

Genetics link between brain and immune system

Speaker: Fabio Macciardi

Università degli Studi di Milano, Italy. University of Toronto.

The connection between the central nervous system (CNS) and the immune system (IS) is a concept that has been considered by the medical research community for a relatively long time, although the lack of solid discoveries in this field has somehow discredited it. However, recent finds have shown that these two systems in fact interact, and even share some components, molecules, and genes that are not only players in this functional interaction, but also in the development and the role of each system in the context of disease. In this talk, Dr. Macciardi wants to show several biological models that exemplify this interaction. Multiple sclerosis (MS) is a relatively “simple” disease that traditionally has been conceived as an affection of the CNS –white matter degeneration– caused by an alteration of the IS. Recent data is showing the possibility of what is really happening in MS is the other way around, that is, the primary lesion is at the CNS, secondarily worsened by an IS malfunction. In this sense, when Macciardi recently participated in a genome-wide scan of MS populations, they found mainly CNS genes predominantly involved in the disease. Furthermore, when they focused in the gene that codifies one of the most relevant key elements in MS, Interferon B (IFNB), and dug into its relevant gene to gene interactions, they learned that the IFNB gene belongs to three different pathways, genetically speaking: the Cytokines (CK) pathway, the Toll-like receptor pathway, and the Jack-Stat pathway, each one highly related with CNS development and function. Particularly, he emphasized the role of CK (IFNB is actually a CK) in neural differentiation and migration, plasticity, neurotransmitter metabolism, and even neurodegeneration. CK regulation of disease processes is influenced by genetic factors, such as polymorphisms, and environmental factors as well. CK also interact with neuronal modulator factors, such as the Brain Derived Neurotrophic Factor (BDNF), in CNS specialization. In the last year to year in a half, very interesting findings have been coming from the imaging genetics field on the effects that haplotype variations of the gene that codifies BDNF have in the brain. Particularly, the effect of BDNF 66met allele in reductions of declarative and episodic hippocampal memory, and that BDNF val alleles exaggerate the negative effect of the 5’-HTTLPR s allele on cingulate gray matter volume, whereas BDNF met alleles have a protective effect against it. Dr. Macciardi presented other two models of the link between immune system and CNS: a) the association of the ever-increasing use of organophosphate pesticides for agriculture in developed countries and a dramatic increase of autism diagnosis. In this regard, he has found a highly significant association between organophosphate use and a polymorphism variation in the gene that codifies the reelin protease enzyme, the “Q192R”, which may be related with reelin bad performance on neuronal migration and CNS shaping, ultimately leading to autism. And b) the recent discovery of a gene that may be related with schizophrenia, derived from a study done in a potential linkage area in the chromosome 6q. This gene turned out to be part of the Abl family genes, a kind of genes highly involved in CNS development, but also involved in immunity, stress response, and oxidative response.