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Selected Publication

Garg M, Gurung RL, Mansoubi S, Ahmed JO, Davé A, Watts FZ, Bianchi A (2014) Tpz^{1TPP1} SUMOylation reveals evolutionary conservation of SUMO-dependent Stn1 telomere association. *EMBO Rep* 15: 871-877

Research Aims and Interests

The Bianchi laboratory at the GDSC studies telomere function in two broad areas: how the telomeric complex assists telomere replication (by both telomerase and the conventional DNA replication machinery) and how it ensures chromosome protection.

We are interested in the interdependence between the general process of DNA replication and telomerase action. We have discovered unexpected links between the two processes and have found that in buddying yeast telomere length affects the timing of firing of subtelomeric origins of DNA replication, though the activity of the yeast ortholog of the ATM checkpoint kinase, Tel1. This length-dependent effect operates independently of the well-known regulator DNA replication Rif1, originally identified as a telomere protein. Our analysis, in buddying and fission yeast, has revealed that Rif1 instead affects replication timing by recruiting the PP1 phosphatase and reversing DDK-dependent MCM phosphorylation. Telomerase-dependent telomere replication and conventional DNA replication are further interconnected as telomerase carries out G-rich strand elongation while DNA polymerases ensure synthesis of the complementary C-strand. We have uncovered a mechanism in fission yeast which we propose regulates the coordination of G and C-strand synthesis at telomeres through the Pli1-dependent SUMOylation of telomere protein Tpz1. Current interests in the laboratory in this area aim at elucidating the molecular events leading to coordinated G- and C-strand synthesis at telomeres and how telomeric proteins might control both telomere DNA replication and telomerase function by assisting replication fork progression through telomeric DNA.

With regard to telomere protection, we are currently investigating, in a number of model systems, how telomeric proteins keep the activity of the MRN complex in check at telomeres. Although the MRN complex is generally recruited to telomeres, where it might contribute to telomerase action, its role in promoting the activity of the ATM kinase is curtailed at this location. We are currently testing the idea that a specific protein motif found in some

telomeric proteins mediates modulation of MRN activity at telomeres.