



## POSTDOCTORAL POSITION: STRUCTURAL BIOLOGY

### **Job summary:**

The Associate Laboratory IBMC-INEB (Porto, Portugal; [www.ibmc.up.pt](http://www.ibmc.up.pt)) is recruiting highly motivated researchers to integrate a multidisciplinary team engaged in the field of the Biochemistry and Structural Biology of proteolytic enzymes. A PhD in the appropriate disciplines is mandatory. Previous post-doctoral research experience and demonstrated skills in Biochemistry or Structural Biology may be a factor of preference.

### **Job description:**

Proteolytic events play a major role in a variety of physiological processes, ranging from blood-clotting to signal transduction, and from digestion to cellular quality control. The necessary tight regulation of those processes is achievable through specific inhibition, spatial and temporal compartmentalization, and post-translational modification of the intervening enzymes. Impairment of any of those regulative mechanisms often results in serious pathologies (e.g. blood-clotting disorders, neurodegenerative diseases), to which specific therapeutic approaches can be conceived by understanding the molecular details of protease specificity, as well as of their strict regulation.

We aim at characterizing the structural aspects of specific proteinase inhibition by natural proteic inhibitors, as well as the role of post-translational modifications

(e.g. monoubiquitination, sumoylation, and phosphorylation) in the regulation of protease specificity, activity, cellular compartmentalization, and turnover. In order to address these questions, we will use protein X-ray crystallography to study the three-dimensional structure of the macromolecular complexes formed between specific proteinases (thrombin, elastase) and naturally-occurring inhibitors from haematophagous animals, in an attempt to better understand the molecular basis of blood-clotting inhibition, and therefore gain insights into better strategies for the design of more efficient and safer anti-thrombotics. Furthermore, a combination of biochemical and biophysical techniques will be employed to study the role of intracellular proteases in neurodegenerative processes. We are especially interested in the characterization of ataxin-3, a polyglutamine tract-containing ubiquitin hydrolase, implicated in Machado-Joseph's disease. A number of biophysical techniques (CD, NMR, MS, X-ray crystallography) will be used in an attempt to dissect the molecular pathway of ataxin-3 aggregation *in vitro*, in parallel with the biochemical characterization of its regulation by post-translational modifications.

### **Conditions of Employment:**

The appointment will be for an initial period of 3 years with a possible extension for an additional 2 years, corresponding to a gross annual income of 43.000 € (before taxes). Payment will be made in accordance with the work contract regulations of Portugal. There are no nationality restrictions, and no teaching obligations.

## Application

The closing date for applications is 30th September, 2008. Candidates should submit a letter of motivation that includes scientific interests, a *Curriculum vitae* and three digitized versions of letters of reference, to IBMC – Ciência 2008, Rua do Campo Alegre, 823, 4150-180 Porto, Portugal or [ciencia2008@ibmc.up.pt](mailto:ciencia2008@ibmc.up.pt).

When applying for this job always mention C2008-IBMC-AMD-001

The Associate Laboratory IBMC-INEB is located in close proximity to the Chemistry, Biology and Physics Departments of University of Porto, as well as to the Botanical garden. Overlooking the Douro River, Porto is one of the most ancient European cities. Its historical center was classified as World Heritage by UNESCO in 1996 (<http://www.portoturismo.pt/index.php>).

Informal enquiries can be addressed to Dr. Sandra Macedo-Ribeiro ([sribeiro@ibmc.up.pt](mailto:sribeiro@ibmc.up.pt)).