A 2-year Postdoctoral position funded by Labex EpiGenMed is available in the team of Dr Dimitris Xirodimas at the Montpellier Cell Biology Research Center (CRBM), France (http://www.crbm.cnrs.fr).

CRBM is within a dynamic research community with excellent facilities and strong scientific interactions. Montpellier in South of France, close to the Mediterranean Sea and mountains is a historic, lively and cultural city providing an excellent standard of living.

Research project

The role of the ubiquitin-like molecule NEDD8 in protein quality control

Organisms are constantly exposed to environmental stress conditions that cause protein damage (proteotoxic stress). A series of sophisticated mechanisms that constitute the so-called protein quality control (PQC) system ensure the detection, repair and/or elimination of protein damage in order to maintain protein homeostasis (proteostasis). Defects in the PQC system lead to the accumulation of misfolded proteins as aggregates, which are linked to human diseases, including neurodegeneration and cancer and are also regarded as the hallmark of aging [1].

Main regulators and effectors of the PQC system are the family of ubiquitin and ubiquitin-like molecules (Ubls) such as SUMO and NEDD8. Protein modification with ubiquitin/Ubls is dynamically balanced by the action of conjugating and deconjugating enzymes. The activity of these enzymes is altered as part of the cellular response to proteotoxic stress and is often deregulated in pathological conditions [2].

The project will follow on our recent findings on the Ubl NEDD8, showing that NEDDylation is a regulator of the protein quality control system under proteotoxic stress conditions [3,4]. The successful candidate will study how changes in the equilibrium of the NEDD8 cycle affect the cellular response to proteotoxic stress. In particular, the studies will focus on the deNEDDylating enzyme NEDP1 (DEN1/SENP8): 1. Determine how defects in NEDP1 function affect protein aggregate formation upon proteotoxic stress. 2. Elucidate the role of NEDP1 in proteotoxicity.

The successful candidate will be involved in a multi-disciplinary project that combines biochemical, biological, live imaging and quantitative proteomic approaches in human cells, with genetic approaches in *C. elegans*.

Applicants are required to have a PhD, ideally in molecular biology/biochemistry, and express interest in post-translational modifications and protein turnover. Experience in the use of *C. elegans* as model organism will be advantageous but not a requirement.

Applications in the form of a CV and covering letter, including the names and addresses of 2 referees, should be sent to Dr Dimitris Xirodimas, dimitris.xirodimas@crbm.cnrs.fr

References

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