Swammerdam Institute for Life Sciences

You are cordially invited to attend the "Yeasterday" keynote lecture:

Molecular competition and cell size control: a link to cell ageing?

by Martí Aldea

Molecular Biology Institute of Barcelona, CSIC, Barcelona, Catalonia, Spain

date: Friday 29 May 2015

venue: Room C1.110

hosts: Matteo Barberis: M.Barberis@uva.nl

Gertien Smits: G.J.Smits@uva.nl

(Abstract and Selected Literature are reported in the next page)

Swammerdam Institute for Life Sciences

Abstract

Coordination of cell growth and DNA replication ensures size adaptation and homeostasis. Cells are able to adapt their size to growth rate both at population and single-cell levels, which suggests that growth is intimately linked to the molecular mechanisms that govern the cell cycle. Budding yeast cells, as most eukaryotic cells, exert this coordination essentially during G1, where a critical size must be attained before cells trigger Start. The most upstream activator of cell cycle entry in budding yeast is Cln3, a cyclin that critically depends on molecular chaperones to accumulate in the nucleus in late G1. On the other hand, chaperones are massively involved in key growth processes, and we have investigated the possibility that coordination between proliferation and growth relies on the competition for limiting stocks of shared chaperones. As deduced from mathematical modeling, a molecular competition device would be able to (1) accumulate Cln3 in the nucleus in a non-linear manner during G1, and (2) trigger Start at a cell size that is proportional to growth rate. We have used different experimental approaches to test predictions of the model, and our data support the notion that competition for molecular chaperones would provide Start with an upstream switch-like mechanism, and adjust the critical size to the individual growth potential.
As protein aggregates accumulate during cell ageing and compromise chaperone function, our findings suggest close connections between proliferation and ageing in cells. We are currently investigating whether a decline in the chaperone armamentarium with age would have negative consequences in the execution of Start and, hence, would decrease the proliferative capacity of cells, a hallmark of ageing.

Selected Literature

1. Yahya G, Parisi E, Flores A, Gallego C, Aldea M. A Whi7-anchored loop controls the G1 Cdk-cyclin complex at start. Mol Cell. 2014; 53:115-26.
2. Ferrezuelo F, Colomina N, Palmisano A, Garí E, Gallego C, Csikász-Nagy A, Aldea M. The critical size is set at a single-cell level by growth rate to attain homeostasis and adaptation. Nat Commun. 2012; 3:1012.
3. Ferrezuelo F, Colomina N, Futcher B, Aldea M. The transcriptional network activated by Cln3 cyclin at the G1-to-S transition of the yeast cell cycle. Genome Biol. 2010; 11:R67.
4. Colomina N, Ferrezuelo F, Vergés E, Aldea M, Garí E. Whi3 regulates morphogenesis in budding yeast by enhancing Cdk functions in apical growth. Cell Cycle. 2009; 8:1912-20.
5. Colomina N, Ferrezuelo F, Wang H, Aldea M, Garí E. Whi3, a developmental regulator of budding yeast, binds a large set of mRNAs functionally related to the endoplasmic reticulum. J Biol Chem. 2008; 283:28670-9.
6. Aldea M, Garí E, Colomina N. Control of cell cycle and cell growth by molecular chaperones. Cell Cycle. 2007; 6:2599-603.