

Department of Anatomy & Cell Biology Chair Search Seminar

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Telomerase and Telomere Regulation in Health and Disease

Telomere maintenance is essential for replicative immortality characteristic of cancer cells. In highly proliferative cells such as blood, stem and most cancer cells, telomere synthesis is catalyzed by the telomerase reverse transcriptase. Mutations in telomere and telomerase protein components cause short (premature aging diseases) and long (cancers) telomere syndromes. We are interested in understanding the mechanisms regulating (1) telomerase assembly and (2) telomerase localization to telomeres, two essential steps required for telomerase function at telomeres. (1) Recent published cryo-electron microscopy structures of the telomerase holoenzyme account for years of accumulated biochemical findings implicating unique domains in the telomerase reverse transcriptase and a telomere protein (including specific premature aging disease-associated residues) in enzyme activity, localization to telomeres and cell immortalization. Moreover, a recently proposed model based on single-molecule imaging suggests telomerase localization to telomeres occurs in two steps that are differentially regulated, a recruitment step and a retention step. The talk will address the coordinated role of these unique domains in telomerase recruitment and retention. (2) Dyskerin is a highly conserved nucleolar protein, and a component of the human telomerase complex that regulates telomerase RNA processing, and the assembly and function of the telomerase complex. The X-linked premature aging and telomere syndrome dyskeratosis congenita is caused by mutations in the gene encoding dyskerin. How dyskerin regulates processing, assembly and function of the telomerase complex remains largely unknown. The talk will address the contributions of the post-translational modification, SUMO, dyskerin-RNA interactions, dyskerin subcellular localization and dyskerin dimerization in the regulation of telomerase biogenesis and function. A better understanding of the mechanisms regulating telomerase recruitment/retention and telomerase biogenesis will inform future therapeutic approaches for short and long telomere syndromes.



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11:30am - 12:30pm

Room 1/12 - Strathcona
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Hosted by: Alba Guarné, PhD



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