SA1 and TRF1 synergistically bind to telomeric DNA and promote DNA-DNA pairing

HONG WANG, JIANGGUO LIN, PRESTON COUNTRYMAN, HAI PAN, North Carolina State University, PARMINDER KAUR TEAM, ROBERT RIEHN TEAM, PATRICIA OPRESKO TEAM, JANE TAO TEAM, SUSAN SMITH TEAM — Impaired telomere cohesion leads to increased aneuploidy and early onset of tumorigenesis. Cohesion is thought to occur through the entrapment of two DNA strands within tripartite cohesin ring(s), along with a fourth subunit (SA1/SA2). Surprisingly, cohesion rings are not essential for telomere cohesion, which instead requires SA1 and shelterin proteins including TRF1. However, neither this unique cohesion mechanism at telomeres or DNA-binding properties of SA1 is understood. Here, using single-molecule fluorescence imaging of quantum dot-labeled proteins on DNA we discover that while SA1 diffuses across multiple telomeric and non-telomeric regions, the diffusion mediated through its N-terminal domain is slower at telomeric regions. However, addition of TRF1 traps SA1 within telomeric regions, which form longer DNA-DNA pairing tracts than with TRF1 alone, as revealed by atomic force microscopy. Together, these experimental results and coarse-grained molecular dynamics simulations suggest that TRF1 and SA1 synergistically interact with DNA to support telomere cohesion without cohesin rings.

Hong Wang
North Carolina State University

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