PROGETTO

Supervisore:: ____Cinthia Farina_____

Titolo/*Title*: _Blood Transcriptomics for multiple sclerosis phenotyping_____

Curriculum: __NEN_____

Link alla pagina personale del sito web di Ateneo o del polo ospedaliero di riferimento: https://research.hsr.it/en/institutes/institute-of-experimental-neurology/immunobiology-of-neurological-disorders.html

Descrizione del progetto (max 3.000 caratteri spazi inclusi)

Background/gap of knowledge

Our lab has great interest in the pathogenic processes occurring in multiple sclerosis (MS), a chronic neurodegenerative inflammatory disorder of the CNS. MS is an erratic disease as its disease course remains unpredictable. The first clinical episode with features suggestive of MS is classified as clinically isolated syndrome (CIS). In 85% of patients the onset form is relapsing-remitting (RR) MS, while the other 15% of patients are diagnosed with primary progressive (PP) MS. People with RRMS generally experience the transition to secondary progressive (SP) MS after several years. Importantly, current immunomodulatory therapies for RR-MS are ineffective in progressive MS, suggesting that immunological phenotypes may vary in distinct disease courses.

Rationale and hypothesis

MS is a complex disease determined by both genetic and environmental factors. Intriguingly, many of the susceptibility genes play a role in the immune system and several of the MS–associated environmental triggers may modulate immunity, raising the hypothesis that MS is a disease of the immune system. Indeed, although MS affects the CNS, there are evidences of altered peripheral immunity in MS patients. Further, the most widely used therapeutic drugs in MS are either immunosuppressive or immunomodulatory agents, indicating that targeting peripheral immune system is beneficial to patients with this CNS disorder. These observations sustain the rationale for employing peripheral blood as an easily accessible and informative source of biological material to study MS pathology and describe its phenotypes. Recent evidence from our group supports this hypothesis, as blood transcriptomics highlighted that, in

addition to transcriptional dysregulations common to all disease courses, blood cells carry gene expression alterations specific to disease stages.

Objectives and specific aims

Starting from archival and newly generated transcriptomics data relative to blood specimens of patients with distinct MS courses or other neurological disorders we want to clarify biological features discriminating neurological subjects from the healthy population, or classifying among neurological cases via differential expression analyses and ad hoc developed machine learning pipelines.

Expected outcomes

Development of transcriptomics data analysis pipelines for clinical applications
Description of the immunological phenotypes for MS and other neurological disorders as detected by blood transcriptomics.
Development of machine learning pipelines exploiting demographic, clinical, paraclinical and biological data for patients classification.

Competenze che deve acquisire lo studente (Max 600 caratteri spazi inclusi):

Deep knowledge of Transcriptomics, Bioinformatics, computational biology, data mining, advanced statistics, machine learning, R for statistical computing, python programmimg.

Basic knowledge of immunology and pathology.

Logical thinking, Scientific English.

Bibliografia (max. 15)

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3 Emanuela Colombo and Cinthia Farina. Lessons from S1P receptor targeting in multiple sclerosis. Pharmacology and Therapeutics 230, 2022.
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5 Massimo Acquaviva, Ramesh Menon, Marco Di Dario, Gloria Dalla Costa, Marzia Romeo, Francesca Sangalli, Bruno Colombo, Lucia Moiola, Vittorio Martinelli, Giancarlo Comi, Cinthia Farina. Inferring Multiple Sclerosis stages from blood transcriptome via machine learning. Cell Rep. Med. 1, 2020.

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7 Martina Severa, Fabiana Rizzo, Sundararajan Srinivasan, Marco Di Dario, Elena Giacomini, Maria Chiara Buscarinu, Melania Cruciani, Marilena P. Etna, Silvia Sandini, Rosella Mechelli, Antonella Farina, Pankaj Trivedi, Paul J. Hertzog, Marco Salvetti, Cinthia Farina, Eliana M. Coccia. A cell type-specific transcriptomic approach to map B cell and monocyte type I Interferon-linked pathogenic signatures in Multiple Sclerosis. J. Autoimmunity 101: 1, 2019

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10 Di Dario Marco, Colombo Emanuela, Govi Chiara, De Feo Donatella, Messina Maria Josè, Romeo Marzia, Sangalli Francesca, Moiola Lucia, Rodegher Mariaemma, Martino Gianvito, Martinelli Vittorio, Comi Giancarlo and Farina Cinthia. Myeloid cells as target of fingolimod action in multiple sclerosis. Neurology: Neuroimmunol. & Neuroinfl. 2: e157, 2015.

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