Poster Presentation

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Towards structural characterization of H. polymorpha telomerase components

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Telomeres are regions of non-coding DNA that cap the chromosomes, preventing the loss of coding DNA during cell division and contributing to chromosomal stability. In actively dividing cells, such as embryonic stem cells, the telomeres need to elongated by telomerase. The telomerase complex consist of the enzyme telomerase reverse transcriptase (TERT), telomerase RNA (TR) and additional proteins. TERT and TR are required for the telomerase activity in vitro. Telomerase is active in vast majority of the cancer cells ensuring continuous cell division and tumor growth. Syndromes leading to premature aging are often associated with short telomeres. Finding ways to regulate the telomerase activity would help to advance therapies for these conditions. However, the structural information available of the telomerase complex is very limited. We have chosen thermophilic yeast Hansenula polymorpha as a model system due to the stability of its proteins. The N-terminal domain of the TERT is essential for telomerase activity and possibly is involved in binding of TR, telomeric DNA and additional protein components of the telomerase complex. We have crystallised the N-terminal domain of H. polymorpha TERT and, in lack of a homologious structure, produced a seleno-methionine derivative of the protein. MAD data on N-terminal domain has been collected to resolution of 2.0 Å at the PETRA-III beamline P13 (EMBL/DESY) in Hamburg. We will discuss the structure-function relationship of the N-domain and the whole TERT component.

Keywords: Telomerase, Cell division, Cancer therapy