

Congratulations to New ICFO PhD Graduate

Dr. Neus Sanfeliu Cerdan graduated with a thesis entitled ?A liquid-to-solid transition governs neuronal mechanotransduction during touch in Caenorhabditis elegans'

March 12, 2024

We congratulate Dr. Neus Sanfeliu Cerdan who defended her thesis today in ICFO's Auditorium.
Dr. Sanfeliu Cerdan obtained her MSc in Advanced Microbiology from the Universitat de Barcelona. She joined the Neurophotonics and Mechanical Systems Biology research group at ICFO led by Prof. Dr. Michael Krieg as a PhD student.
Dr. Sanfeliu Cerdan's thesis entitled ?A liquid-to-solid transition governs neuronal mechanotransduction during touch in Caenorhabditis elegans' was supervised by Prof. Dr. Michael Krieg.

ABSTRACT:

In recent years, our understanding of the ion channels and receptors that orchestrate the conversion of physical stimuli into physiological signals has deepened significantly. Nevertheless, there remains some ambiguity regarding the precise mechanism by which mechanical stresses reach the molecular mechanosensors. While it is well-established that many mechanosensitive ion channels respond to increased plasma membrane tension, emerging evidence underscores the crucial role played by the cytoskeleton within sensory cells. In this thesis, we asked how animals perceive mechanical stress, with specific focus on touch sensation. Our primary objective was to unravel the molecular and the mechanical pathways responsible for transmitting force within the touch receptor neurons of the nematode Caenorhabditis elegans. For over a decade, it has been postulated that the pore-forming subunit of the mechanoelectrical transduction channel forms a connection with the cytoskeleton through a highly conserved and widespread protein known as MEC-2, which bears structural similarities to Stomatin.

Our study presents compelling evidence that MEC-2 assembles in liquid condensates that experience a shift in rigidity, transitioning from a fluid-like pool that allows transport along neurons to solid-like states that are mechanoelectrically active. We provide a new physiologically relevant context in which biomolecular condensates tune their function upon maturation and facilitate neuronal mechanotransduction in response to tactile stimuli. In order to contextualize the function of MEC-2 in force transmission, we developed a genetically encoded tension sensor module, which revealed that only stiffened condensates, as opposed to fluid-like ones, are capable of transmitting force within living organisms. Notably, this stiffening process does not occur autonomously. Within this study, we showed that this transition is instigated by a specific SH3 motif of UNC-89, a protein homologous to Titin and Obscurin, through a direct interaction with a proline-rich domain located in the C-terminal region of MEC-2. We propose that this change in rigidity serves a vital physiological function by contributing to the transmission of forces that vary in frequency during touch to the animal's body wall. Together, our data introduces a novel perspective on the significance of the MEC-2 liquid-to-solid phase transition in the realm of mechanotransduction. It also presents a new conceptual framework for understanding how animals, in a broader sense, perceive and respond to mechanical stresses.

Thesis Committee:

Prof. Dr. Suzanne Wegmann, Neurodegenerative Diseases (DZNE)

Dr. Felix Campelo, ICFO

Prof. Dr. Meital Oren, Weizmann Institute of Science



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