

BOLSA DE INVESTIGAÇÃO (M/F)

Referência: PTDC/BIA-BCM/100088/2008

Título do Projecto: “New host factors hijacked by human bacterial pathogens to promote and establish infection: role of tyrosine-phosphorylated-Myosin IIA and Cytokeratin 18 in infectious processes”

Código interno: PR123203

Está aberto concurso para recrutamento de um(a) bolseiro(a) de Investigação para colaborar no projecto acima referido, financiado pelo programa COMPETE - Programa Operacional Factores de Competitividade na sua componente FEDER e pelo orçamento da Fundação para a Ciência e a Tecnologia na sua componente OE.

A bolsa, em regime de exclusividade, terá a duração de 6 meses, eventualmente renovável, com início previsto em 15 de Maio de 2010.

O valor mensal da bolsa será de € 745,00, pago por transferência bancária (preferencialmente).

Local de trabalho: Group of Molecular Microbiology, IBMC, Porto

Programa de trabalho: ver anexo.

Perfil pretendido:

Os candidatos devem possuir à data de 15 de Maio de 2010 uma Licenciatura em Microbiologia, Biologia, Bioquímica ou áreas afins, e média final de licenciatura igual ou superior a 15 valores. É condição preferencial possuir experiência de investigação em Biologia Cellular.

O prazo para recepção de candidaturas decorre de 26 de Abril a 10 de Maio de 2010.

As propostas deverão incluir carta de motivação, CV, e cartas de referência e ser enviadas por correio electrónico para candidaturas@ibmc.up.pt com indicação do código interno (PR123203).

Após avaliação do CV, os candidatos pré-seleccionados poderão ser chamados para entrevista.

A contratação será regida pelo estipulado na legislação em vigor relativamente ao Estatuto de Bolseiro de Investigação Científica, nomeadamente a Lei 40/2004, de 18 Agosto, e o Regulamento de Bolsas de Investigação Científica do IBMC (www.ibmc.up.pt/fellowships.php).

Role of Cytokeratin 18 in bacterial infections

Project summary:

Listeria monocytogenes is a Gram-positive human foodborne pathogen. It causes invasive illness in well-defined high-risk groups, including elderly, immunocompromized, pregnant women and neonates. Listeriosis is a severe disease characterized by septicemias, meningitis, meningo-encephalitis and abortions. *Listeria* is an intracellular facultative bacterium able to survive and multiply inside phagocytic cells and has the capacity to induce its uptake in epithelial cells. The successive steps of *Listeria* cellular infection have been extensively studied ranking *Listeria* among the most documented pathogens.

We previously reported that, shortly after the interaction of *Listeria* with epithelial cells, host Src kinase is activated and demonstrated that the entry levels of *Listeria* in presence of Src-activity chemical inhibitors are highly reduced. We have been able to show that cortactin is one of the substrates for Src kinase during *Listeria* uptake. We postulated that other host proteins should be tyrosine phosphorylated by Src during entry.

Giving the central role of phosphorylation events in different human bacterial infections and based on our previous results showing the activation of Src after *Listeria* interaction with host cells, we searched for novel host proteins showing a different tyrosine phosphorylation status in the course of infection. We analyzed the tyrosine phosphorylation profile of *Listeria*-infected cells as compared to non-infected cells and showed that eukaryotic cells present a variable protein phosphorylation pattern upon infection. We identified Cytokeratin 18 (CK18) as differentially phosphorylated in response to *Listeria* uptake. We demonstrated that this protein is recruited at the bacteria entry site and play an essential role in *Listeria* infection. These results correlate for the first time CK18 post-translational modifications and bacterial infection.

This project aims to confirm our preliminary data concerning the role of CK18 in *Listeria* cellular infection, and investigate its possible involvement in the infectious of other human pathogens (EPEC, EHEC and Yersinia). In addition, we plan to identify the tyrosine residues that are phosphorylated and address the role of CK18-tyrosine phosphorylation in response to infection. To achieve these objectives siRNA and shRNA techniques, microscopy, biochemical and site-directed mutagenesis will be used.