Title: Radiotherapy beyond cancer: simulating the effect of radiation on pathological protein amyloids associated with neurodegenerative disorders

MSc em Biologia Computacional

Place of work: Departamento de Química e Bioquímica, FCUL

Supervisors: Federico Herrera (fherrera@fc.ul.pt), Daniel Galaviz (galaviz@fc.ul.pt)

Abstract

Radiotherapy (RT) is a relatively safe and established treatment for cancer, where the goal is to kill tumoral cells with the lowest toxicity to healthy tissues. Using it for neurodegenerative disorders involving cell loss is counterintuitive. However, ionizing radiation has a hormetic nature: it can have deleterious or beneficial effects depending on how it is applied. For example, low-dose RT can trigger antioxidant, anti-inflammatory and tissue regeneration responses. RT has been used to treat peripheral amyloidosis, which is very similar to neurodegenerative disorders such as Alzheimer or Parkinson from a molecular perspective. Both types of disorders are associated to the toxic accumulation of proteins in structures known as amyloids. Although some hypotheses have been formulated, the mechanism of action of RT on systemic amyloid deposits is still unclear, and its impact in the central nervous system remains uncertain. We want to explore the potential of RT to destroy or modify pathological amyloids. The student will be trained in Monte Carlo simulations and simulation engines, such as GEANT4-DNA and TOPAS. The student will develop and optimize a simulation tool based on the GEANT4-DNA and TOPAS engines to study the intrinsic characteristics of the effect of traditional and proton RT on toxic protein amyloid structures. If the student is interested, he/she can learn basic cell and molecular biology methods at Herrera´s lab, to confirm simulation results experimentally. Both supervisors have experience in creating multidisciplinary scientific profiles in the edge between computation, physics and biology. 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.