

**Runner-up Technology**  
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**Nanoprobes for Detection or Modification of Molecules**

The available nanoprobes are molecular machines that have the potential to transform current approaches to molecular detection and modification for therapeutic research, diagnostic evaluation, and treatment. This technology provides a *one-step alternative* to multi-step assays, such as ELISA, Southern and Western blots, etc. Additionally, these nanoprobes can be used for nucleic acid sequencing. Thus, commercial availability of this novel technology for identification, modification and destruction of proteins, DNA and RNA *in-vitro* and *in-vivo* would represent a remarkable breakthrough with applications in a broad range of diseases.

The described nanoprobes consist of a rigid molecular rod, having a flexible molecular tether at both ends. Each tether carries a functional group along with a Fluorescent Resonance Energy Transfer (FRET) fluorophore acceptor or donor. When tethered functional groups (e.g. antibodies or oligonucleotides) recognize and bind to the target molecule the FRET donor-acceptor pair is brought in close association, resulting in emission of a detectable signal. Modification or degradation of the target molecule is achievable with the addition of an appropriate enzyme to the functional group, such as a ligase, nuclease or proteinase.

A specific example of the described nanoprobes is Medusa<sup>TM</sup>, which is the subject of a related patent application by the inventors of the current nanoprobe technology. This composition permits sequencing of a nucleic acid molecule with the use of a single reagent. The central component of Medusa<sup>TM</sup> is either a DNA or RNA polymerase or reverse transcriptase enzyme with an attached fluorescent dye, which serves as the donor for FRET. Medusa<sup>TM</sup> consists also of four flexible molecular arms, terminated by one of the four nucleotide bases, each attached with a corresponding distinct fluorescent acceptor. The polymerase binds to the target nucleic acid sequence via a primer and the complementary base at the end of a Medusa<sup>TM</sup> arm hybridizes to the unpaired base of the template. Hybridization of the specific bases to the template is sequential and extends the primer, while bringing the corresponding FRET acceptor in close proximity to the donor fluorophore attached to the polymerase. Interaction of the FRET pair produces a characteristic signal for the given base and exposes Medusa<sup>TM</sup> to next complementary base to be sequenced.

The related technologies are further described and illustrated at <http://www.ccrnp.ncifcrf.gov/~toms/patent/nanoprobe/> and <http://www.ccrnp.ncifcrf.gov/~toms/patent/medusa/>.

Presently the described nanoprobe technology is at an early stage of development and will require the commercial partner to optimize the products for the market.

The commercial benefits of the present nanoprobe technology are demonstrated through the following characteristics:

- Simplicity, only one reagent required and complicated and expensive microfluidic chips are eliminated (BioTechniques Jan 2006, 40:1:85-90)
- Reduction of ELISA, Southern, Northern and Western assays to single molecules
- Speed, only a single molecular reaction is required to detect a target molecule

- Exceptionally low cost per device
- Could be used in the clinic to instantaneously analyze patient's blood and detect genetic diseases
- Could be used to detect biowarfare agents instantaneously.

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