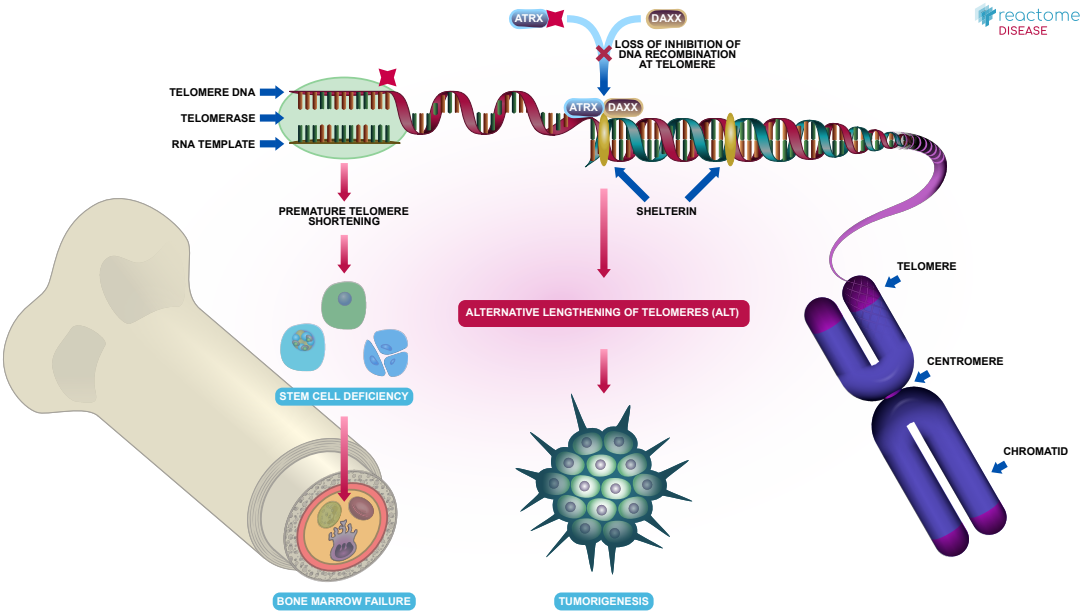
Diseases of Telomere Maintenance



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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.

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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

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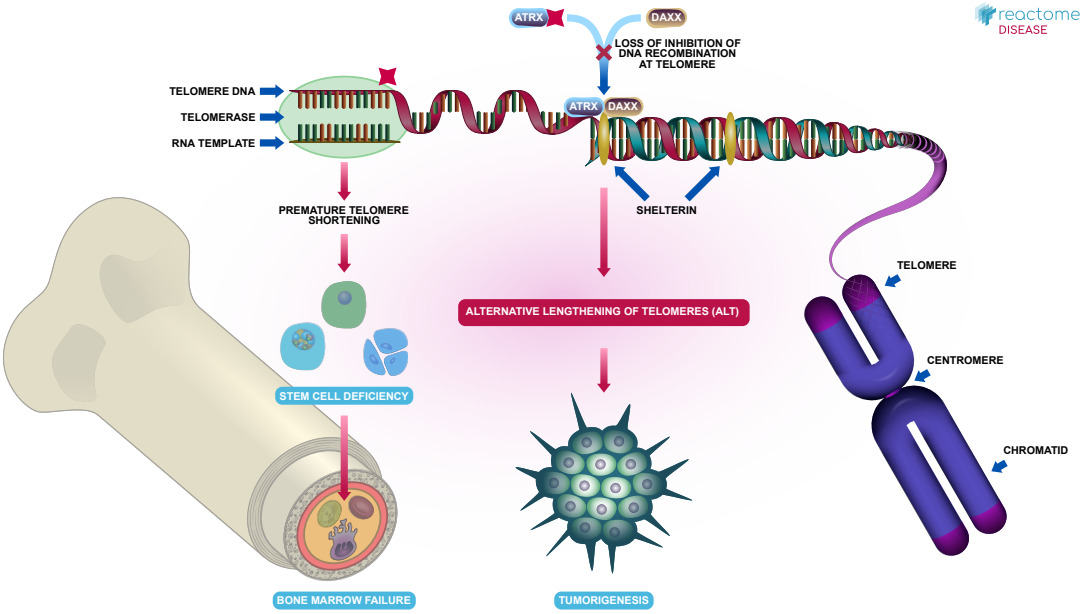
Reactome database release: 88

This document contains 2 pathways (see Table of Contents)

Diseases of Telomere Maintenance ↗

Stable identifier: R-HSA-9673013

Diseases: genetic disease



Somatic mutations or rearrangements in genes involved in telomere maintenance enable immortalization of cancer cells either through upregulation of telomerase activity or through activation of alternative lengthening of telomeres (ALT) (Killela et al. 2013, reviewed by Gocha et al. 2013, Pickett and Reddel 2015, Amorim et al. 2016, Yuan et al. 2019). Germline mutations in telomere maintenance genes lead to telomere syndromes, such as dyskeratosis congenita (DC) and Hoyeraal-Hreidarsson (HH) syndrome, characterized by impaired ability to maintain telomere lengths during growth and development, leading to abnormally short telomere lengths and genomic instability that affects multiple organs and is associated with increased risk of certain cancers (reviewed by Sarek et al. 2015).

Literature references

Santos, G., Soares, P., Vinagre, J., Amorim, JP. (2016). The Role of ATRX in the Alternative Lengthening of Telomeres (ALT) Phenotype. *Genes (Basel), 7*. ↗

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Mandahl, N., He, Y., Hruban, RH., Diaz, LA., McLendon, RE., Zhang, M. et al. (2013). TERT promoter mutations occur frequently in gliomas and a subset of tumors derived from cells with low rates of self-renewal. *Proc. Natl. Acad. Sci. U.S.A., 110*, 6021-6. ↗

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Editions

2020-04-30	Authored	Orlic-Milacic, M.
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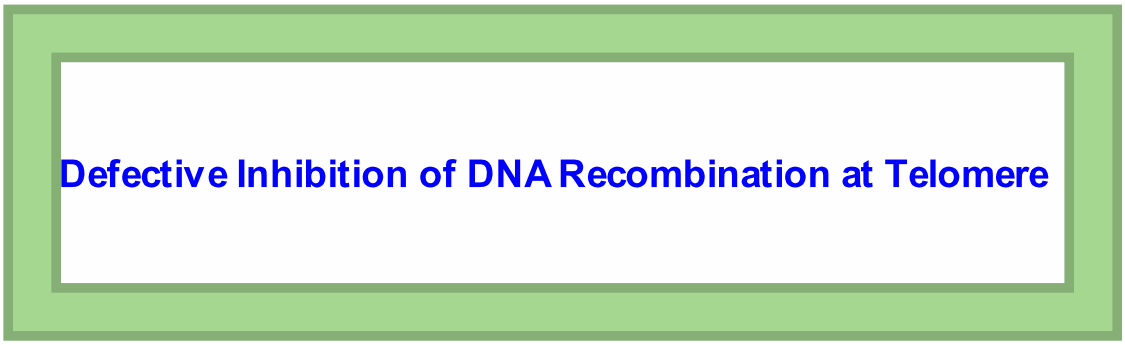
Alternative Lengthening of Telomeres (ALT) ↗

Location: Diseases of Telomere Maintenance

Stable identifier: R-HSA-9006821

Compartments: nucleoplasm

Diseases: cancer



Alternative lengthening of telomeres (ALT) is a homologous recombination repair-directed telomere synthesis that takes place in 5-15% of tumors. ALT positive tumors often harbor loss-of-function mutations in ATRX (Alpha thalassemia mental retardation X-linked) or, more rarely, DAXX (Death domain-associated protein 6) chromatin remodeling factors, which may act to inhibit DNA recombination at telomere ends (reviewed by Gocha et al. 2013). The nuclear receptor complex NuRD-ZNF827 contributes to the recruitment of homologous recombination (HR) machinery to telomeres (Conomos et al. 2014). ALT is most prevalent in subsets of sarcomas, including osteosarcomas and some soft tissue sarcomas, brain cancers and neuroblastomas (Heaphy et al. 2011, Arora and Azzalin 2015). For review, please refer to Nabetani and Ishikawa 2011, Pickett and Reddel 2015, Verma and Greenberg 2016, Amorim et al. 2016, Sommer and Royle 2020, Zhang and Zou 2020.

Literature references

Santos, G., Soares, P., Vinagre, J., Amorim, JP. (2016). The Role of ATRX in the Alternative Lengthening of Telomeres (ALT) Phenotype. *Genes (Basel), 7*. ↗

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Verma, P., Greenberg, RA. (2016). Noncanonical views of homology-directed DNA repair. *Genes Dev., 30*, 1138-54. ↗

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Table of Contents