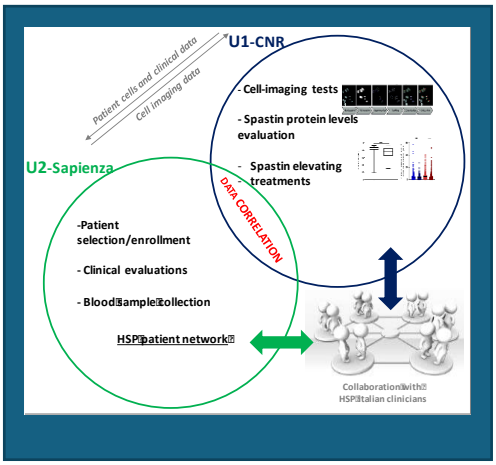
Project title: Cell Imaging-based Approaches to identify non-invasive biomarkers in Hereditary Spastic Paraplegia



Acronym: CIA-HSP

Partners:

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Description:

Hereditary spastic paraplegias (HSP) are inherited rare neurodegenerative diseases characterized by progressive weakness and spasticity of the lower extremities. The most common type of HSP is due to dominant mutations in the SPG4 gene, encoding spastin, a microtubule (MT) severing enzyme. The knowledge about the underlying molecular mechanisms of SPG4-HSP is progressively growing and the future for innovative clinical trial design is encouraging. In particular, SPG4 therapeutics urgently require easily accessible prognostic and predictive biomarkers. Recently, spastin-elevating treatments emerged as promising therapeutic approaches and our group is currently validating spastin-elevating drugs in SPG4 haploinsufficient pre-clinical models.

Aims:

We have developed automated image acquisition/analysis pipelines to detect defective MT in SPG4-HSP patients' peripheral blood cells. We have also shown that these defects can be rescued by spastin-elevating drugs. A cohort of cells from SPG4-HSP patients with different mutations and disease severity will be analysed to

- explore the sensitivity and specificity of our pipelines/treatments and identify monitoring tools for disease severity
- reveal prognostic and therapy response markers.

Expected results:

Capitalising on preliminary data and a long-term fruitful collaboration between the Cell Biology/Imaging Research Unit (U1) and the Clinical Research Unit (U2), this project will lead to

- Define genotype/phenotype correlations
- Identify easily accessible blood-based biomarkers
- Develop low-cost non-invasive image-based tests with prognostic and/or predictive role
- Identify and characterize novel endpoints for future clinical trials

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