University of Basel

BIOZENTRUM
The Center for Molecular Life Sciences

Biozentrum Lectures

Reconstituting chromosome replication

John Diffley

Francis Crick Institute, Clare Hall Laboratory,
South Mimms, United Kingdom

Monday,
December 5, 2016
5.15 pm

John Diffley was born 1958 in New York (USA) and studied in his home town at New York University, where he received his BA and PhD. Following a period as a postdoctoral fellow at Cold Spring Harbor Laboratory in New York, he left for the UK in 1990. He continued his research at the Clare Hall Laboratories, where he became the Director in 2006. In the same year he was made Deputy Director of the London Research Institute, and in 2015 he became Associate Research Director at the Francis Crick Institute. John Diffley was elected as a member of the European Molecular Biology Organization (EMBO) and he is also a Fellow of the American Association for the Advancement of Science. He was awarded the Paul Marks Prize for cancer research in 2003, and the 2016 Louis-Jeantet Prize for Medicine.

John Diffley: Reconstituting chromosome replication

The eukaryotic cell cycle coordinates the accurate duplication and segregation of the genome during proliferation. The large genomes of eukaryotic cells are replicated from multiple replication origins during S phase. These origins are not activated synchronously at the beginning of S phase, but instead fire throughout S phase according to a pre-determined, cell type specific program.

Ensuring that each origin is efficiently activated once and only once during each S phase is crucial for maintaining the integrity of the genome. This is achieved by a two-step mechanism. The first step, known as licensing, involves the loading of MCM proteins into pre-replicative complexes at origins. In the second step, the MCM helicase is activated by a large set of "firing factors". These two steps are differentially regulated by cyclin dependent kinase (CDK): licensing is inhibited by CDK, whilst firing requires CDK. As a consequence, licensing can only happen during G1 phase, when CDK activity is low, and origin firing cannot occur during G1 phase.

We have recently described the reconstitution of the initiation of eukaryotic DNA replication with purified proteins. I will present recent results on the reconstitution of the entire replisome and describe how chromatinised templates are replicated *in vitro*, how nucleosomes displaced during replication are re-deposited on nascent DNA, and how chromatin influences DNA replication origin choice and lagging strand synthesis.

December 5, 2016, 5.15 pm,
Hörsaal 1, Pharmazentrum,
Klingelbergstrasse 50/70, Basel

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