Seminarios internos del IBFG

Roles of the Greatwall-Endosulfine-PP2A/B55 pathway in cell size, autophagy and transcription

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Cell growth, regulated by TORC1, and division, controlled by cyclin-dependent kinases, are two processes tightly regulated and coupled in proliferating cells. The conserved Greatwall-Endosulfine-PP2A/B55 pathway connects these two processes. Greatwall, once is active, triggers the activation of Endosulfine by phosphorylation, which leads to the inactivation of PP2A/B55, which opposes CDK activity. In fission yeast, Greatwall (Ppk18/Cek1) is negatively regulated by TORC1 through S6K (Sck2) phosphorylation. In nitrogen-rich medium, TORC1 is active, and therefore, Ppk18/Cek1 and Igo1 (Endosulfine) are inhibited and are unable to inhibit PP2A/B55. In these conditions, PP2A/B55 is active and opposing CDK activity, thus the cells enter cell division with a large cell size. In nitrogen-poor medium, TORC1 activity is reduced and consequently Ppk18/Cek1 and Igo1 are active and can inhibit PP2A/B55. With reduced PP2A/B55 levels, cells enter division with a smaller size. Deletion mutants of *igo1* and *cek1 ppk18* are unable to arrest in G1 after shifting the cells to minimal medium (MM) without nitrogen (MM-N), barely conjugate and show reduced long-term viability in MM-N. We set to study the transcriptional landscape of these mutants in a time-course in which the cells were shifted from minimal medium to MM-N. RNA-sequencing showed that mutant cells gene expression is similar to the wild-type in MM, but it is vastly different in MM-N. Mutant cells have reduced expression of genes required for mitosis, meiosis and the stress response, and increased expression of metabolic and ribosomal protein genes and transposons.