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Selected Publication

Chan, K.L., Palmai-Pallag, T., Ying, S., & Hickson, I.D. (2009) Replication stress induces sister-chromatid bridging at fragile site loci in mitosis. *Nature Cell Biology* 11:753-760

Research Aims and Interests

The continuity of life requires accurate inheritance and maintenance of genetic information from generation to generation. Our group's research focuses to understand the molecular mechanism of faithful chromosome segregation under normal and challenging condition such as replication stress. It is well known that duplicated sister DNAs are mainly hold by a gigantic tripartite ring complex called cohesin until the onset of anaphase, but increasing evidence from our group and others showed that sister chromatids are indeed still intertwined by DNA structures like double-stranded DNA catenants and/or under-replication DNA intermediates (a product induced by replication stress), even after sister-chromatid separation. Both types of DNA entanglement generate a newly identified mitotic structure named ultrafine anaphase bridges (UFBs) and are unexpectedly recognised by various DNA repair complexes including Bloom's syndrome helicase and Fanconi anemia complex (FANCD2/I). It is still mysterious how cells disjoin these intertwining DNA structures and how their offspring cells repair the associated DNA lesions in the next cell cycle. We are therefore investigating the roles of DNA replication/repair machineries on chromosome segregation and on the repair of replication stress-induced damage. We also investigate the impact of the transgenerational DNA lesions on genome instability and cell pathophysiology. Our aim is to dissect the underlying mechanism of how replication stress may initiate and accelerate the evolution of cancer genomes, and to develop preventative and targeting therapies for cancers.