

**Título do trabalho:**

Exploring the behavior, function and signaling networks of the NKX6-2 transcription factor in health and disease

Nome e contacto do(s) orientador(es):

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Laboratório/Instituição onde o trabalho será realizado:

Cell structure and dynamics laboratory, Dpto. Quimica e Bioquimica, Faculdade de Ciências, Universidade de Lisboa

Plano de trabalho:

NKX6-2 is a barely understood transcription factor essential for normal central nervous system and pancreas development. **NKX6-2 loss of function causes a neurological disorder known as Spastic Ataxia 8 (SPAX8).** Most SPAX8-causing mutations involve the introduction of premature STOP codons, activating nonsense-mediated RNA decay (NMD) mechanisms and/or producing truncated, dysfunctional NKX6-2 proteins. NKX6-2 target genes, protein-protein interactions and signaling networks remain poorly described. **The aim of this project is to unravel the behavior and function of normal and SPAX8-associated NKX6-2 proteoforms, and explore new approaches to restore them in SPAX8.** We have recently developed a series of molecular tools to address these issues, such as mammalian expression plasmids for normal and mutant NKX6-2, a luciferase reporter system to measure NKX6-2 transcriptional activity, or an NKX6-2 minigene containing the 5' and 3' UTRs, exons and introns, to study the role of NMD in SPAX8. The student will further advance this work, **producing an NKX6-2 knockout cell line by CRISPR/Cas9 and additional molecular tools.** The student will characterize these tools by means of a combination of **fluorescence microscopy, flow cytometry and molecular biology** methods, and use them to identify NKX6-2-dependent protein expression and interactions by **proteomics approaches.** The student will also learn **soft skills** related to the preparation of scientific reports, and is expected to assist to regular scientific seminars at the FCUL Campus and the surroundings (Instituto de Medicina Molecular, Faculdade de Farmacia, Instituto de Saúde Ricardo Jorge,...). The responsibilities of the student will include: keeping organized, detailed and rigorous records of their work; regular reporting to bench tutors and supervisors; active participation in lab meetings; contributing actively to the organization of the laboratory and the maintenance of reagent stocks; and helping labmates with their own projects. We are looking for highly motivated, pro-active, hard-working and independent individuals to join our team and enjoy an exciting working environment. **Students selected for this project, after thesis registration, are eligible to apply to the BioISI Junior Programme (supporting 8 students with a 6-month Scholarship(BII), being the selection criterium the academic merit of the candidates.**