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Author: Upasana Roy Orlando D. Schärer

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Involvement of Translesion Synthesis DNA Polymerases in DNA Interstrand Crosslink Repair

Upasana Roy[1] and Orlando D. Schärer[1,2*]

1. Department of Chemistry, 2. Department of Pharmacological Sciences, Stony Brook University, Stony Brook, NY 11794-3400, USA.

*To whom correspondence should be addressed: Tel: +1-631-632-7545; Email: orlando.scharer@stonybrook.edu

ABSTRACT

DNA interstrand crosslinks (ICLs) covalently join the two strands of a DNA duplex and block essential processes such as DNA replication and transcription. Several important anti-tumor drugs such as cisplatin and nitrogen mustards exert their cytotoxicity by forming ICLs. However, multiple complex pathways repair ICLs and these are thought to contribute to the development of resistance towards ICL-inducing agents. While the understanding of many aspects of ICL repair is still rudimentary, studies in recent years have provided significant insights into the pathways of ICL repair. In this perspective we review the recent advances made in elucidating the mechanism of ICL repair with a focus on the role of TLS polymerases. We describe the emerging models for how these enzymes contribute to and are regulated in ICL repair, discuss the key open questions and examine the implications for this pathway in anti-cancer therapy.