reactome

XPC:RAD23:CETN2 and UV-DDB bind distorted dsDNA site

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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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Reactome database release: 77

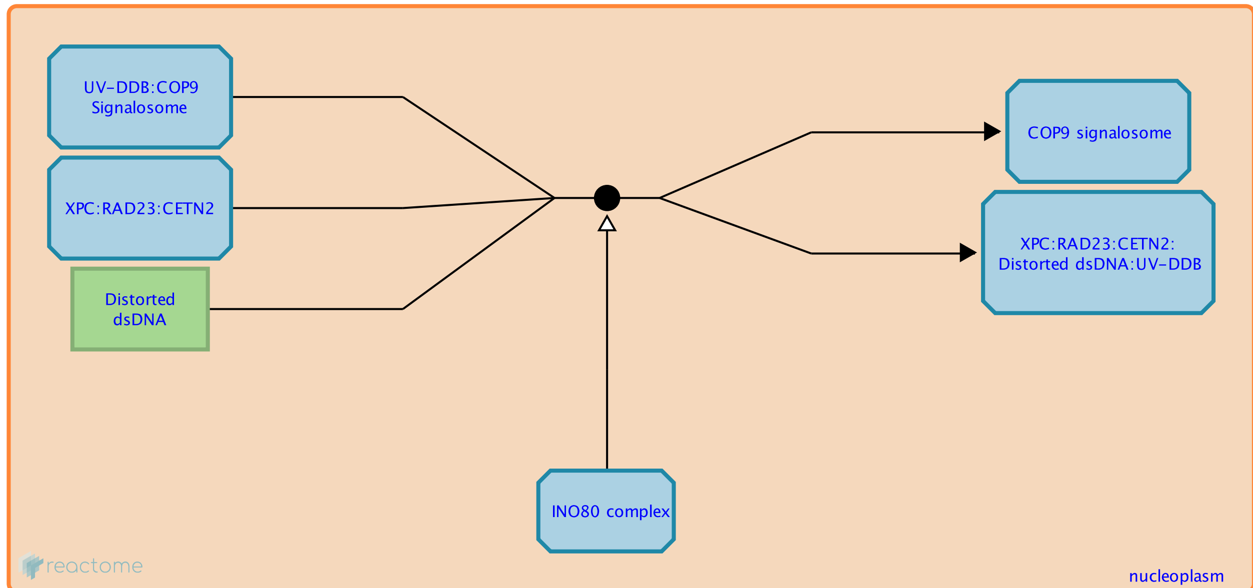
This document contains 1 reaction (see Table of Contents)

XPC:RAD23:CETN2 and UV-DDB bind distorted dsDNA site ↗

Stable identifier: R-HSA-5691006

Type: binding

Compartments: nucleoplasm



XPC, in complex with RAD23B or RAD23A and CETN2, employs a two-stage process to recognize a distorted DNA helix. In the first stage, XPC rapidly probes dsDNA, which is promoted by a DNA repulsive action of a negatively charged beta-turn extension of XPC, located in the vicinity of the XPC DNA-binding domain. In the second stage, the DNA binding domain, consisting of two beta hairpins, binds non-hydrogen bonded bases in dsDNA (Camenisch et al. 2009). Rad4, the yeast ortholog of XPC, recognizes lesions that thermodynamically disrupt normal Watson-Crick base pairing. Rad4 inserts a beta-hairpin through the DNA duplex, causing damaged base pairs to flip out of the double helix. Rad4 associates with the undamaged strand, whereas the DNA strand that contains damaged nucleotides becomes distorted (Min and Pavletich 2007).

Binding of the XPC:RAD23:CETN2 complex to distorted DNA is enhanced in the presence of the DDB1:DDB2 complex, also known as the UV-DDB complex. The UV-DDB complex preferentially binds UV-generated lesions, such as pyrimidine-pyrimidone photodimers (6-4 PPDs) and cyclobutane pyrimidine dimers (CPDs), but also recognizes DNA with apurinic/apyrimidinic (AP) sites, and 2-3 bp mismatches (Fujiwara et al. 1999, Wittschieben et al. 2005). The DDB2 subunit of the UV-DDB complex is a WD40 repeat beta-propeller protein. The beta-propeller domain of DDB2 binds the damaged DNA strand (Scrima et al. 2008). The UV-DDB complex is part of a larger ubiquitin ligase complex that, besides DDB1 and DDB2, also contains CUL4A or CUL4B and RBX1 (Groisman et al. 2003, Sugasawa et al. 2005). In the case of 6-4 PPDs and CPDs, UV-DDB binding to damaged DNA probably precedes the binding of the XPC:RAD23:CETN2 complex. However, in the case of 6-4 PPDs, the XPC:RAD23:CETN2 complex may also recognize damaged DNA in the absence of the UV-DDB complex (Fitch et al. 2003, Moser et al. 2005, Wang et al. 2004), but the UV-DDB complex may be important for retention of DNA repair proteins at the DNA damage site (Oh et al. 2011).

The INO80 chromatin remodelling complex positively regulates GG-NER. INO80 and ACTR5 (ARP5) subunits of the INO80 complex are enriched at GG-NER sites, probably via interaction with DDB1. Chromatin relaxation by the INO80 complex at DNA damage site may be necessary for XPC recruitment (Jiang et al. 2010). In yeast, the interaction between INO80 and the orthologs of XPC and RAD23 has been reported

and it was suggested that this interaction is important for the restoration of chromatin structure after GG-NER completion (Sarkar et al. 2010).

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Editions

2004-01-29	Authored	Hoeijmakers, JH.
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