



**Title:** The effect of melatonin on prokaryotic and eukaryotic respiratory proteins: a possible explanation for its antimicrobial, neuroprotective and antitumoral properties

MSc em Biologia Molecular e Genética

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### **Abstract**

Melatonin is a highly pleiotropic hormone present in all natural kingdoms, from archaeobacteria to humans. Usually associated with regulation of biological responses to light/darkness cycles (e.g. circadian and circannual rhythms or skin pigmentation), melatonin has shown notable and extremely diverse therapeutic potential. Melatonin is generally antioxidant and cytoprotective for normal cells, preventing neuronal death in models of Parkinson or Alzheimer's disease, or preserving frozen sperm quality for longer periods of time. However, it is also antiproliferative and toxic for cancer cells which metabolism is based on aerobic glycolysis (see Warburg effect) and, interestingly, for pathogenic bacteria. The origin of such pleiotropic and apparently opposite effects remains unknown. Herrera and Pereira labs @ FCUL recently joined their expertise in melatonin and bioenergetics to test the hypothesis that melatonin's pleiotropic effects are related to a fundamental effect of the hormone on both eukaryotic and prokaryotic respiratory complexes. To challenge this hypothesis, the student will study the effect of melatonin and other indoles on the activity of recombinant respiratory proteins from pathogenic bacteria (e.g. *Staphylococcus aureus* or *Pseudomonas aeruginosa*) and mammalian cells (e.g. AMiD) *in vitro*. Results will be confirmed in living bacteria and mitochondria isolated from human cells, and the effect of selected concentrations of melatonin in the survival and growth of bacteria and both tumoral and healthy human cells will be analyzed. During this multidisciplinary project, the student will learn bacterial and mammalian cell culture; cloning; production, purification and activity assays of recombinant proteins in bacteria, and other advanced cell and molecular biology methods, as well as improve their 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.