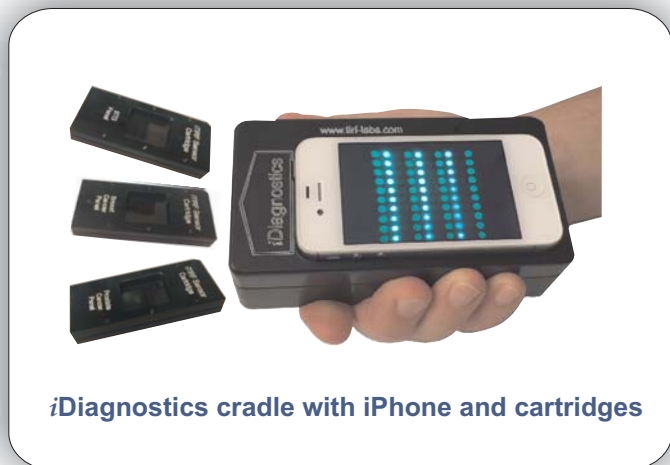




iDiagnostics - the Cellphone Future of Medicine

Open Innovation Platform for Collaborative
Development of Advanced Molecular Diagnostics

Cell Phone Based Molecular Diagnostics - iDiagnostics (iTIRF)



iDiagnostics cradle with iPhone and cartridges

Turn your cell phone into rapid, accurate, yet affordable molecular diagnostics, using iDiagnostics cradle
iDiagnostics works with iPhone, HTC One, and other smartphones

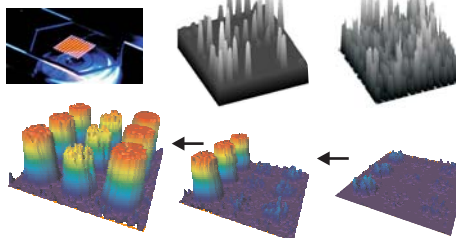
Molecular iDiagnostics (iTIRF Array)

TIRF Labs introduces *iDiagnostics (iTIRF Array)* - a novel molecular diagnostics platform, which is supersensitive, accurate, and rapid, yet affordable for home use. If you are developing fluorescence or electro-chemi-luminescence (ECL) bioassays for diagnosis or prognosis, we invite you to collaborate. We will help you to interface your assays with the *iDiagnostics* platform and will be delighted to license your technology. Ask about our *iDiagnostics* Application Development Kit (ADK).

iDiagnostics features a novel type of real-time microarray that simultaneously detects protein, nucleic acid, and metabolite biomarkers. *iDiagnostics* requires no or minimal sample preparation and is capable of detecting from a single to several thousands of molecular markers in a 50-microliter sample of biological fluids, including whole blood. The Limit of Detection (LOD) for micro-RNA is $\sim 10^{-18}$ M. For proteins and metabolites, the LOD depends on the assay; for certain antibody-based assays, the LOD is at the level of $\sim 10^{-15}$ M. The broad dynamic range of *iDiagnostics* sensor covers the entire spectrum of clinically significant concentrations.

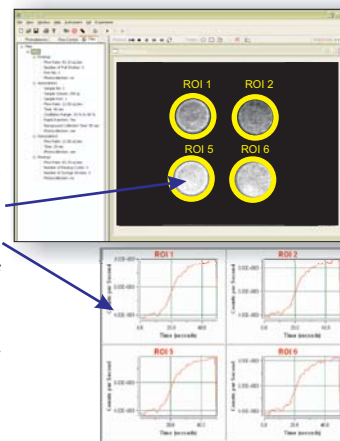
Classical TIRF microarrays operate with small, sub-monolayer amounts of antibodies and DNA probes immobilized on the surface. In classical TIRF fluorescence, the signal is small, thus a low light photodetector, e.g. EMCCD camera is necessary. In *iDiagnostics* the signal of iTIRF arrays is enhanced with silk fibroin. Silk captures the excitation light and becomes an integral part of the lightguide. Classical TIRF is virtually 2-dimensional. One can say that silk extends TIRF into the 3rd dimension. Silk allows for the usage of larger amounts of antibodies per unit area of bioassay spot. The signal from iTIRF arrays is a thousand-fold greater than that in classical TIRF. Therefore, CCD cameras of cell phones are sensitive enough to detect the signal. Silk-enhanced *iDiagnostics* is an ideal platform for interfacing antibody-based bioassays for detecting proteins and molecular beacon assays for measuring nucleic acids. See page 2 for more information.

Real-time protein, nucleic acid, and metabolite iTIRF microarrays



Data Acquisition and Processing

The *iDiagnostics* app selects respective Regions of Interest (ROI), builds sensorgrams for each bioassay, and determines the concentrations of protein, nucleic acid, and metabolite markers. the limit of detection for micro-RNA $\sim 10^{-18}$ M, proteins and metabolites $\sim 10^{-15}$ M.



iDiagnostics (iTIRF Array)

TIRF Spectroscopy

TIRF Microscopy



TIRF Labs

Total Internal Reflection Fluorescence

iDiagnostics Application Development Kit Open Innovation Molecular Diagnostics Platform

***iDiagnostics - the cellphone future of precision medicine
accurate, rapid, personalized, yet affordable diagnostics***

OPEN INNOVATION APPROACH for collaborative development of iDiagnostics applications

If you are developing a molecular diagnostics (MDx) system based on fluorescence or electro-chemi-luminescence assays, we invite you to collaborate. We will help you with hardware, software, cartridge blanks, development tools, reagent kits, methods and protocols to facilitate the interfacing of your assays with the iDiagnostics platform. We will be delighted to license your Intellectual Property (IP) and offer you the opportunity to license our IP to develop precise and rapid, yet affordable devices for molecular diagnosis and prognosis.

The iDiagnostics platform provides unprecedented precision and rapid diagnosing due to its superior sensitivity, multiplicity, and fast response rate. The platform is several orders of magnitude more sensitive and more accurate than alternative methods. One of the advantages of iDiagnostics sensors involves the simultaneous detection of multiple molecular markers of different classes, including proteins, nucleic acids, and metabolites. The detection of different classes of markers minimizes the rate of false positive responses.

iDiagnostics employs silk-enhanced real-time microarrays that include internal controls and standards for normalization and calibration, which provides high reliability and broad dynamic range to iDiagnostics analyses. The platform also supports other luminescence assays, including Electro-Chemi-Luminescence (ECL). iDiagnostics integrates optics, microfluidics, electronics, electrochemical systems, and nanoengineered assays into a small handheld device. Real-time microarrays are capable of parallel detection of up to thousands of analytes, including proteins, nucleic acids, toxins and chemical agents.

iDiagnostics requires no or minimal sample preparation, and can analyze complex biological fluids, including whole blood, saliva, and urine. iDiagnostics employs reagentless bioassays based on molecular beacons or sandwich-format antibody-based assays. Typically, molecular markers are detected in several seconds or a few minutes after the sample is applied.

Applications for the iDiagnostics platform include early diagnosis of cancer, heart diseases, STD, influenza, other infectious diseases, food safety, biodefense, forensic, military, environmental, and agricultural analyses.

Our goal is to make precise, rapid, yet inexpensive iDiagnostics available to everyone. This goal involves numerous challenges and requires the efforts of multiple research groups. The Open Innovation Approach, which we use in this project, is well suited for the collaborative development of advanced diagnostic products. If you are interested in becoming a part of this community please send us an email to <info@tirf-labs.com>.

Business Opportunity in the Area of Molecular Diagnostics

Our goal is to make precise and rapid iDiagnostics available and affordable to every one around the globe. At the initial stage, we will distribute iDiagnostics Application Development Kit (ADK) to the diagnostics research community. In our laboratories in North Carolina we will be developing the tests for breast, prostate, and pancreatic cancer, as well as Alzheimer's disease. We are seeking private and institutional donations, U.S. government and international grants to develop these applications.

Market. iDiagnostics tests are targeting the rapidly growing market. In 2006 the MDx market was \$16B, in 2011 - \$37B. It is anticipated that the market will attain \$92B by 2016.

Social impact. iDiagnostics will change the history of medicine, improve the precision of diagnosis and prognosis, make it affordable for all, help to prevent spreading of infectious diseases such as Ebola, and enable personalized medicine. We will become the owners of information about our health; we will decide what to do with the diagnostic data - email them to our doctor or keep in our files for the future.

Competition. After 9/11 followed by anthrax letters attack, the U.S. government spent over \$70 Billion on biodefense. There is no analytical technique which has not been tried for diagnostics. Competition in the MDx area is intense. However, all existing and emerging methods are inaccurate, slow, bulky, or costly. The iDiagnostics platform is several orders of magnitude more sensitive, accurate, and offers a rapid response, compared to the competition. iDiagnostics biosensors have good chances to become a significant part of the large and rapidly growing MDx market.

Open Innovation Approach. TIRF Labs offers the iDiagnostics Application Development Kit (ADK) for the collaborative development of *medical* molecular diagnosing, and for use in many other areas of life sciences. We have received a large response from the diagnostics community, and will use the feedback from our collaborators to further advance the iDiagnostics platform. We envision rapid progress, and plan to support our collaborators 24/7 to facilitate the interfacing of bioassays, sample preparation, and data analysis.

Applications for the iDiagnostics platform will include the diagnosis and prognosis of cancer, heart diseases, infectious diseases, food safety, environmental, and agricultural applications.

Accurate and Rapid Cell Phone Based Molecular Diagnostics