CCS Annual Report 2024

Annual Highlights

In 2024, the Center for Chromosome Stability (CCS) completed its final full year of operation, with funding due to cease in August 2025. While the CCS has continued to focus on an analysis of fundamental aspects of genome maintenance, increasingly the emphasis has shifted to defining how genome instability is relevant to the etiology of certain pathological disorders, including infertility and cancer. Hence, the overall mission of the CCS is to understand the molecular basis for disease development and to use that knowledge to develop and/or enhance interventions to combat disease and improve 'health-span'.

The CCS has had a very successful year in 2024, with many notable achievements and developments. Several articles have been published in high impact international journals. Gratifyingly, many of these have involved collaborations within the CCS and/or ICMM (the host department for the CCS). A good example of this, and one of the highlights of the year, was the joint publication by the Hoffmann group and the newly incorporated Lerdrup group (see Figure 1 below and discussion later in this report) describing how the chromatin contributed by each parent to an embryo is differentially modified by both methylation and acetylation, as well as being duplicated (replicated) in different ways. This work was published in *Nature Communications*.

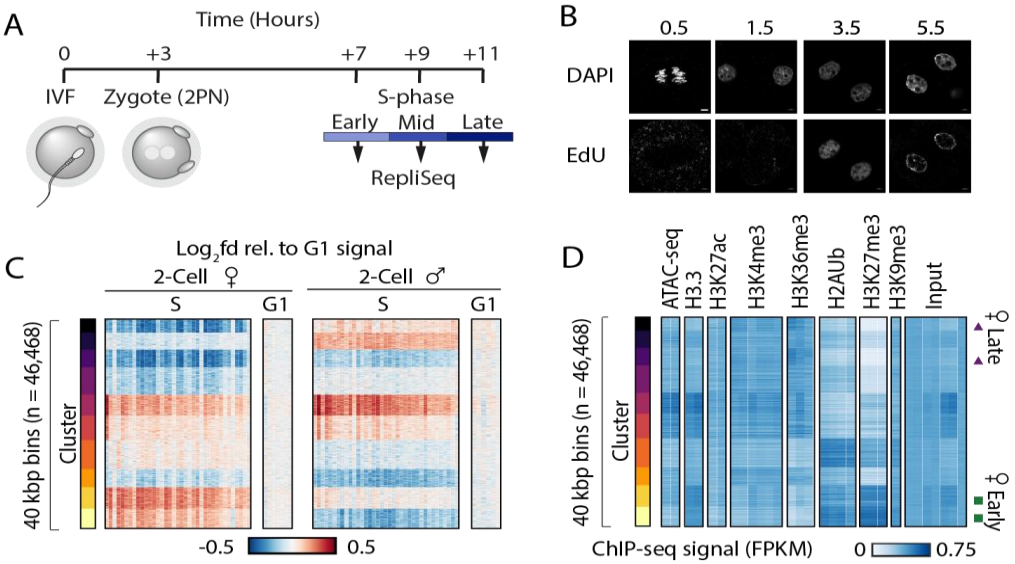

Figure 1: Re-starting life and DNA replication after fertilization. A. Set up of mouse embryo formation; B. Images of DNA (stained with DAPI) and newly replicated DNA (stained for EdU incorporation); C. DNA replication signals according to parent-of-origin (maternal to the left and paternal to the right) Red denotes upregulation and blue downregulation. Note the differences between the profiles in the maternal and paternal genomes. D. Replication timing and its correlation with different chromatin modifications.

A second highlight was the identification of new factors required for histone biosynthesis by the Mailand group (*Molecular Cell*, in press). This process was shown to strongly influence the cellular response to a class of widely used anticancer agents that target Topoisomerase II. This offers the promise of the development of improved therapeutic strategies for a wide range of cancers.

The CCS has also had continuing success in obtaining competitive grant awards in 2024. Most importantly, a consortium of scientists headed by Eva Hoffmann, and including CCS group leaders/affiliated group leaders Blackford, Lerdrup and Miller, secured funding from the DNRF to establish a new center of excellence focusing on fertility and inheritance, which is expected to open in the summer of 2025. Moreover, Niels Mailand was a co-applicant on a second successful DNRF Center application. That Center will also open in 2025 at the Danish Cancer Society laboratories.