



Scuola di Dottorato di SCIENZE NATURALI ED INGEGNERISTICHE

Corso di Dottorato in Biotecnologie

## "ACAD9 deflavination as switching mechanism from fatty acid oxidation to mitochondrial Complex I assembly: insights into amyloid-beta toxicity"

## November 11<sup>st</sup>, 2019 - h. 11.00

## **Dott. Gabriele Giachin**

CIBIO - Trento

## Abstract

Fatty acid  $\beta$ -oxidation (FAO) and the oxidative phosphorylation system (OXPHOS) are critical pathways that transform redox reactions into ATP. Furthermore, evidence indicate a strong association between the OXPHOS Complex I and the amyloid-beta (A $\beta$ ) toxicity that characterizes Alzheimer's disease. Here we show that ECSIT is key for the mitochondrial Complex I assembly (MCIA) complex and its binding to the vestigial domain of ACAD9 induces the ejection of its FAD cofactor, thereby shutting down the ACAD9 dehydrogenase activity and antagonizing its role in FAO. Notably, ECSIT is also the main MCIA factor associated to hyperactive CI in neuronal cells affected by soluble A $\beta$ , suggesting a role of ECSIT as a link between CI deficiencies and neurodegeneration. Overall, our findings are relevant for targeted diagnostics when mitochondria are primarily affected by A $\beta$  toxicity.

The lecture will take place at 11.00 - Aula G - Cà Vignal - Strada Le Grazie, 15

Local organization and contact:

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For each hour of seminar, 1 CFU (provided for the specific activities of PhD Program in Biotechnology) will be recognized to students attending the event.