Open position for the LSM call of applications

Department/Institute: LMU Department of Ophthalmology, LMU Hospital

Subject areas/Research fields: Neuroscience, Bioinformatics, Cell Biology, Developmental Biology

Keywords: Epigenetics, DNA Methylation, Demethylation, Neuron, Retina

Name of supervisor: Prof. Dr. Stylianos Michalakis

Project title: Role of TET3-mediated 5mC oxidation for neuronal differentiation and plasticity

Project description:

Scientific background. Establishment of neuronal cell identity requires precisely orchestrated adjustments in gene expression that are mediated, at least in part, by the fine-tuned activity of a-ketoglutarate (a-KG)-dependent TET (Ten eleven translocation) enzymes. These TETs are dioxygenases that mediate the stepwise oxidation of the repressive DNA modification 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC), 5-formylcytosine (5fC), and 5-carboxycytosine (5caC), thereby activating gene expression.

Among the three TET enzymes, TET3 is the most abundant isoenzyme in the adult brain. TET3 expression steadily increases during early neuronal differentiation and throughout development, which goes in hand with a steady increase in 5hmC. The overarching goal of this project is to investigate the role of TET3 and interacting proteins for differentiation of 2D neuronal cultures and human retinal organoids grown from wildtype and TET3-deficient induced pluripotent stem cell (iPSC) and complement ongoing studies with specific mouse models.

Specific aims and methodology. The functional significance of TET proteins and their enzymatic products in the CNS has not been characterized and will be addressed in the group with specific genetic mouse and cellular models. TET enzymes act in concert with chromatin remodeling proteins and transcription factors. We identified intriguing novel TET interaction partners in mouse retina, mouse brain and/or iPSC-derived

neurons. The potential of selected candidate proteins to functionally engage with TET3 will be assessed in this proposal. We are looking for a highly motivated PhD candidate with genetic and epigenetic background and strong interest in neuroscience and bioinformatics. The candidate will learn and apply genetic, biochemical, cell biological and viral gene transfer methods in vitro and in vivo and bioinformatic methods on different omics datasets (scRNAseq, RNAseq, proteomics, methylation data).

References:

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For further information, please contact: Prof. Dr. Stylianos Michalakis, michalakis(at)lmu.de

Reseach group website:

https://www.lmu-klinikum.de/augenklinik/forschung/gentherapie/1305646bdc184d5c

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