



Università degli Studi di Siena Dottorato di Ricerca in Medicina Molecolare

Scheda Relazione Annuale Dottorando

Pisa, il 25/09/2024

Al collegio docenti del Dottorato in Medicina Molecolare

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Ciclo: XXXVIII° **Tutor:** Prof. Massimo Dal Monte

Attività scientifica svolta ne 2° anno di Dottorato, Anno Accademico 2023/2024

Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a progressive decline in cognitive function. Much evidence about mechanisms underlying AD progression derives from animal models such as 5xFAD, a murine strain carrying five different mutations in amyloidogenic pathways genes. The scientific activity of the 2nd PhD year comprised two main projects. The first project was based on the results obtained during the 1st PhD year and aimed to define a thorough longitudinal analysis of retinal morpho-functional and molecular features (1). In the second project, the morpho-functional cerebral microcirculation features were analyzed over time, and the potential beneficial effect of Acebuche, an olive oil containing remarkable levels of bioactive molecules, was tested (2).

Methods

- Experimental murine model: 5xFAD
- Scotopic, photopic, and pattern electroretinogram: evaluation of visual function
- Optical coherence tomography: evaluation of retinal structure
- Ocular and brain surgery
- Molecular analysis: Western Blot, RT-PCR, genotyping, and immunofluorescence
- Bioinformatic analysis on retinal miRNome
- Observation of pial microcirculation by fluorescence microscopic technique

Results

(1) The morpho-functional analyses highlighted a progressive loss of retinal function followed by retinal thinning starting at 6 months of age. Concurrently, molecular analyses demonstrated retinal beta-amyloid and phospho-Tau accumulation, which correlated with photoreceptor and ganglion cell degeneration, and the progressive increment in antioxidant response, inflammation, and apoptosis markers. The miRNome analysis revealed the presence of dysregulated miRNAs suggesting their potential role in the pathological effects. (2) The preliminary morpho-functional analyses revealed a gradual change of cerebral microcirculation starting from 2 months of age, characterized by a morphological alteration of arteriolar vessels, reduced capillary density, and increased microvascular permeability. The Acebuche oil administration prevented the pathological condition but further analysis will be necessary to understand the mechanisms underlying the protective effects.

Congresses

- **73rd Congress of the Italian Society of Physiology (SIF)**, Pisa, September 6-8, 2023. Poster Session. NaHS protects against cisplatin-induced cytotoxicity in HEI-OC1 cells. Lorenzo Guidotti, E. Tomassi, S. Marracci, R. Pesì, E. Albi, M. Garcia-Gil.
- **17th Annual Meeting of Young Researchers in Physiology (YRP)**, Catania, May 22-24, 2024. Poster session. The retina as a window to the brain: morpho-functional alteration in the retina of a mouse model of AD. Lorenzo Guidotti, R. Amato, M. Lucchesi, S. Marracci, M. Cammalleri, M. Dal Monte.
- **74th Congress of the Italian Society of Physiology (SIF)**, Rome, September 11-13, 2024. Poster Session. Morpho-functional alterations and miRNome dysregulation in the retina of a mouse model of Alzheimer's disease: paving the way for new strategies of gene therapy. Lorenzo Guidotti, R. Amato, M. Lucchesi, U. Borello, M. Cammalleri, M. Dal Monte.

Courses and Webinars

- **"How to become more sustainable in the lab – Approaches, Tips, and Tricks"**, Webinar, November 15, 2023 (2 ore).
- **"Basic Next Generation Sequencing (NGS) procedures"**, Milan, November 22-24, 2023 (20 ore).
- **"Giornata di studio per il Benessere animale e metodi alternativi"**, Pisa, December 18, 2023 (6 ore).
- **"Genomica: Tecnologie avanzate"**, Milan, January 25-26, 2024 (14 ore).
- **"La valorizzazione dei risultati delle attività di ricerca: una opportunità di fare leva sulla specializzazione e sulla massa critica del Centro Nazionale di ricerca – Sviluppo di Terapia Genica e Farmaci con Tecnologia a RNA"**, Webinar, April 5, 2024 (30 minuti).
- **"Seminari Prof. Reggiani e Prof.ssa te Kronnie"**, Webinar, April 15, 2024 (3 ore).
- **"Corso di formazione in materia di Salute e Sicurezza sul lavoro – Formazione generale"**, Siena, April 17, 2024 (4 ore).

PhD Courses

- **“Dual filaments regulation of muscle contraction”**, Florence, February 23, 2024 (1 ora).
- **“The molecular motor of muscle studied in vitro mechanics”**, Florence, February 23, 2024 (1 ora).
- **“Mechanical dysfunction in genetic-based cardiomyopathies: perspectives for the use of novel small molecules and biomimetic polymers”**, Florence, February 23, 2024 (2 ore).
- **“High-throughput sequencing: technologies and application in molecular medicine”**, Florence, February 23, 2024 (2 ore).
- **“Effects of SGLT-2 inhibitors in diseased myocardium”**, Florence, February 23, 2024 (2 ore).
- **“The beta-adrenergic system in the retina: targeting beta-adrenoceptors against retinal neovascular diseases”**, Pisa, April 11, 2024 (8 ore).
- **“Beyond the proteome: non-coding regulatory RNAs in cell pathophysiology”**, Siena, May 20, 2024 (4 ore).

Soft skills courses

- **“La valutazione della ricerca e gli strumenti disponibili per il settore STEM”**, Pisa, April 19, 2024 (3 ore).
- **“Competenze statistiche – La ricerca statistica”**, Pisa, May 6, 2024 (3 ore).
- **“La ricerca e l'innovazione in Europa: strategie, opportunità, progetti”**, Pisa, May 7, 2024 (3 ore).
- **“Academic copyright”**, Pisa, May 27, 2024 (2 ore).
- **“Intellectual monopolies and open science”**, Pisa, May 28, 2024 (2 ore).
- **“Corso Embase”**, Florence, May 31, 2024 (3 ore).
- **“The open access publishing paradigm and FAIR”**, Pisa, June 3, 2024 (2 ore).
- **“Research data management”**, Pisa, June 5, 2024 (2 ore).
- **“LABS: FAIR principles in practice and narrative”**, Pisa, June 7, 2024 (2 ore).
- **“Un progetto di convergenza delle case editrici (Mondadori, De' Agostini e Rizzoli) riguardo all'approccio e alle soluzioni digitali per la didattica, con sviluppo e applicazione di IA”**, Siena, June 21, 2024 (3 ore).

Scientific publication

- Curcio M., Cirillo A., Amato R., **Guidotti L.**, Amantea D., De Luca M., Nicoletta FP., Iemma F., Garcia-Gil M. (2022). Encapsulation of Alpha-Lipoic Acid in Functional Hybrid Liposomes: Promising Tool for the Reduction of Cisplatin-Induced Ototoxicity. *Pharmaceuticals (Basel)*. 2022 Mar 24;15(4):394. doi: 10.3390/ph15040394.
- **Guidotti L.**, Tomassi E., Marracci S., Lai M., Lapi D., Pesi R., Pucci L., Novellino E., Albi E., Garcia-Gil M. (2023). Effects of Nutraceuticals on Cisplatin-Induced Cytotoxicity in HEI-OC1 Cells. *International Journal of Molecular Science*. 2023 Dec 12;24(24):17416. doi: 10.3390/ijms242417416.

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