CRBM external seminar
Thursday May 25th, 11:00 pm Salle Marcel Dorée

Age-dependent aneuploidy, a study case for dissecting the mechanisms of aging

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Yves Barral studied Genetics and Biochemistry at the Ecole Normale Superieure in Paris, and completed his diploma work in Microbiology at The Pasteur Institute in 1989. He then started his Ph.D. studies on the genetic analysis of cell cycle control which he carried out at both the Commissariat à l'Energie Atomique (Saclay, France) and the Friedrich-Miescher Laboratory of the Max-Planck Institute (Tübingen, Germany). In December 1994 he obtained his Ph.D. from the Pierre and Marie Curie University in Paris. He then went on to work as a postdoctoral fellow and postdoctoral associate in the Department of Biology, Yale University (New Haven, USA) up until July 1999, focusing on the regulation of cellular morphogenesis during cell division. He is now full Professor at the Department of Biology at ETH Zürich.

Abstract

Age is the main risk factor for diseases associated with chromosome mis-segregation and aneuploidy, such as cancer. However, whether age itself induces chromosome mis-segregation and if so, how, are still open questions. We have used the budding yeast *Saccharomyces cerevisiae*, a powerful model to study replicative aging, to address these questions. We found that yeast mother cells show a dramatic increase in chromosome loss as they approach their last division. Remarkably, loss was driven by mis-segregation of sister chromatids together the old Spindle Pole Body (SPB, the yeast equivalent of the centrosome) to the bud. This phenotype depends on the accumulation of aging factors such as DNA circles and was amplified upon inactivation of the sirtuin Sir2. I will provide mechanistic details explaining how Sir2, DNA circle accumulation and age induce chromosome drive towards the surviving daughter cell. I will discuss the evolutionary consequences of this observation and the consequent possibility that the mechanisms at play in yeast are also active in other aging organisms, such as most metazoans. Finally, I will provide elements suggesting that the processes driving chromosome mis-segregation with age might be at the root of many of the other effects of age.

Selected publications

Meinema, A.C., Marzelliusardottir, A., et al. (2022). "DNA circles promote yeast ageing in part through stimulating the reorganization of nuclear pore complexes" ***eLife***, doi: 10.7554/eLife.71196

Lengefeld, J., Hotz, et al. (2017). "Budding yeast wee1 distinguishes spindle pole bodies to guide their pattern of age-dependent segregation", ***Nature Cell Biology***, 19(8):941-951

Denoth-Lippuner, A., Krzyzanowski, M.K., Stober, C. and **Y. Barral***, (2014), "Role of SAGA in the asymmetric segregation of DNA circles during yeast ageing", ***eLife***, Nov. 17,3:e03790

Shcheprova, Z., Baldi, S., et al. (2008), "A mechanism for asymmetric segregation of age during yeast budding", ***Nature*** 454;728-34