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Expression and function of the mutator DNA polymerasencoding umuC-like genes in mycobacteria

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ABSTRACT

Mycobacterium tuberculosis is an important human pathogen, claiming more lives per annum than any other single infectious organism. The host environment of *M. tuberculosis* contains DNA-damaging agents that pose a constant threat to the *M. tuberculosis* genome, and as a result, the ability to repair damaged DNA is likely to play an important role in bacterial survival. Y-family polymerases perform translesional synthesis and replicate DNA in an error-prone manner. By characterising the Y-family polymerases in mycobacteria, a better understanding the organism's adaptive mutagenesis may be established.

Through gene expression studies, it was found that UV irradiation of *Mycobacterium smegmatis* resulted in the up-regulation of *dinP3*, which was determined to be a Y-family polymerase by sequence analysis. *DinP3* expression was found to be under control of the SOS response and is the first example of a Y-family polymerase in mycobacteria forming part of the SOS regulon. However, loss of DinP3 did not change the ability of *M. smegmatis* to tolerate UV irradiation. Mutagenesis studies revealed a complex interaction between the different Y-family polymerases in *M. smegmatis*. It was shown that spontaneous mutagenesis was increased in the absence of DinP3, whereas UV-targeted mutagenesis was increased in the absence of DinP, another Y-family polymerase.

In conclusion, these results reflect the differences in control and in the mutational profiles of the Y-family polymerases in *M. smegmatis*. Moreover, these polymerases exhibit distinctive features from other bacterial Y-family polymerases, highlighting the different way in which bacteria have adapted to deal with lesions in their genetic material.