Al collegio docenti del Dottorato in Medicina Molecolare

Dr.ssa/Dott. Elena Battirossi

Ciclo XXXVII Tutor Prof. Pasquale Bianco

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INTRODUCTION

Actin plays crucial roles in cellular processes, like the dynamic remodelling of the cytoskeleton. Non-Muscle Actinopathies (NMAs) are disorders caused by heterozygous mutations in genes encoding for the β- and γ- isoforms of cytoskeletal actin, whose underlying mechanisms remain to be defined. The aim of my project is to develop an analytical toolkit for detailed nanomechanical characterization of neuronal progenitor cells (NPCs), neuronal cells (NCs), and patient-derived Fibroblasts (Fibro) to establish a correlation between the different structural-mechanical-functional parameters of NMAs patient- derived cells.

METHODOLOGY

A Dual Laser Optical Tweezers (DLOT) is applied to characterize the viscoelastic properties of the membrane-cytoskeleton system of wild-type (WT) and expressing the β-R196H and γ-T203M actin mutation cells, associated with malformations of cortical development. Ramp-and-hold pulls to generate tether are imposed on the membrane of NPCs, NCs and Fibro.

RESULTS

Tether formation-elongation is characterized by multiphase force response that were simulated using a 2nd order Maxwell model that provides the estimates of both undamped-damped elastic coefficients and friction coefficients of the tether. The undamped elastic coefficient is higher in WT and β-R196H than γ-T203M NPCs and is not significantly affected by the maturation process. In vivo actin staining marks the presence of F-actin in the tether in all cell lines. These results indicate that γ-actin being responsible of static stiffness.

During maturation, friction and damped elastic coefficients show significant reductions in WT NCs, while in both mutants NCs all the coefficients in NPCs are already reduced to the NCs values. The same mechanical protocols applied to Fibro doesn't show any mutant-associated phenomena.

The DLOT approach to define the structural dynamics of neuron-membrane cytoskeleton system can identify the mechanical fingerprint of β- and γ- actin mutations.

Courses attendance: "Complementary skills for PhD", University of Siena:

- Money for nothing and chicks for free: the story of the European Union and its funding - Dr.ssa Anna Pelagotti (08/05/2023)
- Finanziamenti europei nel settore digitale - www.europedirect.unisi.it/lezioni-deuropa/lezioni-deuropa-2023/ (11/05/2023)
- Europrogettazione: programmi, progetti e rendicontazione- www.europedirect.unisi.it/lezioni-deuropa/lezioni-deuropa-2023/ (18/05/2023)
- Science and Society: continuity and change – Dr.ssa Agnes Allansdottir (29/05/2023)
- PhD and then? Overview on career paths inside and outside the academia – Prof. Gennaro Prota e Dott.ssa Aida Ribera Navarro (12/06/2023)
- Last update in Sustainability reporting regulation – Dr. Maria del Mar Miras (07/09/2023)

Courses attendance:

- How to study genetics in complex diseases – Prof. Stefano Landi, Dipartimento di Biologia dell'Università di Pisa (19-26/01/2023 14.30-17.30)
- Microvescicles in cell-to-cell communication – dr.ssa Laura Governini, Complesso Istituti Biologici San Miniato, Siena (27/02/2023 9.00-13.00)
- Biomarkers discovery in precision medicine – Alice Luddi, Complesso Istituti Biologici San Miniato, Siena (27/02/2023 14.00-18.00)
- Through thick and thin...and titin: Defining titin's role to muscle function - Anthony Hessel (University of Muenster Germany), Università degli studi di Firenze (04/04/2023, 9-11.30)
- Advanced optical methods to monitor and control the cardiac electrical activity - Leonardo Sacconi (Institute of Clinical Physiology, IFC-CNR and LENS – European Laboratory for Non-Linear Spectroscopy) Università degli studi di Firenze (04/04/2023, 11.30-13.30)
- Cellular mechanisms of heart failure - Pieter de Tombe (University of Illinois at Chicago), Università degli studi di Firenze (04/04/2023 14-30-16.30)
- Drug development, sex-dependent difference, pharmacovigilance, Elisabetta Cerbai and Elisabetta Bigagli (University of Florence), Università degli studi di Firenze, (04/04/2023 16.30-18.30)

Lectures and seminars attendance:

- *"Restoring cardiac mechanical function by polymeric artificial muscular tissue (REPAIR) project: mid-way update"*, introduction to REPAIR project - Restoring cardiac mechanical function by polymeric artificial muscular tissue "repair" (Second General Meeting), 16/11/2022 09-10

- *"Extracellular matrix stiffness controls cardiac valve myofibroblast activation through epigenetic remodelling"*, Claudia Crocini (Charité, Berlin, Germany) - Restoring cardiac mechanical function by polymeric artificial muscular tissue "repair" (Second General Meeting), 16/11/2022 10-10.30
- *"Novel 3D model of engineered heart matrix and the stretch of cardiac fibroblasts"*, Frans Van Nieuwenhoven (FYS, Maastricht, Netherlands) - Restoring cardiac mechanical function by polymeric artificial muscular tissue "repair" (Second General Meeting), 16/11/2022 10.30-11.00
- *"Non-coding RNAs as central players in diabetes development"*, Prof. Romano Regazzi, Director, Department of Biomedical Sciences, University of Lausanne) – online seminar, 09/03/2023 17.00
- *"Multiscale modelling of striated muscle contraction"*, Dr. Matthieu Caruel (Université Paris-Est Créteil, Paris, France) – Science Seminar, 14/03/2023, 16/03/2023 13.00
- "*Etica e Intelligenza Artificiale"*, Workshop Careus – online seminar, 27/03/2023 15-17.00
- *"Fluidic Force Microscopy to study Cellular Mechanosensing"*, Prof. Massimo Vassalli (James Watt Scholl of Engineering, University of Glasgow, UK) – 04/07/2023 12.00
- *"Exploring a single nanomotor dysfunction at-a-time: impaired cardiac myosin function triggering pathological cardiac remodelling in cardiomyopathy"*, Mamta Amrute-Nayak (Hannover Medical School, Hannover, DE) – 07/09/2023 15.00

Abstract at National/International conferences:

- **Elena Battirossi**, I. Niehaus, S. Li Puma, I. Pertici[1], M. Reconditi, V. Lombardi, N. Di Donato, P. Bianco. "*Cytoskeleton-membrane dynamics of Neural Progenitor Cells (NPC) and Neuron Cells (NC) studied with Dual Laser Optical Tweezers (DLOT)"*. PhD day, Firenze (FI), Italy, 17 January 2023
- **Elena Battirossi**, I. Pertici, M. Reconditi, V. Lombardi, N. Di Donato, P. Bianco. "*Assessment of the impact on neuron cytoskeleton of b- and g-actin mutations leading to non-muscle actinopathies by means of Dual Laser Optical Tweezers (DLOT)*". Biophysical Society Annual Meeting 2023, San Diego (United States), 18-22 February 2023
- **Elena Battirossi**, I. Pertici, M. Reconditi, V. Lombardi, N. Di Donato, P. Bianco." *Assessment of the impact on neuron cytoskeleton of b- and g-actin mutations leading to non-muscle actinopathies by means of Dual Laser Optical Tweezers (DLOT)".* 16th Annual Meeting of Young Researchers in Physiology, Bertinoro (FC), Italy, 21-23 June 2023
- **Elena Battirossi**, I. Pertici, M. Reconditi, V. Lombardi, N. Di Donato, P. Bianco. "*Assessment of the impact on neuron cytoskeleton of b- and g-actin mutations leading to non-muscle actinopathies by means of Dual Laser Optical Tweezers (DLOT)".* 50th European Muscle Conference, Florence (FI), Italy,2-6 September 2023

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- **Elena Battirossi**, I. Pertici, M. Reconditi, V. Lombardi, N. Di Donato, P. Bianco. *"Assessment of the impact on neuron cytoskeleton of b- and g-actin mutations leading to non-muscle actinopathies by means of Dual Laser Optical Tweezers (DLOT)"*. 73rd SIF National Congress, Pisa (PI), Italy, 6-8 September 2023