**MANUEL MENDOZA**

## Biography

## Project

**European Research Council Starting Grant**
Project acronym: LONGCHROM
Project full title: Chromosome Segregation and Aneuploidy

**Overview**
Accurate partitioning of the genetic material during cell division is critical for the maintenance of genetic stability, both within organisms and across generations. Defects in chromosome segregation produce aneuploidy – an unequal distribution of chromosomes between daughter cells –, which is cause of developmental defects, and one of the cancer hallmarks. To ensure error-free transmission of chromosomes, feedback control systems, known as checkpoints, verify that processes at each stage of the cycle have been completed, before allowing progression into the next stage. In particular, the spindle assembly checkpoint (SAC) prevents initiation of anaphase until chromosomes attach properly to the spindle, whereas the NoCut checkpoint, which I identified, inhibits cytokinesis until chromosome segregation is complete. The discovery of NoCut, which is conserved from yeast to humans, reveals that eukaryotic cells monitor chromosome segregation during anaphase. The molecular mechanisms underlying this, and potentially other anaphase feedback controls remain obscure. The main goal of this proposal is to achieve a detailed understanding of the mechanisms coordinating chromosome segregation and cytokinesis. Key to this task will be the experimental manipulation of chromosome architecture in budding yeast, which allows the generation of cells with extra long chromosome arms. Using this strategy, we have already uncovered at least one novel feedback system, which coordinates axial chromosome compaction with anaphase spindle size. We will characterize this and other anaphase controls through a multidisciplinary approach, which combines classical molecular and genetic techniques with state-of-the-art genomics and proteomics, and an extensive set of reagents we have developed to analyze cell division dynamics and chromosome segregation in living cells. We will identify the mechanisms coordinating chromosome arm length with spindle size, and the molecular basis of chromosome segregation errors during anaphase. The relevance of these novel processes will be confirmed by analysis of cell division in animal cells and in a *Drosophila* tumour model. These approaches will significantly advance our understanding of how eukaryotic cells coordinate cytokinesis with chromosome segregation, how they prevent aneuploidy and genetic instability, and will ultimately be instrumental to identify new therapeutic targets for human cancer.