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Health care costs are of extreme concern now in the US.

Per capita health care costs in 1970 were on the order of $350. Today these same costs in excess of $7500 per person.

Healthcare costs accounts for about 17% of the US economy and is placing extreme financial strain on our society.

The countries in Africa with only 1% of the economic capacity face far greater challenge where the management of HIV is now a huge challenge.

Fortunately, microelectronic and software industries provide some hope.

For past three decades we have witnessed cost reductions for processor power on order of 48% per year.

Healthcare costs are going in the opposite direction increasing at a rate of 7 to 8% per year.
Today most diseases are diagnosed too late when the costs are extremely high.

Biomarkers have the potential to see into the future and allow us to capture diseases before clinical symptoms show up.

Biomarkers are the keys that unlock information about our health and wellness status.

They allow us to see behind these doors that today are locked for most diseases.

For example, for HIV management CD4 testing serves as a main tool for monitoring the immune function for HIV + patients.
Today we live in an exciting time where there is an explosion of scientific and clinical research targeting a detailed understanding of the molecules of life, the biomarkers.

We are now witnessing the “omics revolution” with disciplines like genomics, proteomics, glycomics and metabomics filling scientific journals with exciting findings.

Indeed, there are 20,000 cancer biomarker papers and 6000 in the cardiac area.

However, we only see one biomarker each year secure FDA approval, for all diseases on the planet.

Unless devices that measure biomarkers are approved, they can not be measured.

We now have a huge bottleneck that leads to expensive and inefficient healthcare on a global basis.
Let us imagine a better future. One where individuals are empowered with noninvasive test systems available in their homes, hospitals, pharmacies and the hut in Africa.

Such feedback would provide allow persons to manage their own healthcare in an efficient way.

These new technologies are made by microfabrication and like electronics yield both high performance and low cost.

Better healthcare for less cost.

Global solutions are developed.

Preventative medicine flourishes.
The software and electronics industries provide strong inspiration for healthcare delivery.

Consider the revolution we have had over the past 5 years in the area of smartphones.

Tools like the iPhone that have changed the way we consume information.

The smart phone does much more than take calls. It has become a portable computer, a source of music, a place to surf the internet, a GPS, a display, a digital camera and camcorder.

This has also become a universal hub for hundreds of thousands of specialized applications.

We now have the APP store and for 99 cents we can download tools customized to our personal needs.

The smart phone has changed our lives.
The practice of healthcare would benefit tremendously to have a simple yet powerful tool to gather information about biomarkers.

To empower this area we have developed a universal tool that removes the need for a refrigerator, stable power, shipping of samples, pipetting, trained laboratory staff and specialized lab equipment.

The new tool includes capabilities of a digital camera, a microscope, high power light sources, a full PC, software and a mechanical interface.

The APP store concept is realized with the use of customized lab chips.

This tool exists today… this is not next generation… this is now current generation medical microdevices… lab quality data is now available at the point-of-need.
### This Generation Device

**Reader**
- CCD, and Optics
- LED Light sources
- Stepper motors (loading, fluids)
- Full CPU / memory
- Battery operated
- Wired and wireless connectivity

**Customized Disposables**
- Single-use (one test per card)
- Contains all reagents / fluids

**POC Attributes**
- Portable and low cost
- Lab-based performance
- Simple to operate
- Minimal sample / reagents
- No data interpretation required

### HIV Immune Function Testing
- CD4 absolute counts (adults)
- CD4 % (pediatrics)
- Total lymphocyte counts
- No venipuncture
- No expert user

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The hardware necessary for collecting the biomarker information involves two main parts. An analyzer and a chip.

The analyzer serves as a universal interface.

The same platform services multiple classes of clinical tests.

New combinations of tests can be assembled into bundles.
### Active BNC Trials

<table>
<thead>
<tr>
<th>STUDY</th>
<th>SPONSOR</th>
<th>Study Period</th>
<th>Disease Area</th>
<th># of Study Participants</th>
<th>Clinical Sites</th>
<th>Number of Biomarkers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of A Lab-on-a-Chip System for Saliva Based Diagnostics</td>
<td>NIDCR-VO1</td>
<td>09/01/06-2/28/11</td>
<td>Cardiac Disease</td>
<td>1000 patients</td>
<td>BCM</td>
<td>15 proteins</td>
</tr>
<tr>
<td>Texas Cancer Diagnostics Pipeline Consortium: Oral Cancer</td>
<td>CPRIT</td>
<td>9/1/2010-6/31/2013</td>
<td>Oral Cancer</td>
<td>2200 patients</td>
<td>UTHealth</td>
<td>7 cellular markers</td>
</tr>
<tr>
<td>Texas Cancer Diagnostics Pipeline Consortium: Ovarian Cancer</td>
<td>CPRIT</td>
<td>9/1/2010-6/31/2013</td>
<td>Ovarian Cancer</td>
<td>1250 patients</td>
<td>UTHealth</td>
<td>4 proteins + &gt;10 auto-antibodies</td>
</tr>
<tr>
<td>Texas Cancer Diagnostics Pipeline Consortium: Prostate Cancer</td>
<td>CRPIT</td>
<td>9/1/2010-6/31/2013</td>
<td>Prostate Cancer</td>
<td>400 patients</td>
<td>UK: Home Office</td>
<td>3 proteins</td>
</tr>
<tr>
<td>Advanced Bio-nano-chips for Saliva Based Drug Tests at the Point of Arrest</td>
<td>UK: Home Office</td>
<td>9/1/09-3/31/11</td>
<td>Drugs of Abuse</td>
<td>240 participants</td>
<td>BCM</td>
<td>4 drugs</td>
</tr>
</tbody>
</table>

In addition to HIV management tools which I will touch on next in more detail, the core technology is now moving through 6 major clinical trials.

Major health conditions like cardiac, three types of cancers, drugs of abuse and HIV immune function are covered.
## Towards a Universal Platform

<table>
<thead>
<tr>
<th>Test</th>
<th>Gold Standard</th>
<th>Bio-Nano-Chip Type</th>
<th>Sample Type</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 (HIV Immune Function)</td>
<td>Flow Cytometry</td>
<td>CPU#2</td>
<td>Drop of Whole Blood</td>
<td>$R^2 = 0.93$ to $0.95$ (for $N$ of 200)</td>
</tr>
<tr>
<td>Oral Cancer (OSCC)</td>
<td>Pathologist</td>
<td>CPU#2</td>
<td>Brush Biopsy</td>
<td>$AUC = 0.97$ to $1.00$ (for $N$ of 20)</td>
</tr>
<tr>
<td>Cardiac-AMI</td>
<td>C-Tn-I, Myo, CK-MB</td>
<td>CPU#1</td>
<td>Oral Fluid (saliva)</td>
<td>$AUC = 0.94$ to $1.00$ (for $N$ of 100)</td>
</tr>
<tr>
<td>Roadside drug tests</td>
<td>LC-MSMS</td>
<td>CPU#1</td>
<td>Oral Fluid (saliva)</td>
<td>$R^2 = 0.916$ (for $N$ of 10)</td>
</tr>
</tbody>
</table>

Noninvasive sampling methods are used for each of these tests.

This helps to expand the reach of these tests to more remote settings.

Good agreement with gold standard methods is observed in each case.
Case Study: HIV / AIDS Pandemic

- Over 33MM adults and children living with HIV / AIDS — 6,800 new infections, 5,700 deaths/day
- Antiretroviral drugs more available with cost of $350 to $1500 per DALY averted.
- About 33% of patients on antiretroviral drugs suffer serious side effects.
- CD4 tests are required to determine when to start and monitor HIV / AIDS drug treatments.
- CD4 tests now available in Africa now in Central labs in large cities/towns.
- More rural locations are not addressed. Over 2 of 3 HIV+ persons do not have access these tests.
- The rate of mother-to-child transmission (MTCT) is 30-40% without intervention.
- CD4 levels show strong inverse correlations with MTCT rates.
- Injection drug users represent 19% of those living with HIV.

CD4 testing for HIV patients is critically important now.

This application is a particularly good fit for the lab on a chip as this system can replace the lab infrastructure that does not scale well in Africa.

I want to focus your attention on two areas that are key fits for an accurate point of care CD4 test.

They are MTCT in rural resource poor settings and IV drug use in US indigent populations.
Whole blood is a complex mixture of proteins, electrolytes, lipids and a variety of cells.

To measure the HIV immune function, it is necessary to find the needle in the haystack.

The CD4 cells comprise represent less than 0.1% of the total cell count.

One of the challenges here for the chip was find a way to get ride of the RBCs and find the WBCs.
These electron microscope images show the whole blood and how it is processed by the membrane.

Once the cells are captured we need to count them in a highly accurate way.

This is where chemistry comes into play.

On card reagents are reconstituted in a microfluic circuit and then are passed over the cells to label them red and green.

Images obtained with a video-chip maps out the location of the cells.
Once captured on the flat membrane a series of colored coded images are captured.

Then “pixel logic” comes into play.

T lymphocyte cells carry both CD3 and CD4 surface markers that are color coded red and green respectively.

The overlapping cells with correct intensities and size are efficiently counted by the macro.

The simple image based tests replaces a far more complex flow cytometry measurement that has been dominant for the past 35+ years.
A few brief comments are in order about the cost considerations for the initial chips that are moving into the real world now.

Our first release is targeted for HIV immune function for use in resource poor settings.

Here we see 80% reduction in cost for the instrumentation and 50% cost reductions in the disposables.
Recommendations

1) Develop new programs and policies that help speed release of novel technologies for HIV prevention, management and treatment.

2) Define accelerated approval pathways both in US and resource scarce settings for the new medical microdevices including CD4 tests.

3) Establish new programs and policies that focus on MTCT in rural resource poor settings.

4) Establish new programs and policies that cover the topic of HIV prevention for IVD users in indigent populations in the US.

In finishing up my talk, I would like to leave you with the following recommendations:

See slide…