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Selected Publication

Xie S, Mortusewicz O, Ma HT, Herr P, Poon R, Helleday T, Qian C. (2015) Timeless Interacts with PARP-1 to Promote Homologous Recombination Repair. *Molecular Cell*. 60(1): 163-176.

Research Aims and Interests

One of our research interests is to understand the molecular mechanism mediating the response to replication stress. Replication stress caused by various endogenous and exogenous genotoxic agents can lead to genome instability that has been considered as a hallmark of cancer. My lab applies an integrative structural biology approach to gain molecular insights into the mechanism of cellular response to DNA damage and the implication in cancer treatment.

We have recently identified that human Timeless - the subunit of replication fork protection complex, physically interacts with PARP-1 that is independent of poly(ADP-ribosyl)ation. We present high-resolution crystal structures of Timeless PAB (PARP-1-Binding domain) in free form and in complex with PARP-1 catalytic domain. Interestingly, Timeless PAB domain specifically recognizes PARP-1 but not other PARP family members. Timeless-PARP-1 interaction does not interfere with PARP-1 enzymatic activity. We demonstrate that rapid and transient accumulation of Timeless at laser-induced DNA damage sites requires PARP-1 but not poly(ADP-ribosyl)ation and that Timeless is co-trapped with PARP-1 at DNA lesions upon PARP inhibition. Furthermore, we show that Timeless and PARP-1 interaction is required for efficient homologous recombination repair.