# Master project 2021-2022

| Personal Information | |
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| **Group** | Laboratory of Neuropharmacology |

## Project

## Computational systems biology

**Project Title:**

Intellectual disability can be caused by genetic mutations

**Keywords:**

intellectual disability, treatment, synaptic proteome, synaptic transcriptome, splicing

**Summary:**

Synaptic Intellectual disability may derive from specific genetic alterations, as found in neurodevelopmental disorders such as fragile X syndrome (FXS) and Down syndrome (DS), both disorders associated to relevant alterations in synaptic plasticity. Mouse models of these disorders mimicking the genetic alterations found in humans have demonstrated relevant tools to understand the physiopathology of the disorders and to test pharmacological approaches that may improve cognitive performance. In the lab we have described an approach to improve cognitive performance in models of FXS and DS, but the impact of these treatments in the biology of the synapse has not been addressed. We are now investigating, using high throughput proteomic and transcriptomic analysis of sorted synaptic contacts, the characteristics of pathological synapses, and the effects that pharmacological treatments have in improving synaptic plasticity in both models of intellectual disability.landmarks of intellectual disability

**References:**

Navarro-Romero A, Vázquez-Oliver A, Gomis-González M, Garzón-Montesinos C, Falcón-Moya R, Pastor A, Martín-García E, Pizarro N, Busquets-Garcia A, Revest JM, Piazza PV, Bosch F, Dierssen M, de la Torre R, Rodríguez-Moreno A, Maldonado R, Ozaita A. Cannabinoid type-1 receptor blockade restores neurological phenotypes in two models for Down syndrome. Neurobiol Dis. 2019 May;125:92-106. doi: 10.1016/j.nbd.2019.01.014. Epub 2019 Jan 25. PMID: 30685352. Busquets-Garcia A, Gomis-González M, Guegan T, Agustín-Pavón C, Pastor A, Mato S, Pérez-Samartín A, Matute C, de la Torre R, Dierssen M, Maldonado R, Ozaita A. Targeting the endocannabinoid system in the treatment of fragile X syndrome. Nat Med. 2013 May;19(5):603-7. doi: 10.1038/nm.3127. Epub 2013 Mar 31. PMID: 23542787.

**Expected skills::**

Bioinformatics

**Possibility of funding::**

To be discussed

**Possible continuity with PhD: :**

To be discussed

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**Universitat Pompeu Fabra Barcelona** | **Master in Bioinformatics for Health Sciences**

# Master project 2021-2022

| **Personal Information** | |
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| **Group** | Epitranscriptomics and RNA Dynamics |

**Project**

## Computational systems biology

**Project Title:**

PREDICTING AND MONITORING CANCER USING MACHINE LEARNING ON NANOPORE SEQUENCING DATA

**Keywords:**

nanopore sequencing, RNA modifications, small RNA, machine learning, deep learning, cancer, prognosis, sample classification

**Summary:**

Dysregulation of small RNA abundances and their RNA modifications is a well-known feature in cancer cells, which leads to enhanced expression of specific oncogenic transcripts and proteins [1,2]. Despite the well-established association between small RNA dysregulation and cancer progression and malignancy, small RNA abundances and modifications are still not being used as screening, diagnostic or prognostic markers for cancer detection or progression, mainly due to the lack of a simple, unbiased and cost-effective method to quantify small RNA abundances and their modifications. Our laboratory has pioneered the use of direct RNA sequencing for the detection and quantification of RNA abundances and their modifications, including both development of improved library preparation protocols as well as the development of novel algorithms to predict and quantify RNA modifications [3-5]. Here we propose to use native RNA nanopore sequencing technology to predict the malignancy of biological samples in a high-throughput, rapid, multiplexed and cost-effective manner. Specifically, the candidate MSc student will benefit from a recently developed method in our lab to sequence small RNAs using nanopore sequencing. The candidate will then develop and apply deep learning algorithms

to classify small RNA profiles into "normal", "tumoral" and "metastasic". Once the classification model is benchmarked and validated using cell lines, the methodology will then be applied to patient-derived samples.

**References:**

1. Begik O, Lucas MC, Ramirez JM, Liu H, Mattick JS and Novoa EM#. Integrative analyses of the RNA modification machinery reveal tissue- and cancer-specific signatures. Genome Biology 2020, 21:97. doi: 10.1186/s13059-020-02009-z 2. Gingold et al., A Dual Program for Translation Regulation in cellular profileration and differentiation. Cell 2014, 158(6):1281-1292. 3. Liu H*, Begik O*, Lucas MC, Ramirez JM, Mason CE, Wiener D, Schwartz S, Mattick JS, Smith MA and Novoa EM#. Accurate detection of m6A RNA modifications in native RNA sequences. Nature Comm 2019, 10:4079. doi:10.1038/s41467-019-11713-9 4. Smith MA*, Ersavas T*, Ferguson JM*, Liu J, Lucas MC, Begik O, Bojarski L, Barton K and Novoa EM#. Molecular barcoding of native RNAs using nanopore sequencing and deep learning. Genome Research 2020 30(9): 1345-1353 5. Begik O*, Lucas MC*, Ramirez JM, Milenkovic I, Cruciani C, Vieira HGS, Medina R, Liu H, Sas-Chen A, Mattick JS, Schwartz S and Novoa EM#. Quantitative profiling of native RNA modifications and their dynamics using nanopore sequencing. bioRxiv 2021, 189969 (accepted in Nature Biotechnology)

**Expected skills::**

python (required), R (required), prior experience with machine learning is a plus but not required, familiarity with third-generation sequencing (e.g. nanopore) is a plus but not required

**Possibility of funding::**

To be discussed

**Possible continuity with PhD: :**

To be discussed

**Comments:**

Option for funding, as well as option for PhD continuity.

**Universitat Pompeu Fabra** *Barcelona*

Master in Bioinformatics for Health Sciences

# Master project 2021-2022

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| **Group** | Reprogramming and Regeneration |

# Computational systems biology

**Project Title:**

Identification of master regulators of reprogramming

**Keywords:**

retina, reprogramming, regeneration, master regulators, gene networks

**Summary:**

We use gene regulatory network to identify master regulators of reprogramming and pluripotency. We are now investigating master regulators that can be enhances to induce the regeneration of the retina in mammals.

**Expected skills::**

bioinformatics, math lab,

**Possibility of funding::**

To be discussed

**Possible continuity with PhD: :**

To be discussed