Interaction of tau and microtubules using single molecule approach

Grenoble Institut des Neurosciences (Team Dynamique et structure du cytosquelette ; Leader I. Arnal) – Chemin Fortuné Ferrini, UGA, Site Santé La Tronche

Objective: Deciphering the dynamic interaction of the tau protein with microtubules using real time observation at the single molecule level

CONTEXT:

Microtubules (MT) are a major component of the cell cytoskeleton. They are dynamic polymers involved in essential cell functions such as mitosis, motility or intracellular transport. The spatial organization and the dynamic behavior of MT are regulated by MAPS (Microtubule-Associated Proteins). In our team we focused on the specific MAP tau.

Tau is a neuronal Microtubule-Associated Protein that promotes MT assembly and bundling in axons. Misregulation of tau leads to cytoskeleton alterations and severe neuronal impairments in neurodegenerative pathologies like Alzheimer Disease and related dementia. Although tau is known for years, many of its intrinsic properties remain unknown; for instance, today we lack a clear picture of how tau interacts with and organizes MTs in bundled arrays.

INTERNSHIP:

The student will characterize the dynamic interaction of tau (both normal tau and mutated forms of tau found in the brains of Alzheimer patients) with microtubules using real time TIRF (Total Internal Reflexion Fluorescence) microscopy.

To do so, the applicant will use *in vitro* assays to reconstitute MT cytoskeleton in the presence of tau (a well-established assay in the team) and to develop conditions that allow quantitative measurements of single molecules. Part of the internship will be devoted to image analysis.

KEYWORDS: Biology/physics interface, Single molecule imaging, Tau dynamics

Requested domains of expertise: Excellent and pedantic experimenter – Computer programing (knowledges on Phyton and Matlab are welcome)

Supervisor: Virginie Stoppin-Mellet (virginie.stoppin-mellet@univ-alpes-grenoble.fr)

Relevant publications available on request:

1- Telley IA, Bieling P, Surrey T. (2011). Reconstitution and quantification of dynamic microtubule end tracking in vitro using TIRF microscopy. Methods Mol Biol. 777:127-45.

2- Bieling P, Kandels-Lewis S, Telley IA, van Dijk J, Janke C, Surrey T. (2008). CLIP-170 tracks growing microtubule ends by dynamically recognizing composite EB1/tubulin-binding sites. J Cell Biol. 183:1223-33.