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The role of telomere dynamics in aging and cancer KRASTAN BLAGOEV, EDWIN GOODWIN, Los Alamos National Laboratory — Telomere length changes are far more dynamic than previously thought. In addition to a gradual loss of ∼100 base pairs per telomere in each cell division, losses as well as gains may occur within a single cell cycle. We are investigating how telomere exchange, extension, and deletion affect the proliferative potential of telomerase-negative somatic cells. Experimental techniques are being devised to detect dynamic telomere processes and quantify both the frequency and length changes of each. In parallel, a "dynamic telomere model" is being used that incorporates telomere dynamics to study how the telomere size distribution evolves with time. This is an essential step towards understanding the role that telomere dynamics play in the normal aging of tissues and organisms. The model casts light on relationships not otherwise easily explained by a deterministic "mitotic clock," or to what extent the shortest initial telomere determines the onset of senescence. We also expect to identify biomarkers that will correlate with aging better than average telomere length and to shed light on the transition to unlimited growth found in telomerase-negative tumor cells having the ALT (alternative lengthening of telomeres) phenotype, and to evaluate strategies to suppress the growth of these tumors.

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