Seminarios internos del IBFG

Postranslational regulation of the Greatwall-Endosulfine-PP2A/Pab1 pathway

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Cell growth is normally coupled to cell division in order to generate an organism of certain size. Cell growth is regulated by TORC1, whereas cell cycle is driven by the activity of cyclin dependent kinases (CDKs). Recently, our group have shown that the conserved Greatwall-Endosulfine pathway connects cell growth to cell cycle by regulating the phosphatase activity of PP2A/Pab1 complex. In nitrogen rich medium, TORC1 activity is increased, and therefore, Greatwall and Endosulfine are inhibited, and are unable to inhibit PP2A/Pab1. In these conditions, PP2A/Pab1 is active and opposing CDK activity, thus the cells enter cell division with a large cell size. In nitrogen poor medium, TORC1 is inhibited and consequently, Greatwall and Endosulfine are active and can inhibit PP2A/Pab1. Reduced PP2A/Pab1 levels enables cells enter division with a smaller size.

Over the past few years, we have studied the physiological roles of the Greatwall-Endosulfine-PP2A/Pab1 pathway in the fission yeast. Our results suggest that these proteins are required for G1 arrest, which is needed to initiate the sexual differentiation response, and mating under nitrogen starvation. We have also shown that Greatwall-Endosulfine activity might be crucial in longevity.

According to our model, the Greatwall-Endosulfine module is a hub for cell cycle and nutritional signals. We have preliminary data indicating that Greatwall is activated by Cdk1/Cyclin B and inhibited by nutrient sensing pathways. Using 2D LC-MS/MS, we have analysed the phosphorylation changes in Endosulfine, identifying 3 Cdk1 and 2 PKA phosphosites. Furthermore, we have used mass spectrometry techniques to study the interactomes of Endosulfine and Pab1, which might help us to understand the protein-protein interactions that control this module as well as to identify new targets of these proteins.