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Saliva – A Quintessential Diagnostic Tool

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ABSTRACT *This review examines the promising nature of saliva as a diagnostic tool. Saliva has distinctive advantages over the serum based assays, being cost effective and can be collected non-invasively without any special equipment. Saliva has undergone several advancements in the past years. Research today is not only trying to focus on the ability of saliva to be an ultimate diagnostic tool but also to make the health professionals especially the dentists realise the potential of the same. This review portrays the current scenario of the saliva based innovations.*

INTRODUCTION:

Saliva acts as an attractive alternative to serum which can be analysed for diagnostic purposes, since the whole saliva contains both serum derived and locally produced markers which make it apt for diagnosis of various systemic diseases. Research has evidences of saliva being used to monitor immune responses to viral infections like hepatitis and HIV. Saliva has also proven to be useful in monitoring therapeutic drug levels and hormone levels. The development of saliva, as a diagnostic tool has seen significant advances in the past decade.Saliva is the most sought after medium to be explored as health and disease surveillance and for personalised medicine as well. Saliva being a non-invasive tool has the ability to detect both oral and systemic diseases. Hence a question arises whether the clinicians possess the ability to use saliva as a diagnostic tool in order to detect these oral and systemic diseases.In this article, I intend to discuss the current scenario of how the saliva based innovations are applied in the detection of oral and systemic diseases.

THE NOVEL APPROACHES TOWARDS SALIVA:

Certain terminologies have caused a major breakthrough in the field of salivary sciences, "Salivary diagnostics" is one of them. Another term "Salivaomics" was coined in 2008 toreflect the rapid development of knowledge about the various "omics" constituents of saliva(that is, the study of related sets of biologicalmolecules).In only five years, the terms "salivary proteome," "transcriptome," "microRNA" (miRNA), "metabolome" and "microbiome" have entered the scientific lexicon[1].

These essentials of saliva reflect its ability to be used for both translational and clinical applications, including personalized medicine and dentistry.

Investigators discovered the salivary transcriptome in 20042,3; it consists of a core of 180 messengerRNAs (mRNAs). The core salivary proteomecontains 1,166 proteins[4,5.]

TheUCLA research group, together with the research group headed by Masaru Tomita, PhD, at KeioUniversity, Tsuruoka City, Yamagata, Japan, deciphered the salivary metabolome and demonstrated its utility for detection of oral and systemic diseases.[6]

Farrell and colleagues7 recently showed that the potential for variation in the salivary microbiome could be used in the detection of early resectable pancreatic cancer. Two microbial markers (Neisseria elongataand Streptococcusmitis) yielded a receiver operating characteristic plot area under the curve value of 0.90 (95 percent confidence interval, 0.78-0.96; P < .001), with a 96.4 percent sensitivity and an 82.1 percent specificity in distinguishing patients with early-stage resectable pancreatic cancer from study participants who did not have cancer.

Area under the curve is a measure of the ability of a test to accurately discriminate a result indicating a particular disease state from a result not indicating that disease state.[7]

THE DATA BASE SYSTEMS:

Most of the health professionals are unaware regarding a vast amount of salivaomics data that has been generated with the use of high-throughput technologies.8-11

This data has been generated with the help of the omics including, transcriptomics, genomics, metabolomics, epigenomics and proteomics. These omics have also enabled the emergence of both personalised medicine and omics based tests.

The exploitation, lack of computational access and cross reference of data was encountered. Hence to overcomethese barriers led the researchers at UCLA to develop the Salivaomics Knowledge Base (SKB), a data management system and Web resource that supports salivary diagnostics research.12The research team at UCLA is building it on thebasis of the saliva ontology (SALO) and SDxMart, which allow the SKB to operate with other omics databases as part of a generalstrategy to facilitate integration of heterogeneousand disparate data sources in a systems biology approach.[1]

SALO - The SALO is a detailed ontology of saliva that is optimized to meet the needs of both the clinical diagnostic community and the cross-disciplinary community of omics researchers.[13,1]

BioMart - BioMart is a free, open-source databasesystem.14,15 It is cross-platform and supportsmany popular relational database managementsystems, including MySQL (Oracle, RedwoodShores, Calif.), PostgreSQL (PostgreSQL Global

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Development Group), SQL Server (Microsoft,Redmond, Wash.) and DB2 (IBM, Armonk, N.Y.).The software is database agnostic; therefore, itcan be adapted easily to existing data sets. It isexpandable and customizable through a plug-insystem; because it is open source, the generalcommunity can participate in its development.1

SDxMart.The SDxMart is a BioMart data portal that hosts salivary proteomic, transcriptomic, metabolomic and miRNA data and offers access to the data via use of the BioMart interface and querying environment.

The SDxMart is designed to enable users to make a variety ofqueries—including complex queries that integrate genomic, clinical and functional information to facilitate salivary biomarker discovery.1

THE QUINTESSENCE OF SALIVA:

Saliva is brilliantly sound in the detection of oral diseases (that is, periodontal disease, caries, oral cancer, salivary gland disorders) but its ability to detect the non-oral distal diseases still remains a question. Hence animal models are the best tools to bridge this credibility gap, and investigators in several studies have used rodent tumor models to examine the connection between non-oral cancers and salivary biomarkers.1

[16]Gao and collegues have demonstrated rodent model which identifies and unravels mechanisms of salivary diagnostics for systemic diseases. The demonstration on the rodent model is as follows:

(A) Lung cancer and melanoma tumors are induced in ro dents and allowed to develop fully.

(B) Tumors, blood, saliva and salivary glands are harvested and biomarkers are examined by using high-throughput technologies such as expression microarrays.

(C) Statistical results and bioinformatics are used to identify biomarkers that are differentially present only in saliva of tumor-bearing animals.

(D) Researchers then develop working models and hypotheses to address the mechanistic pathways of distal disease development and onset of salivary biomarkers that reflect the distal diseases.[16]

A working hypothesis currently being tested is that tumorshed microvesicular structures known as exosomes (30-100 nanometers in size) can shuttle tumor specific contents to different parts of the bodyincluding the salivary glands, leading to theappearance of disease-discriminatory markers insaliva.17

Efforts are in place for the study of existing markers for salivary detection of myocardial infarct(heart attack)18,19 and of new markers primarily for Sjögren syndrome in patients with sicca symptoms (dry eyes, dry mouth).20-22

THE ROLE OF THE DENTIST:

Dentists play a very important role in detecting medical and life-threatening conditions, hence; the chair-side screening for medical conditions in dental office is a major mandate. More Americans see dentists regularly than they do physicians. Greenberg and colleagues[23]surveyed 1,900 practicing dentists in the United States and asked them whether they would bewilling to collect a sample of saliva and send it to a laboratory for diagnostic evaluation. Eighty-seven percent of surveyed practitioners responded "yes," demonstrating how receptive the dental profession is to saliva-based screens and risk-assessment technologies.Combined with the fact that about 20 percent more Americans visit their dentists regularly than they do their physicians and that a dentist has, on average, a roster of about 2,000 patients, the 20 percent differential between visits to dentists and visits to physicians translates into substantialopportunities for dentists to engage in the early detection of life-threatening conditions.When clinicians integrate salivary diagnostics fully into dentistry, it will have the potential toadvance the profession into primary health care.[1]

CONCLUSION:

The major drawback salivary diagnostics face is the highly advanced infrastructure of clinical laboratories and blood detection assays which need no replacement. But, diagnosis and early detection of cancer have not been promising through the serum based markers. This enhances the opportunity for the salivary diagnostics to be used for both clinical and translational applications.As health professionals we should foresee the clinical applications of salivary biomarkers for systemic diseases; when there are investments in place to advance the salivary diagnostics, when research looks forward for clinical and translational applications. Eventually we look forward to the day when dentists understand the importance of salivary diagnostics and imply it into dental practice.

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