Title: Asymmetric post-translational modifications (PTMs) as a new regulatory mechanism in self-associating signaling proteins

MSc em Biologia Evolutiva e do Desenvolvimento

Place of work: Departamento de Química e Bioquímica, FCUL

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Abstract

Protein self-association in homodimers and oligomers is very common in nature, playing key roles in both physiological and pathological conditions. Protein homodimers frequently display some structural symmetry and are generally assumed to be formed by identical molecules, not only in terms of amino acid composition, but also in terms of post-translational modifications (PTMs). However, a perfect symmetry is very unlikely considering the high number and dynamic nature of the different PTM proteoforms that can co-exist at any given time and for the same protein (i.e. the proteoform stoichiometry). We have recently reported that asymmetrically phosphorylated huntingtin homodimers/oligomers showed a distinct aggregation pattern, with implications for Huntington´s disease; and that the intracellular distribution of STAT3 homodimers changed strikingly when specific PTMs could not occur on only one of the monomers. Based on these results, we launched the hypothesis that PTM asymmetry could constitute a new level of functional regulation for self-associating proteins. To challenge this hypothesis, the student will study the putative role of asymmetric PTMs on the behaviour and function of STAT3 homodimers by means of a multidisciplinary combination of advanced bioimaging methods in living cells and proteomics. This project is the basis of my last applications to FCT grants, two current projects within FCUL MSc programmes and 4 MSc theses and 1 PhD thesis in my laboratory. During this thesis, the student will learn mammalian cell culture, advanced microscopy methods, flow cytometry, protein biochemistry and proteomics methods, cloning and site-directed mutagenesis, as well as improve his soft skills (writing, presenting, producing professional graphs and statistics). The ideal candidate must be an organized, hard-working and team player individual, and have good English level (the language we use in lab meetings). 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.

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