**Title:** Identification of miRNA and/or circRNA involved with Parkinson Disease

**Cell death in Substantia Nigra** appears to be the central pathophysiologic mechanism of Parkinson’s Disease (PD). While the complete picture of the molecular basis remains to be elucidated, several recent studies have observed dysregulation of the autophagy pathway in the brains of PD patients, leading to emerging interest in the role of this cellular process in the disease. Genetic studies on PD patients have identified mutations in genes encoding components of the autophagy-lysosomal pathway. However, the selectivity for most agents targeting autophagy is limited. Because upstream autophagic-lysosomal components are involved in many other pathways, a broad stimulation of autophagy could result in a wide spectrum of side effects.

We recently identified PD familial cases that carry new mutations in the *PGRN* gene [1], and our preliminary data suggest that its mutant isoforms can affect normal autophagy in the brain. In addition, we have evidence of PGRN involvement in macroautophagy through TOR dependent regulation.

To understand this mechanism, we will **Induce Pluripotent Stem Cells (iPSCs)** using PBMC’s isolated from patients diagnosed with PD with known and unknown mutations. Specific midbrain dopaminergic (mDA) neurons made by this technique are able to recapitulate key phenotypes of PD creating a patient-derived disease model which allow us to identify coding and non-coding transcriptional signatures associated with neurodegenerative phenotype. Then we will be devoted to the characterization of differentially-expressed miRNA and/or circRNA extracted from these cells and finally we will create neuronal cellular models of PD by **CRISPR-Cas9 genome editing technique** to identify any dysregulated molecular network involved in a specific autophagy step.

**References:**

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**Keywords:** progranulin, parkinsonism, genetics, dementia, gaze palsy, CRISPR-Cas9, Induce Pluripotent Stem Cells (iPSCs).

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**Website(s):** http://www.ibbc.cnr.it/research-applications/aging-and-dementia/

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