PROJECT TITLE
Identification of molecular mechanisms driving to pediatric multiple sclerosis

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PROJECT DESCRIPTION
Pediatric form of Multiple Sclerosis (PedMS) is a rare form of MS present in 5% of cases characterized by an onset before 18 years. It represents a privileged condition to explore the mechanisms involved in MS development as close to exposure to etiological factors, with the possibility to study their role with respect to genetic background.
The present project aims to investigate the mechanisms underlying the onset of PedMS taking advantage of a large network of > 25 Italian MS clinical centers which collected prospective cohort of 150 pedMS patients and 150 healthy matched controls (HC).
Main aims of the project are:
a) To identify genetic risk factors associated with pedMS by measuring the genetic burden of pediatric-onset and to detect genetic variants associated with the risk of pedMS by means of case-control association study (GWAS) at genome-wide and mitochondrial DNA levels using array technology and next-generation sequencing technology with exome-sequencing;
b) To assess the epigenetic signature associated with pedMS using whole-genome array technology;
c) To explore the gene-environment interactions associated with pedMS;
d) To explore the role of gut microbial in pedMS. We will compare the gut microbial community profiles in incident cases of pedMS and control children matched for age and sex using 16S ribosomal RNA or shot-gun sequencing based on available funding;
e) To investigate the role of Herpes viruses, and in particular of Epstein-Barr virus, on the emergence of pedMS, we will measure the antibody titre against the virus and we will determine the different latent or lytic phases of the viral infection in patient cells;
The PhD student will be directly involved in the application of array and sequencing protocols, he/she will participate in the bioinformatic steps related to the analyses and interpretation of omics data, as well as in functional studies on target genes identified by the study of novel mechanisms of disease susceptibility.

CANDIDATE SPECIFIC REQUIREMENTS
A degree in the field of Medicine, Molecular and/or Cellular Biology is required. Experience in DNA, mRNA and stool extraction; cell culture; ability to maintain database; basic knowledge of bioinformatic tools

MOST RELEVANT PUBLICATIONS FOR THE PROJECT
.Pilotto S, Gencarelli J, Bova S, Gerosa L, Baroncini D, Olivotto S, Alfei E, Zaffaroni M, Suppiej A, Cocco E, Trojano M, Amato MP, D'Alfonso S, **Martinelli-Boneschi F**, Waubant E, Ghezzi A,

Bergamaschi R, Pugliatti M. **Etiological research in pediatric multiple sclerosis: A tool to assess environmental exposures (PEDiatric Italian Genetic and enviRonment ExposurE Questionnaire).** Mult Scler J Exp Transl Clin. 2021 Dec 1;7(4):20552173211059048. doi: 10.1177/20552173211059048. PMID: 34868629; PMCID: PMC8640303.

2.Esposito F[*], Sorosina M, **Martinelli Boneschi F***, De Jager PL* et al.* **A pharmacogenetic study implicates SLC9A9 in multiple sclerosis disease activity.** Annals of Neurology 2015. Jul; 78(1):115-27.

3. *Peroni S, Sorosina M, Malhotra S, Clarelli F, Osiceanu AM, Ferrè L, Roostaei T, Rio J, Midaglia L, Villar LM, Álvarez-Cermeño JC, Guaschino C, Radaelli M, Citterio L, Lechner-Scott J, Spataro N, Navarro A, Martinelli V, Montalban X, Weiner HL, de Jager P, Comi G, Esposito F, Comabella M,* ***Martinelli-Boneschi F.*** **A pharmacogenetic study implicates NINJ2 in the response to Interferon-β in multiple sclerosis.** Mult Scler. 2019 Jun 21:1352458519851428. DOI: 10.1177/13524585198514281.

*4. Sorosina M, Clarelli F, Ferrè L, …., **Martinelli Boneschi F.*** **Clinical response to Nabiximols correlates with the down-regulation of immune pathways in Multiple Sclerosis**. Eur J Neurol. 2018 Jul;25(7):934-e70.

*5. Giacalone G, Clarelli F, Osiceanu AM, D'Alfonso S, …., **Martinelli Boneschi F.*** **Analysis of genes, pathways and networks involved in disease severity and age at onset in Primary Progressive Multiple Sclerosis.** Mult Scler. 2015; 21(11):1431-42