**Computational identification of universal alterations in DNA methylation and nucleosome positioning in a matched normal/tumor sample**

Jason W. H. Wong[1], Luke B. Hesson[1], Mathew A. Sloane[1], John E. Pimanda[1], Michael J Bourke[2], Nicholas J. Hawkins[3] and Robyn L. Ward[1]

**Affiliation:** [1]Adult Cancer Program, Lowy Cancer Research Centre and Prince of Wales Clinical School, University of New South Wales, Sydney, New South Wales, AUSTRALIA. [2]Department of Gastroenterology and Hepatology, Westmead Hospital, Sydney, AUSTRALIA. [3]School of Medical Sciences, University of New South Wales, Sydney, New South Wales, AUSTRALIA.

**E-mail:** jason.wong@unsw.edu.au

## Abstract

DNA methylation and nucleosome positioning are known to be important in the epigenetic regulation of gene expression. More recently, studies using whole-genome approaches have also suggested that nucleosomes are likely to play an important role in the regulation of alternative splicing. In many tumors, DNA methylation is significantly altered, with the cancer epigenome characterized by global hypomethylation and site-specific hypermethylation. Here, we used MethylMiner (Invitrogen) to enrich for methylated DNA and micrococcal nuclease (MNase) digestion to isolate nucleosome-protected DNA, followed by next-generation sequencing, to explore changes in DNA methylation and nucleosome positioning across gene promoters and intragenic regions in an early colorectal adenoma.

We determined the level of DNA methylation and nucleosome occupancy at a number of different gene regions including transcription start sites, promoter CpG islands and intron/exons. By aligning respective regions across all genes, we computed the average read coverage per base within and around each region. This enabled us to compare the relative methylation or nucleosome occupancy between normal and tumor samples at a global level. Finally, we performed hierarchical clustering and principal components analysis to identify patterns of DNA methylation and nucleosome occupancy across all genes across at the different gene regions analyzed. Our results show an increase in nucleosome occupancy at methlyated promoters and provide interesting insights into the interplay between DNA methylation and nucleosome remodeling in the epigenetic regulation of DNA function.