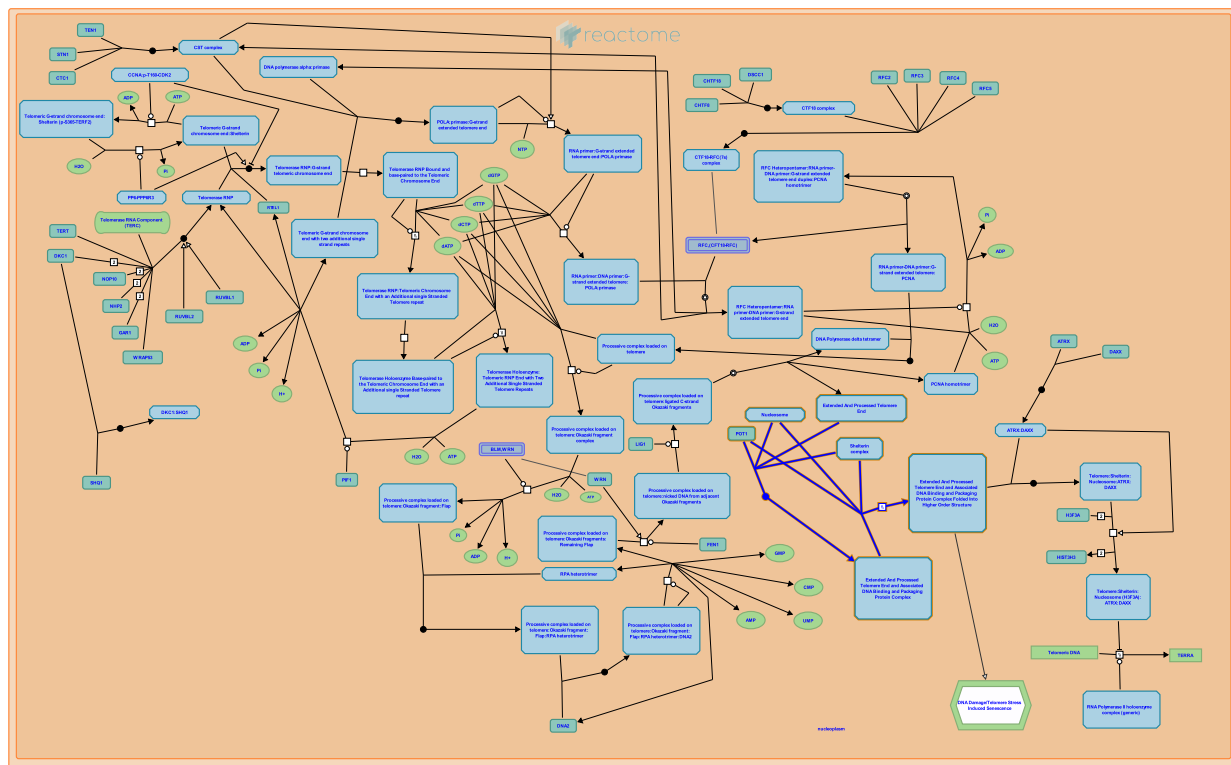


Packaging Of Telomere Ends



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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](https://reactome.org).

10/04/2024

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.

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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. [↗](#)

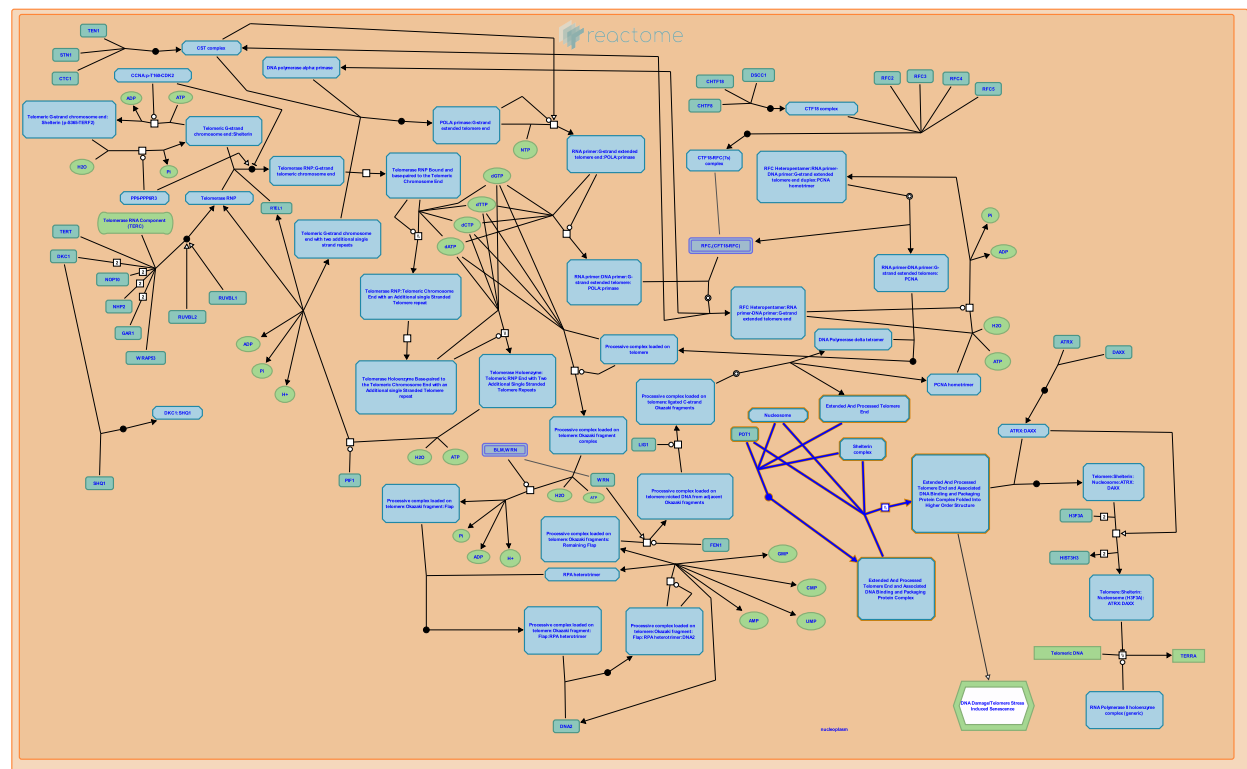
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 88

This document contains 1 pathway and 2 reactions ([see Table of Contents](#))

Packaging Of Telomere Ends ↗

Stable identifier: R-HSA-171306



Multiple steps, including C-strand resection, telomerase-mediated elongation, and C-strand synthesis are involved in processing and maintaining the telomere. Though this module posits a linear transit for the steps, in humans it is not well understood how these steps are coordinated and what other events may be involved.

Telomeric DNA can form higher order structures. Electron microscopy of telomeric DNA isolated from human cells provided evidence for lariat-type structures termed telomeric loops, or t-loops (Griffith et al., 1999). t-loops are proposed to result from the invasion of the 3' G-rich single strand overhang into the double stranded telomeric TTAGGG repeat tract. The function of the t-loop is presumed to be the masking of the 3' telomeric overhang. Multiple protein factors can bind telomeric DNA and likely contribute to dynamic, higher order structures.

Literature references

Moss, H., Bianchi, A., de Lange, T., Stansel, RM., Rosenfield, S., Comeau, L. et al. (1999). Mammalian telomeres end in a large duplex loop. *Cell*, 97, 503-14. ↗

Editions

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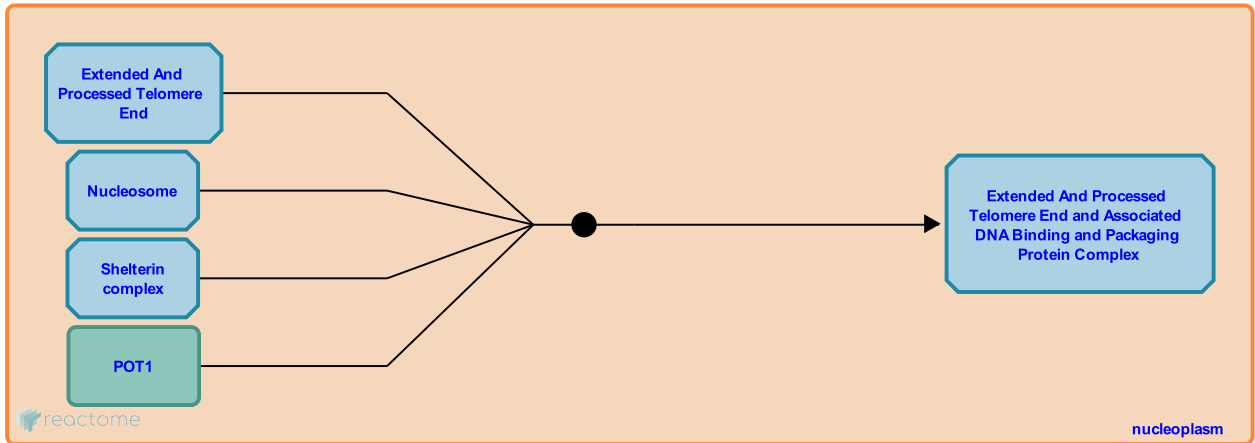
Incorporation Of Extended And Processed Telomere End Into Associated Protein Structure ↗

Location: [Packaging Of Telomere Ends](#)

Stable identifier: R-HSA-181450

Type: binding

Compartments: nucleoplasm



In addition to telomerase-mediated elongation and C-strand synthesis, other DNA processing steps are likely involved in telomere maintenance. In humans, nucleolytic activity is proposed to be involved in generating the G-rich 3' single strand overhang. In addition, differences in the structure of the overhang at telomeres that have undergone leading vs. lagging strand replication suggest that DNA processing may be different at these telomeres (Chai et al. 2006).

Many proteins associate with telomeric DNA. One complex that binds telomeres is called shelterin. Shelterin is a six-protein complex composed of TRF1 and TRF2, which can bind double-stranded telomeric DNA, POT1, which can bind single-stranded telomeric DNA, and three other factors, RAP1, TIN2, and TPP1 (reviewed in de Lange 2006 "Telomeres"). Human telomeric DNA is also bound by nucleosomes (Makarov et al. 1993; Nikitina and Woodcock 2004). A number of other proteins, including some that play roles in the DNA damage response, can be found at telomeres (Zhu et al. 2000; Verdun et al. 2005).

Studies in yeast and humans indicate that the association of many proteins with telomeres is regulated through the cell cycle (Zhu et al. 2000; Taggart et al. 2002; Fisher et al. 2004; Takata et al. 2004; Takata et al. 2005; Verdun et al. 2005). For instance, TRF1, MRE11, POT1, ATM, and NBS1 display cell cycle regulated chromatin immunoprecipitation of telomeric DNA (Zhu et al. 2000; Verdun et al. 2005), and cytologically observable hTERT and hTERC localize to a subset of telomeres only in S-phase (Jady et al. 2006; Tomlinson et al. 2006). These data indicate that telomeres are dynamically remodeled through the cell cycle.

Followed by: [Incorporation Of Extended And Processed Telomere End Into Higher Order T-Loop And Associated Protein Structure](#)

Literature references

de Lange, T. (2005). Shelterin: the protein complex that shapes and safeguards human telomeres. *Genes Dev*, 19, 2100-10. ↗

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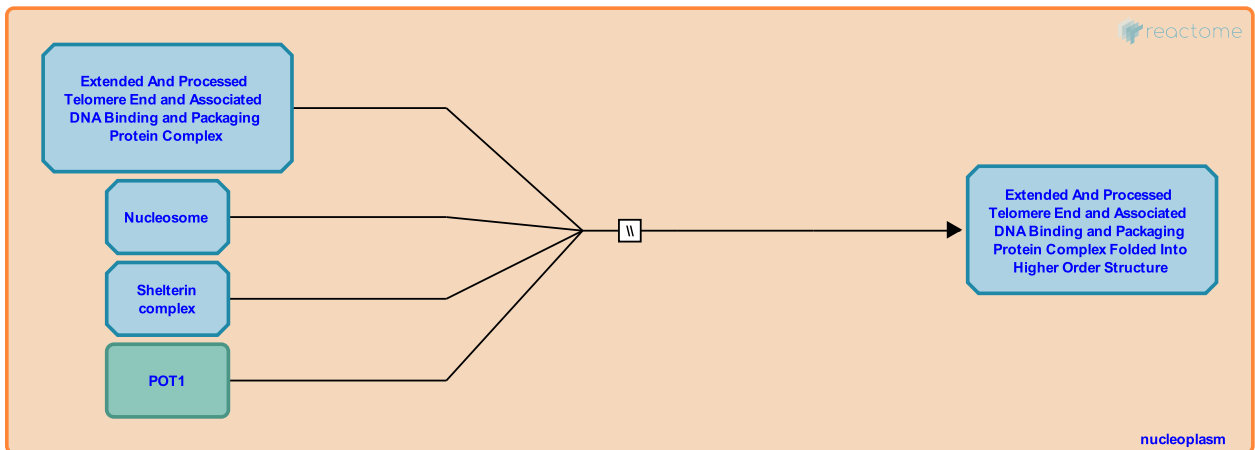
Incorporation Of Extended And Processed Telomere End Into Higher Order T-Loop And Associated Protein Structure ↗

Location: [Packaging Of Telomere Ends](#)

Stable identifier: R-HSA-176700

Type: omitted

Compartments: nucleoplasm



In addition to telomerase-mediated elongation and C-strand synthesis, other DNA processing steps are likely involved in telomere maintenance. In humans, nucleolytic activity is proposed to be involved in generating the G-rich 3' single strand overhang. In addition, differences in the structure of the overhang at telomeres that have undergone leading vs. lagging strand replication suggest that DNA processing may be different at these telomeres (Chai et al. 2006).

Electron microscopy studies of purified human telomeric DNA have provided evidence for telomeric loops, or t-loops (Griffith et al. 1999). t-loops are proposed to result from invasion of the 3' G-rich single strand overhang into the double stranded portion of the telomeric TTAGGG repeat tract. The strand displaced by invasion forms a structure called a D loop. The function of the t-loop is presumed to be the protection of the 3' telomeric end. In vitro, the double strand telomeric DNA binding protein TRF2 can increase the frequency of t-loop formation. The prevalence of the t-loops in vivo is not known.

Many proteins associate with telomeric DNA. One complex that binds telomeres is called shelterin. Shelterin is a six-protein complex composed of TRF1 and TRF2, which can bind double-stranded telomeric DNA, POT1, which can bind single-stranded telomeric DNA, and three other factors, RAP1, TIN2, and TPP1 (reviewed in de Lange 2006 "Telomeres"). Human telomeric DNA is also bound by nucleosomes (Makarov et al. 1993; Nikitina and Woodcock 2004). A number of other proteins, including some that play roles in the DNA damage response, can be found at telomeres (Zhu et al. 2000; Verdun et al. 2005).

Studies in yeast and humans indicate that the association of many proteins with telomeres is regulated through the cell cycle (Smith et al. 1993; Zhu et al. 2000; Taggart et al. 2002; Fisher et al. 2004; Takata et al. 2004; Takata et al. 2005; Verdun et al. 2005). For instance, TRF1, MRE11, POT1, ATM, and NBS1 display cell cycle regulated chromatin immunoprecipitation of telomeric DNA (Zhu et al. 2000; Verdun et al. 2005), and cytologically observable hTERT and hTERC localize to a subset of telomeres only in S-phase (Jady et al. 2006; Tomlinson et al. 2006). These data indicate that telomeres are dynamically remodeled through the cell cycle.

Preceded by: [Incorporation Of Extended And Processed Telomere End Into Associated Protein Structure](#)

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