National Oral Health Conference
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Oral Cancer & Saliva Diagnostics
Enhancing Dentistry & Making Medicine Better

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Jonsson Comprehensive Cancer Center

UCLA
Saliva as a Diagnostic Fluid

Biomarkers & Diseases

Saliva diagnostic alphabets

• Proteomic Biomarkers

• Genomic Biomarkers

Translational Application: Oral cancer detection
NIDCR Initiatives

Technology Development

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

Salivary Proteome

- Susan Fisher (UCSF)
- David Wong (UCLA)
- John Yates (Scripps)
Vision

Use of Saliva for Disease Diagnostics as well as for Normal Health Surveillance
HUMAN SALIVARY PROTEOME

Protein Fractionation → MS/MS → Salivary Proteome Knowledge Base

“Top Down”

“Bottom Up”

Daniel Malamud
Arjan Vissink

UCLA
UO1 DE 16275
www.hspp.ucla.edu
HSP Proteomics Central Repository

Parotid(1026)  SM/SL(1232)

Download Files

- 1026 Parotid Identifications (coming soon)
- 1232 SM/SL Identifications (coming soon)
- 87 ACs Found in Other IPI Versions
- HSP Identification Clusters (coming soon)

Total Identifications (1546)
Discovery of the Salivary Transcriptome

Salivary RNA Pool

3,000 RNA in Saliva

Microarray Technology

200 “Core”

Yang Li, et al. Journal of Dental Research, 83(3), 199-203, 2004
Salivary Diagnostics for Oral Cancer Detection

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

Rationale: OSCC in salivary milieu

As proof-of-principle disease

- 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

Head & Neck Cancer
Proof of Principle of Salivary Transcriptome for Oral Cancer Detection

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

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<thead>
<tr>
<th>Area under ROC curve</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>0.95</td>
<td>0.91</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

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<tr>
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<th>Saliva Transcriptome Diagnosis*</th>
<th>Blood Tests**</th>
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<tbody>
<tr>
<td>Area under ROC curve</td>
<td>0.95</td>
<td>0.88</td>
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Rinse and Spit: Saliva as a Cancer Biomarker Source

It’s home to more than 700 types of bacteria (by current estimates, at least), can be a source of infection, but also has wound-healing properties. It’s essential for swallowing and digestion, but, in many cultures, to expel it at somebody is the ultimate insult. And now this slimy body fluid—saliva—is gaining a reputation in biomedical research circles as an effective source for detecting the hidden presence of disease, including some types of cancer.

Most research into cancer biomarkers has focused on blood components, such as plasma or serum. Saliva, on the other hand, has been largely overlooked as a source of biomarkers. It has long been considered a hostile environment, riddled with bacteria and other debris that would yield adulterated samples incapable of generating reliable and reproducible results.

But that perception is beginning to change. According to Dr. Sudhir Srivastava, director of NCI’s Early Detection Research Network (EDRN), which focuses on identifying and validating novel biomarkers, recent data on saliva-based biomarkers show promising trends, but often not until they have already progressed to late-stage disease—a big reason why 5-year survival rates have been mired in the 50 percent range for several decades.

Detecting these cancers at earlier stages, with the aid, for instance, of a saliva-based diagnostic test, could increase 5-year survival to 80 to 90 percent, according to Dr. Elizabeth Franzmann, of the Department of Otolaryngology at the University of Miami. This could help avoid some of the morbidity associated with treatment, including disfigurement and significant swallowing difficulties.

Public attention to saliva-based biomarker research received a significant boost last December with the publication of a pilot study conducted in the lab of Dr. David Wong, of the UCLA Jonsson Comprehensive Cancer Center. Elevated levels of seven different RNAs, they reported, could distinguish patients with oral squamous cell carcinoma (OSCC) from controls with 91 percent sensitivity and specificity.

Dr. Wong says that his lab has now

Saliva-based detection methods don’t have to be limited to head and neck cancers, Dr. Wong argues. As-yet-unpublished studies by his lab using the same RNA approach to detect early-stage breast cancer, he says, “have been very promising.”

Dr. Wong’s lab is working with newer testing technologies developed with funding from the National Institute of Dental and Craniofacial Research, which is investing significantly in this area. But other researchers are trying to tease out diagnostic clues from saliva using more conventional assays and are finding success.

Dr. Franzmann led a small study published earlier this year in which she used the conventional ELISA test to detect elevated levels of a soluble form of the protein CD44 (solCD44), which was found to reliably identify patients with head and neck squamous cell carcinoma (HNSCC), regardless of the tumor stage. The closer the cancer to the main oral cavity, the more sensitive the solCD44 levels.

“We’ve even had cancers where no tumor can be seen in the upper aerodigestive tract, but there is a metastasis to the lymph node,” she says. “So that’s telling us that it may be capable of picking up disease that we can’t even see.”

Like Dr. Wong’s group, other researchers are also looking at more atypical markers. Dr. Joseph Califano of the Department of Otolaryngology-Head & Neck Surgery at Johns Hopkins Medical
Normal State

Disease State

A B C D E F G H I
• • • • • • • • • • • •

Proteomic Targets

Genomic Targets

Normal State
Early Detection

Unsupervised screening for oral cancer
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 (OFNASET)
“Saliva Health Screen”
at
the 2007 ADA Health Screen Program
Saliva Diagnostics
Powered by
Nano-Technologies, Proteomics & Genomics

Type 2 Diabetes
Breast Cancer
Oral Cancer

NIDCR