



Title: Towards the identification of universal ataxia-related signalling networks

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Abstract / MSc thesis project proposal

Ataxias are an apparently diverse family of neurodegenerative disorders which share common symptoms related to cerebellar alterations and/or white matter loss. We have recently developed a series of cell and molecular tools that allow us to study the mechanisms underlying Spastic Ataxia 8 (SPAX8) and Autosomal Recessive Ataxia of Charlevoix-Saguenay (ARSACS). SPAX8 and ARSACS are caused by loss-of-function mutations in the NKX6-2 transcriptional repressor and the saccin chaperone, respectively. In principle, these two proteins have little in common between them and with other ataxia-related genes. However, the normal function of ataxia-related proteins is barely understood, and so are the molecular and cellular alterations induced by their mutations. We are analyzing these issues in our SPAX8 and ARSACS models by mass spectrometry, at a proteome level, producing a large amount of data. The main aim of this project is to analyze these data, compare it with existing information about other ataxias, and integrate them to obtain a series of meaningful signaling networks common to most ataxias. These analyses will be mainly carried out by means of application packages based on R programming. However, if the student is interested, he/she can also carry out “wet” work at the bench, to produce and analyze the biological samples that will be later analyzed by mass spectrometry and other methods. We intend to train the students in a mixed profile combining informatics and biology skills, which could be very interesting for the career of the students from this particular MSc programme. 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 BiolSI Junior Programme (supporting 8 students with a 6-month Scholarship(BII), being the selection criterium the academic merit of the candidates.