Resolution of Abasic Sites (AP sites)

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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 5 pathways and 1 reaction (see Table of Contents)
Resolution of Abasic Sites (AP sites)

Stable identifier: R-HSA-73933

Compartments: nucleoplasm

Resolution of AP sites can occur through the single nucleotide replacement pathway or through the multiple nucleotide patch replacement pathway, also known as the long-patch base excision repair (BER). Except for the APEX1-independent resolution of AP sites via single nucleotide base excision repair mediated by NEIL1 or NEIL2 (Wiederhold et al. 2004, Das et al. 2006), single nucleotide and multiple-nucleotide patch replacement pathways are both initiated by APEX1-mediated displacement of DNA glycosylases and cleavage of the damaged DNA strand by APEX1 immediately 5' to the AP site (Wilson et al. 1995, Bennett et al. 1997, Masuda et al. 1998). The BER proceeds via the single nucleotide replacement when the AP (apurinic/apyrimidinic) deoxyribose residue at the 5' end of the APEX1-created single strand break (SSB) (5'dRP) can be removed by the 5'-exonuclease activity of DNA polymerase beta (POLB) (Bennett et al. 1997). POLB fills the created single nucleotide gap by adding a nucleotide complementary to the undamaged DNA strand to the 3' end of the SSB. The SSB is subsequently ligated by DNA ligase III (LIG3) which, in complex with XRCC1, is recruited to the BER site by an XRCC1-mediated interaction with POLB (Kubota et al. 1996). BER proceeds via the multiple-nucleotide patch replacement pathway when the AP residue at the 5' end of the APEX1-created SSB undergoes oxidation-related damage (5'ddRP) and cannot be cleaved by POLB (Klungland and Lindahl 1997). Long-patch BER can be completed by POLB-mediated DNA strand displacement synthesis in the presence of PARP1 or PARP2, FEN1 and DNA ligase I (LIG1) (Prasad et al. 2001). When the PCNA-containing replication complex is available, as is the case with cells in S-phase of the cell cycle, DNA strand displacement synthesis is catalyzed by DNA polymerase delta (POLD) or DNA polymerase epsilon (POLE) complexes, in the presence of PCNA, RPA, RFC, APEX1, FEN1 and LIG1 (Klungland and Lindahl 1997, Dianova et al. 2001). It is likely that the 9-1-1 repair complex composed of HUS1, RAD1 and RAD9 interacts with and coordinates components of BER, but the exact mechanism and timing have not been elucidated (Wang et al. 2004, Smirnova et al. 2005, Guan et al. 2007, Balakrishnan et al. 2009).
Literature references


Editions

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Displacement of DNA glycosylase by APEX1

Location: Resolution of Abasic Sites (AP sites)

Stable identifier: R-HSA-110357

Compartments: nucleoplasm

Following cleavage of the damaged base, DNA glycosylase is displaced by APEX1, an AP endonuclease (Parikh et al. 1998).

Literature references


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APEX1 mediates endonucleolytic cleavage at the 5' side of the AP site

Location: Resolution of Abasic Sites (AP sites)

Stable identifier: R-HSA-110359