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DEFENSE OF THE DOCTORAL

DISSERTATION

"DNA Probe Design Approaches to Generate New Assays for the Detection of Cancer Somatic Mutations and COVID19 Variants"

by

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MD/PhD Program

BS, Biochemistry 2015, Boston College, Chestnut Hill, MA

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https://rutgers.zoom.us/j/97934320289?pwd=SUN5OHRsakdKcTJVZXFNdzNWRVJmdz09

Monday, March 27th, 2023
3:00 P.M.
ICPH Auditorium, zoom

Abstract

Analysis of cells' nucleic acids is commonly employed to gain insight into cell state and function. Leveraging thermodynamic characteristics of nucleic acid probes, we have designed probes that can selectively bind mutant targets and produce a signal, called single nucleotide discriminating molecular beacons. By using these technologies, we created laboratory tests that can detect SARS-COV2, the causative agent of COVID19, as well as tests to identify which SARS-CoV2 variant is present in a sample. These tests enable identification of SARS-CoV2 variants for treatment as well as for tracking these variants epidemiologically.

We have also generated assays and techniques which use SuperSelective primers to identify rare mutations in a background of wildtype sequences, a task that is useful in liquid biopsy diagnosis of cancer. We have expanded this work into the realm of sequencing where it is possible to detect more mutations than previously possible via fluorogenic PCR. We show that products of PCR with SuperSelective primers can be analyzed by sequencing. We also explored a pooled SuperSelective primer approach to identify SuperSelective primers designs that are effective in amplifying mutant and ignoring the wildtype sequences.

By using python code, we created a program, COD-FISH, that designs probes for use with single molecule Fluorescent *in situ* Hybridization (smFISH). COD-FISH implements an accessible user interface for users of all levels of experience and uses the ensembl database to identify the appropriate transcripts for the gene you are looking for with smFISH. It uses the blast+ program and the most accurate nucleic acids affinity analysis, nearest neighbor thermodynamics, to predict optimal probe sets. These probe sets should increase signal intensity and reduce signal to background ratio, making smFISH experiments more accurate.

Lastly, we have used our understanding of nucleic acids and their sequencing to perform analysis on a variety of subjects, ranging from mouse models of Tuberculosis to finding unique new cell types in the fetal immune system.