Understanding neurodegenerative disorders with cell-type specificity

LAB & PEOPLE

- *Name of the hosting lab*: Genetics and Neurodegenerative Disorders
- *General activities of the lab*:
  The Munoz-Manchado lab is interested in deciphering the genetic complexity of parkinsonism and other related disorders. Parkinson's Disease (PD) is the most frequent parkinsonism, the second within the neurodegenerative disorders, and the one with the highest growing rate. Its etiology is still unknown, and the current treatments are only efficient in alleviating the symptoms temporarily. In our lab we use single-nucleus RNA sequencing of postmortem brain sample donors from one of the most affected areas (the dorsal striatum), to investigate the main genetic changes underlying the disease with cell type specificity. Defining the critical cell types of the disease will allow for the development of targeted therapies. Our results so far identified both neuronal and glia subclasses with important differences between caudate and putamen.
- Website: https://inibica.es/en/co23-genetics-and-neurodegenerative-diseases/
- Number of staff / PhD: 4/2
- Supervisor name and contact: Ana B. Muñoz-Manchado, ana.munoz@uca.es

TOPIC OF THE INTERNSHIP

- *Scientific context of the internship:* Munoz-Manchado lab is a recent-established group with a strong background in molecular techniques, specifically single-cell and single nuclei-RNA sequencing in the nervous system. In the group we aim to decipher the main critical cell types in PD, identifying the gene regulatory networks involved in the neurodegenerative process. This will be of great use in developing new target therapies, defining molecular differences in the group of diseases under the parkinsonism name and other close disorders, and establishing accurate models of the disease. In the group we have one PhD-student with great expertise in the bioinformatic analysis of single-cell RNA-seq who is currently working in the vast dataset we have built from PD and control patients in collaboration with Harvard Medical School; one PhD-student working in molecular and histology techniques with a main focus in the interneuron populations, and a postdoc with great experience in molecular and histology techniques focused in the modelling of the disease. A neurologist collaborates with us in interpreting the data. We have also the support from the department technician.

- *Keywords* : Parkinson´s Disease, neuroscience, single-cell RNA-sequencing, gene regulatory networks, critical cell types, neurodegeneration.

- *Bibliography*

1. Garma LD, Harder L, Barba-Reyes JM, Díez-Salguero M, Serrano-Pozo A, Hyman B. T., **Muñoz-Manchado AB**. Interneuron diversity in the human dorsal striatum (Preprint). **https://www.biorxiv.org/content/10.1101/2023.03.22.533839v1**
2. **Muñoz-Manchado AB***, Bengtsson-Gonzales C*, Zeisel A*, Munguba H, Bekkouche B, Skene NG, Lonnerberg P, Ryge J, Harris K, Linnarsson, S, Hjerling-Leffler J. Diversity of interneurons in the dorsal striatum revealed by single-cell RNA-sequencing and PatchSeq. *Cell Reports* 2018, 21;24(8):2179-2190.e7. PMID: 30134177.
3. Qian X, Harris KD, HAuling T, Nicoloutsopoulos D, **Muñoz-Manchado AB**, Skene N, Hjerling-Leffler J, Nilsson M. Probabilistic cell typing enables fine mapping of closely related cell types in situ. *Nature Methods*, 2020; 17(1):101-106. PMID: 31740815
4. **Muñoz-Manchado AB***, Bengtsson-Gonzales C*, Zeisel A*, Munguba H, Bekkouche B, Skene NG, Lonnerberg P, Ryge J, Harris K, Linnarsson, S, Hjerling-Leffler J. Diversity of interneurons in the dorsal striatum revealed by single-cell RNA-sequencing and PatchSeq. *Cell Reports* 2018, 21;24(8):2179-2190.e7. PMID: 30134177.
5. **Muñoz-Manchado AB*,** Zeisel A*, Codeluppi S, Lönnerberg P, La Manno G, Juréus A, Marques S, Munguba H, He L, Betsholtz C, Rolny C, Castelo-Branco G, Hjerling-Leffler J, Linnarsson S. Brain structure. Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq. *Science*, 2015, 347; 6226 1138-42. PMID: 25700174.

- *Tasks and duties entrusted to the student:*

  1. Get familiar with literature and techniques in the lab.
  2. Become part of the team and participate in the lab activities (seminars, meetings, mingles...).
  3. Perform experiments and data analysis according to the project development and the student's progress.

- *Skills to be acquired or developed:*

  1. Basics in the lab: safety, organization, general rules.
  2. Knowledge in high-sensitive and state of the art techniques as single-cell RNA-sequencing, *in situ* sequencing and recent-developed histology techniques and analysis methods.
  3. Bioinformatics: use of Python and R for single-cell RNA sequencing analysis.

PROFILE OF THE DESIRED STUDENT

- *Minimum level of study required*: the student should be enrolled in a master related with the field of biomedicine, bioinformatics, genetics, or neuroscience.

- *Field(s) of study*: Neuroscience, Biomedicine, Genetics.

- *Scientific skills:* it will be of value any experience in molecular biology and histology techniques. Experience in bioinformatics (R-studio, Python, matlab…) is meriting. The student is expected to be highly motivated, enthusiastic and be able to integrate in a team and collaborative environment.

Language skills required: fluent in English.

THE INTERNSHIP ASSIGNMENT:

Desired duration of the internship (in months): 3-9 months

Desired Starting date of the mission: (please indicate the level of flexibility) : end 2023, beginning 2024

Indicative weekly schedule: 25h / week

Remuneration : depend on availability of funds

*Erasmus grant :*yes

Internship agreement: *an internship agreement will be signed.*

To SEA-EU students:

If you're interested please send your CV and letter of motivation to Ana Muñoz-Manchado, ana.munoz@uca.es, before 30th October 2023