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Chemical shift assignments and the secondary structure of the Est3 telomerase subunit in the yeast *Hansenula polymorpha*

Sofia S. Mariasina[1,2] · Sergey V. Efimov[3] · Olga A. Petrova[4] · Elena V. Rodina[2] · Alexander N. Malyavko[2,5] · Maria I. Zvereva[2] · Vladimir V. Klochkov[3] · Olga A. Dontsova[2,4,5] · Vladimir I. Polshakov[1]

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Abstract Telomerase is a multisubunit ribonucleoprotein enzyme that is essential for continuous cellular proliferation. A key role of telomerase in cancer and ageing makes it a promising target for the development of cancer therapies and treatments of other age-associated diseases, since telomerase allows unlimited proliferation potential of cells in the majority of cancer types. However, the structure and molecular mechanism of telomerase action are still poorly understood. In budding yeast, telomerase consists of the catalytic subunit, the telomerase reverse transcriptase or Est2 protein, telomerase RNA (TLC1) and two regulatory subunits, Est1 and Est3. Each of the four subunits is essential for in vivo telomerase function. Est3 interacts directly with Est1 and Est2, and stimulates Est2 catalytic activity. However, the exact role of the Est3 protein in telomerase function is still unknown. Determination of the structure, dynamic and functional properties of Est3 can bring new insights into the molecular mechanism of telomerase activity. Here we report nearly complete ^{1}H, ^{13}C and ^{15}N resonance assignments of Est3 from the yeast *Hansenula polymorpha*. Analysis of the assigned chemical shifts allowed us to identify the protein's secondary structure and backbone dynamic properties. Structure-based sequence alignment revealed similarities in the structural organization of yeast Est3 and mammalian TPP1 proteins.

Keywords Telomerase · Protein NMR · Resonance assignment · Secondary structure

Abbreviations

IPTG	Isopropyl-thio-β-D-galactoside
Est1	Telomere elongation protein
Est2	Telomerase reverse transcriptase subunit
Est3	Telomere replication protein
hpEst3	*Hansenula polymorpha* Est3 protein
scEst3	*Saccharomyces cerevisiae* Est3 protein
TEN	Telomerase N-terminal domain
TER	Telomerase RNA
TERT	Telomerase reverse transcriptase subunit
TEV	Tobacco etch virus nuclear-inclusion-a endopeptidase
TPPI	Telomere-binding protein, component of the six-membered shelterin complex

Biological context

Telomerase is a ribonucleoprotein complex that maintains telomeres by the addition of short DNA repeats at the 3′ end of eukaryotic chromosomes. Telomerase in vitro activity minimally requires the catalytic reverse transcriptase subunit (TERT in animals, or Est2 in yeast), and integral telomerase RNA (TER), that provides the template for telomeric DNA synthesis (Wyatt et al. 2010). However, in vivo activity of telomerase requires additional protein components. The

✉ Vladimir I. Polshakov
vpolsha@mail.ru

1 Center for Magnetic Tomography and Spectroscopy, Faculty of Fundamental Medicine, M.V. Lomonosov Moscow State University, Moscow, Russia 119991

2 Department of Chemistry, M.V. Lomonosov Moscow State University, Moscow, Russia 119991

3 NMR Laboratory, Institute of Physics, Kazan Federal University, 18 Kremlevskaya, Kazan, Russia 420008

4 A.N. Belozersky Institute of Physico-Chemical Biology, M.V. Lomonosov Moscow State University, Moscow, Russia 119991

5 Skolkovo Institute of Science and Technology, Moscow, Russia

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