

CCS Annual Report 2023

Summary

The overarching goal of the Center for Chromosome Stability (CCS) is to define how a breakdown in the maintenance of genome stability promotes human disease. Our studies are not focused on any specific disease; instead, we have interests in several pathological conditions that are caused, at least in part, by chromosome abnormalities. For example, we have ongoing studies on fertility and neurodegenerative disorders, as well as cancer. We aim both to understand the molecular basis for disease development and to use that knowledge to develop and/or improve treatments to combat the life-changing consequences of these diseases. In recent years, we have increasingly been studying the mechanisms by which the process of DNA replication (during which the genome is duplicated) can create mutations and rearrangements within chromosomal DNA. This is particularly relevant to the etiology of cancer because many of the oncogenes that are activated during neoplastic transformation perturb DNA replication through the creation of so-called DNA replication stress (RS). This RS, in turn, prevents certain problematic regions of the human genome from being replicated fully or faithfully, and this serves as a driver of cellular transformation. These problematic regions, which we term the ‘enemies within’ the genome, have been a focus of intensive study in the CCS from its inception.

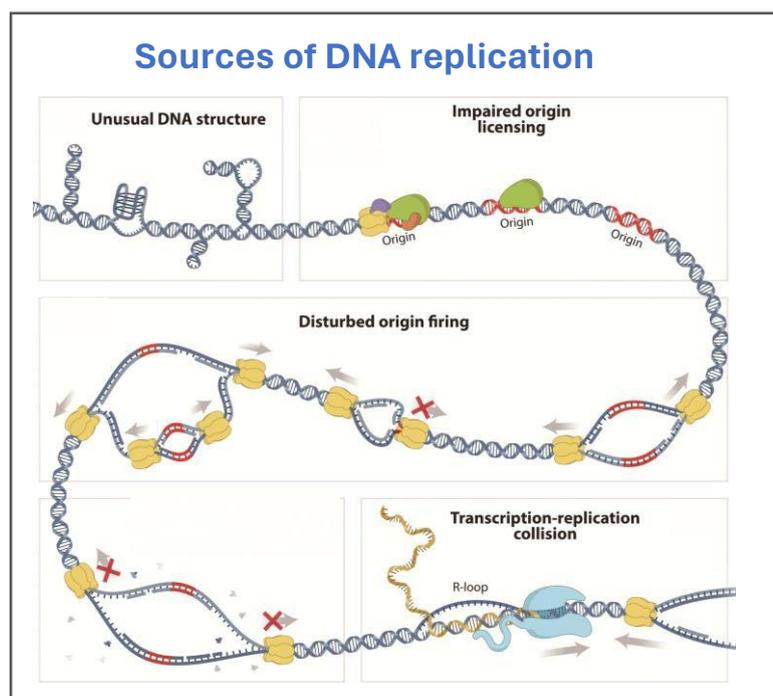


Figure 1: Depiction of a major topic under study in the CCS: the cellular response to perturbation of genome duplication (DNA replication). This process is frequently perturbed when the replication machinery encounters DNA lesions or DNA secondary structures, or when replication comes into conflict with the transcription machinery simultaneously using the same DNA template.

The CCS has had a very successful year in 2023, with many notable achievements and developments. In recognition of the quality of his research over an extended period, the CCS Center Leader, Ian Hickson, was awarded the 2023 Kirsten and Freddy Johansen Prize for outstanding achievements in medical science. Several articles in the very highest impact international journals have also been published and, gratifyingly, many of these have involved collaborations within the CCS or ICMM. Moreover, success with obtaining competitive grant awards has also been a strong

feature of 2023. Most notably, Michael Lisby was awarded a grant of over 16 mio DKK from the Carlsberg Foundation, while several CCS PIs obtained grants from the Novo Nordisk Foundation, the Neye Foundation, Lundbeck or the Danish Council for Independent Research. Moreover, a consortium of ICMM PIs, including Ian Hickson and Tom Miller from the CCS, also obtained an infrastructure grant from the Carlsberg Foundation.