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Monash Biomedicine Discovery Institute Cancer Program

OTHER PROGRAM AFFILIATIONS

Development and Stem Cells

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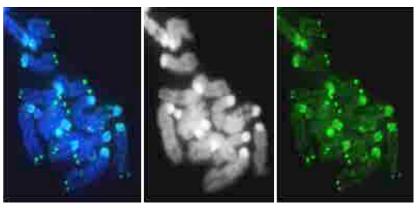
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Both centromeres and telomeres are important chromosomal structures that control genome stability and genetic transmission. Our research interest is to uncover fundamental epigenetic mechanisms and new chromatin factors that regulate centromere and telomere functions. Recent studies have reported the frequent mutations of histone variant H3.3 and chromatin factor ATRX in human cancers including brain and bone cancers. These cancers with H3.3 and ATRX mutations are defective in telomere function, and they use the ALT (Alternative Lengthening of Telomeres) pathway for maintaining telomere length in order to ensure a continual cellular growth capacity. Our aims are: (1) to define the role of H3.3 and ATRX in maintaining telomere function and global DNA stability; (2) to investigate epigenetic defects associated the loss of ATRX function in ALT cancers.

Research Projects:

 Determination of novel chromatin factors that are involved in suppressing ALT activation



Staining of repressive histone mark-trimethylated H4K20 at the centromeres and telomeres in mouse embryonic stem cells.

Selected significant publications:

- Chang FTM, Chan FL, McGhie JDR, Udugama M, Mayne L, Collas P, Mann JR, Wong LH, et al. 2015. CHK1-driven histone H3.3 serine 31 phosphorylation is important for chromatin maintenance and cell survival in human ALT cancer cells. Nucleic Acids Res, 43 (5): 2603-2614.
- Chan FL, Marshall OJ, Kim B, Saffery R, Choo KHA and Wong LH. 2012. Novel RNA polymerase II transcriptional activity at the kinetochore during mitosis. Proc Natl Acad Sci USA. 109(6): 1979 – 1984.
- 3. Wong LH, McGhie JD, Sim M, Anderson MA, Ahn S, Hannan RD, George A, Morgan K, Mann JR and Choo KHA. 2010. ATRX interacts with H3.3 in maintaining telomere structural integrity in pluripotent embryonic stem cells. *Genome Res.* 20: 351-360.
- Chueh AC, Northrop EL, Brettingham-Moore KH, Choo KHA, Wong LH. 2009. LINE retrotransposon RNA is an essential structural and functional epigenetic component of a core neocentromeric chromatin. PLoS Genet. 5: e1000354.
- Wong LH, Ren H, Williams E, McGhie J, Ahn S, Sim M, Tam A, Earle E, Anderson MA, Mann J, and Choo KHA. 2009. Histone H3.3 incorporation provides a unique and functionally essential telomeric chromatin in embryonic stem cells. Genome Res. 19: 404-414.