

A new link between asymmetric inheritance of spindle microtubule organizing centers and cellular aging

Javier Manzano-López, Laura Matellán, Alejandra Álvarez-Llamas, José Carlos Blanco-Mira and Fernando Monje-Casas

CABIMER / Spanish National Research Council (CSIC), University of Seville and University Pablo de Olavide. Avda. Américo Vespucio, 24. 41092 Seville (Spain)

There are many examples of asymmetric cell divisions, which give rise to a newly-generated daughter cell that differs from its mother in size, cellular composition or potential to differentiate. These divisions are essential for many microorganisms and play pivotal roles during development and tissue morphogenesis in animals and plant. As such, the asymmetry during the division of stem cells allows them to self-renew while also producing another cell that, based on the inheritance of specific cell-fate determinants, enters a particular differentiation program. Defects during the asymmetric division of stem cells can lead to tissue degeneration or aging due to a reduction in the number of these cells or, alternatively, to tumorigenesis or tissue hyperplasia if the stem cell pool increases. Thus, it is of pivotal importance to better understand the mechanisms that regulate these processes. A fascinating phenomenon associated to asymmetric cell divisions is the differential distribution of the microtubule-organizing centres (MTOCs) that orchestrate mitotic spindle formation, which was originally described in *Saccharomyces cerevisiae* and later found to be conserved during stem cell divisions in organisms ranging from *Drosophila* to humans. Remarkably, however, the biological meaning of this process was so far unknown. Using budding yeast as a model, and taking advantage of the powerful molecular tools developed for the genetic modification of this organism, we have generated a *S. cerevisiae* strain that displays a constitutively inverted MTOC inheritance pattern. Our results demonstrate that the asymmetric distribution of the MTOCs that orchestrate spindle formation in budding yeast is critical in order to preserve cellular lifespan, and shed light into the mechanisms by which the differential inheritance of these structures contribute to the maintenance of the replicative potential of the cells.