ISTITUTO PASTEUR ITALIA
FONDAZIONE CENCI BOLOGNETTI

Avviso seminario

Il 10 settembre 2024 alle ore 15 nell'aula Magna Regina Elena

"Tunneling Nanotubes Across Biological Scales: Reshaping Connectivity and Their Role in the Spreading of Neurodegenerative Diseases"

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Tunneling nanotubes (TNTs) are actin-based cellular connections that allow the transport of various cellular components between cells. They were first described in a cell line culture almost 20 years ago and are now recognized as an important mechanism of cell-to-cell communication. Since their discovery, the structure and function of TNTs have been characterized in several cell types, including neurons and astrocytes. Under homeostatic conditions, TNTs transport different vesicular cargoes and entire organelles like mitochondria and lysosomes. However, they can be hijacked by different pathogens and amyloid proteins involved in neurodegenerative diseases, such as Parkinson's disease (PD) and Alzheimer's disease (AD). We have previously demonstrated that both alpha-synuclein (α-Syn) and Tau aggregates, respectively the hallmarks of PD and AD, can spread from one cell to another via TNTs. We have proposed that this is a key mechanism for the progression of these diseases and the spreading of pathology throughout the brain. In the context of PD, we have also shown that TNTs form between neurons and microglia. α-Syn aggregates increase TNTs in both neuronal and microglial cells and move preferentially from neuronal cells to microglia. Conversely, microglia deliver healthy mitochondria preferentially to neurons bearing α-Syn aggregates, suggesting a rescuing role of microglia towards dying neurons. Our unpublished data indicate that this is regulated by differential dysfunctions of organelles (lysosomes and mitochondria) in neurons and microglia. In my talk, I will address the similarities and differences between TNT-mediated diffusion of different types of aggregates to identify common pathways leading to neurodegeneration. I will also touch upon our studies on the molecular mechanisms of TNT formation and will assess the likelihood of TNT presence in vivo, specifically using a serial SEM connectome approach in the mouse brain and live imaging approaches in zebrafish embryos. Our recent data indicate that TNT-like connections are present in the developing brain. Our hypothesis is that TNTs precede synaptic connections and may be important for the establishment of mature neuronal networks, while in adult tissue they are induced by stressful and inflammatory stimuli.

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