

BOLSA DE INTEGRAÇÃO NA INVESTIGAÇÃO (M/F)

Título do Projecto: Melanocortin 5 receptor structural aspects underlying its cell-surface transport

Código interno: LA150123

Está aberto concurso para recrutamento de um(a) Bolseiro/a de Integração na Investigação para colaborar no projecto acima referido, co-financiado pela Fundação para Ciência e a Tecnologia e pelo FEDER.

As bolsas, em regime de exclusividade, terão a duração de 12 meses, com início previsto a 1 de Setembro de 2009.

O valor mensal da bolsa será de € 140,00, pago por transferência bancária (preferencialmente).

Local de trabalho: Laboratório de Biologia Celular e Molecular da Faculdade de Medicina da Universidade do Porto

Programa de trabalho: ver anexo.

Perfil pretendido:

Os/as candidatos/as devem frequentar o 1º ciclo em áreas afins a Medicina, Biologia e Bioquímica. É condição preferencial possuir alguma experiência laboratorial.

O prazo para recepção de candidaturas decorre de 8 a 22 de Junho de 2009.

As propostas deverão incluir uma carta de motivação e CV e ser enviadas para:

Alexandra Gouveia
Faculdade de Medicina da Universidade do Porto
Laboratório de Biologia Celular e Molecular
Alameda Prof. Hernâni Monteiro,
Porto
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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).



“Melanocortin 5 receptor structural aspects underlying its cell-surface transport”

Supervisor:

Alexandra Maria Monteiro Gouveia

Project summary:

MC5R belongs to a five member-family of G protein coupled receptors (GPCRs) and has a broad tissue distribution in almost all eukaryotic organisms [1]. Regarding the MC5R physiological role, it may be related with the peripheral regulation of lipid metabolism, a conclusion supported by the MC5R null mice studies, which showed a down-regulation of sebaceous lipid secretion with a consequent defect in water repulsion and thermoregulation [2].

To better understand the mechanisms underlying MC5R expression and maturation, this project focuses on the study of the intracellular trafficking of this receptor. Preliminary results show that the N-terminus of MC5R is crucial to the receptor stability and targeting to cell surface. In order to identify the MC5R specific domains responsible for the Endoplasmic Reticulum-cell membrane receptor movement, the levels and location of N-terminal truncated forms of the receptor will be analysed by co-localization with markers of the different organelles (Endoplasmic Reticulum, Golgi and Plasma Membrane).

Recently we have described a GFP-tagged MC5R heterologous expression system, which allowed the study of the signalling mechanisms activated by this receptor. We concluded that MC5R, after α -MSH activation, signals through PI3K pathway which activates ERK1/2 MAPK in an Akt/PKB independent mechanism [3]. The activation of these signalling pathways will be analysed in the cells expressing the N-terminus truncated forms of the receptor in order to identify the MC5R domains responsible for signalling.

Understanding the molecular and cellular mechanisms controlling GPCR intracellular routing is essential for preventing or correcting the conformational abnormalities associated with disease-causing misfolded receptors.

[1] Getting SJ (2006). Targeting melanocortin receptors as potential novel therapeutics. *Pharmacol Ther* 111(1):1-15.

[2] Chen W, Kelly MA, Opitz-Araya X, Thomas RE, Low MJ, Cone RD (1997). Exocrine gland dysfunction in MC5-R-deficient mice: evidence for coordinated regulation of exocrine gland function by melanocortin peptides. *Cell* 91(6):789-98.

[3] Rodrigues AR, Pignatelli D, Almeida H, Gouveia AM (2009). Melanocortin 5 receptor activates ERK1/2 through a PI3K-regulated signaling mechanism. *Molecular and Cellular Endocrinology* 303, 74-81

