Abstract

New and potentially powerful biomarkers have been constantly emerging due to the continued elucidation of the genetic and epigenetic alterations that drive the disease progression. Many of the methods for rapid and accurate biomarker detections are nucleic acids-based molecular diagnostics, owing to their superior turnaround time, sensitivity and specificity. The DNA hybridization reaction, as the primitive of constructing molecular machineries, the engineer of which enables the rational design of hybridization probes, PCR primers as well as a variety of nucleic acids-based devices and assays.

This thesis is a collection of four projects that demonstrate and characterize nucleic acids-based devices for genetic/epigenetic biomarker diagnostics. An approach of integrating an upstream target-recycled DNA circuit with a downstream self-sustainably triggered nonlinear hybridization chain reaction was developed, which demonstrated improved signal amplifying performance with high detection sensitivity, and specifically the design of amplification circuits is generic in sequences for different analytes. To achieve high specific detection of trace SNVs, we established a new hybridization-based assay combining the approach of competitive DNA hybridization probes with exonuclease III, which selectively amplify the signal in the presence of the intended SNV over WT, enabling better discrimination of single base differences in DNA sequences than hybridization probes relying on competition or amplification alone.

Aberrant DNA methylation alteration is a well-known contributor to carcinogenesis. The current gold standard for base-level resolution and quantitative DNA methylation analysis is based on the sodium bisulfite conversion. We employed the targeted bisulfite sequencing to characterize the bisulfite conversion efficiency, DNA fragmentation and conversion correlation of cytosine pairs. We discussed the principles of multiplexed primer design for bisulfite DNA and sought to identify a panel of robust differential-methylated regions that are exceptional specific to high-grade serous ovarian carcinoma and assess the potential use of the identified loci as methylation biomarkers.

Date: 14 Aug 2019 (Wednesday)
Time: 10:00 am
Venue: Room 4582 (Lifts 27-28)

Examination Committee:
Prof. Xiaoyuan Li (Chair)
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All are welcome!