UNIVERSITÀ POLITECNICA DELLE MARCHE

NUTRITION AND INTEGRATIVE METABOLISM IN AGING (NUMAGE)

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DiSVA

UNIVERSITÀ POLITECNICA DELLE MARCHE

NUTRITION AND INTEGRATIVE METABOLISM IN AGING

Supervisor: Prof. ANDREA FRONTINI

The Supervisor

Associate Professor of Human Anatomy

Research Area: Molecular mechanisms involved in the control of energy balance. This includes central mechanisms of action in the hypothalamus but also peripheral signaling pathways in adipose tissue, muscle and liver. I am interested in the biology of adipose tissue in physiological (cold exposure, physical exercise and aging) as well as in pathological conditions (obesity and diabetes).

Author of 66 **peer-reviewed publications** in international journals and 4 book chapters, with an ***h* index= 39**, i10-index= 51 with 9500 citations (from Google Scholar); *h* index= 37; 6500 citations (from Scopus).
Orcid profile: https://orcid.org/0000-0002-7381-4107

Associate Editor Frontiers in Cell and Developmental Biology, Editorial board member in Biomolecules. **Guest Editor** of 2 special issues for IJMS; ad Hoc **Reviewer** for Nature Communication; Journal of Lipid research; Journal of Clinical Endocrinology and Metabolism.

Memberships:
Italian Society of Anatomy and Histology
Italian Society for the Study of Obesity

Invited speakers in about 20 National and International Congress organized by scientific associations working in the field of obesity and metabolic disorders

Most recent publications and research projects:

- Sahu BS, Razzoli M, McGonigle S, Pallais JP, Nguyen ME, Sadahiro M, Jiang C, Lin WJ, Kelley KA, Rodriguez P, Mansk R, Cero C, Caviola G, Palanza P, Rao L, Beetch M, Alejandro E, Sham YY, **Frontini A**, Salton SR, Bartolomucci A (2023). Targeted and selective knockout of the TLQP-21 neuropeptide unmasks its unique role in energy homeostasis. Mol Metab.;76:101781. doi: 10.1016/j.molmet.2023.101781
- Nodari A, Scambi I, Peroni D, Calabria E, Benati D, Mannucci S, Manfredi M, **Frontini A**, Visonà S, Bozzato A, Sbarbati A, Schena F, Marengo E, Krampera M, Galiè M. Interferon regulatory factor 7 impairs cellular metabolism in aging adipose-derived stromal cells. J Cell Sci. 2021 Jun 1;134(11). doi: 10.1242/jcs.256230
- Lyons CE, Razzoli M, Larson E, Svedberg D, **Frontini A**, Cinti S, Vulchanova L, Sanders M, Thomas M, Bartolomucci A (2020). Optogenetic-induced sympathetic neuromodulation of brown adipose tissue thermogenesis. FASEB J. 34(2):2765-2773
- de Jong JMA, Sun W, Pires ND, **Frontini A**, Balaz M, Jespersen NZ, Feizi A, Petrovic K, Fischer AW, Bokhari MH, Niemi T, Nuutila P, Cinti S, Nielsen S, Scheele C, Virtanen K, Cannon B, Nedergaard J, Wolfrum C, Petrovic N (2019). Human brown adipose tissue is phenocopied by classical brown adipose tissue in physiologically humanized mice. Nature Metab. 1(8):830-843.
- Pellegrinelli V, Peirce VJ, Howard L, Virtue S, Türei D, Senzacqua M, **Frontini A**, Dalley JW, Horton AR, Bidault G, Severi I, Whittle A, Rahmouni K, Saez-Rodriguez J, Cinti S, Davies AM, Vidal-Puig A. Adipocyte-secreted BMP8b mediates adrenergic-induced remodeling of the neuro-vascular network in adipose tissue (2018). Nat Commun. 26;9(1):4974.

Full list of Pubs: https://www.ncbi.nlm.nih.gov/myncbi/andrea.frontini.1/bibliography/public/

Research projects
- Scientific expert on FP7-DIABAT (Recruitment and activation of brown adipose tissue to curb obesity in humans).
- PI on a grant by the company Ethicon endo-surgery (Johnson&Johnson Med Tech) to evaluate the potential application of electrical transdermal stimulation on human supraclavicular brown adipose tissue.
- RSA by Università Politecnica delle Marche

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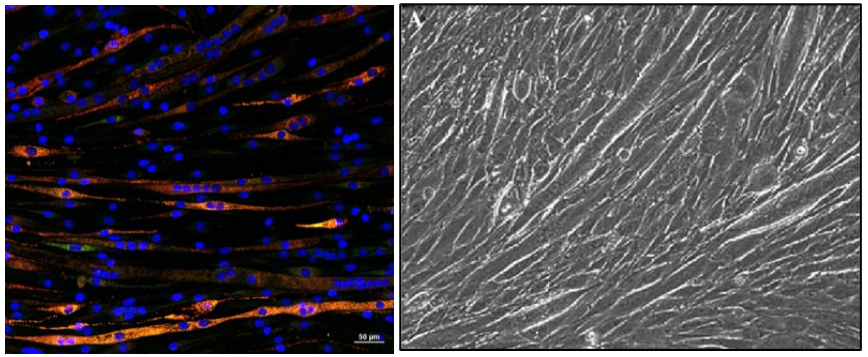
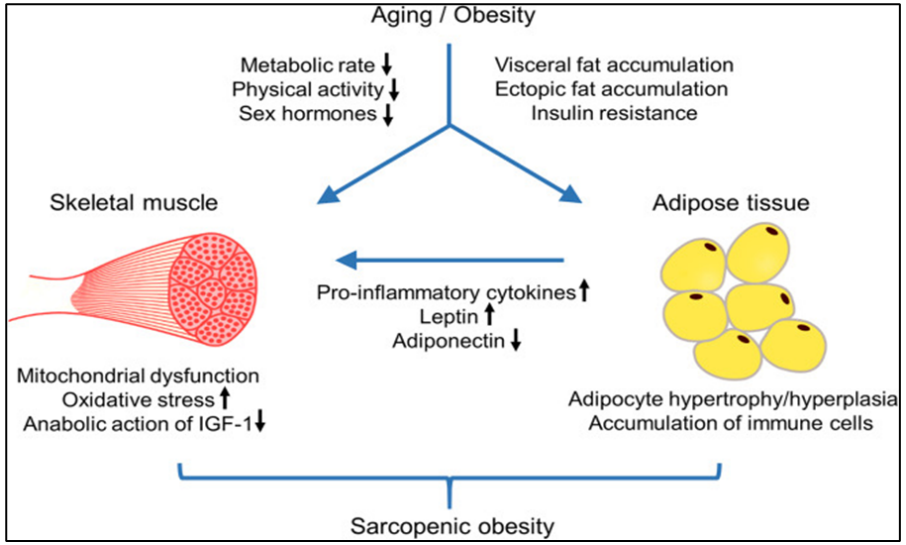


THE RESEARCH GROUP: Morpho-functional aspects and biochemistry of oxidative stress and inflammation in ageing

Research efforts of our research team are primarily concerned with the role of **mitochondrial dysfunction and oxidative stress in models of aging and degenerative disease**. Because of its critical position as an **electron transporter** in the mitochondrial respiratory chain and the **potent antioxidant** capability of its reduced form, we have a thorough understanding of the impacts of **Coenzyme Q10** in biological and clinical settings. CoQ10 may be a crucial molecule during senescence processes since its endogenous biosynthesis and ability to diminish and activate this cofactor both decline. Our laboratory is provided with the expertise to investigate on potential morpho-functional benefits obtained by CoQ10 supplementation on cells/tissues involved in integrated metabolism and which function might be impaired during aging. We could also perform biochemical analysis of oxidative stress and inflammation on several cellular models.



The group has access to an **HPLC facility** equipped with UV/VIS, electrochemical, fluorometric, and chemiluminescent detectors. Cell culture work is carried out in two **cell culture labs** that are outfitted with automated cell counters, incubators with O2/CO2 control, complemented by a wide range of cytometric and molecular biology tools, including fully automated extraction and expression analysis systems for protein and nucleic acids. (King fisher extractor, Quiagility liquid handler, Jess Protein simple)

Moreover, we have access and co-coordinates the activities of the **advanced microscopy Laboratory**, within DISVA Department of Excellence facilities, which is equipped with an image-based flow cytometer,. (Amnis Flowsight) Nikon AR1 Confocal Microscope High-throughput Automated Microscope (Agilent, Lion Heart).

The research group has a multidisciplinary expertise ranging from analytical biochemistry for the quantification of small molecular weight bioactive molecules in food and biological specimens to bioavailability assessment as well as to the histochemical and physiological analysis of nervous tissues. The group has created preclinical stress and senescence models to investigate the efficacy of bioactive substances in enhancing cellular health and delaying the senescence phenotype. Adipose tissue health, skeletal muscle function and sarcopenia, endothelial functionality, and neurodegenerative process of the nerve cells have all received attention. These molecular pathways have also been explored in several clinical research in humans and animal models.


Prof. A. Frontini


Prof. M. Fabri


Dr. P.Orlando


Dr. S.Silvestri


Dr. F.Marcheggiani


Dr. L. Rao


Dr. F. Mengarelli

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THE DEPARTMENT OF LIFE AND ENVIRONMENTAL SCIENCES (DiSVA)

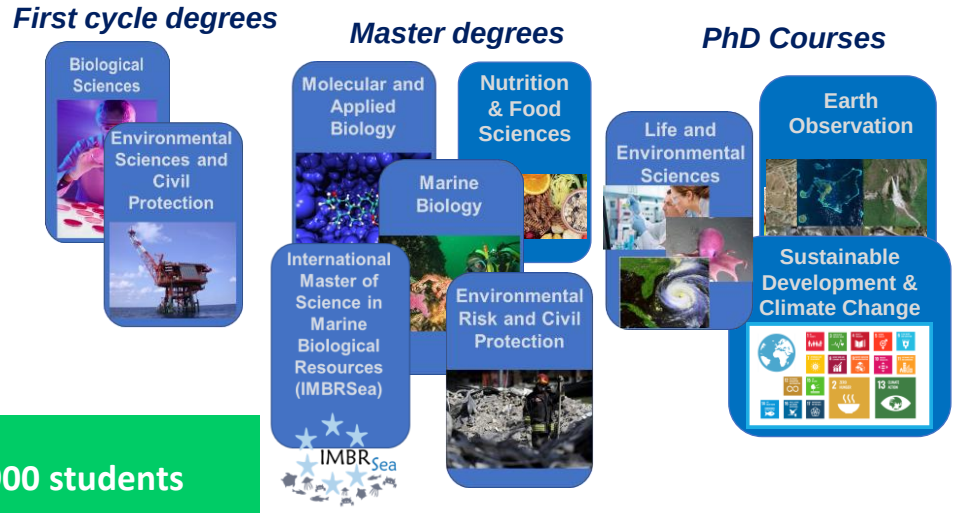
Department of Excellence

100 units of permanent staff (researchers and technicians)
80 PhD students and post-docs

in 2021-23, > 140 national and international projects for > 11 Mil €

in 2023 >220 international publications (>80% in Q1 Journals)

Teaching programmes:
2 First cycle degrees, 4 Master degrees, 3 PhD Courses

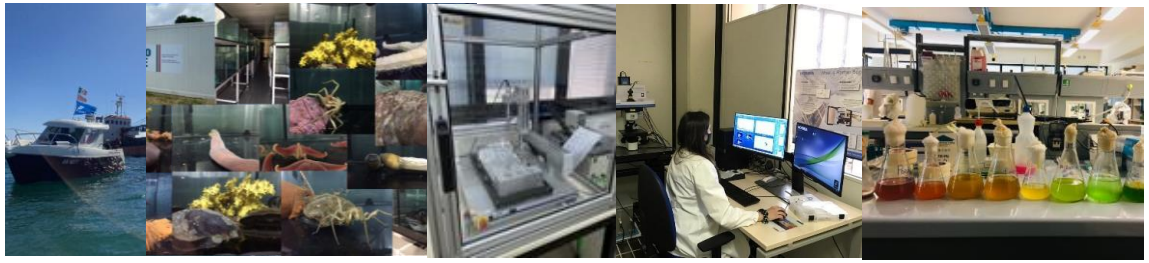


20 Professors have *h* index between 30 and >80, 15 have between 100 and 400 publications, 1 in Highly Cited Researchers (Clarivate)

> 1.900 students

Research Infrastructures & Excellence Laboratories:

- Marche Structural Biology Center (Ma.S.Bi.C.); The Aquarium-Joint Research Unit (JRU) of EMBRC ITALY (EMBRC-IT); Laboratory of Advanced Microscopy Research Instrumentation; Advanced Laboratory of Mass Spectrometry; Computing Data Center-DiSVA-HPC; Covid-19 LABC19; research vessels ACTEA and MYTILUS; Fano Marine Center (FMC), FORTUNAE Oceanographic Buoy.



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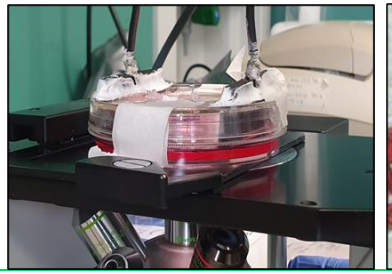
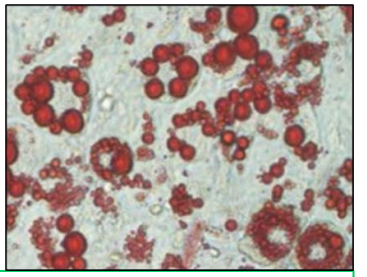




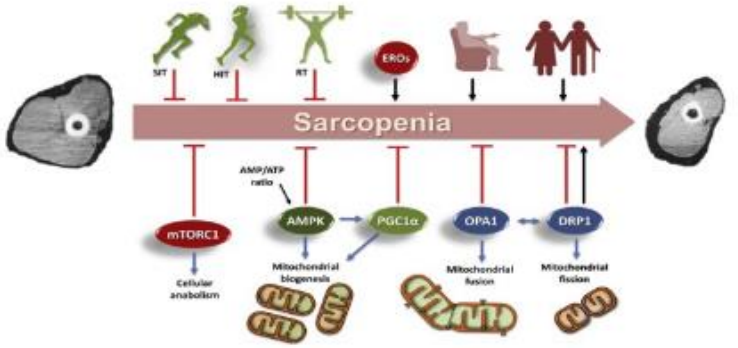
Project Idea: NUMAGE

Backgroud: Ageing is associated with the accumulation of cellular damages, which increases the risk of disease and mortality. More people are at risk of neurological illnesses as life expectancy rises. Alzheimer disease (AD) is expected to climb from 53 million in 2018 to 88 million in 2050 in the US population over the age of 65. Simultaneously, the health and societal costs associated with age-related illnesses will rise, necessitating preventive and/or therapeutic treatments. General human health is directly tied to mitochondrial health, integrity, and quality control, particularly during aging, when muscle mitochondrial ATP generation has been observed to decrease by roughly 8% every decade of age in a population between the ages of 18 and 89. Alterations in mitochondrial dynamics and function appear to be implicated also in age-related degenerative diseases such as Alzheimer's and also in the development of sarcopenic obesity characterized by progressive reduction of muscle mass and increase of deposition of ectopic adipose tissue causing insulin resistance and T2D.

The project **NUMAGE** is designed to study the adaptations induced by exercise and nutritional factors, stimuli which may have important implications in the protection from metabolic and neurodegenerative age-associated disorders. To this purpose, the first objective will be the development of different co-colture systems, such as muscle/neurons, muscle/adipocites and neurons/glia.

The following research objectives will be addressed, aimed at contributing to healthy aging:

1. to detail the molecular mechanisms underlying the combination of physical exercise and nutrients on the modulation of mitochondrial plasticity, improving biogenesis, respiration and consequently fatty acid oxidation and aerobic performance, and indirectly affecting also brain cells.
2. to investigate the molecular mechanisms underlying myelin production and regeneration.
3. to evaluate the role of exercise-induced EVs on adipocytes biology. We'll analyze if oxidative stress and pro-inflammatory conditions can be modulated to curb the development of insulin resistance in sarcopenic obesity.



The project is expected to have tangible impacts in providing new insight on the molecular adaptation, in the young as well as in the senescent cells, underlying physical exercise, brain functionality, and adipose tissue metabolism, with broader implication to the general health of different tissue, exploiting muscle cross talk with brain and adipose cells. Identification of optimal exercise protocols and nutrients combination will provide useful insight on optimizing health at advanced age and achieve a successful ageing.