



## **Computational approaches to understand the selective basis of motor-neuron degeneration**

**Place of work/:** RNA Systems Biology Lab – BioISI, FCUL

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*Hereditary mutations in essential proteins involved in RNA metabolism that also present ubiquitous expression are linked to many human genetic diseases, but show striking association to neurodegenerative and, in particular, motor neuron disorders. Several models have been put forth to explain the unexpected cell-type specific manifestation of the disease phenotype, including the concept that motor-neurons may be more sensitive to changes in splicing or our lab's proposal that these proteins tend to coordinate the expression of proteins that integrate the same tissue-specific functional consortia. This project aims to expand on our previous work and available RNA-seq data by exploring different models that justify the predominant neuronal impact of these proteins. The workplan will explore the impact of disease-associated mutations on the neuronal transcriptome with an emphasis on the analysis of transcript structure based both on our available data and public data-sets though the implementation of different RNA-seq data analysis pipelines. These results will contribute to the second aim of the project, on which the concept of Biolnt libraries, developed by our group to explore tissue-specific protein consortia and how they are altered by disease causing mutations, will be expanded to include information on transcript and protein isoform expression. Finally, a pipeline for cross-species mapping and comparison of these functional proteins networks will be developed.*

*The outputs of this project will contribute to build a better understanding of the molecular functional diversity that is found across tissues and how it connects to the manifestation of disease phenotypes. The student will gain an in-depth know-how on RNA-seq data analysis and protein-network analysis working mostly in R.*

### **References:**

Garcia-Vaquero, M., Heim, M., Flix, B., Pereira, M., Palin, L., Marques, T.M., Pinto, F.R., de Las Rivas, J., Voigt, A., Besse, F., Gama-Carvalho, M. (2022). Analysis of pre-symptomatic *Drosophila* models for ALS and SMA reveals convergent impact on functional protein complexes linked to neuro-muscular degeneration *bioRxiv* 2022.06.20.496821; doi: 10.1101/2022.06.20.496821

Garcia-Vaquero M, Gama-Carvalho M, Pinto FR, De Las Rivas J. 2022. Biological Interacting Units identified in human protein networks reveal tissue functional diversification and its impact on disease. *Computational and Structural Biotechnology Journal* 20: 3764-3778. doi: 10.1016/j.csbj.2022.07.006