PRINCIPE FELIPE
CENTRO DE INVESTIGACION

The Future of Biomedical Research Lecture Series

Remote signaling and stem cell-niche biology in the adult brain

Speaker: **Dr. Isabel Fariñas**
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Date: **13/04/18- 12:30h**
Place: Salón de Actos CIPF

Abstract: Adult stem cells are found at specific locations and their behavior and lifelong maintenance is regulated by both cell intrinsic factors and signals from the microenvironment or niche in which they reside. However, stem cell niches are still poorly characterized due to the complexity of the interactions between stem cells and their neighbors and to the dynamic changes required for the continuous production of new cells. In the adult brain subependymal zone (SEZ), radial glia/astrocyte-like neural stem cells (NSC) continually produce new neurons and oligodendrocytes, via a population of rapidly-diving transit-amplifying progenitor cells. In the adult SEZ, different elements, including innervation, irrigation and the cerebrospinal fluid of the brain lateral ventricles, appear to play important roles in the regulation of NSC behavior, but the signalling pathways involved are still under investigation. Increasing evidence indicates that immune cells and immunological mediators could also modulate NSC behavior. Effects on neurogenesis of pro-inflammatory cytokines that are produced under non-physiological conditions, such as irradiation, inflammation, status epilepticus or stroke, have been described. However, their effects appeared sometimes contradictory, suggesting potentially distinct effects depending on the cell or receptor type involved. Tumor necrosis factor alpha (TNFα), a pro-inflammatory cytokine, is a multifunctional protein with a broad range of activities in different systems. We have evaluated potential roles of TNFα and its receptors in SEZ remodeling/regeneration analyzing direct effects of this cytokine on the proliferation/self-renewal of NSCs in culture and assessing its relevance in different in vivo scenarios where SEZ homeostasis is compromised. We have also analyzed the role of the two TNFα receptors using specific TNFR1 and TNFR2 agonists and TNFR knock-out mice. We found that TNFα modulates proliferation, self-renewal and the balance of symmetrical/asymmetrical divisions of NSCs and that each receptor mediates a distinct biological response.

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