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Selected Publication

Chan KM, Fang D, Gan H, Hashizume R, Yu C, Schroeder M, Gupta N, Mueller S, James CD, Jenkins R, Sarkaria J, Zhang Z. (2013) The histone H3.3K27M mutation in pediatric glioma reprograms H3K27 methylation and gene expression. *Genes & Dev* 2013; 27:985-990

Research Aims and Interests

Genetic information is encoded by the DNA sequence; yet, DNA alone does not account for the complexity of the mammalian genome. Chromatin, comprising DNA, core histone proteins, and other regulatory proteins, regulates gene expression and maintains genome stability.

Recent studies using the next generation sequencing (NGS) technologies have identified for the first time mutations on histone genes in two pediatric brain cancers; diffuse intrinsic pontine gliomas (DIPG) and glioblastoma multiforme (GBM). Two recurrent somatic mutations (K27M and G34R/V) were identified in genes encoding the canonical histone H3.1 (HIST1H3B) and its variant H3.3 (H3F3A). This revealed the important roles of histone modifications in human diseases and links epigenetic changes to tumorigenesis.

We are interested in understanding how histone mutations found in human diseases affect the epigenetic landscapes; alter gene expression and cellular functions. In addition, we are also using X-chromosome inactivation as a model system to elucidate how epigenetic factors maintain gene silencing during cell divisions. We will combine biochemistry, cell biology, and genome-wide ChIP-seq and RNA-seq approaches to address these questions.