

POST-DOCTORAL FELLOWSHIP (M/F)

Reference: PTDC/SAU-MII/098041/2008

Title of the Project: “A systematic method for identifying the ligands of T-cell surface molecules”

Internal Code: PR162506

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, and in collaboration with the T-cell Biology Group, The Weatherall Institute of Molecular Medicine, University of Oxford.

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

Place of Work: 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, Biomedicine, Biology, Physics, Biophysics, Molecular Biology or related areas. We are looking for highly motivated candidates with experience in at least one of the following: protein expression and biochemistry, transfection and expression in eukaryote systems; flow cytometry; biochemistry of signal transduction/cell activation; RNA techniques. Experience with Atomic Force Microscopy and/or bioinformatics is advantageous.

The applications should be received between May 6th and May 20th, 2010.

Proposals must include a letter of motivation, CV, 2 reference letters, and copies of major publications, and should be sent to candidaturas@ibmc.up.pt referring the internal code (PR162506)

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).

A systematic method for identifying the ligands of T-cell surface molecules

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Supervisor: Alexandre M. Carmo

Summary

T lymphocytes are activated by antigen presenting cells (APCs) that express cognate peptides in the context of MHC molecules. A large variety of T-cell surface molecules participate in the activation process, many of them by binding a counter receptor expressed on the APC. Whereas it is believed that virtually all molecules expressed on the T-cell surface are known and have been at least partially characterized, for a large fraction of these receptors the ligands have not been identified. We now propose to establish a method for the systematic identification of ligands of T-cell surface molecules. In the new method, two key steps need to be achieved in order to identify the putative ligands of receptors of interest. In the first step, the receptor of interest is produced in a multivalent form, which will be used to screen for the presence of ligands on the surfaces of different cell lines. In the second step a full transcriptome database of the entire set of cell lines will be generated. Messenger RNA will be obtained from these cells, and analyzed using Illumina Inc's 'Tag-seq' gene expression analysis protocol. By searching for correlations between the binding of the multivalent receptor and the gene expression profiles of the target cells, we expect to obtain a restricted and manageable number of "hits" comprising transcripts encoding putative ligands. Bioinformatic approaches will be employed to limit the set of possible candidate ligands. Increasing the number of cell lines can be used to further restrict the numbers of candidates. The approach should be broadly applicable to any receptor that binds differentially to the set of cells for which we have transcriptome data, both within and outside the immune system. Three query molecules will be used during this project. To establish proof of principle for the experimental approach, we will use as query receptor the surface antigen CD2, whose interaction with CD58 is extensively characterized. To fully validate the method, all identified candidate molecules that are considered probable ligands of the query receptors will be tested for binding and the effects of confirmed interactions will be investigated using a variety of functional approaches.