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## Structural and molecular basis for mitochondrial Complex I assembly and its implication in amyloid pathology

le 27 avril 2017

de 11h30 à 12h30

SÃ©minaire de Montse Soler Lopez (ESRF Structural Biology, Grenoble)

Alzheimer's disease (AD) is a fatal neurodegenerative disorder characterized by amyloid- $\beta$  ( $A\beta$ ) plaques and whose causality remains unclear. There is evidence that  $A\beta$  enters into the mitochondria in brains of AD patients and impairs the mitochondrial respiratory supercomplex system, leading to defective neurotransmission, synaptic damage and cognitive impairments associated with AD. Previously, we identified a respiratory mitochondrial complex I assembly (MCIA) factor as an interacting node between  $A\beta$  producing enzymes and mitochondrial energetics. Our work focuses on the structural and functional analyses of the MCIA core complex composed of NDUFAF1, ECSIT and ACAD9 proteins and their interplay with  $A\beta$  burden regulation. Deciphering the mechanistic details underlying MCIA function will advance our understanding of AD etiology by (i) elucidating how mitochondrial respiration is coupled to  $A\beta$  dynamics and (ii) unveiling the causal link between mitochondrial dysfunction and amyloid pathology in the early stages of AD. It will also establish whether MCIA factors are potential biomarkers that may contribute to mitochondria-targeted therapeutics.

Montse Soler Lopez est invitée par Annie Andrieux.

Mise à jour le 21 avril 2017