

### **New multiple sclerosis gene identified**

Novel advance in understanding multiple sclerosis, a common, neurological disease which usually occurs in young adults and causes a wide range of neurological symptoms. The disease is one of those that arise when the body's immune system attacks one of its own components. In the case of multiple sclerosis, the target of this “friendly fire” is myelin, an electrically insulating material that forms a layer around the axon of the neurons, fundamental for the transmission of the electrical signals and for thus the proper functioning of the nervous system. The exact causes of multiple sclerosis are still largely unknown, but there are clear indications that the joint action of several genes and unknown environmental factors play together an important role. Identifying the precise genetic causes is relevant to understand the mechanisms underlying the disease process. It requires the study of the whole genome in thousands of people to assess relevant genetic differences between affected and non affected individuals, indicative of the changes in the DNA that mediate susceptibility to the disease.

In an article published in *Nature Genetics* on May 9<sup>th</sup>, researchers from the Mediterranean island of Sardinia (Italy), identified a novel gene that contributes to the disease. The population of Sardinia is known to have one of the highest frequencies of multiple sclerosis in the world, along with some other autoimmune maladies like type 1 diabetes.

The study was performed as a collaboration between Sardinian centers: the Istituto di Neurogenetica e Neurofarmacologia of the National Council of Research (Inn-CNR), the Universities and Hospitals of Cagliari and Sassari, and the CRS4 (Center for Advanced Studies, Research and Development in Sardinia) in Pula.

“This gene, CBLB, encodes a multifunction adaptor protein”, says **Francesco Cucca**, director of the Inn-Cnr, Professor of human genetic at the University of Sassari and scientific coordinator of the project, “it regulates the activation of receptors on the surface of the white blood cells, which are the key cells regulating immune and autoimmune responses. Our results are also consistent with what have been observed in animal models: mice deficient for this gene, for example, are affected by autoimmune encephalomyelitis, the animal model of multiple sclerosis.”

The team used a two-staged approach. They initially looked at variations across the entire genome of 882 patients and 872 healthy volunteers, and then assessed the most promising results for confirmation in an additional set of 1775 patients and 2005 controls from the Sardinian population.

Using advanced statistical methods, the information generated in the laboratory (1 million variants characterized) was integrated with that available from the 1000 Genomes Project, an international effort that aims to establish the most detailed catalogue of human genetic variation (8 million variants) “this results in the largest set of variation so far analyzed for multiple sclerosis, which allowed us to detect this association for the first time” says **Serena Sanna**, investigator at the Inn-Cnr, who lead the statistical part of the project.

Underlining the medical impact of multiple sclerosis **Maria Giovanna Marrosu** of the University of Cagliari, notes that, “The disease affects more than 3 million people worldwide, half a million only in Europe, and is one of the major causes of disability in

adults under the age of 65”. “This result contributes to the knowledge of this complex disease, revealing some possible mechanisms and suggesting potential therapeutic targets, although a real treatment may need many years to be developed” concludes **Giulio Rosati** of the University of Sassari.

10 maggio 2010

**Link:**

**<http://www.nature.com/ng/journal/vaop/ncurrent/abs/ng.584.html>**

**Title:** Variants within the immunoregulatory CBLB gene are associated with multiple sclerosis.

**Authors:** Serena Sanna, Maristella Pitzalis, Magdalena Zoledziewska, Ilenia Zara, Carlo Sidore, Raffaele Murru, Michael B Whalen, Fabio Busonero, Andrea Maschio, Gianna Costa, Maria Cristina Melis, Francesca Deidda, Fausto Poddie, Laura Morelli, Gabriele Farina, Yun Li, Mariano Dei, Sandra Lai, Antonella Mulas, Gianmauro Cuccuru, Eleonora Porcu, Liming Liang, Patrizia Zavattari, Loredana Moi, Elisa Deriu, M Francesca Urru, Michele Bajorek, Maria Anna Satta, Eleonora Cocco, Paola Ferrigno, Stefano Sotgiu, Maura Pugliatti, Sebastiano Traccis, Andrea Angius, Maurizio Melis, Giulio Rosati, GonÁalo R Abecasis, Manuela Uda, Maria Giovanna Marrosu, David Schlessinger & Francesco Cucca.

**Contacts:** Francesco Cucca, director Inn-cnr: **[francesco.cucca@inn.cnr.it](mailto:francesco.cucca@inn.cnr.it)**

Serena Sanna, investigator Inn-Cnr: **[serena.sanna@inn.cnr.it](mailto:serena.sanna@inn.cnr.it)**

**Andrea Mamei**, press release office CRS4: **[mamei@crs4.it](mailto:mamei@crs4.it)** -