GENETIC AND BIOCHEMICAL ANALYSIS OF TRANSLESION SYNTHESIS: INVOLVEMENT OF ALL THREE SOS-INDUCIBLE DNA POLYMERASES (POL II, POL IV AND POL V) IN INDUCED MUTAGENESIS.

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A new class of DNA polymerases (the UmuC/DinB family) involved in mutagenesis was discovered recently in bacteria, yeast and mammalian cells. In E. coli, three DNA polymerases, Pol II (polB) and the recently discovered Pol IV (dinB) and Pol V (umuC), are induced as part of the SOS system, a coordinated cellular response to environmental stress. While the umuDC gene products were known to be required for base substitution mutagenesis triggered by UV light or abasic sites, the roles of Pol II and Pol IV in damage induced mutagenesis have not yet been established. Here, we show that while DNA Pol II and DNA Pol V are necessary and sufficient for -2 and -1 frameshift mutagenesis induced by the chemical carcinogen N-2-acetylaminofluorene respectively, benzo(a)pyrene induced -1 frameshift mutagenesis requires both DNA Pol IV and V. Thus, in response to the vast diversity of existing DNA damages, the cell uses a pool of specialised DNA polymerases in order to perform translesion synthesis.

At the biochemical level, both Pol IV and V share with their homologues a low processivity as well as a lack of 3’ to 5’ proofreading activity. Together with the in vitro demonstrations that these polymerases possess a clear propensity to elongate distorted primer/template structures these findings led to a new paradigm for mutagenesis called the DNA polymerase switch. Briefly, translesional DNA
polymerases are thought to be temporarily recruited at the site where the replisome has stalled allowing thus translesional synthesis to occur before highly accurate and processive replication resumes by means of the replicative polymerase. We show here that the activity of native Pol IV is drastically modified by the β clamp, the processivity factor of the replicative DNA polymerase III. In the absence of β, Pol IV is strictly distributive and no stable Pol IV/DNA complexes could be observed. In contrast, β clamp allows Pol IV to form a stable initiation complex (t1/2=2.3 min.) which leads to a dramatic increase in the processivity of Pol IV reaching an average of 300-400 nucleotides. In vivo, the β clamp may thus target Pol IV to its substrate, generating synthesis tracks much longer than previously thought.

References:

The dinB gene encodes a novel E. coli DNA Polymerase (DNA Pol IV) involved in mutagenesis.
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All three SOS-inducible DNA Polymerases (Pol II, Pol IV and Pol V) are involved in induced mutagenesis.
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