CRBM
Centre de Recherche en Biologie Cellulaire de Montpellier

CRBM external seminar
January 25th, 2024 13:00 Salle Marcel Dorée

Neurofilament dynamics and signaling

Pascale BOMONT

***Group leader* - Mechanisms and therapies for neuromuscular diseases in the INMG (Institut NeuroMyoGène), Lyon, France**

Pascale Bomont received her PhD in Human Genetics in 2002 (IGBMC, Strasbourg, France) and identified the mutated genes for several neuropathies. Focusing on rare diseases, in particular giant axonal neuropathy (GAN) caused by loss-of-function of the Gigaxonin-E3 ligase, she conducted a postdoctoral training in Cell Biology (LICR, San Diego, USA) to investigate cytoskeleton alterations in disease. Moving back to France, she was recruited at INSERM in 2007 and was awarded by the ATIP-Avenir prize in 2011 to run a multidisciplinary research program on GAN at Montpellier University. Her group developed tools and biological systems in patients, mouse and zebrafish to unravel the key roles of Gigaxonin in controlling cytoskeleton (Intermediate Filaments) architecture, autophagy machinery and neuromuscular integrity, and to generate diagnosis tests and therapeutic approaches for patients. Presently, she is INSERM Research Director at INMG (Institut NeuroMyoGène) at Lyon and runs an ERC-CoG program on neurofilament biology.

Abstract

Neurofilaments (NFs) are the Intermediate Filaments of the nervous system and the major cytoskeletal component of mature neurons. The assembly mode of NFs, generating intermediate antiparallel tetramers and establishing an interconnected stable network constitutes a major challenge for monitoring their behavior and functions in the neuron. Still, adaptation of imaging methodologies and mouse genetics revealed the dynamic nature of NFs, in their transport and turn-over along nerves. Little is known regarding the roles of NFs, and rare studies in mouse revealed that in addition to their regulation of mechano-resistance, radial axonal outgrowth and nerve conduction, NFs control microtubule dynamics, organelle distribution and neurotransmission at the synapse. Our research program aims to uncover the dynamics and signaling of NFs, which enable the neuron to establish a stable, yet elastic NF array constituting the structural scaffold of the axon, but that are also key dynamic elements to fulfill local demands, respond to stimuli/injury and fine-tune neuronal functions. Integrating disease model systems related to NF degradation (gigaxonin-E3 ligase) and aggregation (NF-L), our goal is to scrutinize the dynamics of NFs in vivo, the downstream signaling sustaining their essential functions and how alterations of this system can cause neurodegeneration. These fundamental questions have not been addressed in a physiological environment, the principal hurdles being the tedious and long investigations in mouse and the lack of knowledge and methodologies to investigate the live dynamics of NFs *in vivo*. Here, we will present how we will tackle the dynamics and signaling of NFs *in vivo*, in the zebrafish (Danio rerio) species that will enable us to combine molecular, cellular and behavioral investigations to boost innovation on NF biology.

Selected publications

Lescouzères L, Hassen-Khodja C, Baudot A, Bordignon B, **Bomont P** (2023) A multilevel screening pipeline in zebrafish identifies therapeutic drugs for GAN. **EMBO Mol Med**. 2023 Jul 10;15(7):e16267.

Gafson AR, Barthélemy NR, **Bomont P**, Carare RO, Durham HD, Julien JP, Kuhle J, Leppert D, Nixon RA, Weller RO, Zetterberg H, Matthews PM. (2020) Neurofilaments: neurobiological foundations for biomarker applications. **Brain**. 143(7):1975-1998.

Arribat Y, Mysiak KS, Lescouzères L, Boizot A, Ruiz M, Rossel M, **Bomont P**. (2019) Sonic Hedgehog repression underlies gigaxonin mutation-induced motor deficits in giant axonal neuropathy. **J Clin Invest**. 129(12):5312-5326.

Scrivo A, Codogno P, **Bomont P**. (2019) Gigaxonin E3 ligase governs ATG16L1 turnover to control autophagosome production. **Nat Commun**. 10(1):780