative splicing of VPS13B generates different mRNA variants with predicted open reading frames (ORFs) ranging from 1,248 to 12,069 nucleotides (nt). The longest transcript (NM_017890.5; isoform 5) encodes a predicted 4,022-amino acid transmembrane protein that plays a critical role in Golgi assembly and membrane transport [1]. Mutation in VPS13B causes Cohen syndrome, a rare autosomal disorder characterized by multisystemic involvement and a broad spectrum of clinical manifestations [2]. Here, we analyzed the VPS13B splicing pattern in a patient with Cohen syndrome who harbors a homozygous ≈250 Kb deletion on chromosome 8, leading to the complete loss of exons 18-24 and partial truncation of exon 25. Using primers spanning exon 17 to exon 29, we demonstrated that the patient expressed an mRNA variant with a complete deletion of exons 18-25. This deletion introduced a premature termination codon in the exon 26, reducing the ORF to 2,538 nt. Subsequently, using real-time PCR and VPS13B isoform-specific primers, we found that isoform 1 (NM_152564.5), which includes the mutually exclusive exon 28b and has an ORF of 11,994 nt, was the most highly expressed mRNA variant in both control and patient-derived fibroblasts and PBMCs. However, the patient exhibited a marked (2-3 fold) reduction of VPS13B isoform 1 mRNA expression compared to control fibroblasts, likely due to nonsense-mediated mRNA decay (NMD). Furthermore, VPS13B isoform 5 (NM_017890.5), which contains the mutually exclusive exon 28, was the second most highly expressed VPS13B mRNA isoform in control fibroblasts and PBMCs but was barely detectable in patient-derived cells. The expression of the other two VPS13B isoforms, namely NM_015243.3 (isoform 3) and NM_18166.1 (isoform 4) were not expressed in control and patient-derived fibroblasts and PBMCs. Interestingly, patient-derived fibroblasts expressed a previously undescribed mRNA isoform that included both exons 28 and 28b. Since both exons lie downstream of the gene mutation in the patient, this alternative splicing event did not alter the ORF length of the mutated VPS13B.
In conclusion, we described a novel VPS13B mutation in a patient with Cohen syndrome. The large DNA deletion in this patient resulted in decreased VPS13B mRNA levels and a partial alteration of the slicing pattern. Further analyses are needed to evaluate the impact of this VPS13B mutation on protein production, localization and function.

References

[1] Seifert W. et al., J Biol Chem. 2011; 286(43):37665-75
[2] Kolehmainen J. et al., Am J Hum Genet. 2003 Jun;72(6):1359-69

contact: f.fanelli3@campus.uniurb.it

A Hybrid Computational Approach to Personalize Neuroinflammation Diagnosis: Targeting TSPO Mutations with Quantum and Machine Learning

Lorenzo Ceccarelli, Martina Cirinciani, Marco Podda, Alessandro Berti, Nadia Pisanti, Eleonora Da Pozzo.

University of Pisa, Department of Pharmacy, Pisa, Italy
Department of Computer Science, University of Pisa, Pisa, Italy
Centre for Instrument Sharing, CISUP, University of Pisa, Pisa, Italy

Personalized medicine, a patient-tailored approach to healthcare, is becoming increasingly relevant in the big data era. By focusing on therapies and diagnoses customized to the unique characteristics of each patient, such as variations in therapy responsiveness or the emergence of symptoms of uncommon diseases, the vast amount of available information enables a deeper understanding of diseases. Mutations, particularly those affecting amino acids, are often associated with these variations. Even if a mutation does not completely impair protein activity, it may alter its affinity for ligands, such as diagnostic molecules, potentially leading to differences in diagnosis. Understanding the consequences of these mutations is crucial for selecting the best course of action for specific patient groups.
The study of biological systems can benefit from the development of quantum computing (QC) techniques, which hold promise for superiority over classical computing in solving complex problems. However, given the current limitations in computing resources, a hybrid approach that combines classical methods with QC techniques may be a practical solution. Here, we propose a computational workflow that begins with the state-of-the-art Machine Learning tool Pocket2Mol to construct a library of approximately 5 million ligands for both the wild-type (WT) TSPO protein, a commonly used target for neuroinflammation, and its mutated variants. Then, ligand descriptors generated with RDKit are analyzed using a quantum-based feature selection algorithm to identify a small set of ligands for in vitro testing, assessing both their binding capability and biological effects. We continuously refined the screening phases, focusing on evaluating the similarity of these ligands with known TSPO binders and assessing their ability to interact with both WT and mutated TSPO. Additionally, we performed in silico ADME evaluation using ADMETLab 3.0 and toxicity assessment with VenomPred, specifically analyzing hepatotoxicity and carcinogenicity. This approach has the potential to evaluate the impact of mutations on TSPO, aiding in the identification of ligands that interact with mutant proteins and could be used in ligand-mediated imaging for neuroinflammation diagnosis. Radiobinding assays were conducted to assess the ligand binding affinity to TSPO.
Furthermore, we optimized the cellular model on which identified ligands can be tested. Currently, we evaluated fibrosis induction in cells through two different in vitro models: (i) conventional radiotherapy and (ii) treatment with TGF-β to establish the most robust pathological model. Future directions will be the assessment of the effects exerted by the identified molecules in these pathological models to determine their potential protective effects.

This work is partially funded by PNRR ECS00000017 "THE - Tuscany Health Ecosystem - Spoke 6 Precision medicine & personalized healthcare

contact: lorenzo.ceccarelli@unipi.it

Red Blood Cells-derived Extracellular Vesicles as a novel RNA delivery system

Perla Elena, Libetti Debora, Tiboni Mattia, Canonico Barbara, Pierigé Francesca, Antonio Nozza, Guescini Michele, Bianchi Marzia, Rossi Luigia, Magnani Mauro, Biagiotti Sara

Department of Biomolecular Sciences, University of Urbino

Introduction

Extracellular vesicles (EVs) are emerging and promising tools for drug delivery. They are physiologically produced by nearly all cell types and play significant role in many physiological and pathological processes. Among these, Red Blood Cells (RBCs) are particularly intriguing EV producers due to their easy accessibility, complete safety, non-immunogenicity, and lack of DNA content. However, Red Blood Cells-derived Extracellular Vesicle (RBCEV) production is still challenging because of issues related to yield, clinical translatability, and loading efficiency.

Materials and methods

We started from pre-loaded RBCs to obtain RNA-loaded RBCEVs with a newly developed and patented method called “soft extrusion”. This non-disruptive physical vesiculation technique mimics the natural processes occurring during RBC passage through the spleen. The encapsulation was conducted through a hypotonic dialysis, using a synthetic mRNA as cargo. This is a modified mRNA with methyl-pseudouridine for enhanced stability and with a codon optimization for murine models. Our RBCEVs were then purified through a ultracentrifugation and characterized by Dynamic Light Scattering (DLS), Nanoparticle Tracking Analysis (NTA), and Flow Cytometry (FC). Finally, RBCEVs underwent total RNA extraction followed by qRT-PCR to assess the loading efficiency.

Results

Thanks to their unique properties, RBCs were efficiently loaded with the above-mentioned synthetic mRNA encoding for the GAMT enzyme, leading to the RBCEV production that effectively retained molecules within them. First, a dose-dependent loading was set up with 4 different concentrations of long RNA that revealed that the two highest concentrations were very similar to each other, likely due to a saturation effect. Then, we successfully obtained GAMT mRNA-loaded, both RBCs and RBCEVs, as reported by qRT-PCR quantification. Thus, we demonstrated the feasibility of producing RBCEVs loaded with long RNAs and with great features in terms of size distribution, and biochemical features. Moreover, the whole process has been monitored at each step through the use of a cell counter to demonstrate that our soft extrusion is non-disruptive. Indeed, our findings showed that we are able to induce RBCs to vesiculate without their breakage. Finally, preliminary pharmacokinetic and efficacy studies are currently ongoing.

Conclusion

Our RBCEV mimetics exhibit efficient loading and delivery of biological molecules, making them a promising tool for the development of RNA-based therapies. Their advantages include easy translation into clinical applications and the ability to be fully automated, providing a robust and scalable solution for therapeutic delivery. Furthermore, the absence of chemicals makes them non-toxic; thus, confirming their potential use for therapeutic applications, such as for metabolic disorders

contact: e.perla1@campus.uniurb.it

Taste sensitivity and salivary antioxydants in feeding and eating disorders: the role of integrated therapy

Tiziana Di Crescenzo1, Alice Di Paolo1, Valentina Membrino1, Sonila Alia1, Laura Nanetti2, Lucia Emanuela Svarca2, Michele Severini2, Arianna Vignini1

1 Department of Clinical Sciences, Section of Biochemistry, Biology and Physics, Università Politecnica delle Marche, Ancona, Italy.
2 Department of Neuropsychiatry, Children's Hospital "G. Salesi", AOU Ospedali Riuniti delle Marche, Ancona, Italy

Feeding and Eating disorders (FEDs), including anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED), have become a prevalent public health problem due to their rising prevalence, earlier onset, and complex multifactorial etiology. These disorders are influenced by a combination of biological, psychological, familial, and sociocultural factors, underlining the necessity for advanced treatment strategies. Taste sensitivity, defined as the ability to perceive and differentiate between different tastes, is crucial for maintaining overall health. This sensory function can be impaired in various health conditions, and when altered, it may contribute to the development of further health problems. Recent studies have investigated its potential correlation with body mass index (BMI).

Consequently, the objective of this study was to examine the effects of integrated therapy (nutritional rehabilitation, psychotherapy, pharmacotherapy) on taste sensitivity and salivary antioxidant levels [Total Polyphenols Content (TPC), Total Flavonoids Content (TFC), Antioxidant Capacity by ORAC method and Superoxide Dismutase activity (SOD)] in patients suffering from AN and/or BN. The study involved 51 adolescents diagnosed with FEDs, of which 39 had AN and 12 had BN. Anthropometric data, saliva samples, and taste sensitivity assessments were collected at baseline (t0), 3 months (t1), and 6 months (t2) during the integrated therapy. After six months of therapy, improvements in both BMI and taste sensitivity were observed in the AN and BN patients. In particular, the sensitivity to umami and water tastes increased significantly in AN patients, with a similar significant increase in BN patients for umami and sour tastes; on the contrary, the sensitivity for oleogustus was unchanged. However, no significant changes were observed in the salivary antioxidant levels.

Given the fluctuating and non-linear course of FEDs, it is acknowledged that some treatment benefits may become evident in the short term, while others require longer monitoring. The findings of this study suggest that integrated therapy plays a crucial role in the management of these disorders, emphasizing the need for a multidisciplinary approach. These results stress the importance of comprehensive care to improve the physical and psychological health of individuals suffering from FEDs.

contact: tiziana98.tdc@gmail.com

Exploring the Role of ZFHX2 in Neuroinflammation: Implications for Microglia Activation

O.F.Biasco, F.Finetti, A.M. Aloisi, L.Trabalzini

1 Department of Biotechnology, Chemistry and Pharmacy,
2 Department of Medical, Surgical and Neuroscience, University of Siena

ZFHX2 (Zinc Finger Homeobox Domain 2) is a \"dark gene\" identified in a rare pathology known as Marsili syndrome, a hereditary condition with an autosomal dominant inheritance pattern. This syndrome is characterized by congenital insensitivity to pain, where affected individuals exhibit significantly reduced pain perception while maintaining normal sensitivity to touch and temperature[1]. This syndrome has been linked to mutations in the ZFHX2 gene, which encodes a putative transcription factor involved in nervous system development and pain modulation. However, to date, the functions of ZFHX2 and the molecular pathways associated with it remain completely unknown.
Neuroinflammation is a pathological condition observed in many diseases of the nervous system. It represents the response of reactive components in the central nervous system that disrupt homeostasis, with microglia playing a key role in the neuroinflammatory process [2].
The aim of this work is to evaluate the role of ZFHX2 in the neuroinflammatory process, with a particular focus on microglia, and to investigate the underlying molecular pathways.
By using U373 (human glioblastoma) and immortalized astrocytes as cellular models, along with Prostaglandin E2 (PGE2), Interleukin-1 beta (IL-1β), and Substance P (SP) as microglia-activating factors, we observed a modulation of ZFHX2 protein expression and intracellular localization. Additionally, ZFHX2 silencing affected astrocyte responses to neuroinflammatory stimuli. The outcomes of this study indicate that ZFHX2 may play a crucial role in microglia activation during neurogenic inflammation and, for the first time, suggest a possible molecular pathway associated with this protein. Understanding the role of ZFHX2 in neuroinflammation could provide new therapeutic targets for the management of neuroinflammatory disorders.

This research was funded by European Union – Next-GenerationEU - National Recovery and Resilience PLAN (PNRR) - Mission 4, Component 2, Investment 1.4 - “National Center [CN3] for Gene Therapy and Drugs based on RNA Technology”; WP 5.3 Circulating RNA therapeutic target discovery and delivery strategies in autoimmune and inflammatory diseases.

References
1 Habib AM et al. Brain 2018; 141(2):365-376. doi: 10.1093/brain/awx326.
2 DiSabato DJ et al. J Neurochem 2016;139 Suppl 2(Suppl 2):136-153. doi: 10.1111/jnc.13607

contact : omarfrancesco.bia@student.unisi.it

Fibrinogen-Mediated Neuroinflammation: How Extra virgin Olive Oil Polyphenols Defend the Brain

Carnemolla Federica, Manuela Leri, Serena Borghi, Flavia Argento, Elvira Giurranna, Francesca Nencini, Claudia Fiorillo, Niccolò Taddei, Matteo Becatti, Monica Bucciantini

Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence

Polyphenols are natural compounds found in a variety of plants and are widely recognized for their antioxidant properties and potential health benefits, particularly in relation to inflammation and neuroprotection.
Among these, Oleuropein Aglycone (OleA) and its main metabolite Hydroxytyrosol (HT) from extra virgin olive oil (EVOO) and olives have the potential to counteract pro-inflammatory signals in the brain, including those triggered by fibrinogen, a key protein involved in blood clotting.
Fibrinogen is known to activate microglia, the resident immune cells of the central nervous system, leading to the production of inflammatory cytokines that exacerbate neuroinflammatory conditions.
The aim of our study was to enhance the understanding of the molecular mechanisms underlying the protective effects of EVOO polyphenols at different concentrations on fibrinogen-induced damage by conducting in vitro experiments using the human microglia C13NJ and SH-SY5Y neuronal cell models, where cellular viability and oxidative stress were assessed.
Additionally, immunofluorescence analysis was performed to measure the levels of neuroinflammatory markers, and we investigated the mitochondrial efficiency in microglia and neuronal cells treated with C13NJ-conditioned medium.
Our results indicate that both OleA and HT prevent the activation of TRL4 and p-NF-κB and the release of pro-inflammatory chemokines and cytokines, as evidenced by conditioned medium treatments on SH-SY5Y cells.
Moreover, OleA and HT promote an increase in TREM2 levels and act as epigenetic modulators on histone 4 lactylation while also increasing the mitochondrial function.
The ability of OleA and HT to promote an anti-inflammatory microglial phenotype positions them as promising molecules for reducing neuroinflammation, protecting neurons from damage, and supporting overall brain health.
Dietary or supplemental strategies incorporating these polyphenols could provide preventive approaches and strategies aimed at mitigating inflammation before the onset of neurodegenerative diseases.
Additionally, they may serve as complementary therapies to existing treatments that focus on managing neuroinflammation and supporting neuronal health.

contact: federica.carnemolla@unifi.it

Branched oncolytic peptides target HSPGs, inhibit metastasis, and trigger the release of immunogenic cell death-related DAMPs in pancreatic cancer

Rencinai Alessandro, Tollapi Eva, Marianantoni Giulia, Brunetti Jlenia, Henriquez Tania, Pini Alessandro, Bracci Luisa, Falciani Chiara

Dipartimento di Biotecnologie Mediche, Università degli Studi di Siena

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, largely due to its immunosuppressive microenvironment, aggressive metastatic behavior, and poor response to conventional therapies. A major challenge in treating PDAC is its resistance to immune system activation, making it a prime candidate for strategies that enhance tumor immunogenicity. Immunogenic cell death (ICD) is a regulated form of cell death that eliminates malignant cells and activates the immune system, transforming dying tumor cells into endogenous vaccines. ICD is characterized by the release of key damage-associated molecular patterns (DAMPs) from dying tumor cells, including the translocation of calreticulin to the cell surface, extracellular ATP secretion acting as a \"find-me\" signal for dendritic cells, and the release of HMGB1, which binds Toll-like receptor 4 (TLR4) on antigen-presenting cells to enhance antigen processing. These signals promote dendritic cell recruitment and antigen presentation to cytotoxic T cells, fostering a robust adaptive immune response. Unlike non-immunogenic forms of cell death, ICD establishes long-term tumor immunity, making it a promising avenue for cancer therapy.
In this study, we investigated the anticancer properties of two novel branched oncolytic peptides (BOPs), BOP7 and BOP9. Our findings demonstrate that BOP7 and BOP9 selectively target PDAC cell lines (PANC-1 and Mia PaCa-2) while sparing non-tumoral cells, effectively inducing cytotoxicity and inhibiting key metastatic traits such as adhesion and migration. Mechanistically, BOPs exert their anticancer effects through multivalent interactions with HSPGs, which are overexpressed on cancer cells and play a key role in tumor progression and metastasis. Moreover, BOP-induced cytotoxicity contributes to ICD induction, as evidenced by the sustained release of DAMPs from dying tumor cells, including HMGB1, ATP, and IFN-β. Notably, BOP-induced DAMP release persists significantly longer than that of conventional chemotherapeutics such as irinotecan and daunorubicin, suggesting a more sustained immunostimulatory effect. These results imply that BOPs may enhance antitumor immunity by stimulating antigen-presenting cells, promoting adaptive immune responses, and potentially overcoming the immune evasion mechanisms characteristic of PDAC. In vivo, BOP9 demonstrated a 20% reduction in tumor growth in a murine PDAC model, underscoring its potential as a therapeutic agent. Importantly, BOPs exhibit systemic bioavailability, stability against proteolysis, and low hemolytic activity, key advantages for clinical translation. Given their dual anticancer and immunostimulatory properties, BOPs represent promising candidates for combination therapies, particularly in synergy with immune checkpoint inhibitors, to improve the treatment of immunologically silent tumors such as PDAC.

contact: alessandro.rencin@student.unisi.it

The mini recombinant protein ED-sRGN: a compact and versatile genome editing tool

Forte Federica1, De Angeli Pietro2, Tasini Filippo1, Sparti Angelo1, Libetti Debora1, Anjum Ruhi1, Magnani Mauro1, Bianchi Marzia1

1. Department of Biomolecular Sciences, University of Urbino Carlo Bo, Urbino, Italy
2. Institute for Ophthalmic Research, Centre for Ophthalmology, University of Tübingen, Germany

The aim of our project is to develop engineered recombinant enzymes that overcome the limitations of protein expression in cellular hosts, preserving biological activity and improving their performance. Our goal with sRGN (Synthetic RNA-Guided Nuclease), a mini-Cas9 recombinant protein, is to address a key limitation of the Cas9 endonuclease: its large size of 160 kDa, which affects the formulation and delivery processes, both critical for the efficiency of the CRISPR-Cas genome editing system. Indeed, advances in knowledge of the conserved Cas9 domains, combined with recent structural studies, highlighted the potential of engineered mini-Cas9 proteins for more efficient delivery systems, improving the overall efficacy of genome editing technologies.
The ED(Enhanced Deletion)-sRGN protein is made up of the mini-Cas9 (124.3 kDa) fused with TREX2 (25.8 kDa), a 3'->5' exonuclease protein to degrade the Cas9 generated ends thus preventing its re-cutting and further stress to the cell or a possible wild type repair.
While sRGN alone was produced as recombinant enzyme in bacterial hosts and proved to be active in an in vitro assay, the expression of ED-sRGN in bacteria was very challenging.
Therefore, the coding sequence has been cloned into a pKLV2 Lentiviral vector and stably integrated in eukaryotic HEK293T cells. The construct presents a PGK promoter, a N-terminal His-Tag, two nuclear localization signals, the TREX2 and the sRGN coding sequences, a T2A before the puromycin resistance gene. The construct was designed for three different variants of the protein: sRGN (no TREX2 sequence); ED-sRGN and ED-sRGN-3R (bearing mutations in the nuclease DNA binding site). These constructs were used for both stable and transient expression in HEK293T cells. WB assay using an Anti-His Ab, however, failed to detect the ED-sRGN protein in transfected cells. RT-qPCR assay with sRGN-specific primers on total RNA extracted from transfected cells and DNase-treated, confirmed the presence of the transcript. This evidence, combined with the failure to detect the protein, suggests that alterations may occur at post-transcriptional level affecting the ED-sRGN expression.
In-silico analyses were conducted to assess any instability or alteration of the protein structure and any bias of the lentiviral construct. No abnormalities were found. Therefore, our strategy involves a new design of the ED-sRGN construct to express a new version of the protein, by moving the His-Tag to the C-terminus and by introducing site-specific mutagenesis of amino acid residues responsible for TREX2 homodimerization to promote maintenance in its active monomeric form as it could affect the expression of the recombinant protein.

This work has been funded by the European Union - NextGenerationEU, Mission 4, Component 1, under the Italian Ministry of University and Research (MUR) National Innovation Ecosystem grant ECS00000041 - VITALITY - CUP H33C22000430006."

contact: federica.forte@uniurb.it

Short-Chain Fatty Acid Supplementation Mitigates Oxidative Stress and Thrombosis Risk in Behçet's Syndrome

Serena Borghi1, Flavia Rita Argento1, Elvira Giurranna1, Francesca Nencini1, Ilenia Barbaro1, Niccolò Taddei1, Giacomo Emmi2, Matteo Becatti1, Claudia Fiorillo1

1 Department of Experimental Clinical Biomedical Sciences "Mario Serio", University of Firenze, Firenze, Italy
2 Department of Medical, Surgery and Health Sciences, University of Trieste, 34100 Trieste, Italy

Introduction
Behçet's Syndrome (BS) is a systemic vasculitis of unknown aetiology, characterized as a multisystemic immune-inflammatory disorder affecting vessels of all sizes and frequently complicated by thrombosis. Systemic redox imbalance and heightened neutrophil activation in BS patients are believed to contribute to impaired coagulation. Our group has already demonstrated in BS patients altered fibrinogen structure and reduced fibrin susceptibility to plasmin-induced lysis, primarily due to increased reactive oxygen species (ROS) production by neutrophils. This supports the idea that BS serves as a model for inflammation-driven thrombosis. Moreover, BS has been associated to a peculiar dysbiosis in gut microbial ecosystem, represented by a depletion in Clostridium cluster, involved in short-chain fatty acids (SCFAs) production. Among SCFAs, patients show a decrease in butyrate production, which exerts anti-inflammatory and trophic activity.
Methods
To clarify the relationship between butyrate, blood redox status and cardiovascular risk, we assessed the effects of 3 months butyrate-enriched diets in 30 BS patients, 15 patients were randomized to supplementation with oral butyrate (2.4 g/die), whereas 15 to lacto-ovo-vegetarian diet containing insulin and resistant starch-rich foods whose fermentation increases butyrate production. Before and after dietary interventions (T0–T3), we evaluated intracellular leukocytes ROS production, plasma malondialdehyde (MDA) concentration, as an index of lipid peroxidation, and plasma total antioxidant capacity (TAC). On purified fibrinogen fractions, fibrin susceptibility to plasmin-induced lysis was also evaluated.
Results
Both butyrate-enriched interventions showed a significant reduction in leukocyte ROS production and in plasma lipid peroxidation and an increase in plasma total antioxidant capacity. Notably, a significant improvement in fibrin susceptibility to plasmin-induced lysis was observed in both T3 groups compared to T0.
Conclusions.
Our data indicate that a butyrate-enriched diet can restore blood redox status and fibrin degradation, suggesting its potential benefits for cardiovascular prevention in BS patients.

contact: serena.borghi@unifi.it

Enhancing RNA Delivery via Extracellular Vesicles: Loading Efficiency, Cargo Characterization, and Functional Uptake

Germelli Lorenzo 1, Luisotti Lucrezia 1, De Felice Martina 2, Piccarducci Rebecca 1, Grieco Giuseppina 3-4, Sebastiani Guido 3-4, Dotta Francesco 3-4, Falleni Alessandra 5, Cella Zanacchi Francesca 2, Giacomelli Chiara 1, Marchetti Laura 1, Martini Claudia 1

1 Department of Pharmacy University of Pisa, Italy
2 Department of Physics 'Enrico Fermi'-University of Pisa
3 Diabetes Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy
4 Fondazione Umberto Di Mario ONLUS c/o Toscana Life Sciences, Siena, Italy
5 Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Therapeutic RNAs have paved new avenues in drug discovery, but the lack of efficient and tissue-specific delivery systems limits their clinical application. Extracellular vesicles (EVs) are cell-derived nanosized carriers involved in intercellular communication and are enriched in functional non-coding RNAs (ncRNAs) that can modulate gene expression in target cells1. EVs are promising candidates for RNA delivery, yet their clinical translation is hindered by the lack of standardized loading protocols, precise cargo quantification, RNA stability assessment, and functional delivery evaluation2. Here, electroporation, sonication, and transfection with a cell-penetrating peptide (Exo-Fect™) were compared as methods for the loading of a siRNA against GFP (siRNA-GFP) into HEK293-derived EVs. Transfection proved to be the most efficient, yielding roughly 23 siRNA molecules/EV after RNase treatment, and preserving the structural properties of the EVs. The siRNA loading distribution within EVs was further characterized using STORM super-resolution microscopy and stepwise photobleaching. EVs were also loaded with a therapeutic antago-miR (anti-miR-375), and transcriptomic analysis was performed to characterize the total endogenous small RNA content of loaded EVs, as well as to compare the loading efficiency for both cargoes. Transfection efficiency was evaluated in a stable GFP-expressing HEK293 cells using different doses of loaded EVs. Notably, a dose-dependent reduction in GFP expression was observed, reaching up to 50% inhibition with 10^9 EVs per 10^5 cells; however, a plateau effect was detected at higher doses. Conversely, 10^{10} EVs loaded with anti-miR-375 exhibited suboptimal efficiency in reducing the expression of miRNA target in a human pancreatic β-cell line (EndoC-βH1). These findings suggest an inefficient RNA delivery in recipient cells depending on the EVs' cell of origin, likely due to heterotypic membrane interactions. Thus, EVs were engineered to express the viral fusogenic glycoprotein VSVG on their surface. This modification significantly increased the RNA-mediated silencing effects and RNA release in recipient cells, enhancing functional uptake in HEK293 and EndoC-βH1 cells. Overall, this study tackles key challenges in the development of EV-based RNA therapeutics, including the quantification and distribution of loaded RNA within EVs, the characterization of total endogenous small RNA content, the minimum EV dose required per cell for efficient transfection, and the optimization of membrane fusion as an uptake mechanism to enhance functional RNA release across different cellular contexts.

[1] O'Brien K et al.(2020),Nat Rev Mol Cell Biol.,21:585¬606. [2] Zeng H et al.(2023),Cells,12:1416.
Project funded by: PNRR Missione 4, Componente 2, Investimento 1.4, Sviluppo di terapia genica e farmaci con tecnologia a RNA (National Center for Gene Therapy and Drugs based on RNA Technology)-CN3 Spoke8 (WP 8.1.4). CN00000041; CUP I53C22000710007

contact: lorenzo.germelli@farm.unipi.it

Exploring Limbal Stem Cell Aging: The Role of Extracellular Vesicles in Microenvironment Modifications

Guzzetti Martina1, Chiasserini Davide1, Barbaro Vanessa2, Manfredi Marcello3, Romani Rita1,4, Mezzasoma Letizia1,4 Di Michele Alessandro3,5, Demarinis Anna6, Di Iorio Enzo6,7, Bellezza Ilaria1,4.

1 Department of Medicine and Surgery, University of Perugia, Italy.
2 Fondazione Banca degli Occhi del Veneto, Mestre, Venezia, Italy.
3 Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy.
4 Extracellular Vesicles network of UniPG, Italy.
5 Department of Physics and Geology, University of Perugia, Italy.
6 Department of Molecular Medicine, University of Padova, Italy.
7 Clinical Genetics Unit, Azienda Ospedaliero Universitaria di Padova, Italy.

Limbal epithelial stem cells (LESCs) are essential for the maintenance and regeneration of the corneal epithelium, ensuring the continuous renewal of the ocular surface and preventing limbal stem cell deficiency (LSCD), a condition associated with severe visual impairment. The ability of stem cells to proliferate and differentiate is hindered by senescence, a complex and multifaced process that results in an irreversible proliferation arrest, and resistance to apoptosis. Understanding the molecular mechanisms underlying LESC senescence is critical for developing strategies to prevent LSCD, which leads to corneal conjunctivalization, neovascularization, scarring, chronic inflammation, and vision loss. Extracellular vesicles (EVs) are membrane-enclosed particles secreted by virtually all cells which contribute to intercellular communication by transporting protein, lipids and nucleic acids such as miRNA. Data in the literature suggest that EVs are involved in the spreading of senescence signals within tissues. To investigate the molecular events underlying cellular senescence, LESCs were cultured until proliferative arrest and proteomic analyses were performed at early (p2) and senescent (p6) passages. The analysis showed 450 upregulated and 671 downregulated proteins in LESCs P6 versus P2 (logFC >2; adj.P.Val <0.01). Pathway analysis reveal an upregulation of processes such as extracellular matrix organization and glucose metabolism and a downregulation of cell adhesion, respiratory electron transport and integrin-mediated pathways. To characterize the ability of LESC to influence tissue microenvironment, EVs were isolated from conditioned media and analyzed using scanning electron microscopy (SEM), nanoparticle tracking analysis (NTA), and EV-specific protein markers. miRNAomic profiling revealed an enrichment of microRNAs implicated in important biological pathways, such as protein metabolism, cell cycle, membrane trafficking, and stress response. These findings shed light on the molecular mechanisms underlying LESC aging and identify EVs as key mediators of microenvironmental changes, presenting new opportunities for therapeutic interventions in LSCD.

This work was supported by: grant number 20223FW48B – PJ PRIN_2022_BELLEZZA financed by the European Union—Next Generation **EU CUP: J53D23006150006**.

contact: martina.guzzetti@unipg.i

ELENCO NUMERATO DEI POSTER

1 Bertoldi Agnese, Calzoni Eleonora , Cusumano Gaia, Buratta Sandra, Urbanelli Lorena and Emiliani Carla
Evaluation of Plant-Derived Extracellular Vesicle modulate the Epithelial-Mesenchymal Transition process in an In Vitro cellular Hepatic Model

2 Ricci Anastasia, Biancucci Federica, Morganti Gianluca, Magnani Mauro, Menotta Michele
ATM variants activation by endogenous ATM

3 Andrea Carlotta Conti, Elena Casarotto, Cristina Cecchi, Fabrizio Chiti, Angelo Poletti, Valeria Crippa and Roberta Cascella
The alterations of proteostaisi network promotes the secretion and propagation of toxic TDP-43 species

4 Angela Subbiani, Francesca Bonechi, Nicla Lorito, Alice Santi, Marina Bacci, Alfredo Smiriglia, Edoardo Pagliantini, Sven Rottenberg, Paola Francica and Andrea Morandi
Identification of ALDH18A1 as a metabolic vulnerability in ER+ breast cancer cells resistant to estrogen deprivation using RNA interference screening

5 Moccia Annalisa, Santi Alice, Iannuccilli Francesca, Taddei Maria Letizia, Sodano Rebecca, Joechler Veronika, Vizzoni Lucia, Nesti Siria Emily, Piras Anna Maria, Zambito Ylenia, Paoli Paolo, Caselli Anna, Cirri Paolo
Targeting tumor cells with custom antigen transferred by monocyte-derived EVs: a novel immunotherapy strategy to enhance T cell-mediated cytotoxicity

6 Visibelli Anna, Coppola Carmen, Sinicropi Adalgisa, Spiga Ottavia, Santucci Annalisa
A Combined ML and DFT Strategy for the Prediction of Dye Candidates for Indoor DSSCs

7 Antonio Nozza, Rachele Agostini, Mattia Tiboni, Stephanie Fondi, Paola Ceccaroli, Emanuela Polidori, Patrick Orlando, Sonia Silvestri, Andrea Frontini, Luca Casettari, Michele Guescini
Bioinspired exosome-mimetic nanovesicles for targeted delivery of Coenzyme Q10

8 Chirco Antony, Meacci Elisabetta, Margheri Giancarlo
SPADE: biosensori ottici SPR per la rilevazione in tempo reale di biomolecole target in quantità minime di campione biologico.

9 Ranocchi Bianca, Pennesi Alessandro, Baglieri Egizia, Amicucci Antonella
In silico characterization of the Yap1 transcription factor in Tuber genus fungi: a study on the mechanisms of response to oxidative stress

10 Polini, Beatrice, Mazzierli, Anna, Brogi, Etrusca, Corradi, Francesco, Forfori, Francesco, Chiellini, Grazia
Cranberry juice (CJ) counteracts the inflammatory process in inflamed human microglial HMC3 cell line

11 Mannini Benedetta,, González Díaz Alicia, Sarracco Eleonora, Antonio Urrutia Gustavo, Belli Elisa, Chia Sean, Vendruscolo Michele
Advancing Preclinical Models for Alzheimer's Disease

12 Carmela Conte, Michela Bulfoni, Federico Fiorani, Samuela Cataldi, Nicolò Gualandi, Ornella Calderini Mercedes Garcia-Gil, Giorgia Vesca, Rita Paroni, Michele Dei Cas, Cataldo Arcuri, Alessandra Mirarchi, Tommaso Beccari, Toshihide Kobayashi, Nario Tomishige, Paola Signorelli, Francesco Curcio and Elisabetta Albi
Microdomains of the inner nuclear membrane contain sphingomyelin and RNase-resistant RNA.

13 Mancini Caterina , Desideri Dayana , Pranzini Erica , Mattei Gianluca , Lori Giulia , Taddei Maria Letizia
PHGDH expression modulates arachidonic acid pathway and 5-FU resistance in colorectal cancer

14 Baccioni Caterina, Agostini Giada, Stincarelli Maria Alfreda, Nass Kebapcioglu Ismael Cem, Munagala Uday, Giannecchini Simone, Conticello Silvo G.
Unraveling the role of ADARs in SARS-CoV-2 Infection

15 Chiara Rucci, Laura Bordoni, Enrica Sordini, Giuseppe Persico, Noemi Pappagallo, Giulia Matacchione, Marco Giorgio, Daniele Fraternale, Mirco Fanelli, Maria Cristina Albertini, Stefano Amatori, Rosita Gabbianelli
Exploring the transcriptomic and epigenetic impact of Mela Rosa Marchigiana callus extract on cellular aging: insight from an in vitro study

16 Bernardi Clizia, Finetti Federica, Trabalzini Lorenza
Common Beans and Gut Health: Investigating Their Role in Inflammation, miRNA Modulation, and Colorectal Cancer Prevention

17 Cicchi Costanza, Tena Garitaonaindia Mireia, Ceacero Heras Diego, Jiménez Ortas Ángela, Sánchez de Medina Fermin, Martinez Augustin Olga, Leri Manuela, Bucciantini Monica, Paoli Paolo, Luti Simone, Pazzagli Luigia
Bioactive peptides from fermented sourdough: potential role in modulation of intestinal homeostasis and barrier function

18 Flavia Di Re, Serena Vetri, Maria De Angioletti, Francesca Mari, Silvestro G. Conticello
Molecular Killers: exploiting cell death from the inside

19 Edoardo Pagliantini, Dario Romagnoli, Simone Romagnoli, Matteo Benelli and Andrea Morandi
Development of a peroxisome activity-related gene expression signature with prognostic potential in ER+ breast cancer

20 Germelli Lorenzo, Rebecca Piccarducci, Lorenzo Ceccarelli, Laura Marchetti, Tito Calì, Da Pozzo Eleonora
Microglial exosome biogenesis and release: roles of cholesterol and organelle contact sites.

21 Fiorani Federico, Quattrone Alda, Cataldi Samuela, Roberto Maria Pellegrino, Carla Emiliani, Arcuri Cataldo, Mirarchi Alessandra, Curone Giulio, Laura Menchetti, Beccari Tommaso, Floridi Claudia, Brecchia Gabriele, Mandarano Martina, Albi Elisabetta
Role of sphingomyelin and vitamin D3 rich diet in rabit brain

22 Elisabetta Romano, Nicla Lorito, Marina Bacci, Alfredo Smiriglia, Francesca Bonechi, Edoardo Pagliantini, Sven Rottenberg, Pola Francica, Andrea Morandi
Targeting LIPH-mediated signaling potentiates CDK4/6 inhibition in ER+ breast cancer

23 Elvira Giurranna, Serena Borghi, Francesca Nencini, Flavia Rita Argento, Ilenia Barbaro, Giacomo Emmi, Niccolò Taddei, Claudia Fiorillo, Matteo Becatti
Oxidative Stress-Driven Fibrinogen Alterations in Systemic Lupus Erythematosus: Unraveling the Mechanisms of Thrombotic Risk

24 Emilio Ermini, Martina Gennari, Alessandra Bigi, Cristina Cecchi, Roberta Cascella and Fabrizio Chiti
Unraveling the Protective Role of Estrogens in ALS: A Study of TDP-43 Dynamics in Neuronal Cells

25 Shaba Enxhi, Vantaggiato Lorenza, Carullo Gabriele, Ciccone Valerio, Donnini Sandra, Morbidelli Lucia, Gemma Sandra, Butini Stefania, Campiani Giuseppe, Bini Luca, Landi Claudia
Proteomics based evaluation of potential treatment for Idiopathic Pulmonary Fibrosis: investigation of HDAC6i effects on lung fibrotic fibroblasts

26 Eva Tollapi, Alessandro Rencinai, Giada Meogrossi, Silvia Scali, Chiara Falciani
Antibacterial and anti-biofilm activity of branched peptides derived from antimicrobial peptides

27 Francesca Del Debbio, Maria Sofia Bertilacchi, Damiano Del Sarto, Andrea Cavalieri, Giovanni Gadducci, Noemi Giannini, Alessandra Gonnelli, Taiusha Fuentes, Francesca Cella Zanacchi, Benedetta Noferi, Antonella Catanzariti, Vittorio Parenti, Martina De Felice, Chiara Giacomelli, Fabiola Paiar, Fabio Di Martino, Claudia Martini, Eleonora Da Pozzo, Simone Capaccioli
Exploring the molecular mechanism of FLASH Radiotherapy: In Vitro Assessment on Healthy Bronchial Epithelial Cells

28 Iannuccilli Francesca, Santi Alice, Moccia Annalisa, Sodano Rebecca, Joechler Veronika, Paoli Paolo, Caselli Anna, Cirri Paolo
Role of Bisphosphoglycerate mutase (BPGM) in Tumour-Mediated Metabolic Reprogramming in Proliferative Cancer-Associated Fibroblasts (CAF)

29 Nardi F, Del Prete R, Drago R, Di Rita A, Vallone FE, Ciofini S, Malchiodi M, Pezzella L, Tinti L, Cicaloni V, Salvini L, Licastro D, Pezacki AT, Chang CJ, Marotta G, Naldini A, Deaglio S, Vaisitti T, Gozzetti A, Bocchia M, Kabanova A.
Apoliprotein E induces ferroptosis in leukemic B cells

30 Francesca Monittola, Sofia Masini, Gianni Gori Savellini, Giulia Scopa, Marta De Angelis, Elena Piselli, Gabriele Anichini, Maria Grazia Cusi, Lucia Nencioni, Alessandra Fraternale and Rita Crinelli
Glutathione metabolic pathways in SARS-CoV2-infected Calu-3 cells and their modulation by synthetic low molecular weight thiol molecules

31 Errico Silvia, Fani Giulia, Ventura Salvador, Schymkowitz Joost, Rousseau Frederic, Trovato Antonio, Vendruscolo Michele, Bemporad Francesco, Chiti Fabrizio
Structural Commonalities Determined by Physicochemical Principles in the Complex Polymorphism of the Amyloid State of Proteins

32 Francesco Maria Grasselli, Laura Bonfili, Gregorio Sonsini, Massimo Ubaldi, Massimiliano Cuccioloni, Valentina Cecarini, Anna Maria Eleuteri
Effect of a multi-strain probiotic under chronic hypoxic conditions with a focus on brain damages and cognitive functions

33 F. Morena, C. Cencini, M. Lucariello, S. Giannoni, L. Donati, M. Valicenti, C. Emiliani, S.Martino
RoseTTAFold diffusion-guided short peptide design: a case study of binders against Keap1/Nrf2

34 Gabriele Tani, Alfredo Smiriglia, Marina Bacci, Nicla Lorito, Francesca Bonechi, Edoardo Pagliantini, Sven Rottenberg, Paola Francica, Andrea Morandi
CYP1A1 regulates estrogen receptor activity and response to Palbociclib in Estrogen Receptor-positive breast cancer cells

35 Giada Agostini, Caterina Baccioni, Maria Alfreda Stincarelli, Ismael Cem Nass Kebapcioglu, Uday Munagala, Simone Giannecchini, Silvo G. Conticello
Unraveling the role of ADARs in SARS-CoV-2 infection

36 Cusumano Gaia, Bertoldi Agnese, Calzoni Eleonora, Buratta Sandra, Urbanelli Lorena, Angelini Paola, and Emiliani Carla
Comparative Evaluation of Mushroom-Derived Extracellular Vesicles from Pleurotus eryngii: Antioxidant and Anti-Inflammatory Properties

37 Gioena Pampalone, Marilena Pariano, Emidio Camaioni, Claudia Stincardini, Magdalena Davidescu, Lara Macchioni, Mirco Dindo, Consuelo Fabi, Julie Saba, Giorgio Giardina, Stefano Giovagnoli, Luigina Romani, Claudio Costantini, Barbara Cellini
Biochemical characterization of A6770 as dual species inhibitor of sphingosine-1-phosphate lyase in cystic fibrosis.

38 Genny Scacci, Giorgia Isinelli, Sandra Buratta, Lorena Urbanelli, Roberta La Starza, Ilaria Iacobucci, Carla Emiliani, Cristina Mecucci, Rocco Piazza, Daniele Ramazzotti, Charles G. Mullighan, Danika Di Giacomo
Dissecting the mechanisms of leukemogenesis in NUP98::DDX10-driven leukemia

39 Feliziani Giulia, Tagliasco Marianna, Pellegrini Nicoletta, Suo Xinying, Vittadini Elena, Bordoni Laura, Gabbianelli Rosita.
Bioactive properties of Grano Mischio: effects on antioxidant activity, intestinal barrier function, and inflammatory response

40 Gangarossa Giulia, Iozzo Marta, Ippolito Luigi, Pecoraro Matteo, Pardella Elisa, Pranzini Erica, Comito Giuseppina, Capatano Carlo, Giannoni ELisa and Chiarugi Paola
The role of lactate-mediated histone H3 lysine 18 lactylation (H3K18la) in prostate cancer aggressiveness

41 Lori Giulia, Mancini Caterina, Desideri Dayana, Paffetti Caterina, Pranzini Erica, Manicone Fedele, Spatafora Pietro, Magherini Francesca and Taddei Maria Letizia
Role of the senescent stroma-derived glutamine in the aggressiveness of prostate and ovarian cancer cells

42 Buffi Gloria, Fiorani Mara, Guidarelli Andrea, Bagherlou Nazanin, Spina Andrea, Scocchia Lorenzo, Renna Giorgia Maria, Zito Ester, Cantoni Orazio
Myotube specific vulnerability to clozapine: potential correlation with muscle-related side effects

43 Ismael Cem Nass Kebapcioglu, Caterina Baccioni, Uday Munagala, Silvo G. Conticello
Fine-tuning site-directed RNA editing: controlled gRNA synthesis with T7 RNA polymerase

44 Balloni Irene, Angeloni Elisa, Dell'Amico Claudia, Coppini Allegra, Marchetti Laura, Onorati Marco, Raffa Vittoria, Barresi Elisabetta, Da Settimo Federico, Taliani Sabrina, Costa Barbara, Da Pozzo Eleonora, Trincavelli Maria Letizia
Pharmacological modulation of 18KDa translocator protein in different neuronal models: exploration of new neuroprotective mechanisms

45 Isabella Marzi, Fabrizio Chiti
Insights into the Structure and Aggregation of C-terminal domain of TDP-43 and its ALS-associated mutants

46 Katia Capitani, Flavia di Re, Umberto Greco, Caterina Baccioni, Silvestro G. Conticello
Harnessing MMEJ for Precise DNA Cassette Integration Using CRISPR/Cas

47 Laura Bianchi, Rossana De Salvo, Rita Vignani, Monica Scali, Riccardo Fedeli, Sara Desideri, Stefano Loppi, Luca Bini
Genetic and Proteomic Characterization of Triticum monococcum L. and Old and Modern Triticum aestivum L. Varieties: Implications for Nutritional Value

48 Malandrino Laura, Pucciarelli Stefania, Renzi Sofia, Vici Giorgia, Polzonetti Valeria, and Vincenzetti Silvia
Protein characterization of almond beverage and almond-based cappuccino.

49 Gatticchi L, Bellezza I, Rumsby G, Glover M, Cellini B
Functional analysis of amino acid substitutions within human AGT1 in a cell-based platform to support the diagnosis of primary hyperoxaluria type 1

50 Depau Lorenzo, Garfì Marta, Paolocci Maria Francesca, Silvi Giada, Bonucci Giulio, Falciani Chiara, Brunetti Jlenia, Bracci Luisa
HSPGs at the Frontline of Cancer Cell Migration: Functional and Therapeutic Insights

51 Lorenza Vantaggiato, Marco Frisenda, Enxhi Shaba, Chiara Splendore, Luca Bini, Alessandro Sciarra and Claudia Landi
Proteomic analysis identifies distinct molecular pattern among non-muscle-invasive bladder cancer subtypes.

52 Luana Ruta, Gioena Pampalone, David J. Sas, John C. Lieske, Peter C. Harris, Barbara Cellini
The minor allele polymorphism in human AGT modulates pathogenicity of Ile279Thr variant associated with primary hyperoxaluria type 1

53 De Marchi Lucia, Oliva Matteo, Pretti Carlo, Meucci Valentina, Vasarri Marzia, Degl'Innocenti Donatella, Lacchetti Ines, Mancini Laura, Chiesa Luca Maria, Nobile Maria, Intorre Luigi
Beyond the treatment: environmental risks and toxicity of ectoparasiticides used in pets

54 Piazza Lucia, Balestri Francesco, Moschini Roberta, Felice Francesca, Cappiello Mario, Allegrini Simone, Del Corso Antonella, Mosca Rossella, Avanatti Martina, Cecchettini Antonella, Rocchiccioli Silvia, Signore Giovanni
Chestnut shell-derived inhibitors of aldose reductase AR: from extraction to functional evaluation

55 L. Paradisi, L. Poliseno, J.F. Marshall, F. Finetti, L. Trabalzini
KRIT1 as a Key Regulator of Cytoskeletal Dynamics and Tumor Cell Migration: Implications for Cancer Progression

56 Frusciante Luisa, Geminiani Michela, Trezza Alfonso, Olmastroni Tommaso, Mastroeni Pierfrancesco, Shabab Behnaz, Palazli Ava, Bernini Andrea, Grasso Daniela, Spiga Ottavia, and Santucci Annalisa
Unlocking the Potential of Chaetomorpha linum: A Natural Ally Against Inflammation

57 Raucci Luisa, Perrone Cosimo Damiano, Barbera Stefano, de Boer Laurens Julius, Tosi Gian Marco, Brunetti Jlenia, Bracci Luisa, Pozzi Cecilia, Galvagni Federico, Orlandini Maurizio
Structural definition of the interacting surface between CD93 and an antiangiogenic antibody

58 Magdalena Davidescu, Sandra Buratta,, Roberto Maria Pellegrino, Leonardo Gatticchi, Pier Luigi Orvietani, Lorena Urbanelli, Carla Emiliani, Ilaria Bellezza and Lara Macchioni
Hydroquinone induces cardiolipin profile alterations in retinal pigmented epithelial cells

59 Cirinciani Martina, Germelli Lorenzo, Da Pozzo Eleonora, Priami Corrado, Martini Claudia, Milazzo Paolo
A network-based drug repurposing study for neuroinflammation: a systems biology approach in human microglia

60 Martina Gennari, Emilio Ermini, Alessandra Bigi, Martina Banchelli, Denise Barbut, Michael Zasloff, Fabrizio Chiti, Cristina Cecchi and Roberta Cascella
Trodusquemine modulates the formation of TDP-43 inclusions suppressing their associated neurotoxicity

61 Vasarri Marzia, Bergonzi Maria Camilla, Leri Manuela, Castellacci Rebecca, Bucciantini Monica, De Marchi Lucia, Degl'Innocenti Donatella
Oleanolic Acid Shields Human Keratinocytes from Exogenous Damage: Study Insights

62 Avanatti Martina, Piazza Lucia, Mosca Rossella, Sardelli Gemma, Felice Francesca, Cappiello Mario, Signore Giovanni, del Corso Antonella, Moschini Roberta, Balestri Francesco
Modulation of Aldose Reductase-like 1 enzyme (AKR1B10) activity by thiols

63 Martina Contestabile, Jacqueline Fátima Martins de Almeida, Ilaria Tonazzini, Simona Daniele
Exploring expression and signalling pathways of Adenosine receptors in cellular models of Angelman Syndrome

64 Michela Geminiani, Pierfrancesco Mastroeni, Tommaso Olmastroni, Collins Nyaberi Nyong'a, Ghaith Jabbour, Luisa Frusciante, Alfonso Trezza, Anna Visibelli, Annalisa Santucci
An in vitro cell model for exploring inflammatory and amyloidogenic events in alkaptonuria

65 Mirco Dindo, Jakob Metson, Weitong Ren, Michalis Chatzittofi, Kiyoshi Yagi, Yugi Sujita, Ramin Golestanian, Paola Laurino
Enzymes can activate and mobilize the cytoplasmic environment across scales

66 Morosetti Marco, Barbarossa Sara, Lucci Paolo, Damiani Elisabetta, De Beer Dalene, Orlando Patrick
Role of Red and Green Rooibos in wet and dry marinades for pork subjected to different cooking methods

67 Mastroeni Pierfrancesco, Trezza Alfonso, Geminiani Michela, Frusciante Luisa, Visibelli Anna, Santucci Annalisa
HGA Triggers SAA Aggregation and Accelerates Fibril Formation in the C20/A4 Alkaptonuria Cell Model

68 Rachele Agostini, Emanuela Polidori, Paola Ceccaroli, Laura Graciotti, Stephanie Fondi, Michela Battistelli, Francesca Luchetti, Silvia Codenotti, Gabriella Pocsfalvi, Joao Ferreira, Lorena Urbanelli, Sandra Buratta, Alessandro Fanzani, Vilberto Stocchi, Michele Guescini
Caveolin-1-overexpression increases the release of extracellular vesicles with altered protein-lipid cargo, thereby modulating tumor development

69 Rebecca Innocenti, Elisabetta Coppi, Gloria Mulas, Lucia Frulloni, Anna Maria Pugliese, Chiara Giacomelli, Maria Letizia Trincavelli, Paola Bruni, Francesca Cencetti
Investigating the molecular mechanisms underlying myofibroblast-to-lipofibroblast transition in idiopathic pulmonary fibrosis: a role for SK/S1P axis

70 Sodano Rebecca, Joechler Veronika, Pecora Lucia, Moccia Annalisa, Iannuccilli Francesca, Santi Alice, Caselli Anna, Cirri Paolo, Paoli Paolo
The effects of Bisphenol AF on glucose metabolism and cell differentiation

71 Tania Vanzolini, Giacomo Mari, Gian Marco Elisi, Francesca Monittola, Federica Forte, Marzia Bianchi, Fabio Mantellini, Giovanni Bottegoni, Gianfranco Favi, Rita Crinelli
Biochemical and computational analyses of potential Usp2 inhibitors selected from an in-house library and sub-library of small organic compounds

72 Mosca Rossella, Balestri Francesco, Signore Giovanni, Moschini Roberta, Sardelli Gemma, Piazza Lucia, Felice Francesca, Cappiello Mario, Allegrini Simone, Del Corso Antonella
Metabolic Rewiring in Chemoresistant Pancreatic Cancer: Redox Metabolism and Lipid Alterations

73 Martina Pergola, Husam B.R. Alabed, Dorotea Frongia Mancini, Carla Emiliani, Roberto Maria Pellegrino
Functional lipid analysis: development of a new feature to be integrated into the LipidOne bioinformatics platform

74 Rossana De Salvo, Alfonso Carleo, Isabella Damiani, Silvia Castiglioni, Clara Rossi, Camilla D'Alonzo, Alberto Corsini, Luca Bini, Stefano Bellosta, and Laura Bianchi
Unraveling the Impact of Cigarette and Alternative Smoke Products on Vascular Smooth Muscle Cells: Inflammation, Migration, and Phenotypic Shifts

75 Barbarossa Sara, Morosetti Marco, Lucci Paolo, Damiani Elisabetta, De Beer Dalene, Osimani Andrea, Orlando Patrick
Role of green and red Rooibos on oxidation and shelf-life of wet and dry marinated pork

76 Giannoni Samuele, Valicenti Maria Luisa, Donati Leonardo, Lucariello Miriam, Morena Francesco, Emiliani Carla, Martino Sabata
Unveil Sporadic Alzheimer's Disease trough an innovative Adipose-Derived Stem Cells Ex Vivo Model

77 Sara Biagiotti, Elena Perla, Rachele Agostini, Antonio Nozza, Mattia Tiboni, Barbara Canonico, Amatori Stefano, Mirco Fanelli, Michele Guescini and Mauro Magnani
Biotinylated Red Blood Cell-derived Extracellular Vesicles as a promising tool for drug delivery and targeting

78 Roccabianca Sara, Pardella Elisa, Ippolito Luigi, Pranzini Erica, Iozzo Marta, Gangarossa Giulia, Bertoli Greta, Grillo Caterina, Santi Alice, Comito Giuseppina, Chiarugi Paola, Giannoni Elisa.
Glutamate–Oxaloacetate Transaminase 2 (GOT2)-dependent aspartate availability confers ferroptosis resistance to detached prostate cancer cells

79 Silvia Bellini Baldelli, Federico Fiorani, Valentina Trovarelli, Martina Mandarano, Samuela Cataldi, Alessandra Mirarchi, Stefano Bruscoli, Tommaso Beccari, Claudia Floridi, Cataldo Arcuri3 and Elisabetta Albi
Effect of C6 ceramide on embryonic hippocampal cells

80 Silvia Errico, Giulia Fani, Alessandra Bigi, Benedetta Mannini, Fabrizio Chiti
Protective role of berberine and its natural derivatives against misfolded protein oligomers associated with Alzheimer's disease

81 Grottelli S, Gutturi M, Mezzasoma L, Beccari G, Romani R, Ederli L, Covarelli L, Bellezza I
Mycotoxins enniatin B and deoxynivalenol compromise intestinal barrier integrity

82 Simona Daniele, Jacqueline Fátima Martins de Almeida, Martina Contestabile, Ilaria Tonazzini, Claudia Martini
Involvement of the ubiquitin-proteasome/autophagy system in cellular models of Angelman Syndrome

83 Sundas Javed, Gabriella Jacomelli, Giulia Bernardini
MALDI-TOF MS-Based Peptidomic Profiling of Plasma in Lesch Nyhan Syndrome

84 Masini Sofia, Monittola Francesca, De Angelis Marta,Gori Savellini Gianni, Piselli Elena, Anichini Gabriele, Bruschi Michela, Cusi Maria Grazia, Nencioni Lucia, Crinelli Rita, Fraternale Alessandra
Thiol-based redox-modulating molecules ameliorate inflammation induced by lipopolysaccharide and viral infections

85 Sofia Renzi, Stefania Pucciarelli, Valeria Polzonetti, Laura Malandrino, Giorgia Vici , Maria Magdalena Coman, Paolo Polidori, Silvia Vincenzetti
Development and characterization of fermented donkey milk drinks: a novel source of the bioavailable form of folic acid

86 Stella Nappi, Claire Staton, Chiara Cassioli, Nagaja Capitani, Anna Hoyle, Iolanda Vendrell, Michael L. Dustin, Cristina Ulivieri1 and Cosima T. Baldari
The U373 glioma cell line releases perforin-1 positive proteinaceous particles that promote migration

87 Henriquez Tania, Falciani Chiara
Characterization of extracellular vesicles from clinical strains of Pseudomonas aeruginosa

88 Vanzolini Tania, Di Mambro Tomas and Magnani Mauro
The antifungal humanized monoclonal antibody Dia-T51 and its synergy with amphotericin B: in vitro and in vivo studies

89 Kersikla Tena, Peppicelli Silvia, Menegazzi Giulio, Bianchini Francesca, Nediani Chiara, Calorini Lido
Morphological and functional characterization of anoikis-resistant melanoma cells

90 Trezza Alfonso, Anna Visibelli, Michela Geminiani, Annalisa Santucci
Molecular and Evolution In Silico Studies Unlock the h4-HPPD C-Terminal Tail Gating Mechanism

91 Valentina Trovarelli, Federico Fiorani, Bellini Baldelli S. , Martina Mandarano, Samuela Cataldi, Cataldo Arcuri, Alessandra Mirarchi, Angelo Sidoni, Elisabetta Albi, Michela Codini
Vitamin C Increases ceramide level in luminal A breast cancer cell line

92 Joechler Veronika, Sodano Rebecca, Santi Alice, Iannuccilli Francesca, Moccia Annalisa, Caselli Anna, Cirri Paolo, Paoli Paolo
Study of the effects of the T457M mutation of hexokinase 1 (HK1) on the enzyme activity and metabolism of human fibroblasts

93 Ylenia Martinini, Assia Duatti, Alfredo Smiriglia, Elisa Pardella, Giuseppina Comito, Monica Mangoni, Simonetta Bianchi , Luca Visani, Icro Meattini, Giorgio Giurato, Carlo Ferravante, Annamaria Salvati, Giovanni Nassa, Lorenzo Livi, Andrea Morandi
STARD9 dysregulation potentiates therapy sensitivity in ER+ breast cancer

94 Lorenzo Casbarra, Matteo Ramazzotti
PathLay: a novel graphical server for -omics integration and interpretation

Questo evento è stato sponsorizzato da