Highlights of 2020

The Center for Chromosome Stability (CCS) aims to define how cells preserve the integrity of their genome, with a particular focus on how human health is compromised when chromosomal DNA damage is not repaired efficiently. We adopt a multidisciplinary approach to addressing this issue by combining cell biological, genetic, biochemical and organismal systems in our research. One major focus that bridges studies conducted by all of the CCS groups is a study of how the human genome is duplicated (DNA replication) and how perturbation of this process drives genomic instability (Figure 1). Ultimately, the aim is to develop new strategies for the prevention and/or treatment of human disease.

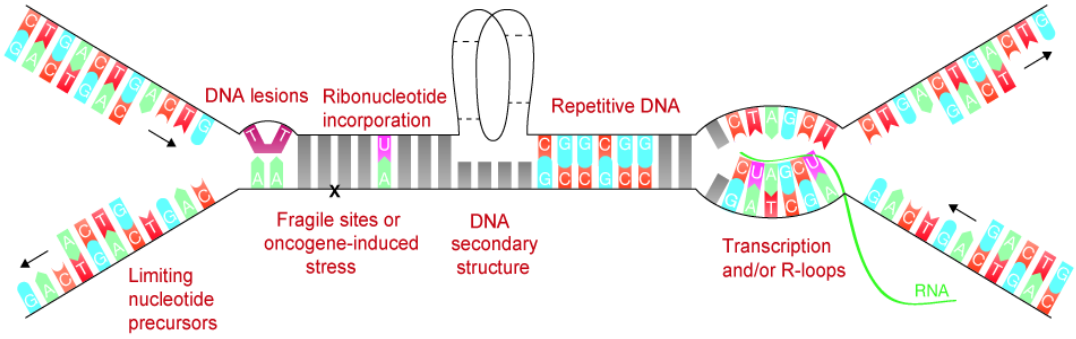

Figure 1: *Graphical depiction of one of the major topics under study in the CCS: the cellular response to perturbation of DNA replication. This process can be perturbed by several factors, including the replication machinery encountering DNA lesions, secondary structures or the transcription machinery simultaneously using the same DNA template.*

The CCS has succeeded in generating several major research findings in 2020, despite the disruption caused by the ongoing pandemic. Our publication output has been impressive, with nine papers in Nature series or Cell Press journals. Gratifyingly, we have again generated several major publications that reflect successful collaborations involving at least two CCS groups. The successful analysis of chromosomal fragile sites (inherently unstable loci in the human genome) has continued in 2020 with several major findings published in high impact journals. We fulfilled one of our key original aims in defining, at high resolution, the location of all fragile sites in the human genome (Macheret/Bhowmick et al. **Cell Res.** [1]). This has opened the way to numerous future studies on defining the molecular basis of chromosome fragility. This work, coupled with two other successful projects on defining why fragile sites exist in the human genome (Wu/Bhowmick et al., **Nature Struct. Molec. Biol.**, [2] and Garribba/Bjerregaard et al., **P.N.A.S**. [3]) has highlighted the key role played by RNA transcription in interfering with the faithful duplication of the genome, and hence being a major driver of fragility.

Our highly successful program to understand the molecular basis of genome instability in the human germline has continued. We revealed in 2020 the importance of epigenetic changes in oocytes for the successful development of the zygote (Sankar/Lerdrup/Manaf et al. **Nature Cell Biol**. [4]). Other notable achievements by the CCS in 2020 include: (i) identification of a novel protease that influences genome stability and human health (Hoffmann et al., **EMBO Rep**. [5]); (ii) Defining a role for the ZGR1 protein in supporting the process of DNA replication under stress conditions (Brannvoll et al., **Cell Rep**. [6]); (iii) Contributing to the discovery that perturbation of DNA replication causes non-random segregation of sister chromatids during mitosis (Xing et al., **Mol. Cell** [7]).

We congratulate CCS group leaders Eva Hoffmann and Andres Lopez-Contreras on being elected to membership of the European Molecular Biology Organization (EMBO), and on being awarded the Danish Cancer Society Junior Research Prize, respectively. Finally, we thank all of the staff at the CCS for contributing to the successful renewal of the CCS for a second funding period.