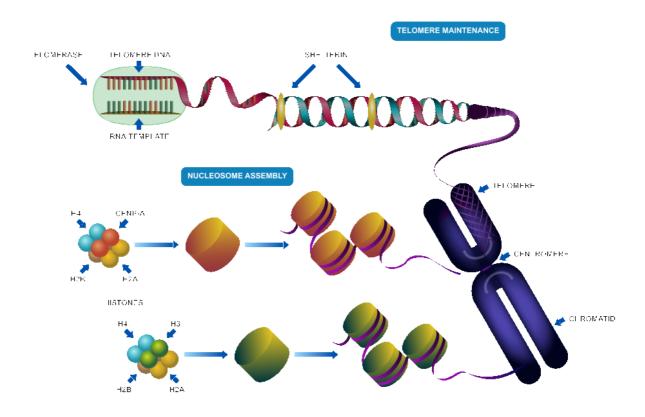


Chromosome Maintenance



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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

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 data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

Reactome database release: 77

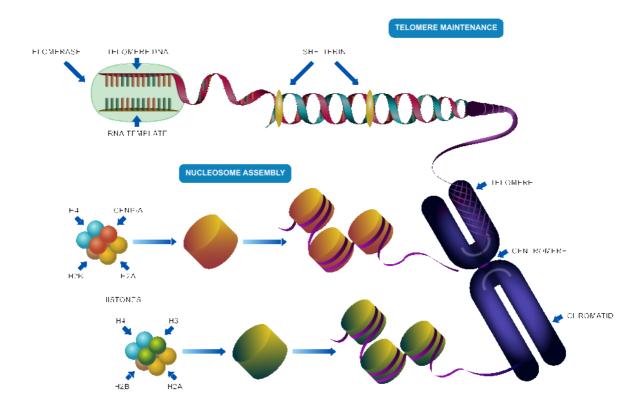
This document contains 3 pathways (see Table of Contents)

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Chromosome Maintenance

Stable identifier: R-HSA-73886

Compartments: nucleoplasm, nuclear envelope



Maintenance of chromosomal organization is critical for stable chromosome function. Two aspects of maintenance annotated in Reactome are centromeric chromatin assembly outside the context of DNA replication, involving **nucleosome assembly** with the histone H3 variant CenH3 (also called CENP-A), and the **maintenance of telomeres**, protein-DNA complexes at the ends of linear chromosomes that are important for genome stability.

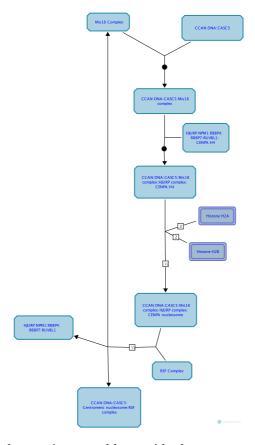
Editions

2021-05-18	Authored	Gillespie, ME.
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Nucleosome assembly 对

Location: Chromosome Maintenance

Stable identifier: R-HSA-774815



The formation of centromeric chromatin assembly outside the context of DNA replication involves the assembly of nucleosomes containing the histone H3 variant CenH3 (also called CENP-A).

Editions

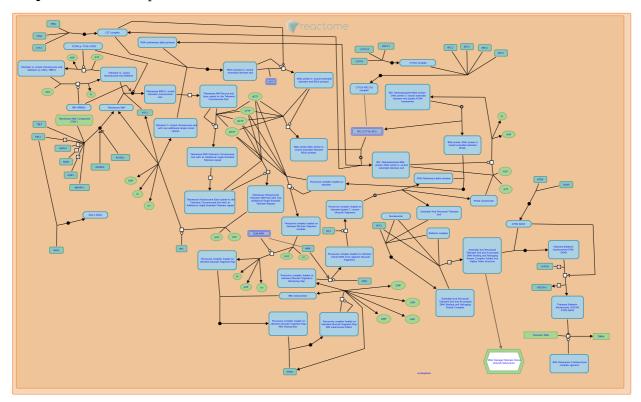
2010-05-21	Authored	Matthews, L.
2010-05-24	Edited	Matthews, L.

Telomere Maintenance

Location: Chromosome Maintenance

Stable identifier: R-HSA-157579

Compartments: nucleoplasm



Telomeres are protein-DNA complexes at the ends of linear chromosomes that are important for genome stability. Telomeric DNA in humans, as in many eukaryotic organisms, consists of tandem repeats (Blackburn and Gall 1978; Moyzis et al. 1988; Meyne et al. 1989). The repeats at human telomeres are composed of TTAGGG sequences and stretch for several kilobase pairs. Another feature of telomeric DNA in many eukaryotes is a G-rich 3' single strand overhang, which in humans is estimated to be approximately 50-300 bases long (Makarov et al. 1997; Wright et al. 1997; Huffman et al. 2000). Telomeric DNA isolated from humans and several other organisms can form a lasso-type structure called a t-loop in which the 3' single-strand end is presumed to invade the double stranded telomeric DNA repeat tract (Griffith et al. 1999). Telomeric DNA is bound by multiple protein factors that play important roles in regulating telomere length and in protecting the chromosome end from recombination, non-homologous end-joining, DNA damage signaling, and unregulated nucleolytic attack (reviewed in de Lange 2005).

DNA attrition can occur at telomeres, which can impact cell viability. Attrition can occur owing to the "end-replication problem", a consequence of the mechanism of lagging-strand synthesis (Watson 1972; Olovnikov 1973). Besides incomplete replication, nucleolytic processing also likely contributes to telomere attrition (Huffman et al. 2000). If telomeres become critically shortened, replicative senescence can result (Harley et al. 1990). Thus, in order to undergo multiple divisions, cells need a mechanism to replenish the sequence at their chromosome ends.

The primary means for maintaining the sequence at chromosome ends in many eukaryotic organisms, including humans, is based on telomerase (Greider and Blackburn, 1985; Morin 1989). Telomerase is a ribonucleoprotein complex minimally composed of a conserved protein subunit containing a reverse transcriptase domain (telomerase reverse transcriptase, TERT) (Lingner et al. 1997; Nakamura et al.

1997) and a template-containing RNA (telomerase RNA component, TERC, TR, TER) (Greider and Black burn, 1987; Feng et al 1995). Telomerase uses the RNA template to direct addition of multiple tandem repeats to the 3' G-rich single strand overhang. Besides extension by telomerase, maintenance of telomeric DNA involves additional activities, including C-strand synthesis, which fills in the opposing strand, and nucleolytic processing, which likely contributes to the generation of the 3' overhang.

Literature references

- Vega, LR., Mateyak, MK., Zakian, VA. (2003). Getting to the end: telomerase access in yeast and humans. *Nat Rev Mol Cell Biol*, 4, 948-59.
- Smogorzewska, A., de Lange, T. (2004). Regulation of telomerase by telomeric proteins. *Annu Rev Biochem, 73*, 177-208.
- Olovnikov, AM. (1973). A theory of marginotomy. The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon. *J Theor Biol, 41*, 181-90.
- Blackburn, EH., Gall, JG. (1978). A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in Tetrahymena. *J Mol Biol*, 120, 33-53.
- Greider, CW., Blackburn, EH. (1989). A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis. *Nature*, 337, 331-7. *¬*

Editions

2006-03-10	Authored	Blackburn, EH., Seidel, J.
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