Global Genome Nucleotide Excision Repair

(GG-NER)

Fousteri, M., Gopinathrao, G., Hoeijmakers, JH., Joshi-Tope, G., Orlic-Milacic, M.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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: 68

This document contains 5 pathways (see Table of Contents)
The DNA damage in GG-NER is recognized by the joint action of two protein complexes. The first complex is composed of XPC, RAD23A or RAD23B and CETN2. The second complex, known as the UV-DDB complex, is an ubiquitin ligase composed of DDB1, CUL4A or CUL4B, RBX1 and a GG-NER specific protein DDB2. In vitro, the UV-DDB complex is only necessary for GG-NER mediated repair of UV-induced pyrimidine dimers. In vivo, however, where DNA repair occurs in the chromatin context, the UV-DDB complex likely facilitates GG-NER mediated repair irrespective of the DNA damage type.

After DNA damage recognition, the TFIIH complex, together with XPA, verifies the DNA damage and unwinds the DNA helix around the damage, creating an open bubble. Two DNA endonucleases, ERCC5 (XPG) and the complex of ERCC1 and ERCC4 (XPF), excise the oligonucleotide that contains damaged base(s) from the affected DNA strand. DNA polymerases delta, epsilon and/or kappa perform DNA repair synthesis, followed by DNA ligation, thus completing GG-NER.

For a recent review, please refer to Marteijn et al. 2014.

**Literature references**


**Editions**

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DNA Damage Recognition in GG-NER

Location: Global Genome Nucleotide Excision Repair (GG-NER)

Stable identifier: R-HSA-5696394

Compartments: nucleoplasm

In global genome nucleotide excision repair (GG-NER), the DNA damage is recognized by two protein complexes. The first complex consists of XPC, RAD23A or RAD23B, and CETN2. This complex probes the DNA helix and recognizes damage that disrupts normal Watson-Crick base pairing, which results in binding of the XPC:RAD23:CETN2 complex to the undamaged DNA strand. The second complex is a ubiquitin ligase UV-DDB that consists of DDB2, DDB1, CUL4A or CUL4B and RBX1. The UV-DDB complex is necessary for the recognition of UV-induced DNA damage and may contribute to the retention of the XPC:RAD23:CETN2 complex at the DNA damage site. The UV-DDB complex binds the damaged DNA strand (Fitch et al. 2003, Wang et al. 2004, Moser et al. 2005, Camenisch et al. 2009, Oh et al. 2011).

Literature references


## Editions

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Formation of Incision Complex in GG-NER

**Location:** Global Genome Nucleotide Excision Repair (GG-NER)

**Stable identifier:** R-HSA-5696395

**Compartments:** nucleoplasm

After the XPC complex and the UV-DDB complex bind damaged DNA, a basal transcription factor TFIIH is recruited to the nucleotide excision repair (NER) site (Volker et al. 2001, Riedl et al. 2003). DNA helicases ERCC2 (XPD) and ERCC3 (XPB) are subunits of the TFIIH complex. ERCC2 unwinds the DNA around the damage in concert with the ATPase activity of ERCC3, creating an open bubble (Coin et al. 2007). Simultaneously, the presence of the damage is verified by XPA (Camenisch et al. 2006). The recruitment of XPA is partially regulated by PARP1 and/or PARP2 (King et al. 2012).

Two DNA endonucleases, ERCC5 (XPG) and the complex of ERCC1 and ERCC4 (XPF), are recruited to the open bubble structure to form the incision complex that will excise the damaged oligonucleotide from the affected DNA strand (Dunand-Sauthier et al. 2005, Zotter et al. 2006, Riedl et al. 2003, Tsodikov et al. 2007, Orelli et al. 2010). The RPA heterotrimer coats the undamaged DNA strand, thus protecting it from the endonucleolytic attack (De Laat et al. 1998).

**Literature references**


## Editions

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**Dual Incision in GG-NER**

**Location:** Global Genome Nucleotide Excision Repair (GG-NER)

**Stable identifier:** R-HSA-5696400

**Compartments:** nucleoplasm

Double incision at the damaged DNA strand excises the oligonucleotide that contains the lesion from the open bubble. The excised oligonucleotide is ~27-30 bases long. Incision 5' to the damage site, by ERCC1:ERCC4 endonuclease, precedes the incision 3' to the damage site by ERCC5 endonuclease (Staresincic et al. 2009).

**Literature references**


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Global genome nucleotide excision repair (GG-NER) is completed by DNA repair synthesis that fills the single stranded gap created after dual incision of the damaged DNA strand and excision of the ~27-30 bases long oligonucleotide that contains the lesion. DNA synthesis is performed by DNA polymerases epsilon or delta, or the Y family DNA polymerase kappa (POLK), which are loaded to the repair site after 5’ incision (Staresincic et al. 2009, Ogi et al. 2010). DNA ligases LIG1 or LIG3 (as part of the LIG3:XRCC1 complex) ligate the newly synthesized stretch of oligonucleotides to the incised DNA strand (Moser et al. 2007).

Literature references


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