Finanziato dall'Unione europea NextGenerationEU
Ministero dell'Università e della Ricerca
Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA

Innovation Ecosystem:

Innovation, digitalisation and sustainability for the diffused economy in Central Italy (Vitality)

Bruna Sinjari
Coordinatrice del WP1-Spoke 4 –One Health Telemedicine and Environment

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WP1: Molecular diagnostics

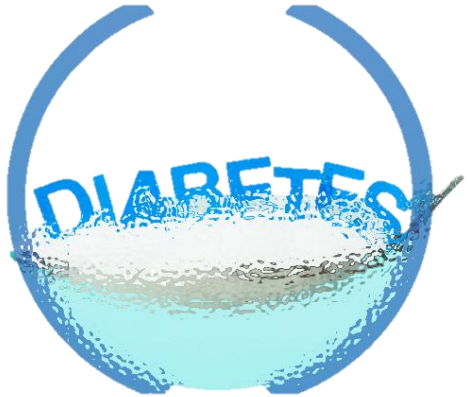
- **Objective 1:** Identificare biomarcatori predittivi rilevanti per la diagnosi molecolare e l'imaging non invasivo di specifiche patologie a base infiammatoria, cronica e degenerativa per il follow-up e il monitoraggio della terapia dal punto di vista della medicina personalizzata.
- **Objective 2:** Identificare nuovi biomarcatori basati sul profilo proteomico mirato per la diagnosi clinica, la stratificazione del rischio, il monitoraggio della progressione della malattia e la risposta terapeutica in specifiche condizioni cliniche cardiometaboliche e infiammatorie.
- **Objective 3:** Identificare i potenziali effetti sulla salute dell'esposizione a miscele di gas atmosferici in tracce e particolato in un modello di laboratorio e in ambienti interni.

WP1 Molecular Diagnostics

1) An **observational** no pharmacological and no profit study on One-Health telemedicine and environnement **approved** by the ethic committee on 9th of December 2023→waiting for the patient data sharing from the Asl 2.

It aims to **analyse** the data of " Sanitamica" of the local health system Asl 2 and **develop algorithms aimed at managing health datasets and study relationships between different pathologies and/or clinical parameters.**

2) An **experimental**, no pharmacological, no profit study One-Health telemedicine and environnement in chronic disease.



It aims to identify **molecular** and **imaging biomarkers** that predict the occurrence of target organ damage in patients with **diabetes** and study the potential **connection** between the **diabetes occurrence** and **atmospheric compounds concentrations.**

Under EC revision

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Università degli studi "G. d'Annunzio" Chieti - Pescara

Urine and saliva extraction

AIM: Analysis of urine biomarkers to evaluate the extent of platelet activation and oxidative stress.

MATERIALS AND METHODS: Semi-automatic extractor able, with a negative pressure, to extract 48 urine samples with specific C18 and Silica pre-custom columns making the whole procedure quicker. The semi-automatic extractor has been tested and optimized to perform perfectly all the phases of the urine purification procedures. The saliva samples will be also collected through a non invasive method.

PROCEDURE: different steps of purification with organic compounds and specific controls added to evaluate the performance of the extraction. The final samples, obtained by the extraction phase, will be conserved at -80°C to perform Immune-enzymatic assays (EIA-ELISA).

semiautomatic extractor PPM48 J2Scientific – document BC1085 of 09/11/2023, order n° 0052134

Ultrasound

AIM: Generate pivotal and integrated data on clinical, molecular and imaging biomarkers that predict the occurrence of target organ damage in patients with diabetes. Stratify patients with type 2 diabetes according to the presence of Non Alcoholic Fatty Liver Disease, diabetic cardiomyopathy, carotid plaques, lower extremity peripheral artery disease.

MATERIALS AND METHODS: Ultrasound machine "Esaote My Lab X8" will allow evaluating target organ damages.

PROCEDURE: Using ultrasound machine, different organs can be explored to investigate injuries: liver (hepatic steatosis), heart (diabetic cardiomyopathy), epiaortic vessels (carotid artery atheromas). Patients with and without signs of target organ damage will be analysed for a number of circulating, urinary and protein molecules to deepen our understanding of the pathogenesis of complications and to identify possible biomarkers of diabetic target organ damage. Finally, we will evaluate whether any therapeutic intervention may modulate the levels of such potential biomarkers .

Ultrasound machine "Esaote My Lab X8"

Review 2023

This review, submitted for publication, emphasizes the role of isoprostanes (IsoPs) in the pathophysiology of cardiovascular diseases, and their role as possible biomarkers for the diagnosis, prognosis and drug response in different settings. The formation of IsoPs in vivo can be monitored reliably and non-invasively, by analytical approaches, such as urinary 8-isoPGF2a, that provide us with information on the state of oxidative stress in humans. IsoPs are potential and interesting biomarkers of the level of oxidative stress in vivo. They are mediators of cardiovascular and non-cardiovascular diseases and responsible for the increase in cardiovascular risk. In addition, they are considered a pivotal link between oxidative stress and platelet activation in cardiovascular diseases.

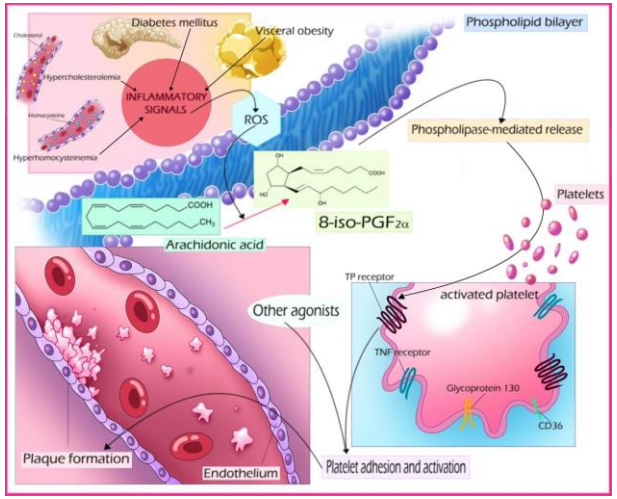

Image created by Dr. Stefano Lattanzio (CAST)

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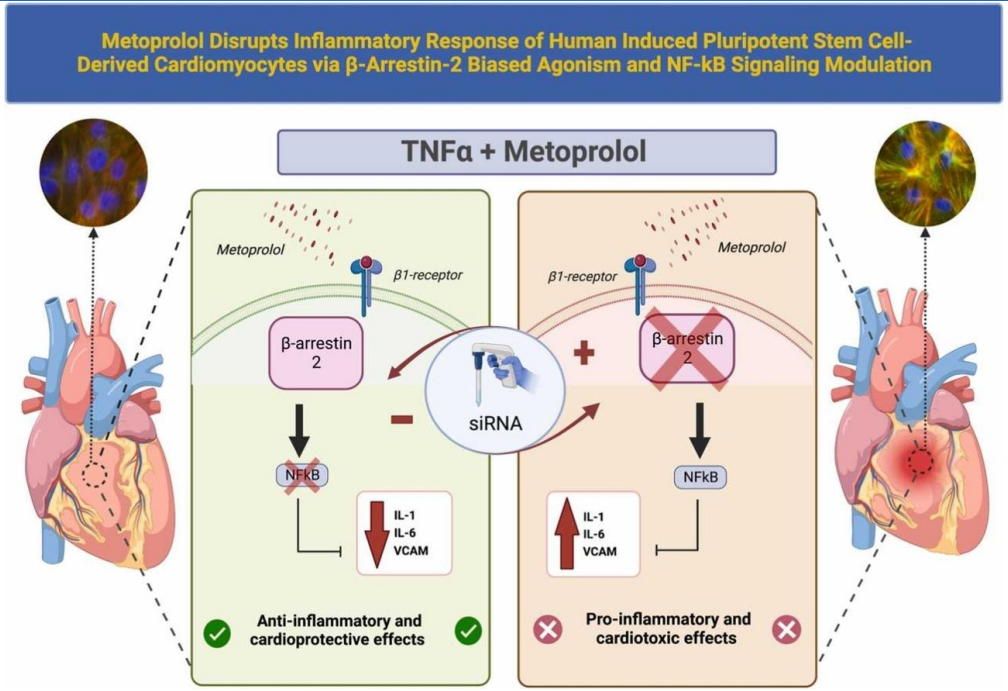
Metoprolol disrupts inflammatory response of human cardiomyocytes via β-arrestin2 biased agonism and NF-κB signaling modulation

Fabrizio Ricci [a,b,1], Andrea Di Credico [c,1], Giulia Gaggi [c], Giovanni Iannetti [a], Barbara Ghinassi [c], Sabina Gallina [a], Brian Olshansky [d], Angela Di Baldassarre [c,*]

[a] Department of Neuroscience, Imaging and Clinical Sciences, G.d'Annunzio University of Chieti-Pescara, 66100 Chieti, Italy and University Cardiology Division, Heart Department, SS Annunziata University Hospital, Chieti, Italy
[b] Department of Clinical Sciences, Lund University, 214 28 Malmö, Sweden
[c] Department of Medicine and Aging Sciences, and Reprogramming and Cell Differentiation Lab, Center for Advanced Studies and Technology (CAST), G. D'Annunzio University of Chieti-Pescara, 66100 Chieti, Italy
[d] University of Iowa, Iowa City, IA, USA



Translational perspective

We provide compelling evidence that **metoprolol**, a β1-selective blocker, **exhibits non-class anti-inflammatory effects on** human induced pluripotent **stem cell-derived cardiomyocytes exposed to TNF-α-induced inflammation**. β-arrestin 2 biased agonism plays a crucial role in mediating these effects by regulating NF-κB activity and the synthesis of inflammatory and adhesion molecules. **The role of β-arrestin 2 in mediating the anti-inflammatory effects of metoprolol suggests a biased agonism as a therapeutic strategy**. Further research is needed to validate these findings *in vivo*.

ESC European Society of Cardiology
European Heart Journal Open (2024) **4**, oeae030
https://doi.org/10.1093/ehjopen/oeae030

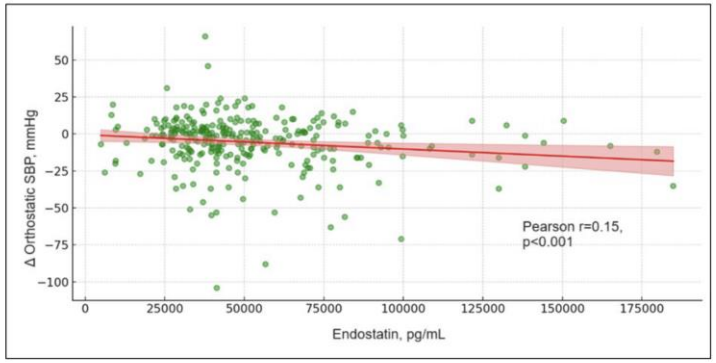
ORIGINAL ARTICLE
Miscellaneous

Orthostatic hypotension is associated with higher levels of circulating endostatin

Fabrizio Ricci [1,2,3], Anders Larsson [4], Toralph Ruge [1,5], Kristian Galanti[2], Viktor Hamrefors [1,6], Richard Sutton [7], Brian Olshansky [8], Artur Fedorowski [1,9,10], and Madeleine Johansson [1,6,*]

[1]Department of Clinical Sciences, Lund University, Malmö, Sweden, Jan Waldenströms gata 35, 214 28 Malmö, Sweden; [2]Department of Neuroscience, Imaging and Clinical Sciences, 'G.d'Annunzio' University of Chieti-Pescara, Chieti, Italy; [3]Heart Department, 'SS Annunziata' Polyclinic University Hospital, Chieti, Italy; [4]Section of Clinical Chemistry, Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [5]Department of Emergency and Internal Medicine, Skåne University Hospital, Malmö, Sweden; [6]Department of Cardiology, Skåne University Hospital, Malmö, Sweden, Jan Waldenströms gata 15, 214 28 Malmö, Sweden; [7]Department of Cardiology, Hammersmith Hospital, National Heart and Lung Institute, Imperial College, London, UK; [8]Division of Cardiology, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, USA; [9]Department of Cardiology, Karolinska University Hospital, Stockholm, Sweden; and [10]Department of Medicine, Karolinska Institute, Stockholm, Sweden

Received 20 January 2024; revised 25 March 2024; accepted 9 April 2024; online publish-ahead-of-print 10 April 2024



- **Key Question**
  Is there a relationship between plasma endostatin levels and blood pressure regulation in patients with orthostatic hypotension (OH)?
- **Key Finding**
  Higher plasma levels of endostatin are associated with increased magnitude of systolic blood pressure drop upon standing in patients with OH.
- **Take-home Message**
  Endostatin is linked to OH independently of prevalent cardiovascular disease and traditional cardiovascular risk factors, suggesting that endostatin is an independent risk factor in OH.

Clinical Relevance

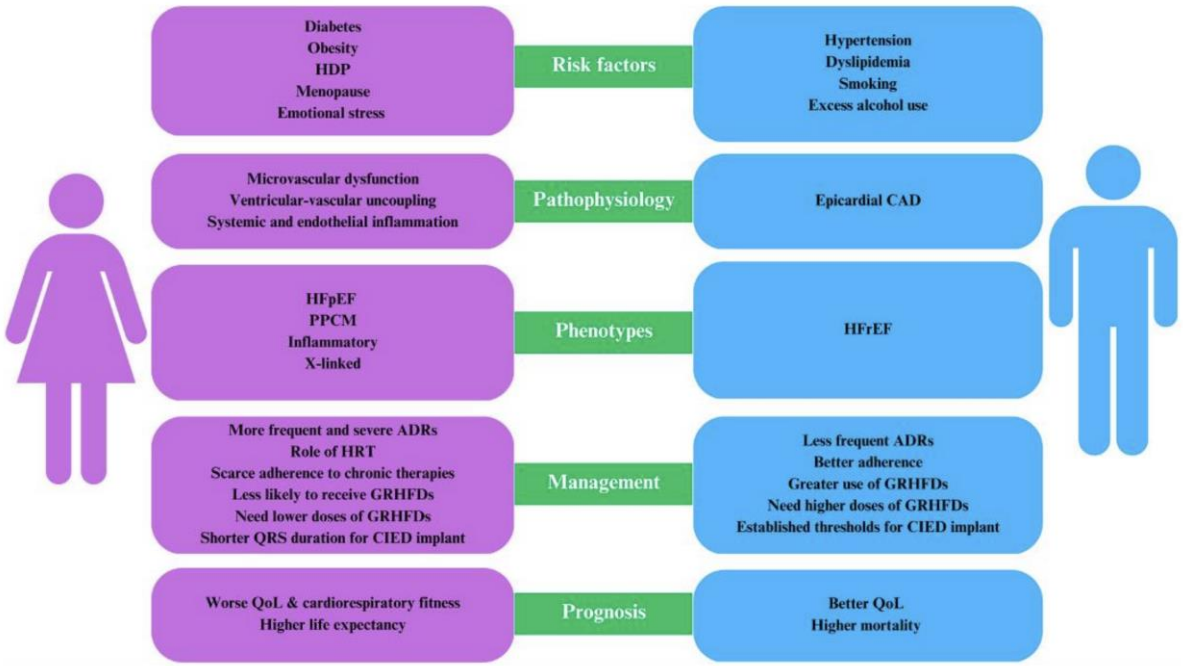
We provide insights into novel mechanisms possibly underlying the **independent association between orthostatic hypotension,** a cardinal sign of autonomic dysfunction and a common cause of syncope and falls in the elderly, **and molecular pathways related to endostatin**, an endogenous angiogenesis inhibitor proposed to be involved in blood pressure regulation by inducing nitric oxide release. Our findings call for external validation and **further research on the effect of nitric oxide synthase inhibitors for treatment of orthostatic hypotension**.

Journal of *Cardiovascular Development and Disease*
MDPI

Review

Sex Differences in Heart Failure: What Do We Know?

Allegra Arata [1,†], Fabrizio Ricci [1,2,3,*,†], Mohammed Y. Khanji [2], Cesare Mantini [1], Francesco Angeli [4], Roberta Aquilani [5], Angela Di Baldassarre [6], Giulia Renda [1], Anna Vittoria Mattioli [7], Savina Nodari [8] and Sabina Gallina [1]



To address sex disparities and improve health outcomes in heart failure

Transformative solutions include fostering a greater understanding of the biological and sociocultural factors contributing to sex-specific differences in HF, advocating for the inclusion of women and underrepresented minorities in clinical research, implementing guidelines that account for sex-specific risk factors and presentation, and providing equitable access to diagnostic and therapeutic strategies

Clinical biomarker discovery holds the potential to profoundly address sex disparities in heart failure and enhance clinical outcomes through several key mechanisms. By identifying specific biomarkers that vary between sexes, we can develop more targeted and effective diagnostic and treatment strategies. These biomarkers can help elucidate the underlying biological mechanisms that contribute to the differences in HF presentation and progression between men and women and could help bridge the gap in outcomes

https://doi.org/10.3390/jcdd10070277

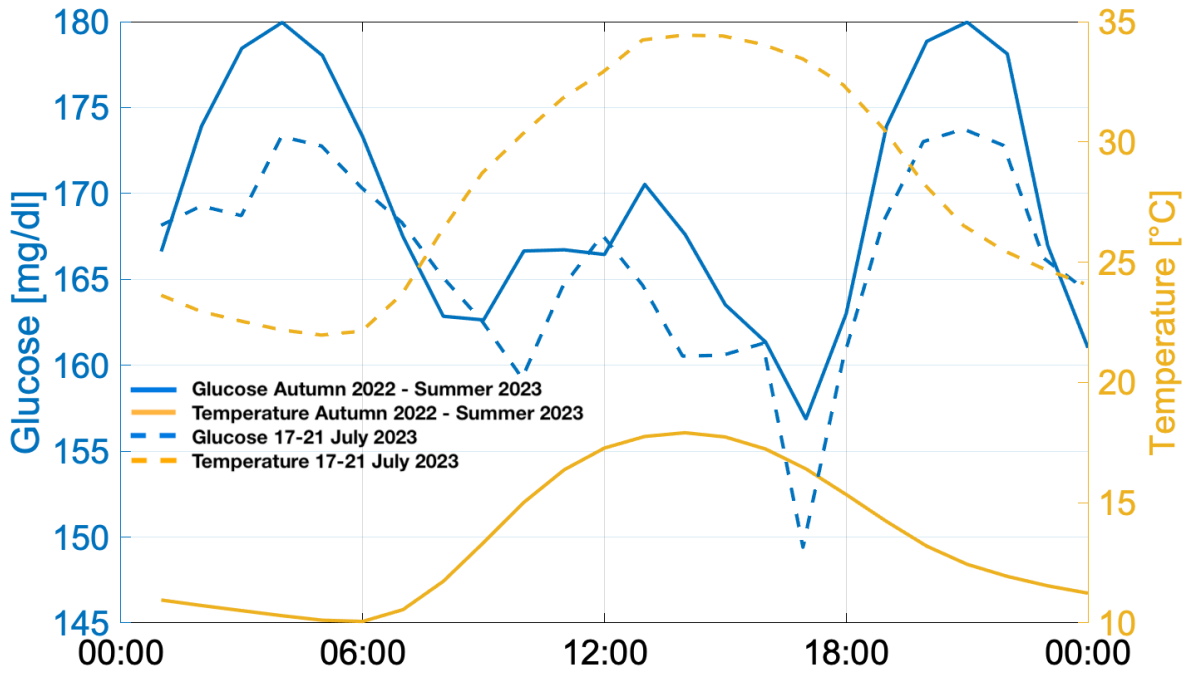
Objective n. 2

WP1 Molecular Diagnostics

The team worked on the **setup** and **calibration** of **small sensors** that can be used to **monitor indoor air pollution.** These small sensors will be used to **densify the monitoring network** and consequently to **have more local environmental data**

The team also kept developing **data analysis algorithms aimed at managing environmental and health datasets**

Preliminary results showed the **close link between environmental parameters**, such as temperature, **and diabetes.** Analysis on metrics and seasonal patterns allowed to evaluate the **relation between temperature and hypoglycaemia episodes.**



Work Package 1: **Molecular diagnostic**

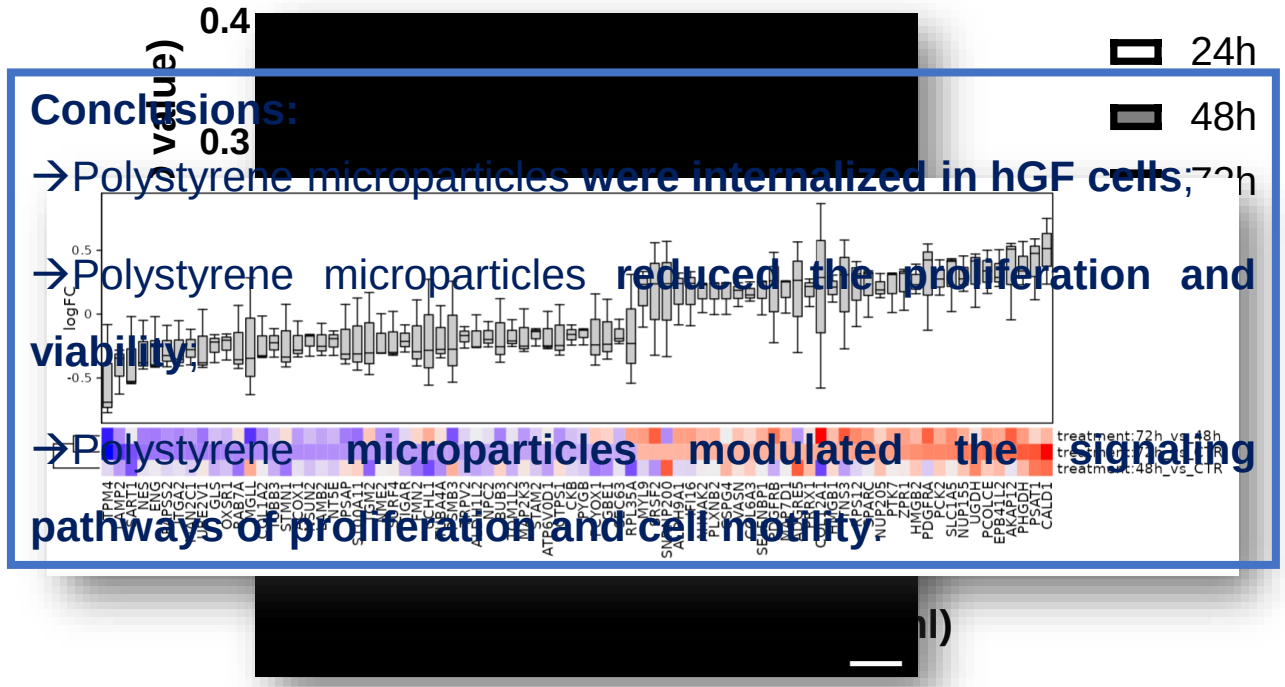
-**Microparticles:** Polystyrene microplastics of 1µm;

-**Cell line model:** human gingival fibroblast cells (hGF)

-**Cell Proliferation and Viability:** MTT assay;

-Internalization Study: Confocal Microscopy and Flow Cytometry;

-**Protein expression**: Proteomic analysis;



Conclusions:

→Polystyrene microparticles **were internalized in hGF cells**;

→Polystyrene microparticles **reduced the proliferation and viability;**

→Polystyrene **microparticles modulated the signaling pathways of proliferation and cell motility.**

- Development of an in vitro model to generate a 3D Culture to evaluate the biological effects of the pollutants through the study of the involved molecular pathway.
- Identification of the potential effects of pollutants on an in vitro model based on the human oral mesenchymal stem cells culture.
- Development of an in vitro of oral mesenchymal stem cells differentiated in dopaminergic cells to establish an in vitro model for neurodegenerative diseases is undertaken.