PROJECT 1

DoS: Marco Bacigaluppi

Title: Mapping age related changes of the immune response occurring in ischemic stroke

Curriculum: Neuroscience and Experimental Neurology

Link to OSR/UniSR personal page:

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):
During ageing the brain as well as the immune system undergoe a series of structural and functional modifications that result in increased susceptibility to diseases. One of the consequences of this decline is that ischemic stroke mainly affects the elderly population that, compared to young, shows a worse clinical outcome in terms of disability and mortality.

On the one hand ischemic brain injury is known to trigger a profound systemic immune response by direct stimulation of hematopoiesis mainly through the autonomic nervous system. As a consequence of stroke, levels of circulating monocytes increase and myeloid cells are recruited to the brain where they contribute to recovery but also to injury. On the other hand a deranged or improperly activated immune system, and in particular myeloid cells, has been described to trigger thrombosis and cerebrovascular as well as cardiovascular ischemia. Importantly recent studies have evidenced that ageing is characterized by the increased frequency of clonal hematopoiesis with somatic mutations predisposing to both cancer but also to increased cardiovascular events. Remarkably elderly people might thus suffer from increased cerebrovascular events and worse outcome due to a derangement of the tightly controlled hematopoiesis and in particular of the myeloid cell compartment limiting their potential protective mechanisms in favor of detrimental immunity.

Aim of this project is to investigate how age-induced dysfunctions of the hematopoietic niche altering the systemic inflammatory response in particular of myeloid cells after ischemic stroke contribute to the worse outcome in terms of stroke related mortality and morbidity.

Skills to be acquired by the student:

Handling of transgenic mouse lines, experimental stroke induction, confocal microscopy, immunohistochemistry and immunofluorescence staining, flow cytometry, rt-PCR, RNA-seq and bioinformatics analysis, PCR, in vivo administration of compounds and drugs (e.g. intracerebroventricular injections, intravenous injections). Detailed knowledge and update of the current literature in the field, construction of a hypothesis and experimental plan to investigate the hypothesis, writing of periodic scientific reports, analysis and discussion of results and of published papers (e.g. Journal Club).

References (max. 3)

- Bacigaluppi M, Russo GL, Peruzzotti-Jametti L, Rossi S, Sandrone S, Butti E, De Ceglia R, Bergamaschi A, Motta C, Gallizioli M, Studer V, Colombo E, Farina C, Comi G, Politi LS, Muzio L, Villani C, Invernizzi RW, Hermann DM, Centonze D, Martino G. Neural Stem Cell Transplantation Induces Stroke Recovery by Upregulating Glutamate Transporter GLT-1 in Astrocytes. J Neurosci. 2016 Oct 12;36(41):10529-10544.

-De Feo D, Merlini A, Brambilla E, Ottoboni L, Laterza C, Menon R, Srinivasan S, Farina C, Garcia Manteiga JM, Butti E, Bacigaluppi M, Comi G, Greter M, Martino G. Neural precursor cell-secreted TGF-β2 redirects inflammatory monocyte-derived cells in CNS autoimmunity. J Clin Invest. 2017 Nov 1;127(11):3937-3953

- Jaiswal, S., et al., Clonal Hematopoiesis and Risk of Atherosclerotic Cardiovascular Disease. N Engl J Med, 2017. 377(2): p. 111-121.