G1/S DNA Damage Checkpoints

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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: 76

This document contains 3 pathways (see Table of Contents)
In the G1 phase there are two types of DNA damage responses, the p53-dependent and the p53-independent pathways. The p53-dependent responses inhibit CDKs through the up-regulation of genes encoding CKIs mediated by the p53 protein, whereas the p53-independent mechanisms inhibit CDKs through the inhibitory T14Y15 phosphorylation of Cdk2. Failure of DNA damage checkpoints in G1 leads to mutagenic replication of damaged templates and other replication defects.

Editions

2003-06-05 Authored Hoffmann, I., Khanna, KK.
The arrest at G1/S checkpoint is mediated by the action of a widely known tumor suppressor protein, p53. Loss of p53 functions, as a result of mutations in cancer prevent the G1/S checkpoint (Kuerbitz et al, 1992). P53 is rapidly induced in response to damaged DNA. A number of kinases, phosphatases, histone acetylases and ubiquitin-conjugating enzymes regulate the stability as well as transcriptional activity of p53 after DNA damage.

**Literature references**


**Editions**

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The G1 arrest induced by DNA damage has been ascribed to the transcription factor and tumor suppressor protein p53. To be effective within minutes after DNA damage, induction of the G1 block should exploit transcription and protein synthesis independent mechanisms.

Upon exposure to ultraviolet light (UV) or ionizing radiation (IR), the abundance and activity of a protein, Cdc25A, rapidly decreases; this DNA damage response is not dependent on p53. The rapid destruction of Cdc25A phosphatase prevents entry of a cell into S-phase, by maintaining the CyclinE:Cdk2 complexes in their T14Y15 phosphorylated form.

**Literature references**

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