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Model based analysis of bisulfite sequencing and its application in liquid biopsy

Abstract: Bisulfite sequencing (BS-seq) is the gold standard for studying genome-wide and base-resolution DNA methylation. We developed MOABS to increase the speed, accuracy, statistical power and biological relevance of BS-seq data analysis. MOABS detects differential methylation with 10-fold coverage at single-CpG resolution based on a Beta-Binomial hierarchical model. Based on exact numerical solution to the model, we developed the Credible Difference concept which is a conservative estimation of true methylation ratio difference adjusted by sequencing depth. The Credible Difference turns out to have combined biological significance and statistical significance, and can be used to rank all the cytosines in the genome instead of combinations of p-value and nominal methylation ratio difference. MOABS is capable of processing two billion reads in 24 CPU hours.

Liquid Biopsy is a powerful approach to detect cancer through circulating tumor DNA in blood. Most common methods of liquid biopsy are genome sequencing or exome sequencing. We use Whole Genome Bisulfite Sequencing and MOABS to analyze DNA methylation of the cell-free DNAs. We can obtain high sensitivity and specificity of cancer detection in both simulation studies and real human sample validations. In the resulting biomarker region, we also found a substantial presence of the recently discovered epigenetic feature DNA methylation Canyon, a large Undermethylated region from several thousand bases to tens of thousand bases.

Keck Seminar

Friday, September 15, 4pm

BioScience Research Collaborative

Room 280 (2nd Floor)

Gulf Coast Consortia

QUANTITATIVE BIOMEDICAL SCIENCES

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