Formation of TC-NER Pre-Incision 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


Reactome database release: 72

This document contains 1 pathway and 7 reactions (see Table of Contents)
Formation of TC-NER pre-incision complex is initiated when the RNA polymerase II (RNA Pol II) complex stalls at a DNA damage site. The stalling is caused by misincorporation of a ribonucleotide opposite to a damaged base (Brueckner et al. 2007). Cockayne syndrome protein B (ERCC6, CSB) binds stalled RNA Pol II and recruits Cockayne syndrome protein A (ERCC8, CSA). ERCC8 is part of an ubiquitin ligase complex that also contains DDB1, CUL4A or CUL4B and RBX1. This complex is implicated in the regulation of TC-NER progression probably by ubiquitinating one or more factors involved in this pathway, which may include RNA Pol II and ERCC6 at the later stages of repair (Bregman et al. 1996, Fousteri et al. 2006, Grossman et al. 2006). XPA is recruited to the TC-NER site through its interaction with the TFIIH complex (Furuta et al. 2002, Ziani et al. 2014). The XAB2 complex, which probably regulates the accessibility of the DNA damage site through its RNA-DNA helicase activity, binds the TC-NER site via the interaction of its XAB2 subunit with RNA Pol II, ERCC6, ERCC8 and XPA (Nakatsu et al. 2000, Sollier et al. 2014). TCEA1 (TFIIS) is a transcription elongation factor that may facilitate backtracking of the stalled RNA Pol II, enabling access of repair proteins to the DNA damage site and promotes partial digestion of the 3' protruding end of the nascent mRNA transcript by the backtracked RNA Pol II, allowing resumption of RNA synthesis after damage removal (Donahue et al. 1994). Access to DNA damage site is also facilitated by chromatin remodelers HMGN1 (recruited to the TC-NER site through RNA Pol II and ERCC8-dependent manner) and histone acetyltransferase p300 (EP300), recruited to the TC-NER site through ERCC6-dependent manner (Birger et al. 2003, Fousteri et al. 2006). UVSSA protein interacts with ubiquitinated ERCC6 and RNA Pol II, recruiting ubiquitin protease USP7 to the TC-NER site and promoting ERCC6 stabilization (Nakazawa et al. 2012, Schwertman et al. 2012, Zhang et al. 2012, Fei and Chen 2012).

**Literature references**


**Editions**

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RNA Pol II initiates transcription from damaged DNA template

Location: Formation of TC-NER Pre-Incision Complex

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