ATR phosphorylates RPA2, FANCI, FANCD2 and FANCM at ICL-DNA

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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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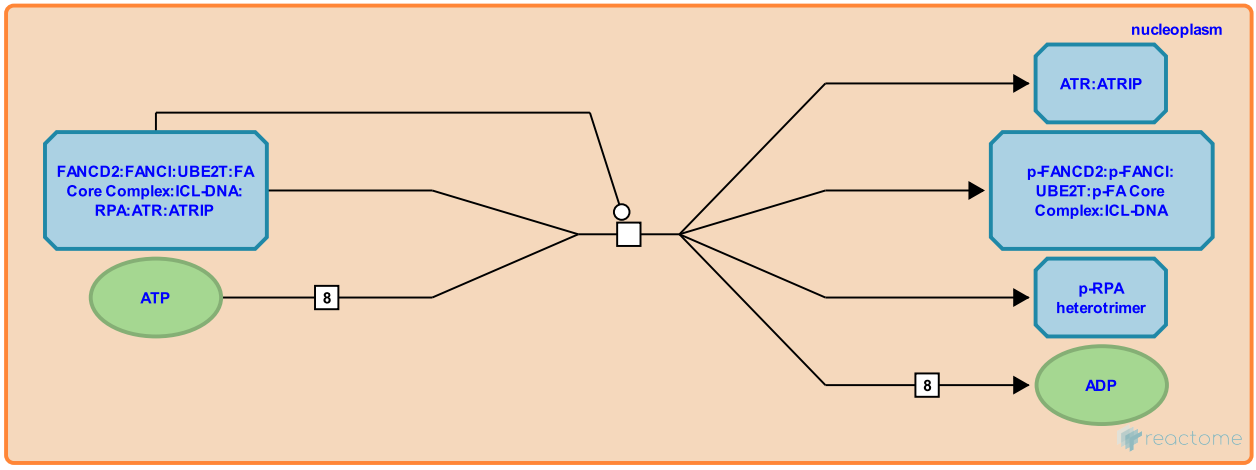
Stable identifier: R-HSA-6788392

Type: transition

Compartments: nucleoplasm



ATR phosphorylates several proteins at DNA insterstrand crosslinks (ICL-DNA), with ATR activity at ICL-DNA being independent of the presence of RAD17 and TOPBP1 (Shigechi et al. 2012, Tomida et al. 2013). Besides phosphorylating the RPA2 subunit of the RPA heterotrimeric complex (Huang et al. 2010), activated ATR also phosphorylates the Fanconi anemia core complex component FANCM on serine residue S1045 (Singh et al. 2013). ATR-mediated phosphorylation of FANCM is thought to be important for the progression of ICL repair, although the mechanism is not known. The critical ATR substrate at ICL-DNA is considered to be FANCI component of the ID2 complex. ATR-mediated phosphorylation of FANCI, at least on serine residues S556, S559, S565 and S617, is a prerequisite for FANCD2 monoubiquitination (Ishiai et al. 2008, Shigechi et al. 2012). FANDC2 itself is also phosphorylated by ATR on threonine residue T691 and serine residue S717, which promotes FANCD2 monoubiquitination and enhances cellular resistance to DNA crosslinking agents (Ho et al. 2006).

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