PROMEMO / DANDRITE Topical Seminar

Tuesday 25 September 2018

at 12:00 – 13:00

The Library, building 1170, 4th floor

Beatriz Alvarez-Castelao

Postdoc in Erin Schuman's group – Synaptic Plasticity,

Max Planck Institute for Brain Research,

Frankfurt, Germany

Neuronal proteostasis

We developed a transgenic mouse line where Cre-recombinase-induced expression of a mutant methionyl-tRNA synthetase (L274G) enables the cell-type-specific labelling of nascent proteins in vivo with a non-canonical amino-acid and click chemistry. We use our transgenic mouse to label, identify and compare the proteomes of excitatory principal neurons and Purkinje neurons. Additionally, we demonstrate that our technique can be used to study protein homeostasis identifying 200 proteins differentially regulated in hippocampal excitatory neurons by exposing mice to an environment with enriched sensory cues. Overall, this approach can be used to isolate, analyze and quantitate cell-type-specific proteomes and their dynamics in healthy and diseased tissues. Additionally, we wonder how are the regulatory feedback mechanisms by which the cells are able to couple protein synthesis and degradation to maintain and optimize protein concentrations in the face of intra- and extracellular perturbations. To tackle this question we examined the feedback between one of the major protein degradation pathways, the ubiquitin-proteasome system (UPS), and protein synthesis in primary neurons. When protein degradation by the UPS was inhibited we observed a coordinate dramatic reduction in nascent protein synthesis in both neuronal cell bodies and dendrites. The mechanism for translation inhibition involves the phosphorylation of eIF2a, mediated by EIF2AK kinase. Under basal conditions, neuronal expression of this kinase is low owing, at least in part, to its less than optimal codon usage.

Host: Prof. Marco Capogna, PROMEMO Group Leader, DANDRITE affiliated researcher, Dept. of Biomedicine, Aarhus University.