

## **Project:**

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### **Function and regulation of SPAK Signalling Pathways in Eukaryotic Cells**

To maximize the probability of survival and proliferation, cells coordinate various intracellular activities in response to changes in the extracellular environment. Eukaryotic cells transduce diverse extracellular stimuli through the cell by multiple MAP kinase cascades. Exposure of cells to stress results in rapid activation of a highly conserved family of MAPKs, known as SAPKs (stress-activated protein kinases). Activation of SAPKs results in the generation of a set of adaptive responses that leads to the modulation of several aspects of cell physiology essential for cell survival, such as cellular metabolism, growth control, proliferation, morphogenesis and development. Consequently, altered signalling through SAPK pathways by genetic or physiological changes is associated to disease processes. However, the regulatory mechanisms of the stress MAPK cascade, particularly, how stress stimuli is perceived and transmitted to the MAPK cascade is only beginning to be uncovered. The main objective of this project is the study of the molecular mechanisms of SAPK signalling, from sensing to signal transduction, as well as, to understand the complexity of adaptive responses generated by these enzymes in response to cellular stress. For this, we will study the mechanisms by which the yeast Hog1 MAPK and its mammalian homologue p38 MAPK regulate gene expression and cell cycle progression. Moreover, we will proceed to a systematic identification of novel targets for these proteins to unravel novel biological functions for SAPKs. Together, a comprehensive molecular picture of the function and regulation of stress-activated kinases should emerge from the proposed research.

## **Comments:**

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The project is at the forefront of signaling pathways research (osmoregulation) in eucaryotic cells. Major contribution to the field foreseen.

Francesco Posas is already an established independent researcher who leads a group of 8 people and has a very impressive publication record.

The ambitious project is based on original ideas and previous results of the candidate. The proposal is positioned in a well chosen but fairly specialized niche, based on the response to hyperosmolarity in yeast. More recent analysis moves to the mammalian system, because almost all the yeast elements of this signal transduction pathway are conserved in evolution. It is very strong in molecular biology, a little less strong in physiology. A EURYI award would enable the candidate to consolidate his research and establish a leading group. He would stay in Barcelona if he received the grant. Otherwise, given the uncertainties of the Spanish funding scene he might be tempted to move somewhere else. Obtaining the grant is essential to him if he is to stay competitive.

Barcelona is rapidly expanding and becoming a real centre of excellence in Europe. The panel felt that an award would help establish these relatively young institutions on the map.

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