

POST-DOCTORAL FELLOWSHIP (M/F)

Reference: PTDC/SAU-GMG/105344/2008

Title of the Project: “LIMP-2 studies: from clinical genetics to functional genomics and back”

Internal Code: PR131406

A Fellowship is open for recruitment of a Post-doctoral fellow to collaborate in the Project referred above, financed by the Program “COMPETE - Programa Operacional Factores de Competitividade” in its FEDER component and by the Foundation for Science and Technology budget in its OE component.

The fellowship is for one year, eventually renewable up to a maximum of 3 years, starting on 1st of September 2010. The monthly amount of the fellowship is € 1,495.00.

Place of Work: Lysosome and Peroxisome Biology Unit, Institute for Molecular and Cell Biology, Porto, Portugal

Work Program: See attached.

Candidate profile:

The candidate should possess a PhD in the fields of Biochemistry, Biology, Biomedicine, Molecular Biology or related areas and have experience in cellular biology and molecular biology. We are looking for highly motivated candidates with experience in at least one of the following: isolation of organelles, namely lysosomes; protein expression and purification, transfection and expression in eukaryote systems.

The applications should be received between May 6th and June 30th, 2010.

Proposals must include a letter of motivation, CV, and 2 letters of reference, and should be sent to candidaturas@ibmc.up.pt referring the internal code (PR131406)

The fellowship is regulated by current laws relating to the Statute of Science Research Fellows, namely Law 40/2004 of August 18, and the Regulation of Scientific Research Studentships of the IBMC (www.ibmc.up.pt/fellowships.php).

“LIMP-2 studies: from clinical genetics to functional genomics and back”

Supervisor:

Maria Clara Sá Miranda, PhD

Head, Lysosome and Peroxisome Biology Unit

Project Summary:

The main goal of this project is to investigate the function of the lysosomal integral membrane protein type 2 (LIMP-2), by using a complementary approach of medical genetics and genomic function studies. LIMP-2 is a transmembrane glycoprotein with a role in the biogenesis and maintenance of the endosomal/lysosomal system (1), although its cellular function is not yet well defined. Recently, almost simultaneously, we and other group, described alterations in the SCARB2 (MIM 602257) gene that codes for LIMP-2 (2, 3) in patients with Action Myoclonus-Renal Failure (AMRF). AMRF is a very rare genetic disease transmitted in an autosomal recessive manner, whose genetic defect was unknown until very recently. In our paper we described by the first time, that in humans, similarly to what was described in the LIMP-2 knockout (KO) mice (4), LIMP-2 is the GCCase (GCCase) lysosomal sorting receptor (2). However, accordingly to the studies carried out in the Portuguese LIMP-2 deficient patients, this mechanism seems to be cell-type specific. In fact, GCCase activity is deficient in fibroblasts but normal in leukocytes. Moreover the LIMP-2 deficient patients do not present a Gaucher disease (GD) clinical phenotype neither the lipid-laden macrophages characteristic of GD, the lysosomal disease originated by defects in the gene that encodes GCCase. In summary, even though the significant improvement in knowledge, as the result of the identification of the genetic defect in a rare disease and the identification of LIMP-2 as the GCCase lysosomal sorting receptor, many questions remain unanswered. This project aims to investigate: 1) the LIMP-2 mediated transport mechanism of GCCase to the lysosome in different human and rat cells and tissues; 2) to identify new LIMP-2 cargo proteins sorted to lysosomes.