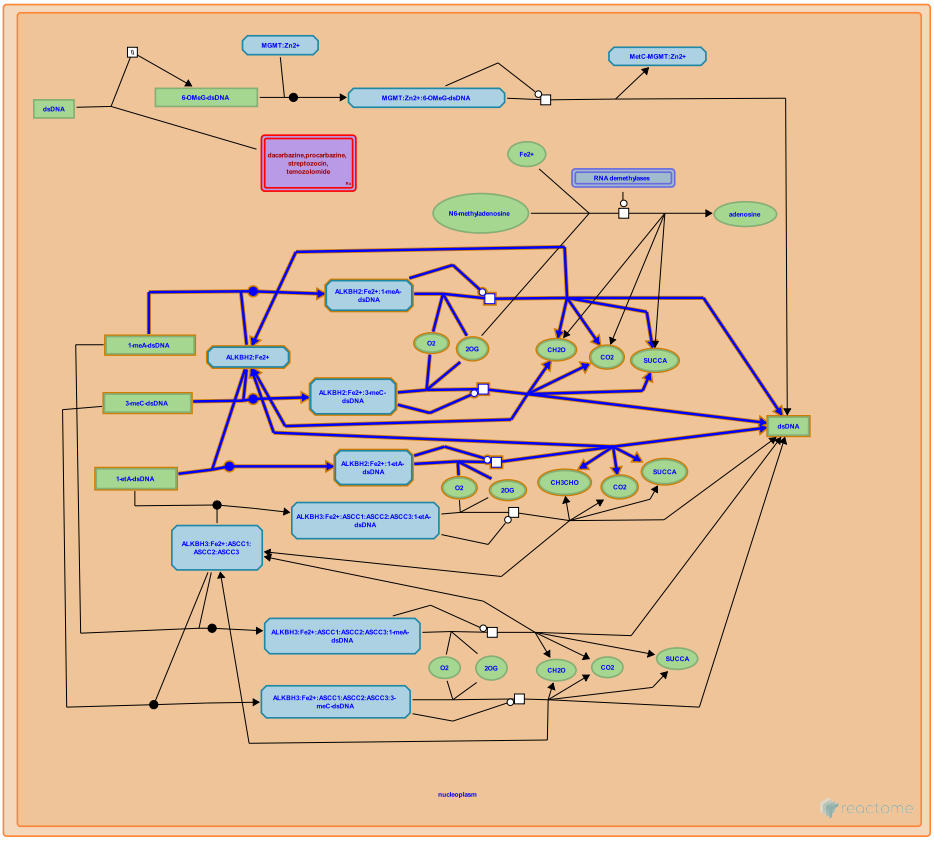
ALKBH2 mediated reversal of alkylation damage



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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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

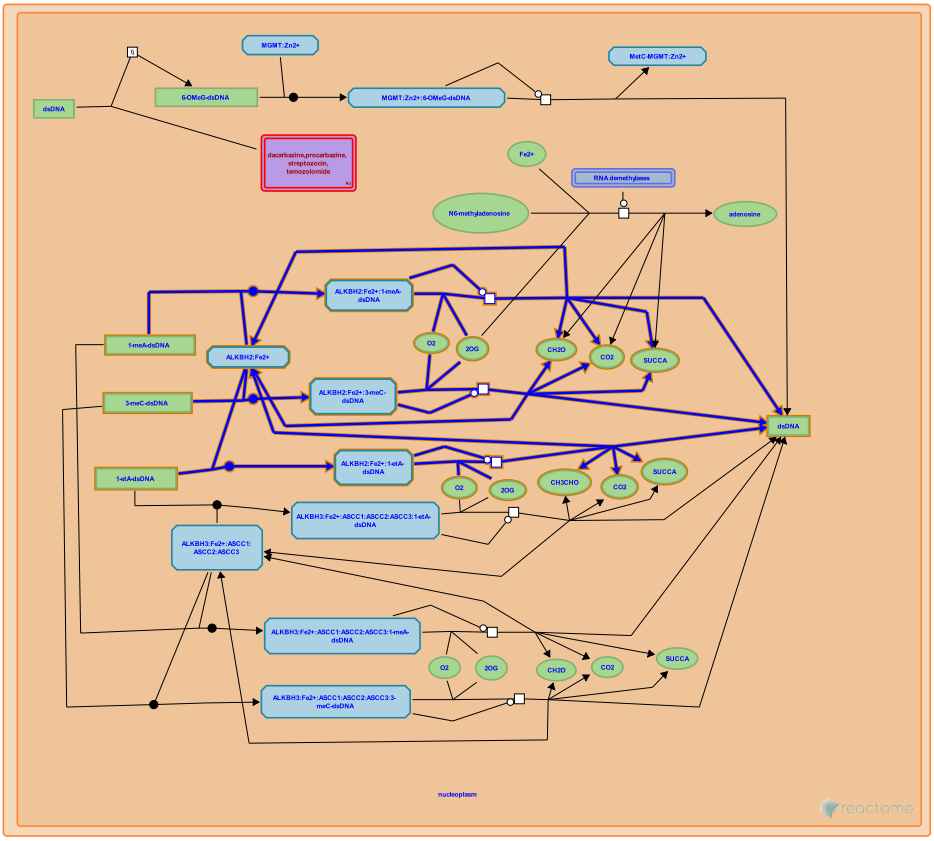
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

ALKBH2 mediated reversal of alkylation damage ↗

Stable identifier: R-HSA-112122

Compartments: nucleoplasm



AlkB is an E.coli alpha-ketoglutarate- and Fe(II)-dependent dioxygenase that oxidizes the relevant methyl groups and releases them as formaldehyde. Two human homologs of AlkB, ALKBH2 and ALKBH3, both remove 1-methyladenine (1-meA) and 3-methylcytosine (3-meC) from methylated polynucleotides in an alpha-ketoglutarate-dependent reaction. They act by direct damage reversal with the regeneration of the unsubstituted bases. E.coli AlkB and human ALKBH2 and ALKBH3 can also repair 1-ethyladenine (1-etA) residues in DNA with the release of acetaldehyde (Duncan et al., 2002, Lee et al. 2005).

Literature references

Sedgwick, B. (2004). Repairing DNA-methylation damage. *Nat Rev Mol Cell Biol, 5*, 148-57. ↗

Cai, S., Lee, DH., O'Connor, TR., Jin, SG., Pfeifer, GP., Chen, Y. (2005). Repair of methylation damage in DNA and RNA by mammalian AlkB homologues. *J Biol Chem, 280*, 39448-59. ↗

Editions

2004-02-04	Edited, Reviewed	Joshi-Tope, G.
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2014-12-16	Edited	Orlic-Milacic, M.
2015-02-06	Reviewed	Gillespie, ME.

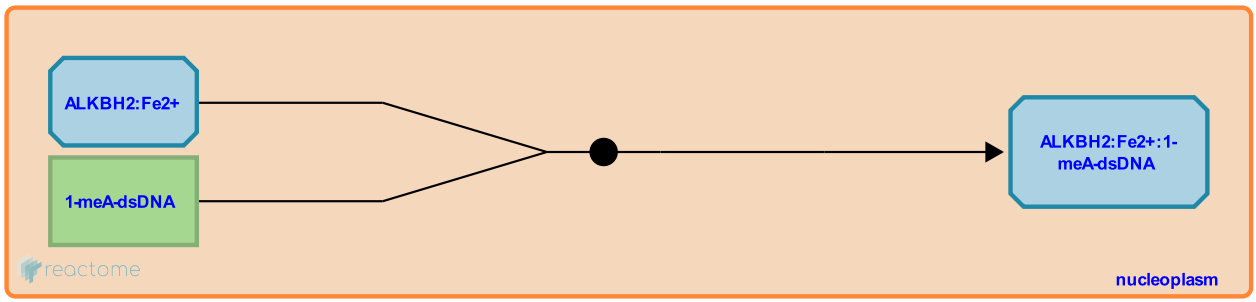
ALKBH2 binds alkylated DNA containing 1-meA ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-5657641

Type: binding

Compartments: nucleoplasm



ALKBH2 binds alkylated DNA containing 1-methyladenine (1-meA). ALKBH2 preferentially binds double strand DNA (dsDNA) (Duncan et al. 2002, Aas et al. 2003, Chen et al. 2010). Iron (Fe2+) is needed for the catalytic activity of ALKBH2 (Duncan et al. 2002).

Followed by: Oxidative demethylation of 1-meA damaged DNA by ALKBH2

Literature references

Falnes, PO., Otterlei, M., Seeberg, E., Akbari, M., Slupphaug, G., Vågbø, CB. et al. (2003). Human and bacterial oxidative demethylases repair alkylation damage in both RNA and DNA. *Nature, 421*, 859-63. ↗

Sun, X., Chen, B., Liu, H., Yang, CG. (2010). Mechanistic insight into the recognition of single-stranded and double-stranded DNA substrates by ABH2 and ABH3. *Mol Biosyst, 6*, 2143-9. ↗

Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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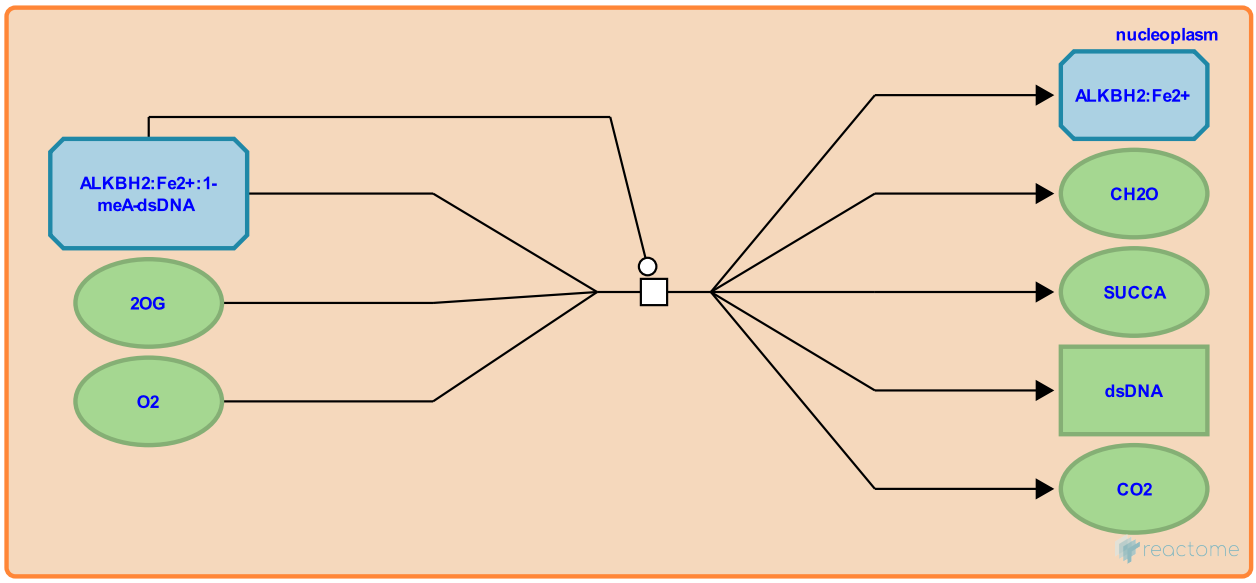
Oxidative demethylation of 1-meA damaged DNA by ALKBH2 ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-112118

Type: transition

Compartments: nucleoplasm



ALKBH2 catalyzes the removal of the methyl group from 1-methyladenine (1-meA) in a reaction that depends on oxygen, alpha-ketoglutarate and Fe2+. ALKBH2 thus directly reverses alkylation damage of DNA in the form of 1-meA, releasing formaldehyde. ALKBH2 is ~4-fold more active on dsDNA containing 1-methyladenine than 3-methylcytosine (Duncan et al. 2002).

Preceded by: ALKBH2 binds alkylated DNA containing 1-meA

Literature references

Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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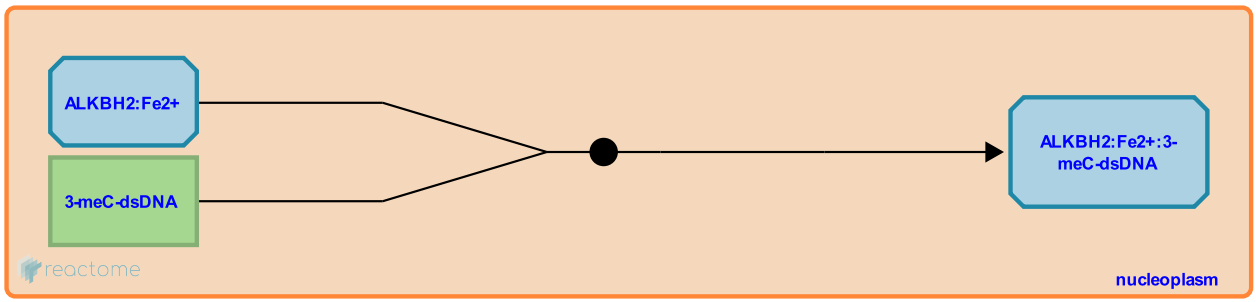
ALKBH2 binds alkylated dsDNA containing 3-meC ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-5657665

Type: binding

Compartments: nucleoplasm



ALKBH2 binds alkylated DNA containing 3-methylcytosine (3-meC). ALKBH2 preferentially binds double strand DNA (dsDNA) (Duncan et al. 2002, Aas et al. 2003, Chen et al. 2010). Iron (Fe2+) is needed for the catalytic activity of ALKBH2 (Duncan et al. 2002).

Followed by: Oxidative demethylation of 3-meC damaged DNA by ALKBH2

Literature references

Falnes, PO., Otterlei, M., Seeberg, E., Akbari, M., Slupphaug, G., Vågbø, CB. et al. (2003). Human and bacterial oxidative demethylases repair alkylation damage in both RNA and DNA. *Nature, 421*, 859-63. ↗

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Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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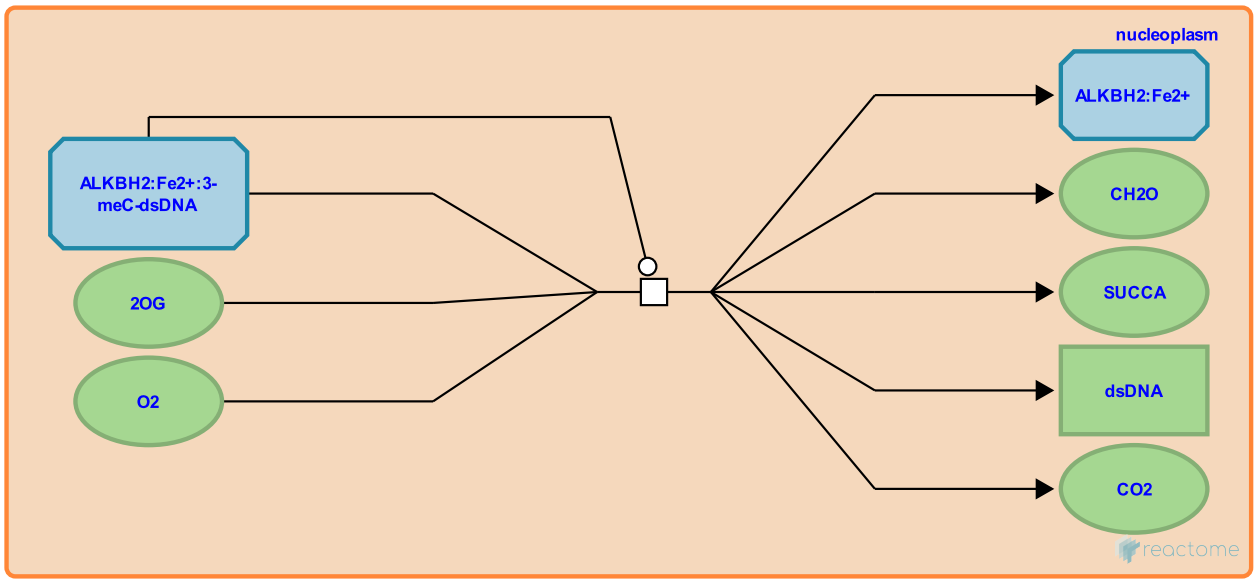
Oxidative demethylation of 3-meC damaged DNA by ALKBH2 ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-112120

Type: transition

Compartments: nucleoplasm



ALKBH2 catalyzes removal of the methyl group from 3-methylcytosine (3-meC) in a reaction that depends on oxygen, alpha-ketoglutarate and Fe2+. ALKBH2 thus directly reverses alkylation damage of DNA in the form of 3-meC, releasing formaldehyde (Duncan et al. 2002).

Preceded by: ALKBH2 binds alkylated dsDNA containing 3-meC

Literature references

Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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2015-02-06	Reviewed	Gillespie, ME.

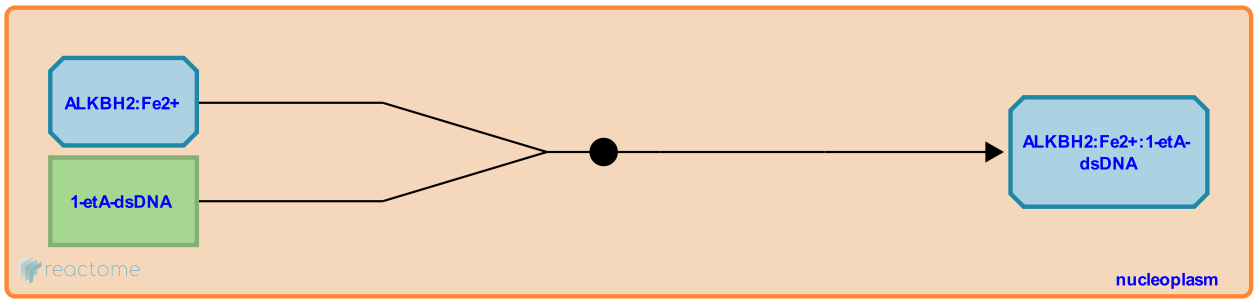
ALKBH2 binds alkylated DNA containing 1-etA ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-5657649

Type: binding

Compartments: nucleoplasm



ALKBH2 binds alkylated DNA containing 1-ethyladenine (1-etA). ALKBH2 preferentially binds double strand DNA (dsDNA) (Duncan et al. 2002, Aas et al. 2003, Chen et al. 2010). Iron (Fe2+) is needed for the catalytic activity of ALKBH2 (Duncan et al. 2002).

Followed by: Oxidative dealkylation of 1-etA damaged DNA By ALKBH2

Literature references

Falnes, PO., Otterlei, M., Seeberg, E., Akbari, M., Slupphaug, G., Vågbø, CB. et al. (2003). Human and bacterial oxidative demethylases repair alkylation damage in both RNA and DNA. *Nature, 421*, 859-63. ↗

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Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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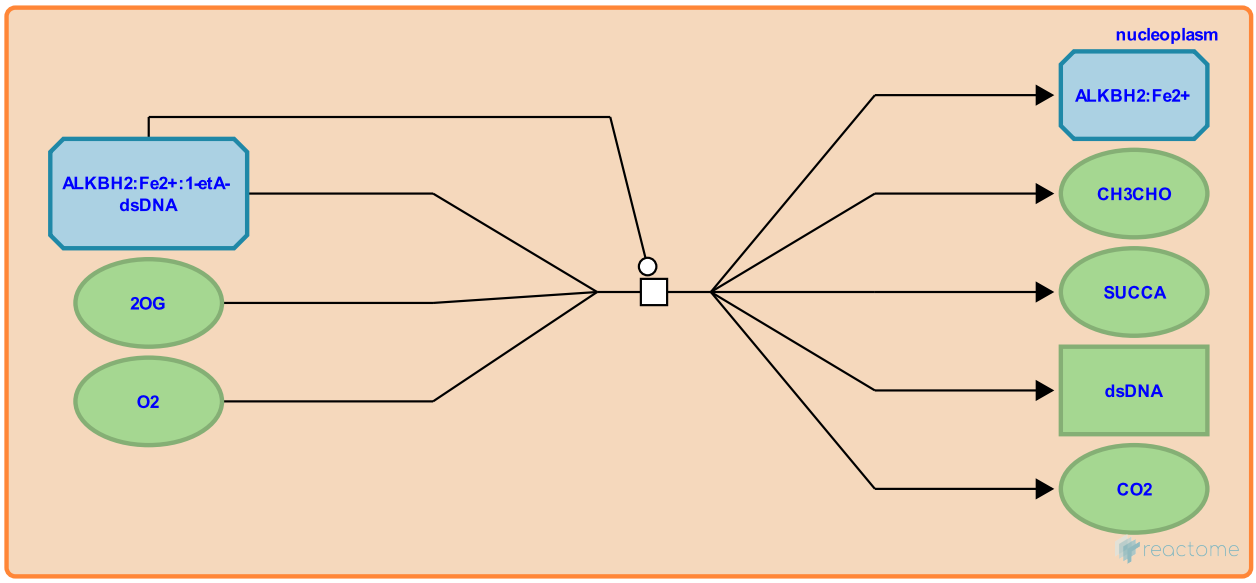
Oxidative dealkylation of 1-etA damaged DNA By ALKBH2 ↗

Location: ALKBH2 mediated reversal of alkylation damage

Stable identifier: R-HSA-112121

Type: transition

Compartments: nucleoplasm



ALKBH2 catalyzes removal of the ethyl group from 1-ethyladenine (1-etA) in a reaction that depends on oxygen, alpha-ketoglutarate and Fe2+. ALKBH2 thus directly reverses alkylation damage of DNA in the form of 1-etA, releasing acetaldehyde (Duncan et al. 2002).

Preceded by: ALKBH2 binds alkylated DNA containing 1-etA

Literature references

Lindahl, T., Duncan, T., Bates, PA., Sedgwick, B., Trewick, SC., Koivisto, P. (2002). Reversal of DNA alkylation damage by two human dioxygenases. *Proc Natl Acad Sci U S A, 99*, 16660-5. ↗

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