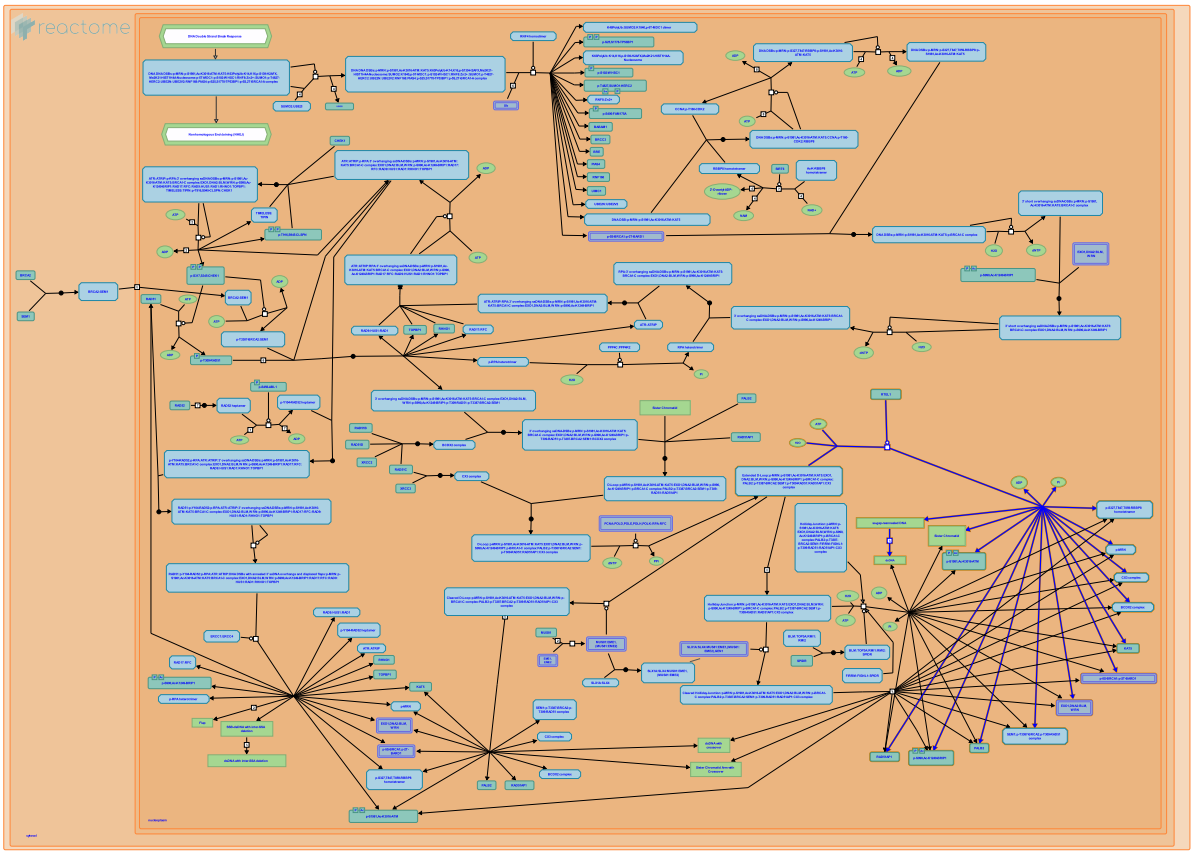
Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA)



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

19/05/2024

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

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. ↗

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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. ↗

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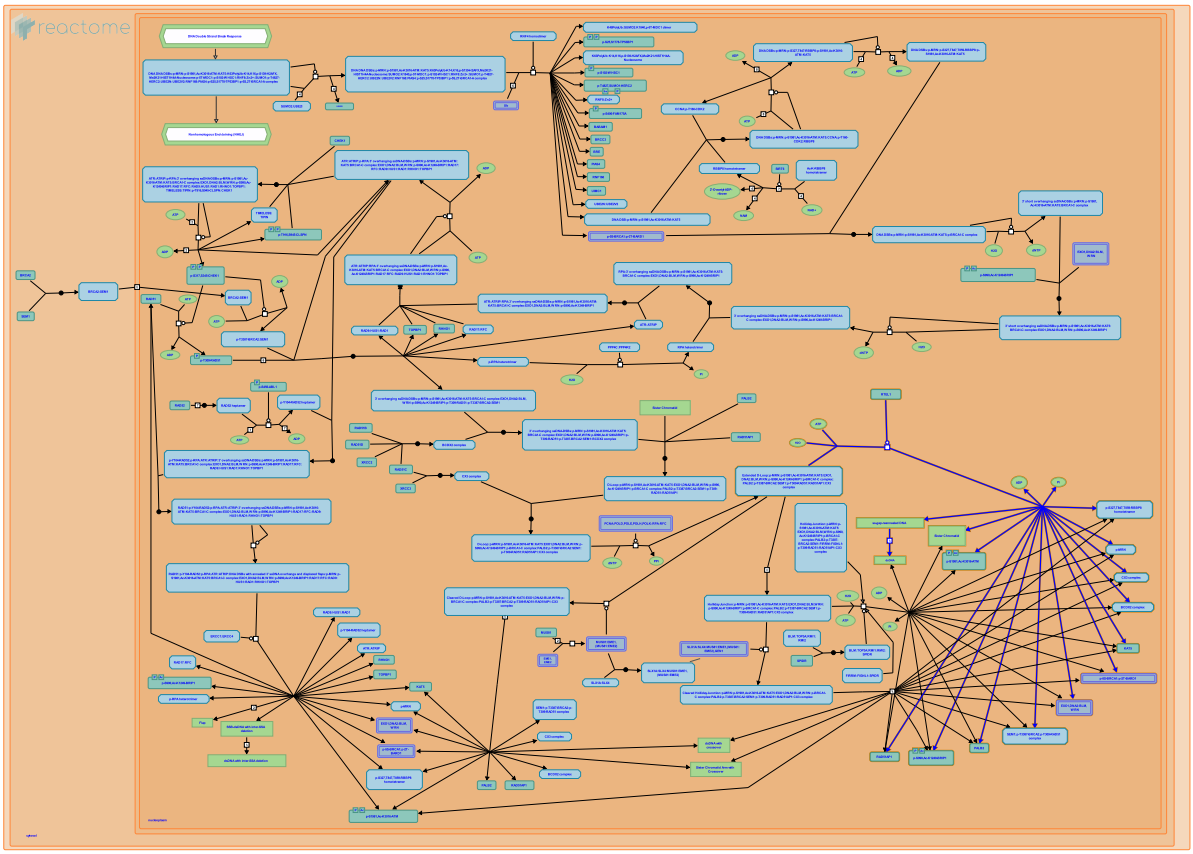
Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA) ↗

Stable identifier: R-HSA-5693554

Compartments: nucleoplasm



In the synthesis-dependent strand-annealing (SDSA) model of D-loop resolution, D-loop strands extended by DNA repair synthesis dissociate from their sister chromatid complements and reanneal with their original complementary strands, resulting in non-crossover products (Mitchel et al. 2010). SDSA is promoted by the DNA helicase RTEL1 (Barber et al. 2008, Uringa et al. 2012). Additional DNA synthesis occurs to fill the remaining single strand gap present in the reannealed DNA duplex. DNA polymerase alpha has been implicated in this late step of DNA repair synthesis (Levy et al. 2009), although RTEL1-mediated recruitment of PCNA-bound DNA polymerases may also be involved (Vannier et al. 2013). The remaining single strand nicks are closed by DNA ligases, possibly LIG1 or LIG3 (Mortusewicz et al. 2006, Puebla-Osorio et al. 2006).

Literature references

West, SC., Collis, SJ., Barber, LJ., Cantor, SB., McIlwraith, MJ., Rose, AM. et al. (2008). RTEL1 maintains genomic stability by suppressing homologous recombination. *Cell, 135*, 261-71. ↗

Ding, H., Petalcorin, MI., Sandhu, S., Boulton, SJ., Wu, X., Vannier, JB. et al. (2013). RTEL1 is a replisome-associated helicase that promotes telomere and genome-wide replication. *Science, 342*, 239-42. ↗

Zhu, C., Alt, FW., Puebla-Osorio, N., Lacey, DB. (2006). Early embryonic lethality due to targeted inactivation of DNA ligase III. *Mol. Cell. Biol., 26*, 3935-41. ↗

Bresson, A., Maiorano, D., de Murcia, G., Van Dorsselaer, A., Oehlmann, M., Ménissier-de Murcia, J. et al. (2009). XRCC1 interacts with the p58 subunit of DNA Pol alpha-primase and may coordinate DNA repair and replication during S phase. *Nucleic Acids Res., 37*, 3177-88. ↗

Rothbauer, U., Mortusewicz, O., Leonhardt, H., Cardoso, MC. (2006). Differential recruitment of DNA Ligase I and III to DNA repair sites. *Nucleic Acids Res., 34*, 3523-32. ↗

Editions

2003-11-24	Authored	Matthews, L.
2015-05-12	Edited, Revised	Orlic-Milacic, M.
2015-06-12	Reviewed	Borowiec, JA.

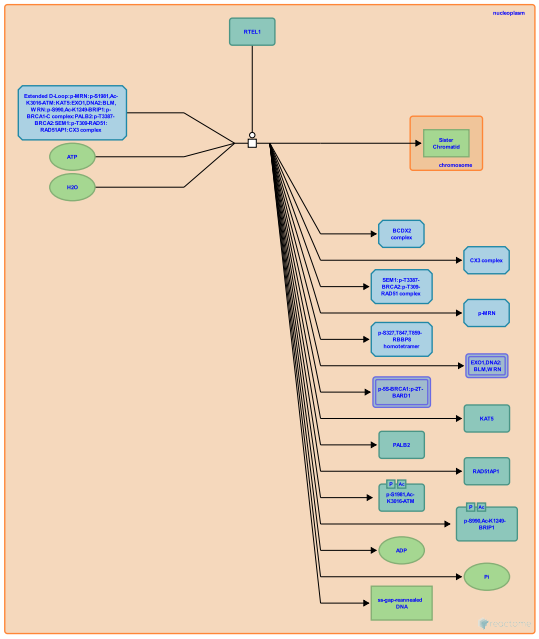
D-loop dissociation and strand annealing ↗

Location: Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA)

Stable identifier: R-HSA-5693589

Type: transition

Compartments: nucleoplasm, chromosome



Following repair synthesis, the extended D-loop strands may disassociate from their sister chromatid complements and reanneal with their original complementary strands. A DNA helicase RTEL1 disrupts preformed D-loops and promotes synthesis-dependent strand annealing, yielding non-crossover products and preventing excessive recombination between mitotic sister chromatids (Barber et al. 2008, Uringa et al. 2012).

Followed by: Gap-filling DNA synthesis in SDSA

Literature references

West, SC., Collis, SJ., Barber, LJ., Cantor, SB., McIlwraith, MJ., Rose, AM. et al. (2008). RTEL1 maintains genomic stability by suppressing homologous recombination. *Cell, 135*, 261-71. ↗

Zelensky, A., Essers, J., Pickett, HA., Lisaingo, K., Uringa, EJ., Lansdorp, PM. et al. (2012). RTEL1 contributes to DNA replication and repair and telomere maintenance. *Mol. Biol. Cell, 23*, 2782-92. ↗

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2015-06-12	Reviewed	Borowiec, JA.

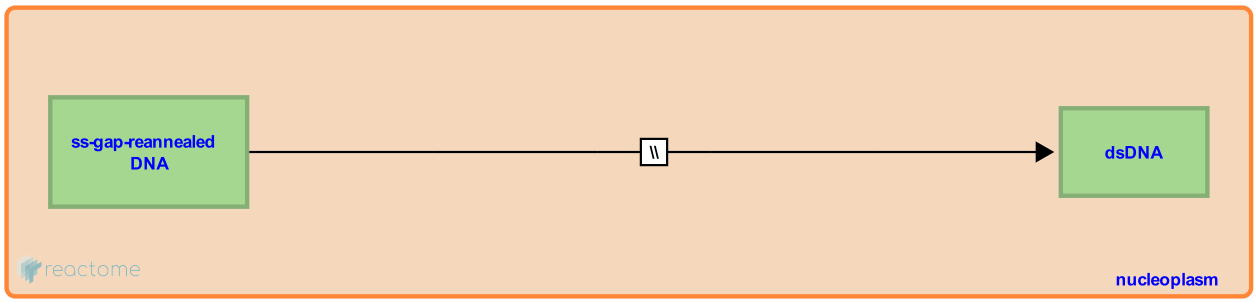
Gap-filling DNA synthesis in SDSA ↗

Location: Resolution of D-loop Structures through Synthesis-Dependent Strand Annealing (SDSA)

Stable identifier: R-HSA-5693558

Type: omitted

Compartments: nucleoplasm



After synthesis-dependent strand annealing (SDSA), the reannealed DNA molecule contains a single strand nick (SSB) in the newly synthesized strand, between the 3' end of the newly added stretch of nucleotides and the resected 5' end of the strand. In addition, the complementary strand contains a gap created by resection that was not filled during DNA repair synthesis. Additional DNA synthesis occurs to fill in this remaining single-strand gap present in the reannealed DNA duplex. SSBs between newly added stretches of nucleotides and resected 5' ends need to be closed by DNA ligases. The identity of DNA polymerase(s) and DNA ligase(s) involved in the completion of DNA double-strand break repair through SDSA is not known. RTEL1 DNA helicase, which resolves D-loops in SDSA, binds PCNA and may promote DNA synthesis after reannealing (Vannier et al. 2013). DNA polymerase alpha is implicated in late steps of DNA repair synthesis (Levy et al. 2009), but other PCNA-bound DNA polymerases may also be involved. LIG1, as well as LIG3 in complex with XRCC1, may act to ligate SSBs (Fan et al. 2004, Mortusewicz et al. 2006, Mortusewicz et al. 2007, Puebla-Osorio et al. 2006).

Preceded by: D-loop dissociation and strand annealing

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Mortusewicz, O., Leonhardt, H. (2007). XRCC1 and PCNA are loading platforms with distinct kinetic properties and different capacities to respond to multiple DNA lesions. *BMC Mol. Biol., 8*, 81. ↗

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Zhu, C., Alt, FW., Puebla-Osorio, N., Lacey, DB. (2006). Early embryonic lethality due to targeted inactivation of DNA ligase III. *Mol. Cell. Biol., 26*, 3935-41. ↗

Otterlei, M., Wilson, DM., Fan, J., Wong, HK., Tomkinson, AE. (2004). XRCC1 co-localizes and physically interacts with PCNA. *Nucleic Acids Res., 32*, 2193-201. ↗

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