Targeting RLF and RLF-MYCL Fusion: A Novel Regulator of Replication Fork Speed and Cancer Epigenetics

Project Description

Project duration:	Honours, PhD or MPhil
Description:	Accurate DNA replication is essential for genome integrity, and disruptions in replication fork dynamics contribute to developmental disorders and cancer. This project focuses on the Rearranged L-myc Fusion (RLF) gene, a newly identified regulator of replication fork speed and chromatin architecture. RLF is a zinc-finger transcription factor involved in epigenetic regulation and replication factory organisation. Its fusion with MYCL (RLF-MYCL) in certain cancers suggests a gain-of-function mechanism that drives oncogenesis and disrupts genome stability. We aim to unravel how RLF and RLF-MYCL fusion regulate DNA replication, cohesin positioning, and 3D genome organisation using innovative tools including DNAscent, a world-first replication mapping assay based on nanopore sequencing, and genome-wide ChIP-seq and Hi-C. This research will provide foundational insights into the role of RLF in normal and cancer cells and guide the development of targeted therapeutics.
Expected outcomes and deliverables:	Students will: • Study how RLF and RLF-MYCL fusion influence replication fork speed, origin usage, and cohesion dynamics • Gain expertise in genome-wide methods such as ChIP-seq, RNA-seq, Hi-C, and nanopore-based replication profiling (DNAscent) • Contribute to functional validation of RLF-regulated loci using CRISPR knockout cell lines • Explore strategies to therapeutically target the RLF-MYCL fusion in cancer models • Deliverables include a written thesis, oral presentations, and potential contributions to high-impact publications

Suitable for:	Ideal for students interested in cancer biology, genomics, gene regulation, DNA replication, or epigenetics. A background in molecular biology, bioinformatics, or biotechnology is beneficial but not required. Enthusiasm for discovery science and interest in translational applications is highly valued.
Primary Supervisor:	Dr Murugan Kalimutho and Professor Kum Kum Khanna
Further info:	Interested applicants are encouraged to contact the research team prior to applying: e: Murugan.kalimutho@mater.uq.edu.au