Project Title: Telomere deprotection and cancer	**Code: CMRI1**
Host School / Institute: Children's Medical Research Institute	**Address:** 214 Hawkesbury Road, Westmead
Certificates & Clearances required: No	
Primary Supervisor: Dr Anthony Cesare	
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Co-Supervisor/team: Post-doctoral researchers Sam Rogers and David Van Ly	
Project Type: Laboratory based	
Project Category: Molecular biology; Cancer	
Skills / Attributes of a successful student: Talented and inquisitive student, interested in pursuing research in cutting edge cell and molecular biology. Ideally the candidate will have laboratory experience in a molecular and cell biology lab. We will provide all the necessary training related to experimentation and research topic. Projects will be directed towards student interest and capability. Individuals with a desire to pursue a Ph.D. will be given priority.	
Project Keywords: Telomeres; DNA Damage response; Microscopy; Molecular Biology; Cell Biology	

Project Description: Telomeres are the structures at human chromosome ends that regulate cellular aging and tumour suppression. This project will explore how telomeres cooperate with the DNA damage response to control these phenomena.

Telomeres are the protective nucleoprotein structures at chromosome ends. They function to protect chromosome termini, and prevent activation of the DNA damage response and illicit DNA repair activity at the naturally occurring chromosome ends. As a consequence of normal ageing, telomeres shorten each time a cell divides. In human cells, progressive telomere shortening is a potent tumour suppressor mechanism that prevents unlimited cell growth in the presence of cancerous mutations.

Our laboratory has identified that telomeres exist in three different structural states. "Closed-state" telomeres prevent activation of the telomere DDR, while "Uncapped-state" telomeres are subjected to DNA repair activity that covalently links chromosome ends together. In between these fully protected and completely unprotected states, lies an "Intermediate-state", which is the critical feature governing Telomere-dependent tumour suppression. Intermediate-state telomeres are unique in that they can activate the DNA damage response and arrest cell growth, while simultaneously inhibiting DNA repair. This enables aged cells to activate a warning signal, and stop proliferation, while simultaneously preventing further genomic instability that can lead to cancer. We were also part of the team that identified telomeres transition from the closed- to intermediate-state during prolonged mitosis, and that this serves as a signalling mechanism to kill human cells with genome instability. This discovery exposed a complex, but poorly understood, relationship between telomeres and cell division, which we continue to actively explore.

Much of our research now focuses on understanding how telomeres govern cell cycle arrest, and the relationship between telomere protection and mitosis. We have opportunities in our laboratory to study telomere biology in relation to genome stability, tumour suppression, cell signalling and mitosis, using cutting edge techniques. Projects will be tailored to applicants interests and strengths on an individual basis.