Salivary Diagnostics: Impact on Global Oral Health

Impact on Global Health

Enhancing Dentistry and Making Medicine Better

Improving Access to Care & Reducing Health Disparities

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Dental Research Institute, Molecular Biology Institute
Jonsson Comprehensive Cancer Center
Saliva as a Diagnostic Fluid

Saliva diagnostic alphabets

- Proteomic Biomarkers
- RNA Biomarkers

Clinical utilities: Early Detection of Oral Cancer

Point of care technology development

Impact on oral and global health
NIDCR Initiatives

Technology Development ↔ Salivary Proteome

- John McDervitt (U. Texas)
- Dan Malamud (NYU)
- David Walt (Tufts University)
- David Wong (UCLA)

- Susan Fisher (UCSF)
- David Wong (UCLA)
- John Yates (Scripps)
Road Map of Salivary Diagnostics
Vision

Use of Saliva for Disease Diagnostics as well as for Normal Health Surveillance
Why is Saliva not yet a mainstream diagnostic biofluid?

- Social taboo
- Cultural taboo
- Psychological taboo

- Lubricant for speech & mastication
- Antimicrobial factors
- Immunological factors
- Growth factors (EGF, NGF)
- Positive cultural values
- Real time monitoring of physiological changes
Human Salivary Proteome Central Repository

**Download Files**

- 914 Parotid Protein Identifications
- 917 SM/SL Protein Identifications
- 25 Accessions Found in Other IPI Versions
- HSP Identification Clusters
- HSP Annotation

SM/SL: Submandibular/Sublingual  
HSP: Human Salivary Proteome  
Protein Database: Human IPI v3.24

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Bioinformatics User Facility  
www.hspp.ucla.edu
Salivary Exon Expression Profiling
(SEEP)

1.4 million data points
Salivary Transcriptome Diagnostics for Oral Cancer

Patient-based genome-wide technologies to identify molecular biomarkers for HNSCC

Head & Neck Cancer

- Incidence: 6th
- 30,000 new cases annually
- 5-year survival rate < 50% not changed in the last 30 years
- Squamous cell carcinoma (HNSCC) < 40% survival rate
- Increased risk of developing metastasis and second malignancies

Rationale: OSCC in salivary milieu

As proof-of-principle disease
Proof of Principle of Salivary Transcriptome for Oral Cancer Diagnostics

Using 4 Saliva RNA Biomarkers: IL-1B, OAZ1, SAT and IL-8

<table>
<thead>
<tr>
<th>Area under ROC curve</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>0.95</td>
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Salivary Transcriptome Diagnosis is Better than Blood Tests for Oral Cancer Detection

Saliva and blood test of oral cancer detection

<table>
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<th>Area under ROC curve</th>
<th>Saliva Transcriptome Diagnosis*</th>
<th>Blood Tests**</th>
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Value Proposition of Early Detection of Oral Cancer

Early Detection

Unsupervised screening for oral cancer
Saliva Screen
"The REACH"

Lesion Localization
"The LOCATION"

Definitive Biopsy
"The DIAGNOSIS"

Supervision - Not Required

Supervision - Required

Supervision - Required
A next-generation handheld diagnostic platform delivers precision analysis of oral fluids.

It’s **smart**. Distinguish between several oral pathogens and cancer biomarkers.

It's **fast**. Perform targeted tests in just minutes.

It's **painless**. Make use of the body's natural diagnostic medium, no needles required.

It's **easy to use**. A technological fusion: microfluidics, optical cell detection and nanobiotechnology come together in a compact diagnostic tool for any clinic.

Administer the patient sample directly into a disposable microfluidic cartridge.

The detector analyses the bio-content of the sample and provides a concise, reliable readout.

The surface of the fluid channel houses a micro-patterned array of active biomolecules.
Oral Fluid NanoSensor Test
Diagnostic Opportunities

Dentists are the most involved in the oral cavity and they do see a large segment of the population . . .

- **There were 550 Million dental visits in 1999**
  - If average per patient is 2 visits per year
  - If 75% of patients were over 18 (at-risk for OSCC)

- **There was the opportunity to examine over 200 Million relevant patients for Oral Cancer**
Disease Overview

OSCC has a high survival rate if caught early. But it is not, and this carries a terrible human and financial cost . . .

• Aside from the human cost of late diagnosis, the economic costs, just in terms of treatment, are large:
  – Cost of treating a Stage 1 – 2 patient $15,000
  – Cost of treating a Stage 3 – 4 patient $200,000 - $500,000

• US total cost of treatment is estimated at $3.7 billion . . .

. . . If improved diagnostic capabilities enabled 70% of OSCC to be detected in Stages 1 or 2, direct savings to the healthcare system would be over $2 Billion per year
Given the magnitude of the need, it is not surprising that there are numerous initiatives underway to develop better screening tools . . .

**Characterization by Current UCLA Development Team**

- Saliva based proteomic & genomic biomarkers
- Chair side
- Card and reader
- Simple
- Less than 20 minutes
- Greater than 90% sensitivity and specificity
- Positive predictive values

**Handheld Oral Health Diagnostics Using Bio-active Nanoscale Detection**

A next generation handheld diagnostic platform delivers precision analysis of oral fluids.

In smart: Distinction between several oral pathogens and cancer biomarkers.

In fact: Perform targeted tests in just minutes.

In painless: Move use of the body’s natural diagnostic medium—mucus—directly impacting.

It is easy to use: A technological fusion of microfluidics, optical detection and nanotechnology come together in a compact diagnostic tool for any clinic.

Administer the patient’s sample directly into a disposable microfluidic cartridge.

The diagnostic analyzes the biomarker content of the sample and provides a concrete, reliable readout.

The surface of the fluid channel houses a micro-patterned array of active biomarkers.
Forthcoming soon:

In addition to the anticipated model / business scenario development, the following unanticipated issues need to be addressed . . .

• Cross over into the Medical channel
  – Coverage
  – Practices
  – Interest
  – Wants and needs

• Dental +/or Medical Channel Assessment
  – Pricing / Reimbursement
  – Cost of Coverage
  – Promotional costs
  – Use / penetration
    – OSCC and beyond

• Product Embodiment Roll-Out Implications
  – Chair side
  – Reference transitioning to chair side

• Business Model Development
• Oral Cancer
• Sjögren’s Syndrome
• Lung Cancer
• Breast Cancer
• Pancreatic Cancer
• Diabetes Type II
• Alzheimer’s Disease
• Ovarian Cancer
• Early Disease Detection
Distribution of Molecular Diagnostics Testing in the U.S.

- Gene/Chromosome Disease: 60%
- Infectious Disease: 16%
- Blood Bank: 15%
- Cancer: 7%
- Pharmacogenetics: 2%

Source: Kalorama Information 2005
## The Fast Growing Molecular Diagnosis Segment in Global IVDs Market

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<th>Type</th>
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*CAGR Cumulative Average Growth Rate

Source: Kalorama Information 2005
A New Industry
Saliva

• Diagnostics
• Pharmaco-proteomics
• Pharmaco-genomics

*Personalized Individual Medicine*
Saliva Diagnostics
Powered by
NanoTechnologies, Proteomics & Genomics

Research
Education
Curriculum
Advocacy

Type 2 Diabetes
Breast Cancer
Oral Cancer

NIDCR
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Road Map of Salivary Diagnostics