The Summer Undergraduate Research Fellowship (SURF) Symposium
3 August 2017
Purdue University, West Lafayette, Indiana, USA

Pathogenic DNA detection using DNA hairpins: a Non-Linear Hybridization Chain Reaction Platform

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ABSTRACT

Currently, 3.2 billion people are at risk of being infected with malaria, with 1.2 billion of those being at high risk (>1 in 1000 chance of getting malaria in a year). Thus, there is a need for a biosensor that is highly sensitive, cost effective, and simple to use for point-of-care diagnosis. The biosensing platform, PathVis, has achieved this by measuring changes in fluid properties after a loop-mediated isothermal amplification (LAMP). LAMP is a DNA amplification system that requires enzymes and a temperature of 65 degrees C. LAMP currently limits PathVis by being costly, requiring refrigeration, and difficult to design. We seek to overcome these limitations by replacing this reaction with a non-enzymatic, low-cost, shelf stable, room temperature DNA amplification reaction. The hybridization chain reaction system (HCR) consists of two DNA hairpins that polymerize into long chains in the presence of target DNA. HCR can be designed to grow as linear polymers or branching polymers, the ladder providing exponential signal growth. We have developed an algorithm to generate hairpin systems for a given target DNA sequence. Using this algorithm, we have developed a branching HCR system for detecting malaria. We have found that this algorithm is extremely versatile and can generate hairpin systems for whole chromosomes (>1,000,000 base pairs) in under five minutes. We have found that this malaria detection system theoretically amplifies in the presence of its target; resulting in a system that is ready to be optimized, experimentally tested, and validated on the PathVis biosensing platform.

KEYWORDS

HCR, Dendritic Growth, Malaria, plasmodium falciparum, 3D7, hybridization, DNA