Institut de Bioenginyeria de Catalunya

COLLABORATIVE IBEC INTERNATIONAL PhD PROGRAMME

Position

1. Project Title:
   Photoswitchable stabilizers of protein-protein interactions for light-driven patterned stimulation of axonal outgrowth and formation of neuronal contacts

2. Research project/ Research Group description

Research Project. Damaged neurons and neuronal connections have a limited capacity for spontaneous regeneration, leading to persistent functional deficits following injury. Targeting protein-protein interactions represents a promising therapeutic avenue for **treatment of the central nervous system (CNS) injuries**. For instance, it has been demonstrated that stabilizing protein-protein interactions of **14-3-3 interactome** of phosphoprotein-binding molecules promotes neurite outgrowth, highlighting these proteins as a promising target for developing novel strategies to stimulate neurite extension and the formation of novel neuronal connections (Kaplan et al., 2017).

In this context, the PhD Project will aim at developing photoswitchable small molecules (molecular glues) for light-controlled stabilization of 14-3-3-protein interactions involved in stimulation of neurite outgrowth. Regulating the strength and likelihood of 14-3-3 binding to its targets, using small photoswitchable molecules, will enable us to **stimulate, in a light-dependent manner, neurite outgrowth and formation of synaptic contacts in desired locations**. We expect that such tools will have a strong impact on both our understanding of how protein-protein interactions affect elongation of neurites and on the development of novel therapeutic strategies to treat CNS injuries.

Research Group. This PhD Project will be developed under the supervision of Dr Galyna Malieieva (IBEC, Nanoprobes and Nanoswitches Group) who works on the development of new ways to control functioning of CNS with light and Dr Luc Brunsveld (Eindhoven University of Technology) who is a world-leading expert in the development of small molecules stabilizers for protein-protein interactions.

The Nanoprobes and Nanoswitches group at IBEC focuses on developing nanoscale light-driven tools for the control of biological systems. Compounds developed by the group have enabled photocontrol of cellular signaling mediated by ion channels and G protein-coupled receptors, photocontrol of cardiac activity and locomotion, sensory restoration, and photocontrol of brain waves.

The Chemical Biology group at ICMS (at TU/e) develops molecular concepts to modulate protein-protein interactions. Next to supramolecular protein engineering, the group has strong focus on

developing small molecule molecular glues that stabilize protein-protein interactions. Specifically, the 14-3-3 protein and its interactome provide an enormous wealth of regulatory roles for molecular glues for many disease states.

3. Job position description

We are seeking a motivated PhD student interested in developing new approaches for studying and controlling protein-protein interactions in central nervous system.

Requirements:

- The candidate for the position must hold a Master´s degree in Organic Chemistry, Biochemistry or other related disciplines.
- The PhD candidate is expected to be involved in the collaborative development and synthesis of the compounds as well as in their *in vitro* testing.
- The PhD candidate should have strong communication skills and enthusiastic to perform research both at IBEC in Barcelona and ICMS in Eindhoven.

What we offer:

- An innovative training in the synthesis of organic photoswitchable compounds, and their photochromic, biochemical and structural characterization.
- An innovative training in *in vitro* cell based assays for testing photoswitchable molecules and studying molecular physiology of central nervous system using photoswitchable molecules.
- Theoretical training in molecular physiology of the nervous system, protein-protein interactions and photochemistry.
- An international, vibrant, and collaborative environment that will ensure the PhD student's professional growth and innovative research resulting in published work in top journals.
- Support in applications for summer schools and other competitive calls.

Group Leader at IBEC

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Collaborator at ICMS

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