

Group name: Nuclear organization and division

"Living cells have a fascinating ability to generate complex and dynamic internal structures. This property is most evident during cell division: in a very short time (often of the order of a few minutes) cells alter their shape, partition equal copies of their internal components to opposite poles, and constrict in the middle to divide into two seemingly identical halves - which often go on to develop different identities. These dramatic changes need to be carefully coordinated with each other in space and time.

Critically, the cells' DNA – contained in rod-like structures called chromosomes – must travel to opposite sides of the cell before this splits in two. Chromosomes that are delayed in their journey risk being caught by the constriction machinery and damaged, potentially leading to severe pathologies such as cancer. We study a control system that prevents this catastrophic event, called the "NoCut checkpoint": a mechanism that delays cell division until all chromosomes are safely away from the constriction site. We study this process in a simple experimental system, the yeast *Saccharomyces cerevisiae*. We then validate key findings made in yeast, and we extend them, in human cells.

Our lab is also interested in the process of asymmetric cell division, a key strategy by which a mother cell generates daughters with different size, age, and transcriptional profiles. Asymmetric division is thus a key process during metazoan development and is at the basis of stem cell self-renewal and tissue homeostasis. We have identified a novel deacetylation-based mechanism controlling nuclear reorganization in asymmetrically dividing yeast cells. We speculate that similar processes might establish nuclear identity and cell fate in yeast and multicellular organisms. The characterization of this novel mechanism will likely reveal new concepts of medical relevance, as defects in asymmetric division (for instance in stem cells) are associated with a host of human pathologies including microcephaly and cancer."

Key Publications:

1. Amaral, A., Vendrell, A., Funaya, C., Idrissi, F., Maier, M., Kumar, A., Neurohr, G., Colomina, N., Torres-Rosell, J., Geli, M.I. and Mendoza, M. (2016). The Aurora B dependent NoCut checkpoint prevents damage of anaphase bridges after DNA replication stress. *Nat Cell Biol*, 18, 516-526.
2. Titos, I., Ivanova, T. and Mendoza, M. Chromosome length and perinuclear attachment constrain resolution of DNA intertwinings (2014). *J Cell Biol* 206, 719–733.
3. Neurohr, G., Naegeli, A., Titos, I., Theler, D., Greber, B., Díez, J., Gabaldón, T., Mendoza, M.# and Barral, Y.# (2011). A Midzone-Based Ruler Adjusts Chromosome Compaction to Anaphase Spindle Length. *Science* 332, 465-468
4. Mendoza, M., Norden, C., Durrer, K., Rauter, H., Uhlmann, F., and Barral, Y. (2009). A mechanism for chromosome segregation sensing by the NoCut checkpoint. *Nat Cell Biol* 11, 477-483
5. Norden, C.*, Mendoza, M.*, Dobbelaere, J., Kotwaliwale, C.V., Biggins, S., and Barral, Y. (2006). The NoCut pathway links completion of cytokinesis to spindle midzone function to prevent chromosome breakage. *Cell* 125, 85-98.