RESEARCH TOPIC-MEM3

A HUMANIZED MODEL OF BLOOD BRAIN BARRIER TO INVESTIGATE IMMUNE CELLS INFILTRATION IN MULTIPLE SCLEROSIS: TOWARD A PERSONALIZED MEDICINE APPROACH

Curriculum MEM Standard

Laboratory name: Laboratory of Pharmacology and Brain Pathology, Humanitas Clinical and Research Center - IRCCS

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Abstract

Among the most accepted hypotheses to explain the disease mechanism underlying multiple sclerosis (MS), is the fact that immune cells (T lymphocytes) cross the barrier that protects the brain, the blood brain barrier (BBB), formed by astrocytes and endothelial cells, triggering inflammatory and neurodegenerative processes. The objective of the project is to exploit and further develop a miniaturized, personalized, bio-mimetic BBB platform employing human endothelial, astrocytic cells and patient-derived T cells, to study the pathological processes and the altered neuroimmune cross talk that occur when lymphocytes migrate across BBB cells in MS. The aim is to evaluate and optimize therapeutic strategies in a patient-specific manner. This step toward a personalized medicine approach in MS is highly desirable, given the enormous heterogeneity of both disease course and treatment responses.

Main technical approaches

The post will suit an ambitious and talented individual who is interested in applying his/her skills at the interface of neuroimmune and cellular biology. Familiarity with the following techniques will be an advantage but is not mandatory: flow cytometry, cell culture, and microscopy.

Scientific references

1. Lauranzano E., Campo E., Rasile M., Pizzocri M., Passoni L., Molteni R., Bello L., Pozzi D., Pardi R., Matteoli M. and Ruiz A. (2019) Setting of a microfluidic human model of blood brain barrier employing primary human astrocytes., Adv. Biosys. 2019, 3, 1800335

2. J. Brummelman, E.M.C. Mazza, G. Alvisi, F.S. Colombo, A. Grilli, J. Mikulak, D. Mavilio, M. Alloisio, F. Ferrari, E. Lopci, P. Novellis, G. Veronesi, E. Lugli, High-dimensional single cell

analysis identifies stem-like cytotoxic CD8(+) T cells infiltrating human tumors, J Exp Med, 215 (2018) 2520-2535.

3. K. Pilipow, E. Scamardella, S. Puccio, S. Gautam, F. De Paoli, E.M. Mazza, G. De Simone, S. Polletti, M. Buccilli, V. Zanon, P. Di Lucia, M. Iannacone, L. Gattinoni, E. Lugli, Antioxidant metabolism regulates CD8+ T memory stem cell formation and antitumor immunity, JCI insight, 3 (2018).

4 E. Colombo, F. Calcaterra, M. Cappelletti, D. Mavilio, S. Della Bella, Comparison of Fibronectin and Collagen in Supporting the Isolation and Expansion of Endothelial Progenitor Cells from Human Adult Peripheral Blood, Plos One, 8 (2013) e66734.

5. F. Filipello, D. Pozzi, M. Proietti, A. Romagnani, S. Mazzitelli, M. Matteoli, C. Verderio, F. Grassi, Ectonucleotidase activity and immunosuppression in astrocyte-CD4 T cell bidirectional signaling, Oncotarget, 7 (2016) 5143-5156.

Type of contract

PhD scholarship awarded by Humanitas University of € 18.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

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