National Oral Health Conference
Annual Meeting
Denver CO
May 1, 2007

Oral Cancer & Saliva Diagnostics

Enhancing Dentistry & Making Medicine Better

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Dental Research Institute
Division of Head & Neck Surgery/Otolaryngology
Jonsson Comprehensive Cancer Center

UCLA

Saliva as a Diagnostic Fluid

Biomarkers & Diseases

Saliva diagnostic alphabets

- Proteomic Biomarkers
- Genomic Biomarkers

Translational Application: Oral cancer detection

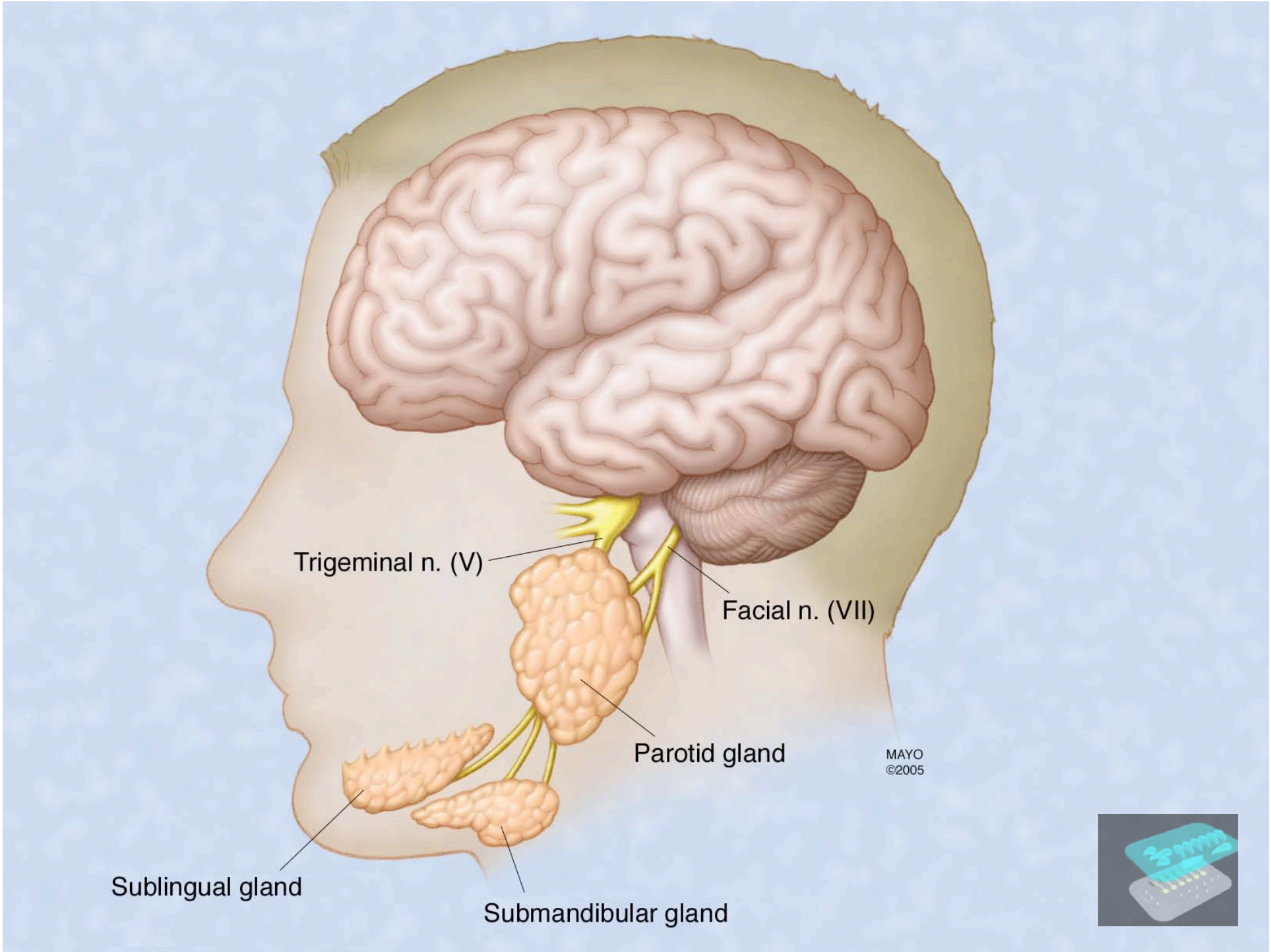
NIDCR Initiatives

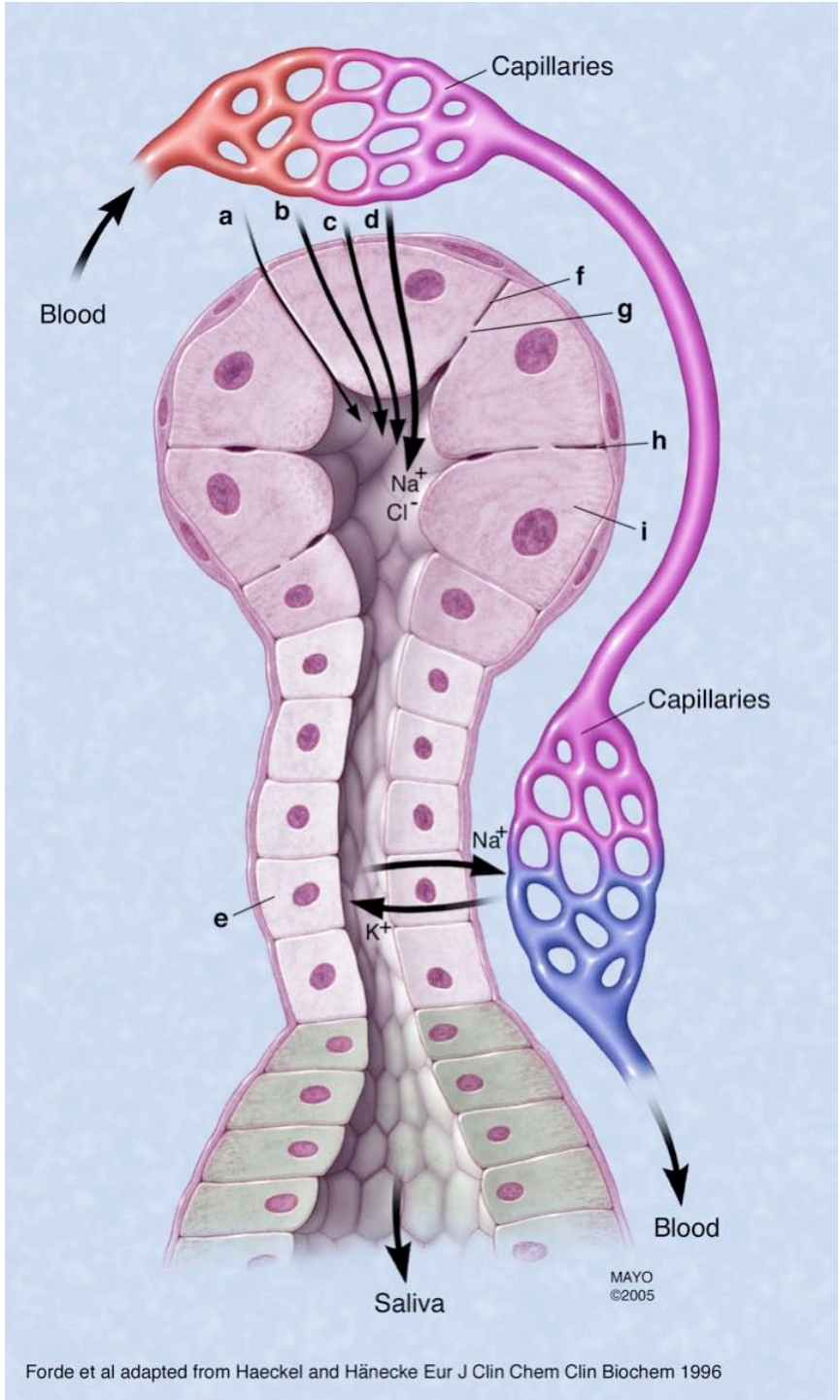
Technology Development ⇌ Salivary Proteome

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

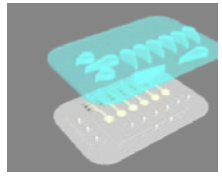
- Susan Fisher (UCSF)
- David Wong (UCLA)
- John Yates (Scripps)

Vision
Use of Saliva for Disease Diagnostics as well as for Normal Health Surveillance


Trigeminal n. (V)
Facial n. (VII)
Parotid gland
MAYO
©2005
Sublingual gland
Submandibular gland

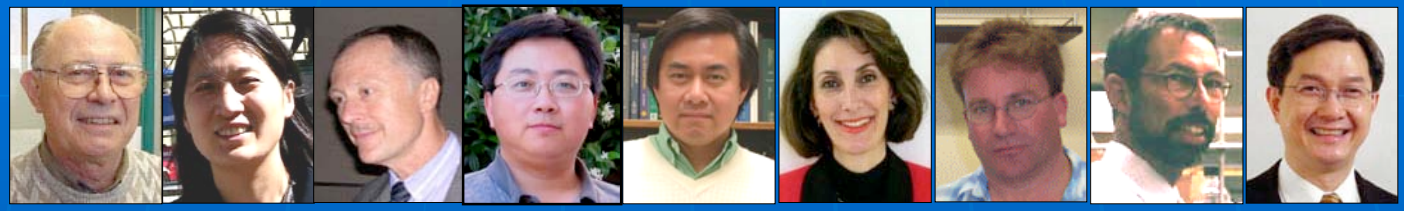


Forde et al adapted from Haeckel and Hänecke Eur J Clin Chem Clin Biochem 1996



UCLA Human Salivary Proteome Project

HUMAN SALIVARY PROTEOME



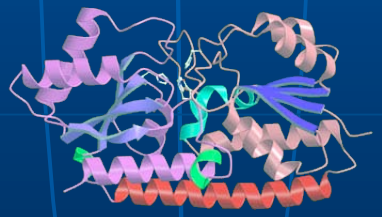
"Top Down"

Protein Fractionation

"Bottom Up"

MS/MS

MIRERICACVLALGMLTGFTHAFGSKDAAADGKPLVV
TTIGMIADAVKNIAQGDVHLKGLMGPGVDPHLYTATA
GDVEWLGNADLILYNGLHLETKMGEVFSKLRGSRLVV
AVSETIPVSQRLSLEEAEFDPHVWFDVKLWSYSVKAV
YESLCKLLPGKTREFTQRYQAYQQQLDKLDAYVRRK
AQSLPAERRVLVTAHDAFGYFSRAYGFEVKGLQGVS
TASEASAHDMQELAAFIAQRKLPAIFIESSIPHKNVEAL
RDAVQARGHVVQIGGELFSDAMGDAGTSEGTYVGMV
THNIDTIVAALAR



Salivary Proteome Knowledge Base

Daniel Malamud
Arjan Vissink

UCLA

UO1 DE 16275

www.hspp.ucla.edu

SPKB Salivary Proteome Knowledge Base

Supported by NIDCR

Home | DB Schemas | Participating Groups | Search Proteins | Wiki | Tools | Log Off

David Wong login

HSP Proteomics Central Repository

Parotid(1026) SM/SL(1232)

Total Identifications (1546)

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)

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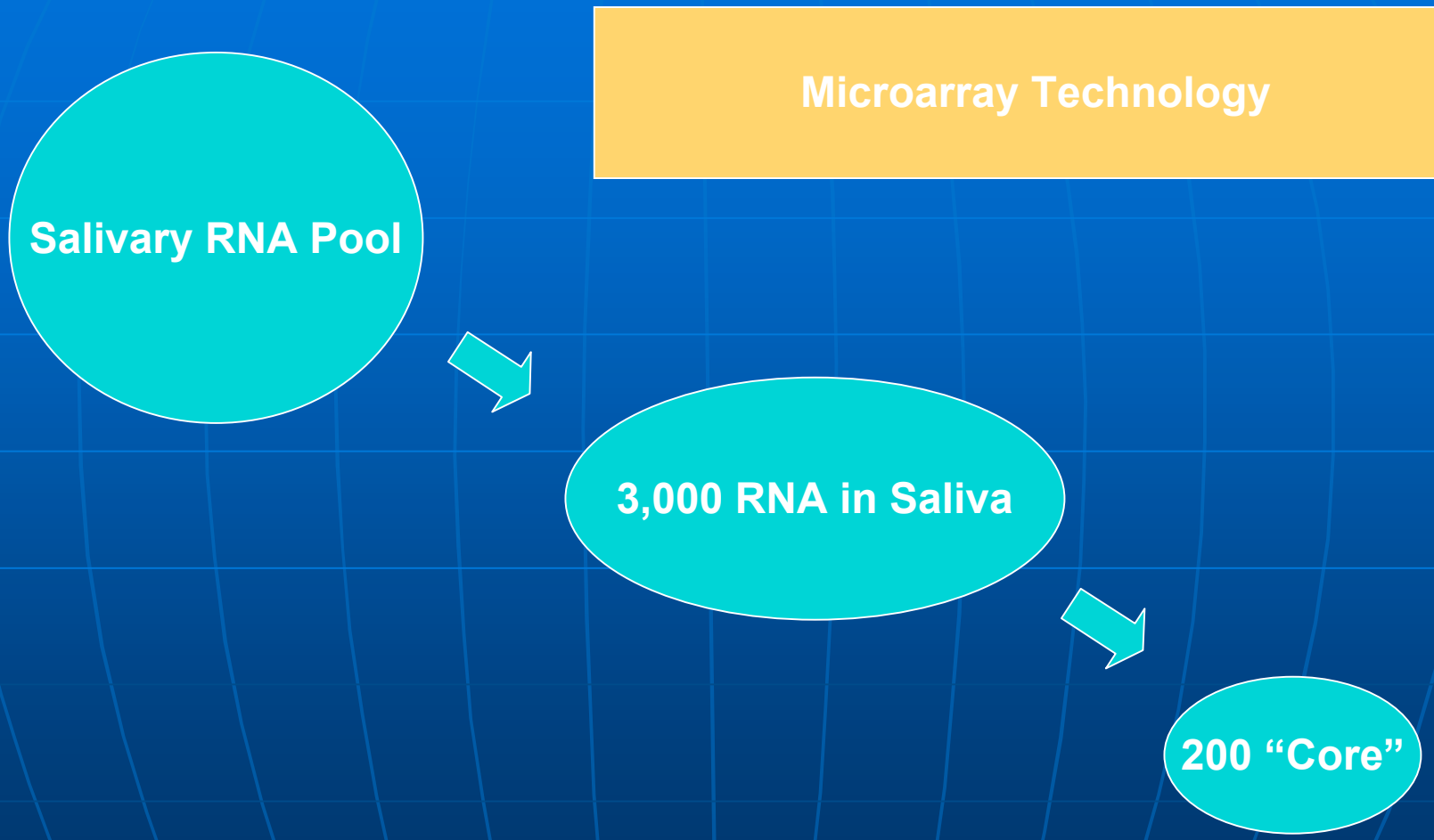
Bioinformatics User Facility

www.hspp.ucla.edu

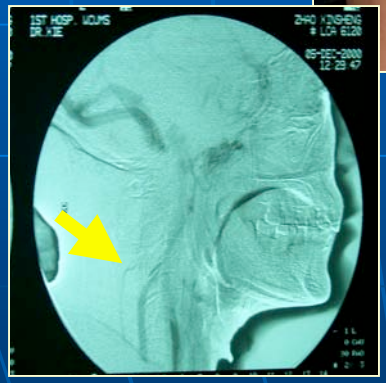
Discovery of the Salivary Transcriptome



UCLA

Yang Li, et al. *Journal of Dental Research*, 83(3), 199-203, 2004

Salivary Diagnostics for Oral Cancer Detection



Head & Neck Cancer

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

Rationale: OSCC in salivary milieu

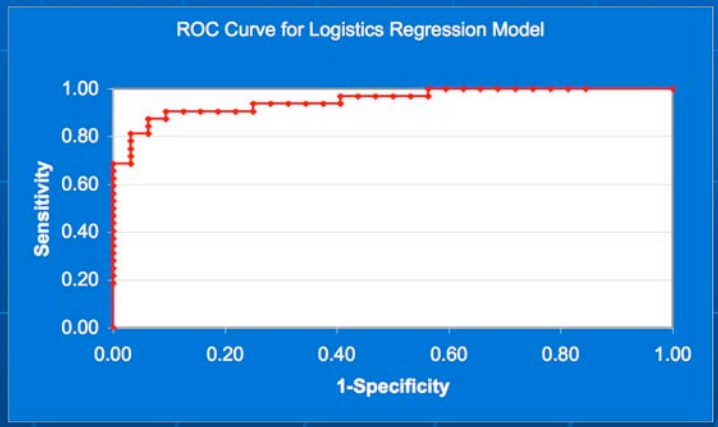
As proof-of-principle disease

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

Proof of Principle of Salivary Transcriptome for Oral Cancer Detection

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

Area under ROC curve	Sensitivity	Specificity
0.95	**0.91**	**0.91**



Li Y, St John MA, Zhou X, Kim Y, Sinha U, Jordan RCK, Eisele D, Abemayor E, Elashoff D, Park NH and Wong DT. Salivary Transcriptome Diagnostics for Oral Cancer Detection. ***Clin Cancer Res****: 10: 8442-8450, 2004.*

Salivary Transcriptome Diagnosis is Better than Blood Tests for Oral Cancer Detection

Saliva and blood test of oral cancer detection

	Saliva Transcriptome Diagnosis*	Blood Tests**
Area under ROC curve	**0.95**	**0.88**

**Yang Li, et al. Clinical Cancer Research, 10: 8442-8450, 2004.*

***Yang Li, et al., J. Clin. Oncology, 24: 1754-1760, 2006.*

NATIONAL CANCER INSTITUTE

NCI Cancer Bulletin

Eliminating the Suffering and Death Due to Cancer

Spotlight

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 detritus 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—although

tions, 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 Research 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."

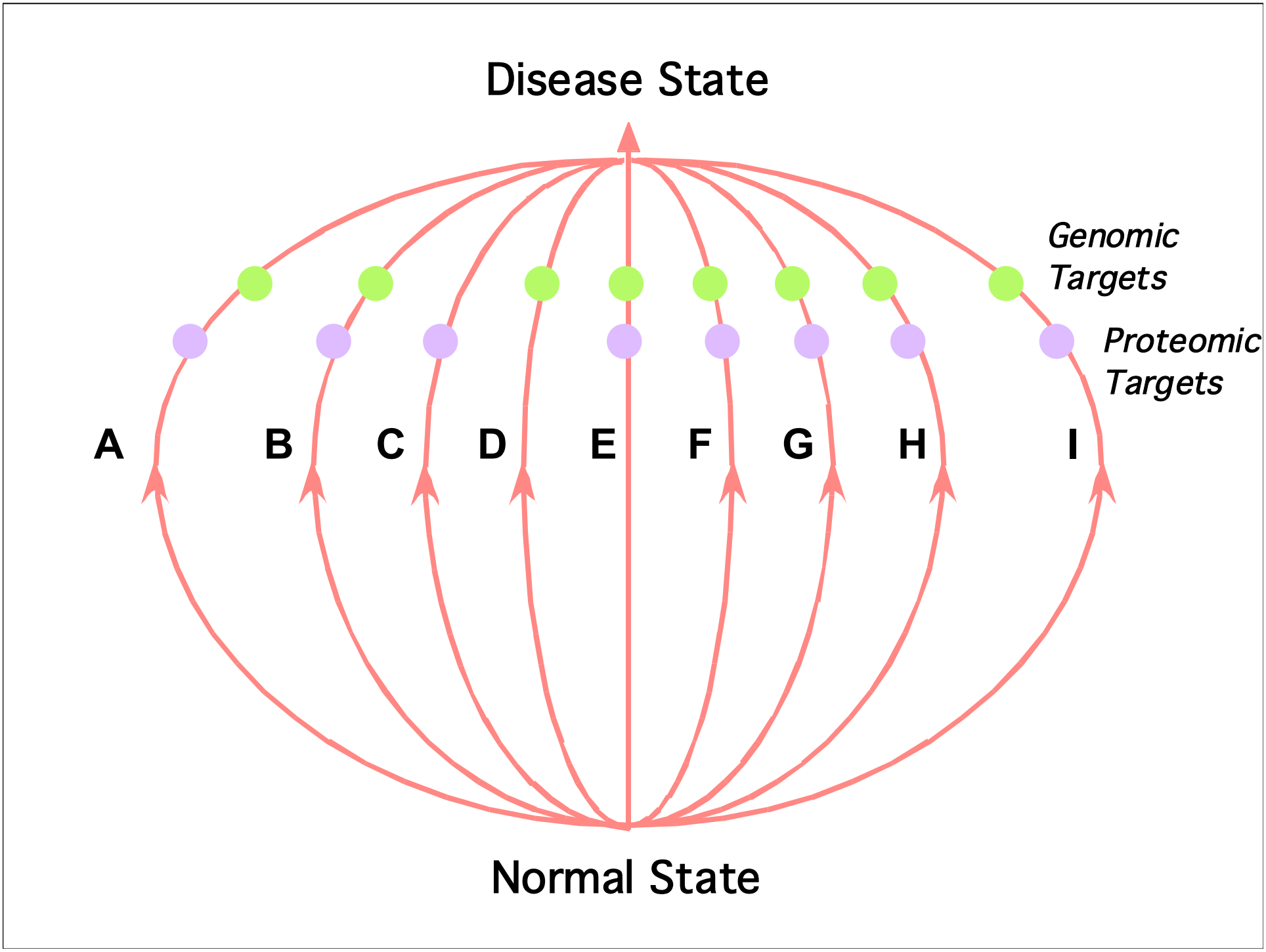
Dr. Wong's lab is working with newer testing technologies developed with funding from the National Institute of Dental and Craniofacial Research, which is investing significantly in this area. But other researchers are trying to tease out diagnostic clues from saliva using more conventional assays and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

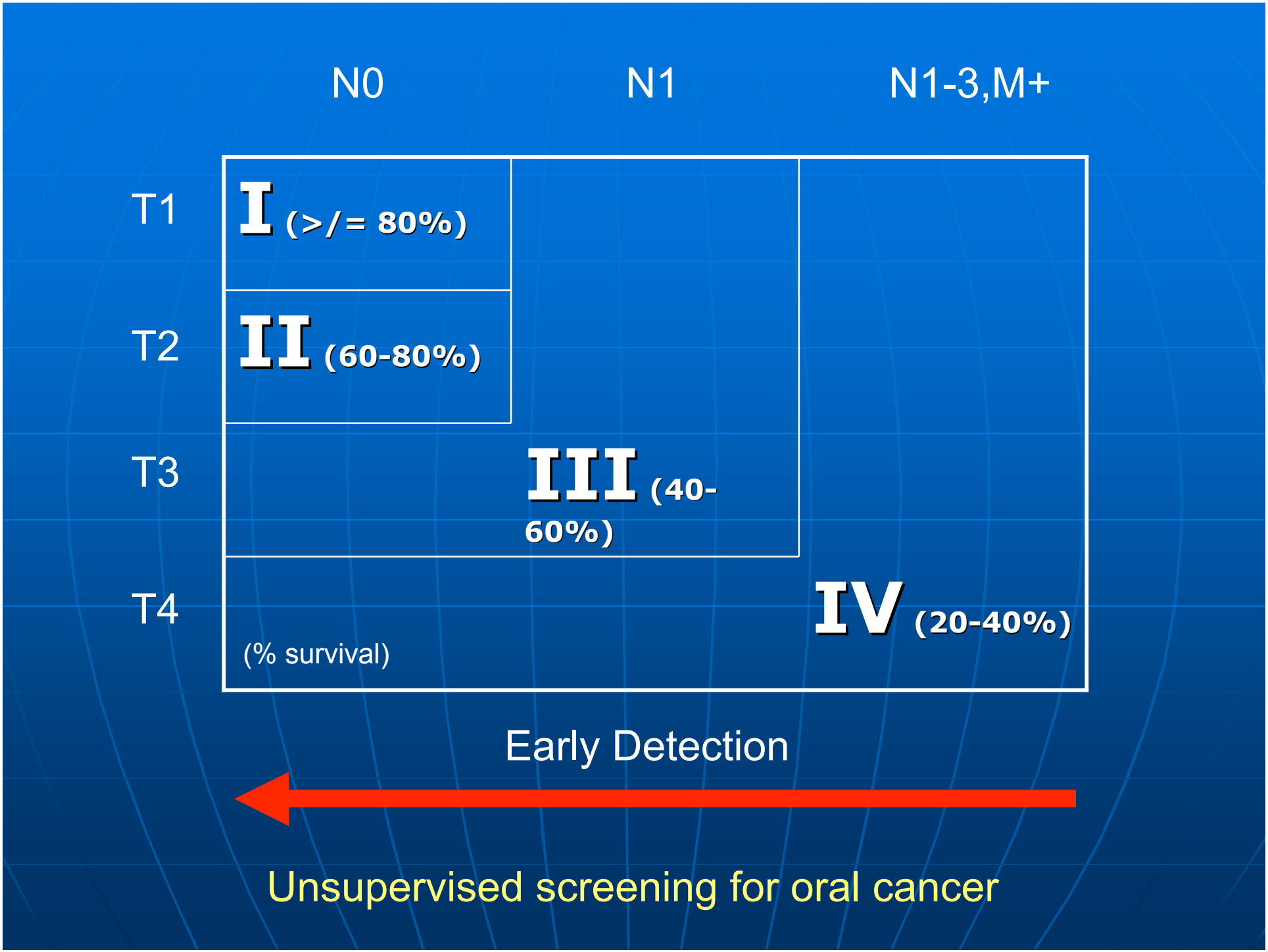
Dr. Franzmann led a small study published earlier this year in which she used the conventional ELISA test to detect elevated levels of a soluble form of the protein CD44 (solCD44), which was found to reliably identify patients with head and neck squamous cell carcinoma (HNSCC), regardless of the tumor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


Disease State
Genomic Targets
Proteomic Targets
A
B
C
D
E
F
G
H
I
Normal State


N0
N1
N1-3,M+
T1
T2
T3
T4
I (>/= 80%)
II (60-80%)
III (40-60%)
IV (20-40%)
(% survival)
Early Detection
Unsupervised screening for oral cancer

Handheld Oral Health Diagnostics Using Bio-active Nanoscale Detection

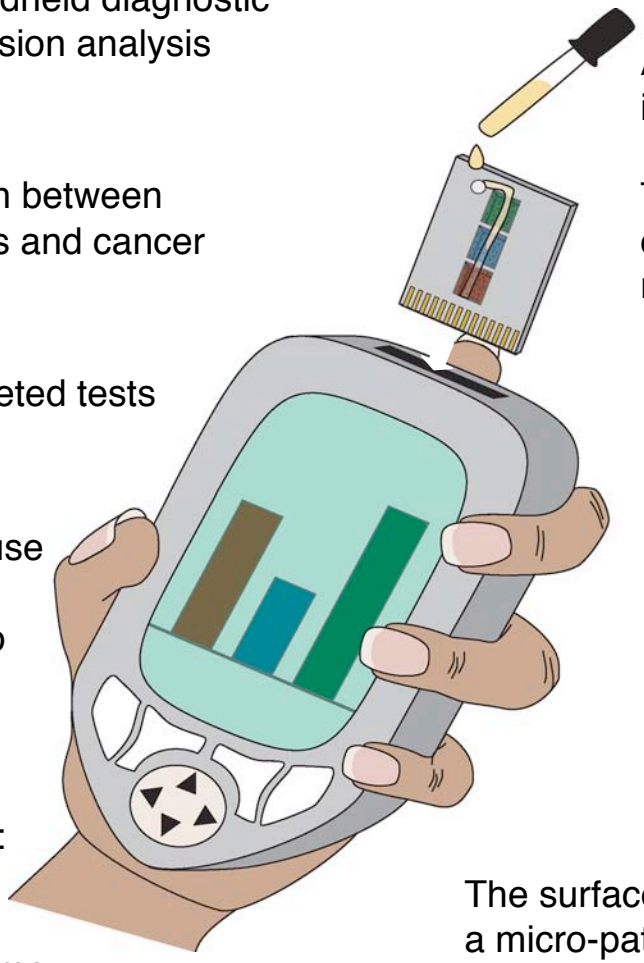
A next-generation handheld diagnostic platform delivers precision analysis of oral fluids.

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

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

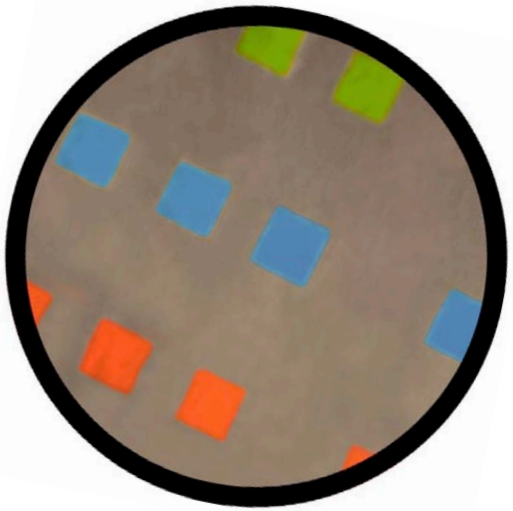
It's **painless**. Make use of the body's natural diagnostic medium, no needles required.

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.

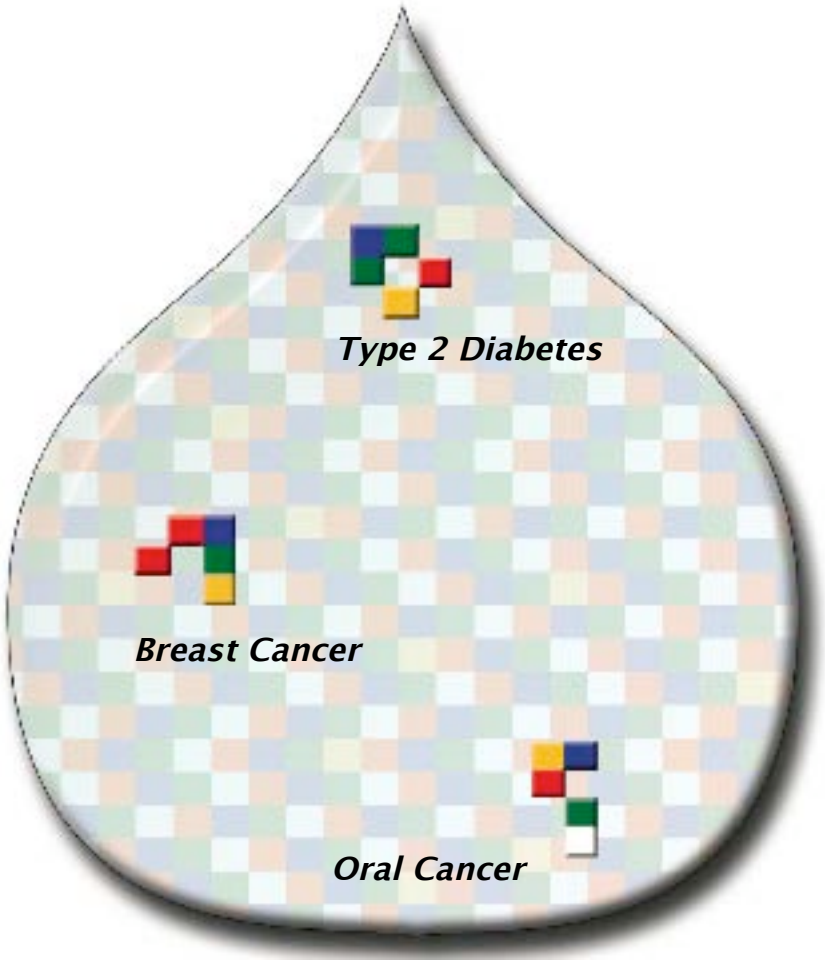
Oral Fluid NanoSensor Test (OFNASET)

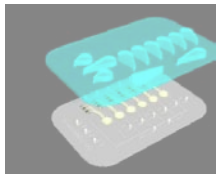
"Saliva Health Screen"
at
the 2007 ADA
Health Screen Program

QIAGEN

HENRY SCHEIN®

Saliva Diagnostics
Powered by
Nano-Technologies, Proteomics & Genomics





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