Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

How cells coordinate growth and division

By

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Cells grow and divide. Growth increases cell size, division decreases it. Although the size of individual cells in a proliferating cell population keeps changing, the population maintains a narrow cell size distribution. The ability of cells to maintain a narrow size distribution is "size homeostasis". Cells achieve size homeostasis by coordinating growth and division. But how do cells coordinate?

In my dissertation, I investigated how cell size homeostasis is maintained and how cell size control works. I used RNA-seq to quantitate the transcriptome of yeast cells of different sizes (generated by multiple methods), and found that the activators of cell cycle increase in concentration with cell size whereas inhibitors do not. We think cells might sense size by the ratio of cell cycle activators over inhibitors. This idea predicts that deletion of a single activator or inhibitor would change the size at which a cell commits to cell cycle (set-point), but not size homeostasis (narrowness of the distribution). Indeed, experimentally, I found cell cycle activator or inhibitor deletion mutants have altered setpoint, but not homeostasis. In fact, we could hardly find a single deletion mutant with altered homeostasis. How to disrupt the size sensor? Theoretically, inverting the size scaling of an activator and/or an inhibitor could make the activator-over-inhibitor ratio less sensitive to cell size. When I swapped the promoters between one activator and one inhibitor, the cells indeed had a broader size distribution.

After showing how growth talks to division, I then completed the loop by demonstrating how division influences growth. I showed a key molecule controlling cell division, CDK, directly regulates metabolism-related enzymes, namely Nth1 and Gph1, which break down stored carbohydrates, trehalose and glycogen. Upon nutrient exhaustion, cells in which Nth1 and Gph1 were mutated and non-responsive to CDK were larger than wild-type cells. This was the first time direct regulation of metabolism-related proteins by CDK had been shown in yeast. Potentially, CDK regulates other metabolic enzymes, and cell division could influence growth in a CDK-regulated manner.

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