Title: Understanding the role of inflammatory cells in the post-acute recovery phase after ischemic stroke.

Ischemic stroke is caused by an occlusion of a cerebral artery, leading to focal brain tissue injury. The brain responds to stroke with an acute as well as prolonged tissue repair process characterized by rapid activation of resident endogenous neural stem cells, astrocytes, microglial cells, and infiltration of various types of blood borne immune cells. CNS-resident and blood-borne CNS-infiltrating inflammatory cells were considered for decades to be detrimental after stroke. However, recent evidence supports the role of these cells in the repair process. It has been in fact shown in other brain pathologies that the local immune response is important for neuroprotection, and for promoting the repair process, including axonal regeneration and cell renewal. In addition, over the last few years, it became clear that brain’s resident neural stem cells (NSCs) participate in a reciprocal relationship with immune cells that is critical to the repair by endogenous cells as well as by exogenously introduced therapeutic NSCs. These progenitor cells exert an immunomodulatory function and act as source of trophic factors beyond cell replacement.

The main aim of the proposed PhD project is to study the role of microglia in post-acute functional recovery after experimental stroke. In particular the main objectives of the project will be:

i. To explore the contribution of microglia to the post-acute recovery phase occurring after stroke;

ii. To explore the contribution of microglia to drive neuronal plasticity processes after stroke;

iii. To study the role of microglia in regulating long-term cell genesis from endogenous NSCs.

To achieve these goals, two different experimental stroke models such as proximal and distal middle cerebral artery occlusion will be used in naïve (treated pharmacologically with CSFR1 inhibitors to ablate specifically microglia) or transgenic mice (NestinTK, NestinCreERT2-iDTR, CX3CR1CreERT2-iDTR, CX3CR1CreERT2-iDTR) either to ablate endogenous NSCs or inflammatory cells. Moreover, in vitro co-culture models with NSC, astrocytes, microglial and endothelial cells will be used to dissect the cross-talk between the different cell types.

Website: http://www.hsr.it/ricerca/divisioni-centri-istituti-e-programmi-di-ricerca/istituto-di-neurologia-sperimentale-inspe/gianvito-martino/

References:


