DimaSense™: 
A Novel Nucleic Acid Detection System

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Technology Description

Recently, we developed a suite of methods for the rational design and fabrication of well-defined nanoparticle architectures, including clusters using bio-encoded nanoscale building blocks and layer-by-layer stepwise assembly on a solid support. In particular, the Nano-Assembly platform using Encoded Solid Supports (NAESS) allows for controlled interactions, purification of side products, modularity of design, and the construction of complex nanoparticle architectures. This approach offers several advantages over the current art of designing nanoparticle clusters, which include the high-yield synthesis of desired architectures, a “plug-and-play” design allowing for the introduction of a variety of sensing modalities, and ease of scalability in high-throughput and synthesis yield.

As a utility proof of concept, we implemented our unique cluster fabrication platform to design gold nanoparticle dimers which are linked via a single-stranded DNA oligonucleotide recognition motif. The design of this motif is such that binding of complementary nucleic acids results in specific, selective and rapid dimer dissociation, which can be monitored by Dynamic Light Scattering (DLS). We demonstrated single level mismatch selectivity using this approach. The limit of detection was determined to be $10^{11}$ molecules of synthetic target RNA or DNA within 30 minutes of incubation at 33°C. This detection limit is determined by the dimer’s concentration which can be probed by currently used standard DLS instruments. We also demonstrated a specific detection of target RNA in a solution containing competing 1,000-fold excess of non-complementary DNA fragments, 10% BSA, and endonucleases.

Markets and Applications

Molecular diagnostic companies, RNA-based technology developers, and personalized medicine companies have applications that could benefit from using DimaSense™.

The technology represents a platform which enables the simple and reasonably inexpensive design and fabrication of highly selective genetic sensors. These sensors operate with very low concentrations of target, can utilize standard instrumentation, produce detection results rapidly, and are robust enough to function in the presence of many competing genetic targets.

Many current genetic target detection products/approaches/technologies rely upon methods (such as qPCR) which are more complicated, cumbersome, and costly to perform, and are not well suited to point-of-care diagnostic applications.

Several clinical diagnostic applications, particularly point-of-care (POC) diagnostics for infectious diseases, are possible and appear to be a good fit for the technology. In addition, the advent of personalized medicine will create opportunities for molecular diagnostic companies with the capabilities of rapidly and quantitatively detecting nucleic acid sequences. The global POC market was ~$7.7B in 2010, with a recent annual growth rate of ~7%. A specific disease or disease-class diagnostic would need to be identified before a more meaningful sub-market value could be stated.

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Sensor design tuning of specificity, selectivity, and reaction kinetics
• modifications to single-stranded recognition region of linker
• number of base pairs between target and linker

Commercial Readiness

Additional validation of the technology to show that it displays appropriate performance parameters for a commercial application on ‘real world’ samples is required for true commercial readiness. In addition, optimization of sensor design parameters, to effect a 10-fold increase in sensitivity, may be required to produce a commercially ready sensor system. These validation and sensor design optimization are estimated to require 3-4 months and ~$75k.

For an unregulated product to give this sensor system a distinct competitive advantage, 2-3 years of product development and $1.5-3M are likely required. For regulated markets, time to market (through clinic) and cost would depend upon the product.

Intellectual Property

U.S. and Foreign Patent Applications are pending. They claim the structures and methods of making them, as well as platform technologies used during fabrication. During scale-up to commercial production it is likely that patentable methods will be developed relating to materials processing. An industrial partner may also choose to protect certain know-how gained during scale-up as trade secrets.

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