MRN activates ATM

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15/05/2024

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

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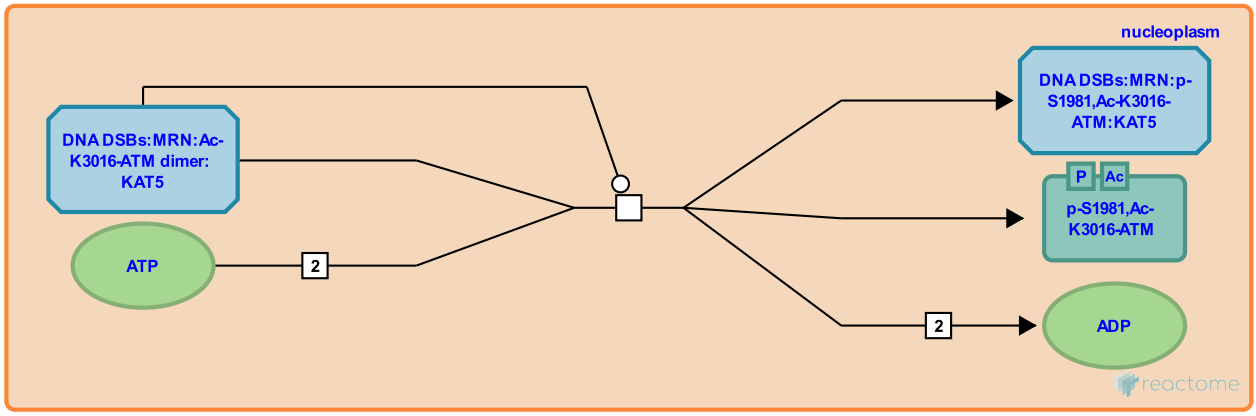
Stable identifier: R-HSA-5693540

Type: transition

Compartments: nucleoplasm



MRN promotes dissociation of ATM dimers to ATM monomers which is accompanied by ATM trans-autophosphorylation on serine residue S1981 (Bakkenist et al. 2003, Du et al. 2014). ATM autophosphorylation at serine residues S367 and S1893 is also implicated in ATM activation (Kozlov et al. 2006). Dissociation of ATM dimers requires the ATP-dependent DNA-helicase activity of the MRN subunit RAD50 (Lee and Paull 2005). KAT5 (Tip60) mediated acetylation of ATM dimers at lysine K3016 is a prerequisite for ATM kinase activity (Sun et al. 2007). Upon the dissociation of ATM dimers induced by DNA double-strand breaks (DSBs), a fraction of activated ATM is retained at DSB sites, co-localizing with the MRN complex (Andegeko et al. 2001, Uziel et al. 2003) at ionizing radiation-induced foci (IRIF). MRN facilitates the binding of a portion of ATM substrates to ATM (Lee and Paull 2004).

After DSBs are repaired, ATM is dephosphorylated by an unidentified PP2A phosphatase complex, leading to dimer reformation (Goodarzi et al. 2004).

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Editions

2013-07-15	Edited	D'Eustachio, P., Matthews, L.
2013-07-15	Authored	Orlic-Milacic, M.
2013-09-03	Reviewed	Samarajiwa, S.
2015-05-12	Edited, Revised	Orlic-Milacic, M.
2015-06-12	Reviewed	Borowiec, JA.