PROJECT

Supervisor:	Yuri Matteo Falzone
Title:	**Complement-Mediated Mechanisms and Biomarker Discovery in CIDP: A multicentre, Multiparametric Longitudinal Study**
Curriculum:	Neurosciences and Experimental Neurology
Link to the personal page of the University or relevant hospital site website:	https://www.hsr.it/dottori/yuri-falzone

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare immune-mediated neuropathy characterized by progressive or relapsing-remitting demyelination of peripheral nerves, leading to motor and sensory impairment. Despite advances in diagnosis and treatment, CIDP remains a highly heterogeneous disorder in presentation, disease course, and response to therapy, likely reflecting distinct and still poorly understood pathogenic mechanisms.

CIDP pathogenesis involves both cell-mediated and humoral immune responses. While T-cell and macrophage-mediated processes contribute to segmental demyelination, humoral mechanisms amplify nerve injury through autoantibody deposition and downstream effector pathways. Among these, complement activation has emerged as a key mediator linking antibody binding to tissue damage, supported by increased circulating complement components and deposition in sural nerve biopsies.

However, the role of complement in CIDP and its ability to define clinically distinct subgroups remain unclear. In parallel, the lack of reliable biomarkers limits prediction of disease course and treatment response, and clinical management remains largely empirical.

Rationale and hypothesis

Improved understanding of disease mechanisms and identification of biomarkers will enable more precise, individualized treatment. We hypothesize that complement-mediated mechanisms contribute to nerve injury in a subset of CIDP patients and that integrating longitudinal clinical data with circulating biomarkers and tissue proteomics will allow the identification of predictors of disease activity, progression, and treatment response.

Objectives and specific aims

Primary objective

To identify biomarkers predictive of disease activity, progression, and treatment response in CIDP through an integrated longitudinal and multiparametric approach.

Specific aims

- To longitudinally characterize clinical (INCAT, I-RODS, MRC, grip strength), neurophysiological, and imaging (nerve ultrasound) features;

- To quantify circulating biomarkers of nerve damage (α-tubulin, neurofilaments, periaxin) and complement activation;

- To perform proteomic analysis of sural nerve biopsies to assess complement involvement and identify novel biomarkers to be validated in the longitudinal cohort;

- To develop an in vitro model using iPSC-derived neuronal cultures exposed to patient serum and exogenous complement to investigate pathogenic mechanisms and treatment response.

Expected outcomes

To identify biomarkers associated with disease activity, progression, and treatment response, improving patient stratification and clinical decision-making. To clarify the role of complement in CIDP pathophysiology and its relevance in defining disease subsets.

Integration of clinical, proteomic, and experimental data will enable biomarker validation and provide a platform for investigating mechanisms and therapeutic responses supporting a more personalized approach to CIDP management.

Skills that the student should acquire (max. 600 characters including spaces):

Ability to independently formulate research questions, perform autonomous literature searches, and select appropriate investigative methodologies. Advanced skills in longitudinal clinical research, multimodal phenotyping, and structured database management. Expertise in biomarker analysis, sample processing, proteomics and sural nerve biopsy interpretation. Experience in iPSC-derived neuronal culture models and immunofluorescence assays. Competence in data analysis, integration of clinical and experimental findings, and scientific writing.

References (max. 15)

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