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Construction of an interstrand lock for single-molecule site-specific DNA methylation in a nanopore

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In this report, we utilized the nanopore single-molecule sensor to investigate a base-pair specific metal ion/nucleic acids interaction, and explored its potential application in locus-specific DNA methylation analysis. We identified that divalent Mercury ion (Hg21) can selectively bind a uracil-thymine mismatch (U-T) in a dsDNA. The Hg21 binding creates a reversible interstrand lock, called MercuLock, which enhances the hybridization strength by two orders of magnitude. Such MercuLock cannot be formed in a 5-methylcytosine-thymine mismatch (mC-T). By nanopore detection of dsDNA stability, single bases of uracil 5-methylcytosine can be distinguished. Since uracil is converted from cytosine by bisulfite treatment, cytosine and 59-methylcytosine can be discriminated. We have demonstrated multiple CpG methylation analysis in a p16 gene CpG island. This single-molecule assay may have potential in detection of epigenetic cancer biomarkers in biofluids, with an ultimate goal for early diagnosis of cancer.

Biography

Li-Qun Gu, an Associate Professor of Bioengineering at the University of Missouri, is leading an interdisciplinary laboratory that has a long term vision: Integrating biomolecular engineering with nanobiotechnology to explore life science problems and to develop sophisticated molecular diagnostic tools for personalized medicine. He received the NSF CAREER award the NIH grant to develop ultrasensitive single-molecule technology for disease biomarker detection. He has published over 40 peer-reviewed papers in high tier journals including *Nature, Nature Nanotechnology, Science and PNAS*. The nanopore-nanosensor he developed can detect circulating microRNAs in cancer patient plasma, offering a non-invasive approach to screening and disease diagnose.

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