University of Zurich[UZH]

Institute for Regenerative Medicine • IREM

InReMed

Innovations in Regenerative Medicine

Monday, 25.3.2024, 13:00 – 14:00

WAD P-106, Wagistrasse 12 (9th floor), 8952 Schlieren

Prof. Anne-Claude Gavin

Department of Cell Physiology and Metabolism, University of Geneva

Impact of APOE polymorphism on lipid transport capacity

Apolipoprotein E (APOE) produced by astrocytes (the brain's feeder cells) is the main lipid transporter in the brain. These local lipid transports ensure the survival of neurons under conditions of stress and hyperactivity by supplying them with essential metabolites and ridding them of toxic peroxidized fatty acids (by-products of neuronal metabolism). In humans, APOE exists in three common variants which, combined with environmental stresses or age-related alterations in astrocytic function (i.e. in reactive astrocytes), influence the risk of developing Alzheimer's disease. APOE4 is a risk factor, APOE3 is neutral and APOE2 is protective. Other rarer APOE mutations have been reported to have an impact on the risk of developing Alzheimer's disease. Among these, protective variants such as APOE3 Christchurch, APOE3 Jacksonville and APOE4-R251G are of particular interest, as they demonstrate that modulation of APOE function can have a beneficial impact. However, the molecular mechanisms involved remain poorly understood, in particular, there are no data comparing the ability of these variant forms to recognize and load specific lipids, and the composition of the lipoprotein particles they assemble in the context of the brain remains enigmatic. How brain-derived APOE handles lipids, the type of lipoprotein particles it assembles, and how these processes are influenced by APOE polymorphism or by factors altering astrocytic functions are the basic molecular biology questions we will discuss.

Chair: Christian Tackenberg