Translesion synthesis by REV1

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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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 73

This document contains 1 pathway and 5 reactions (see Table of Contents)
REV1 (hREV1) encodes a template-dependent dCMP transferase that can insert a C residue opposite an abasic site (Lin et al. 1999, Gibbs et al. 2000). Interaction with monoubiquitinated PCNA at a DNA damage site enhances REV1-mediated translesion synthesis (TLS) (Garg and Burgers 2005, Wood et al. 2007). After REV1 incorporates dCMP opposite to the apurinic/apyrimidinic (AP) template site, TLS is continued by the DNA polymerase zeta complex (POLZ). POLZ consists of the catalytic subunit REV3L and the accessory subunit MAD2L2 (REV7). MAD2L2 binds REV1, thus recruiting POLZ to DNA damage site (Hara et al. 2010, Kikuchi et al. 2010, Xie et al. 2012). POLZ is error-prone and contributes to TLS-related mutagenesis (Shachar et al. 2009, Lee et al. 2014). POLZ has a low processivity and dissociates from the DNA template after incorporating less than 30 nucleotides (Nelson et al. 1996, Lee et al. 2014).

**Literature references**


**Editions**

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**REV1 binds AP-dsDNA**

**Location:** Translesion synthesis by REV1

**Stable identifier:** R-HSA-110307

**Type:** binding

**Compartments:** nucleoplasm

REV1 is a deoxycytidyl transferase that belongs to the DNA polymerase type-Y family. REV1 was cloned as the human homolog of yeast REV1. Similar to its yeast counterpart, REV1 binds damaged DNA, with the preferred substrate being DNA with an AP (abasic - apurinic/apyrimidinic) site. The mechanism for DNA damage recognition has not been elucidated (Lin et al. 1999, Gibbs et al. 2000). Besides DNA binding, REV1 has a ubiquitin binding motif in its C-terminal domain that interacts with monoubiquitinated PCNA, which enhances REV1-mediated translesion synthesis (Garg and Burgers 2005, Wood et al. 2007).

**Followed by:** REV1 inserts dCMP opposite to AP sites in DNA

**Literature references**


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REV1 inserts dCMP opposite to AP sites in DNA

**Location:** Translesion synthesis by REV1

**Stable identifier:** R-HSA-110308

**Type:** transition

**Compartments:** nucleoplasm

REV1 acts as a deoxycytidyl transferase to incorporate a single dCMP opposite a damaged DNA residue. REV1 most efficiently incorporates dCMP opposite apurinic/apyrimidinic (AP, abasic) sites. REV1 enables DNA damage bypass without repair of damaged DNA bases, but its low fidelity results in a mutagenic effect (Nelson et al. 1996, Lin et al. 1999, Gibbs et al. 2000, Zhang et al. 2002).

**Preceded by:** REV1 binds AP-dsDNA

**Followed by:** REV1 recruits POLZ to (AP:Cyt)-DNA Template

**Literature references**


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REV1 recruits POLZ to (AP:Cyt)-DNA Template

**Location:** Translesion synthesis by REV1

**Stable identifier:** R-HSA-5652151

**Type:** binding

**Compartments:** nucleoplasm

REV1, bound to the replication complex, recruits DNA polymerase zeta (POLZ, REV3L:MAD2L2) to the damaged DNA template. REV3L does not bind REV1 directly. Instead, REV3L binding to MAD2L2 (REV7) during the formation of POLZ complex causes a conformational change in MAD2L2 that allows the C-terminal domain of MAD2L2 to bind the C-terminus of REV1 (Nelson et al. 1996, Hara et al. 2010, Kikuchi et al. 2012, Xie et al. 2012)

**Preceded by:** REV1 inserts dCMP opposite to AP sites in DNA, Formation of Pol zeta complex

**Followed by:** POLZ extends translesion synthesis

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Formation of Pol zeta complex

**Location:** Translesion synthesis by REV1

**Stable identifier:** R-HSA-110322

**Type:** binding

**Compartments:** nucleoplasm

REV3L (hREV3), the catalytic subunit of DNA polymerase zeta (POLZ) belonging to B family of DNA polymerases, binds the adapter protein MAD2L2 (hREV7) to form a functional POLZ complex (Murakamo et al. 2000, Murakamo et al. 2001, Hara et al. 2010).

**Followed by:** REV1 recruits POLZ to (AP:Cyt)-DNA Template

**Literature references**


After REV1 inserts a nucleotide directly opposite the template lesion, translesion synthesis (TLS) is continued by DNA polymerase zeta (POLZ), a complex of REV3L and MAD2L2 (REV3 and REV7 in yeast) (Nelson et al. 1996a, Neal et al. 2010). POLZ is a poorly processive enzyme in both yeast and humans and usually incorporates less than 30 nucleotides before it dissociates from the template. In human cells, the processivity of POLZ is increased in the presence of DNA polymerase delta (POLD) subunits POLD2 and POLD3, which act as accessory subunits for POLZ (Nelson et al. 1996b, Lee et al. 2014). POLZ is error-prone, especially in the context of TLS across AP (apurinic/apyrimidinic) sites, resulting in incorporation of mispaired dNTPs, which contributes to TLS-related mutagenesis (Shachar et al. 2009, Lee et al. 2014).

**Preceded by:** REV1 recruits POLZ to (AP:Cyt)-DNA Template

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