DNA nucleases bind monoubiquitinated ID2 complex

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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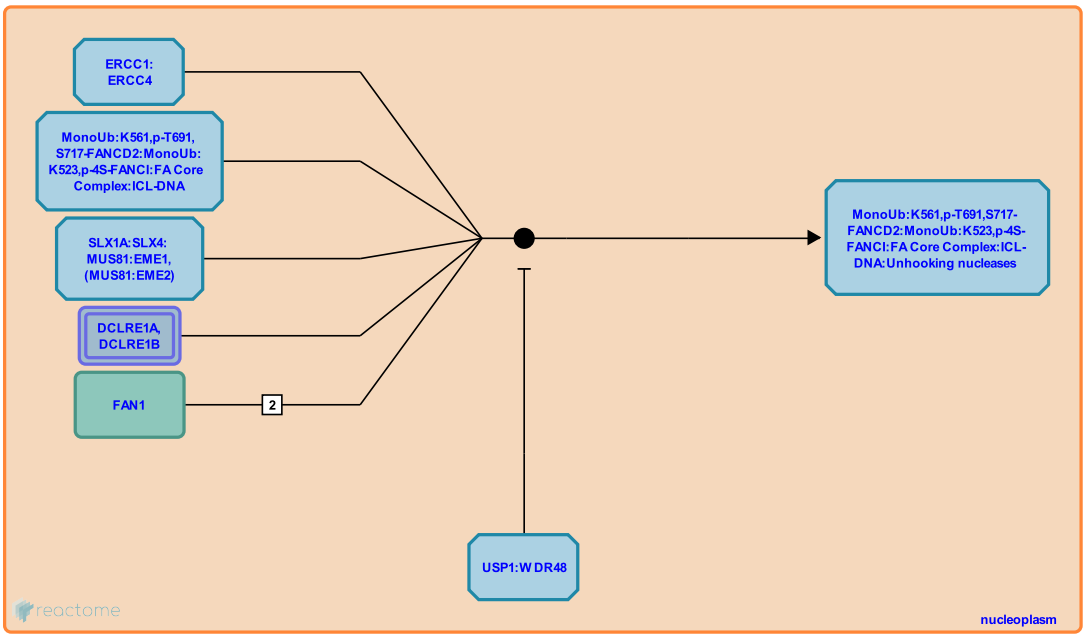
Stable identifier: R-HSA-6785732

Type: binding

Compartments: nucleoplasm



Several DNA nucleases bind to interstrand crosslinks (ICL-DNA) and participate in ICL "unhooking". The ubiquitin-binding zinc finger (UBZ) domain of the DNA nuclease FAN1 binds to monoubiquitinated FANCD2, enabling the recruitment of FAN1 to the ICL-DNA repair site (Liu et al. 2010, MacKay et al. 2010, Smogorzewska et al. 2010, Kratz et al. 2010). Once recruited to ICL-DNA, FAN1 forms head-to-tail homodimers. Homodimerization is important for the endonucleolytic activity of FAN1 (Zhao et al. 2014). SLX4 (FANCP) serves as a docking platform for recruitment of SLX1A, MUS81 and EME1 or EME2, resulting in formation of the SLX1A:SLX4:MUS81:EME1 (or SLX1A:SLX4:MUS81:EME2) endonucleolytic complex (Fekairi et al. 2009, Wyatt et al. 2013). SLX4 can also bind the endonucleolytic complex composed of ERCC1 and ERCC4 (XPF) (Fekairi et al. 2009). SLX4 is recruited to ICL-DNA through interaction of the UBZ domain of SLX4 with monoubiquitinated FANCD2 (Yamamoto et al. 2011). Targeted deletion of the UBZ domain of SLX4 confers sensitivity to ICL-inducing agents, but the UBZ domain seems to be dispensable for the role of SLX4 in homologous recombination repair (Yamamoto et al. 2011).

DNA exonucleases DCLRE1A (SNM1A) and DCLRE1B (SNM1B) likely function redundantly in ICL repair. Similar to FAN1, they are able to digest the DNA past the ICL, thereby unhooking one of the DNA strands (Wang et al. 2011, Sengerova et al. 2012). Monoubiquitination of the PCNA subunit of the stalled replicative polymerase complex by RAD18 may provide the docking site for DCLRE1A (or DCLRE1B) (Yang et al. 2010). In addition, PIAS1 may facilitate loading of DCLRE1A (or DCLRE1B) to ICL sites (Ishiai et al. 2004).

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Editions

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