CHILDREN'S MEDICAL RESEARCH INSTITUTE
Jeans for Genes®

Finding cures for children's genetic diseases

Post-doctoral position in the CMRI Genome Integrity Unit/Cesare Laboratory

- **Make an important contribution to the health of children through medical research**
- **Work with one of Australia's most respected national and independent medical research institutes**
- **Located in Westmead, one of Sydney's and Australia's major biomedical research hubs**

A three-year post-doctoral position in the Genome Integrity Unit, funded by an Australian Research Council Discovery Project, is now available. We are looking for a highly motivated researcher to explore the molecular mechanisms governing telomere protection and telomere replication in pluripotent stem cells. The successful applicant will have a PhD (or be in the final stages of completion) with a strong background in stem cells and molecular biology.

Position Summary
The CMRI Genome Integrity Unit is led by Associate Prof. Tony Cesare and studies how mammalian cells maintain their DNA health, the physiological consequences when these processes are perturbed, and the implication on human diseases including cancer. Post-doctoral scientists are expected to lead their own projects, contribute to internal or external collaborations, and when possible guide student research. The ability to work as part of a team is essential.

Key experience and competencies
The individual employed will be an ambitious post-doctoral scientist with a bold and creative approach to research. They will be capable of independent thought and project design and will be able to work in a collaborative or team setting. Exceptional candidates will be eligible for internal CMRI training fellowships and the possibilities provided by this unique funding opportunity.

Essential characteristics
- PhD in the biomedical sciences (molecular and cell biology, biochemistry, etc). Candidates in the final stages of PhD submission are welcome to apply.
- Expert knowledge of pluripotent stem cell culture.
- Technical expertise in microscopy and standard molecular biology techniques.
- Independent experimental design and completion.
- Track record of scientific publication.
- Track record of presentation at scientific meetings.

Desirable characteristics
- Experience in genome stability, telomere biology, and or DNA repair.
- Academic career ambition
- Experience culturing naïve and primed stem cells.
- Experience with in vitro embryo culture.
- Experience in genome editing.
- Experience in live or super-resolution imaging.

Project specifics
This project will investigate how the specialized chromosome end structures, termed telomeres, are protected and replicated in pluripotent stem cells. This is part of an on-going collaboration with the Boulton Lab (Crick Institute, UK) and the CMRI Embryology Unit led by Patrick Tam.

In somatic tissues, the telomere protein TRF2 plays an essential role in delineating and protecting chromosome ends. Deleting TRF2 in somatic cells results in a robust telomere-specific DNA damage response and end-to-end chromosome fusions. Data from our laboratory indicates that TRF2 protects chromosome ends through formation of a lariat 'telomere loop (t-loop)' structure (Cesare et al, 2013, *Molecular Cell*; Van Ly et al, 2018 *Molecular Cell*; Sarek et al, 2019 *Nature*). In collaboration with the Boulton lab, we made the surprising discovery that TRF2 is dispensable in pluripotent stem cells (Ruis et al, 2021 *Nature*). This revealed that critical telomere functions are not conserved between pluripotent and somatic cells.

We will continue this study and address several open questions related to telomere protection and replication in pluripotent stem cells. Additionally, we will address how cellular mechanisms that respond to telomere dysfunction differ in somatic and pluripotent tissues. The candidate will address these questions through a molecular and cell biology approach in pluripotent and somatic cells measured through super-resolution-, live- and fixed-microscopy, cell-based assays, and proteomic approaches. The position holder will benefit from the collective telomere and stem cell biology expertise within CMRI (laboratories led by A/Prof. Cesare and Profs. Reddel, Pickett Bryan, and Tam), dedicated microscopy and proteomic facilities, and our international collaborative network.

Laboratory details
The Genome Integrity Unit/Cesare laboratory is currently supported by two NHMRC ideas grants, an NHMRC project grant, and an ARC Discovery project. In the past three years we have published 16 papers total in journals including *Nature* (two articles), *Nature Cell Biology*, *Molecular Cell*, and *Nature Communications*. We are looking for outstanding individuals to join the research team at all levels. For more information please visit:
https://www.cmrijeansforgenes.org.au/research/research-teams/genome-integrity, or
https://twitter.com/TheCesareLab

Position compensation
The candidate will be compensated with a competitive remuneration package in accordance with qualifications and experience. Additional benefits include the provision of a Public Benevolent Institution salary packaging scheme and participation in an employer-contributed superannuation fund.

Application
Applications should include a cover letter (citing **PV2110**), curriculum vitae and contact details (phone/email) of three professional referees and be forwarded to recruitment@cmri.org.au

The position will remain open until a suitable candidate is found. We are amenable to the candidate starting late in 2021 pending completion of their PhD or relocation from out-of-state or overseas.

Please direct enquiries Tony Cesare (project principal investigator) at tcesare@cmri.org.au