In Vivo Pathogenesis of Neurodegeneration in Multiple Sclerosis

March 21

Tuesday, 12:30 pm

Zoom Only

SPEAKER:



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Host: Edmund Hollis II, Ph.D.

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Abstract

Here, I want to discuss how in vivo microscopy techniques can be used to better understand the emergence of neurodegeneration during CNS inflammation.

To illustrate this I will discuss two lines of work. First I will present our recent insights into the in vivo pathogenesis of immunemediated axon damage in an animal model of multiple sclerosis. I will highlight how in vivo imaging can help us reveal



how immune cells damage axons in the inflamed spinal cord. In particular I will focus on recent insights that explore the emergence of mitochondrial pathology in neuroinflammatory lesions and identify a dysbalance of the TCA cycle as a critical checkpoint for axonal energy homeostasis that can be targeted therapeutically. In the second part of my talk I will focus on the structural and functional pathology of neurons in the inflamed gray matter. Here I will focus on the role of synaptic pathology, the mechanisms that induce it and its relation to altered neuronal function.

Publications

1. Jafari M, Schumacher AM, Snaidero N, Ullrich Gavilanes EM, Neziraj T, Kocsis-Jutka V, Engels D, Jürgens T, Wagner I, Weidinger JDF, Schmidt SS, Beltrán E, Hagan N, Woodworth L, Ofengeim D, Gans J, Wolf F, Kreutzfeldt M, Portugues R, Merkler D, Misgeld T, Kerschensteiner M. (2021) *Phagocyte-mediated synapse removal in cortical neuroinflammation is promoted by local calcium accumulation.* Nat Neurosci 24, 355-367.

2. Witte ME, Schumacher AM, Mahler CF, Bewersforf JP, Lehmitz J, Scheiter A, Sánchez P, Williams PR, Griesbeck O, Naumann R, Misgeld T, Kerschensteiner M (2019) *Calcium influx through plasma-membrane nanopores drives axon degeneration in a model of multiple sclerosis.* Neuron 101, 615-624

3. Locatelli G, Theodorou D, Kendirli A, Jordão MJC, Staszewski O, Phulphagar K, Cantuti-Castelvetri L, Dagkalis A, Bessis A, Simons M, Meissner F, Prinz M, Kerschensteiner M (2018) *Mononuclear phagocytes locally specify and adapt their phenotype in a multiple sclerosis model.* Nat Neurosci 21, 1196-1208



