May 30th, 9:00 AM - 10:00 AM

Cell Size Control in Budding Yeast by Titration of Regulatory Proteins

John Tyson
Virginia Tech and University of Oxford

Cell Size Control in Budding Yeast by Titration of Regulatory Proteins

John J. Tyson, F. Stefan Heldt & Bela Novak
Department of Biochemistry
University of Oxford, UK

Abstract: The size of a cell sets the scale for all biochemical processes within it, thereby affecting cellular fitness and survival. Hence, cell size needs to be kept within certain limits and relatively constant over multiple generations. Despite the evident importance of "size control", how cells measure their size and use this information to regulate growth and division remains uncertain and controversial. In this talk, we consider two mathematical models of the cell cycle in budding yeast (*S. cerevisiae*) to investigate two competing hypotheses on size control: an inhibitor-dilution mechanism and a mechanism based on titration of nuclear sites. Our results suggest that the inhibitor-dilution mechanism, in which cell growth dilutes the transcriptional inhibitor Whi5 against the constant concentration of an activator, Cln3, can account for many features of size homeostasis in budding yeast; however, it is inconsistent with the observed sizes of mutant cells with altered overall ploidy and/or *WHI5* gene copy number. By contrast, the second model of size control, by titration of Cln3 against a constant number of genomic binding sites for the transcription factor SBF, recapitulates both size homeostasis and the observed sizes of these mutant strains. The nuclear-sites titration model is also consistent with other features of size control in budding yeast and other types of eukaryotic cells. Our theoretical considerations provide renewed support for a specific molecular mechanism of size control at the START transition in budding yeast. Because the "restriction point" in the mammalian cell cycle bears many functional and molecular similarities to START, our conclusions may have broader significance in terms of normal and dysregulated growth of proliferating cells in human physiology.

Reference: F.S. Heldt, R. Lunstone, J.J. Tyson & B. Novak (2018). Dilution and titration of cell-cycle regulators may control cell size in budding yeast (submitted for publication).