Mark D Sutton, Mol Biol 2018, Volume 7
DOI: 10.4172/2168-9547-C2-005

3rd International Conference on
Molecular Biology & Nucleic Acids
August 27-28, 2018 | Toronto, Canada

Mechanism underlying the coordination of high fidelity replication with mutagenesis translesion synthesis

Mark D Sutton
University at Buffalo, USA

Statement of the Problem: Replicative polymerases (Pols), such as *E. coli* Pol III, cannot replicate past most DNA lesions, leading to stalled replication forks. Organisms have therefore evolved specialized Pols that function in translesion DNA synthesis (TLS), a mechanism that bypasses DNA lesions and permits continued replication. Recent evidence supports the view that TLS Pol IV switches with the replicative *E. coli* Pol III to coordinate replication with lesion bypass. As part of this mechanism, genetic evidence and in silico modeling suggests that direct interactions of both Pols with clamp and each other are required for switching. In previous work, a Pol IV mutant bearing a T120P substitution (Pol IV-T120P) was impaired for the Pol III-Pol IV switch. Here we show Pol IV is capable of directly interacting with Pol III core (αεθ), including the Pol IIIα catalytic and the Pol IIIεθ proofreading subassemblies. Biochemical evidence suggests Pol IV binds two distinct sites on both Pol IIIα and the Pol IIIεθ. Further, Pol IV-T120P is impaired for these interactions as only a single binding site between Pol IV-T120P-Pol IIIα and Pol IV-Pol IIIεθ was identified. Mutagenesis of the region surrounding T120 and subsequent analysis in a genetic assay suggests a distinct surface on Pol IV is required to displace Pol III during the Pol III-Pol IV switch. Additionally, we have identified a novel interaction between the β clamp and Pol IV. Taken together, these results support a new model for the Pol III-Pol IV switching mechanism. Interestingly, Pol-Pol interactions are not unique to Pol III-Pol IV, as Pol-Pol interactions were also identified among other *E. coli* Pols, suggesting a fundamental role for these interactions in Pol switching.

Biography

Mark Sutton has expertise in DNA replication, DNA repair, and DNA damage tolerance. He uses a combination of genetic and biochemical approaches to understand the coordination of these functions with a focus on defining the mechanisms underlying the coordination of the actions of replicative, repair and translesion synthesis DNA polymerases.

mdsutton@buffalo.edu

Notes: