PROJECT 1

DoS: Cinthia Farina

Title: A role for astrocytes in Neuroinflammation

Curriculum: PhD in Neuroscience and Experimental Neurology

Link to OSR/UniSR personal page:
http://research.hsr.it/en/institutes/institute-of-experimental-neurology/immunobiology-of-neurological-disorders.html

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):

Our lab has great interest in the pathogenic processes occurring in multiple sclerosis (MS), a chronic neurodegenerative inflammatory disorder of the CNS. A hallmark of CNS injury is the formation of scar tissue composed of activated ("reactive") astrocytes and microglia. An inflammatory response takes place within this clearly demarcated area (Farina et al. Trends in Immunol. 2007, Cordiglieri et al. Current Immunol. Rev. 2010). This reaction is commonly regarded as detrimental, as the glial scar may mechanically block axonal elongation and regeneration after injury. On the other hand, scar formation is important to restrain the damage and spatially restrict the inflammatory reactions. Thus, a crucial issue is the identification of pathways in astrocytes modulating neuroinflammation, neurodegeneration and/or demyelination, key pathogenic processes in MS. Recently, our lab made significant contributions to the field (Colombo et al. J. Exp. Med 2012, Colombo et al. Ann. Neurol 2014). In particular, we have shown that both neurotrophic and inflammatory mediators may induce neurodegeneration via astrocyte activation, and that inhibition of phospholipid signaling in astrocytes may result protective for CNS tissue. With this project we want to gain further knowledge about astrocyte phenotypes contributing to tissue damage or repair during neuroinflammation. In fact, we are interested in determining those glia features regulating immune responses, (de)myelination, and/or neuronal activity by in vitro cell biology experimentations with primary cultures of relevant cell types followed by phenotypical and functional in vitro characterizations. The in vitro observations will be further analyzed in the in vivo setting using distinct animal models of multiple sclerosis. Finally, relevance for the human disease will be pursued by neuropathological examination of human MS and control tissues.

Skills to be acquired by the student:

Immunology, Neurobiology, Neuroimmunology, Statistics.

Molecular and cellular Biology, Immunohistochemistry, Immunofluorescence and confocal imaging, Flow cytometry, Animal Experimentation.

Logical thinking, Scientific English.

References (max. 3)

1) Emanuela Colombo, Chiara Cordiglieri, Giorgia Melli, Jia Newcombe, Markus Krumbholz, Luis Parada, Enzo Medico, Reinhard Hohlfeld, Edgar Meinl and Cinthia Farina. *Stimulation of the neurotrophin receptor TrkB on astrocytes drives nitric oxide production and neurodegeneration.* Journal of Experimental Medicine 209 2012.
2) Emanuela Colombo, Marco Di Dario, Eleonora Capitolo, Linda Chaabane, Jia Newcombe, Gianvito Martino and Cinthia Farina. *Fingolimod may support neuroprotection via blockade of astrocyte nitric oxide*. Annals of Neurology 76 2014.
3) Colombo Emanuela, Farina Cinthia. *Astrocytes: key regulators of Neuroinflammation.* Trends in Immunology 37, 2016.