

Saliva as a Diagnostic Tool-Current & Futuristic Potentials

Dr. Vandana Gupta

Asst. Professor
Dept. of Prosthodontics

Dr. Shipra Gupta

Asso. Professor
Dept. of Periodontics

Dr. Nandini Bhaskar

Sr. Asst. Professor
Dept. of Periodontics

Dr. Arun K. Garg

Asso. Professor
Dept. of Orthodontics

Dr. Harvansh Singh Judge Institute of Dental Sciences & Hospital, Panjab University, Chandigarh, India

Abstract

Saliva, often regarded as the 'mirror of the body' is a perfect surrogate medium to be applied for clinical diagnostics. Salivary diagnostics is a dynamic and emerging field utilizing nanotechnology and molecular diagnostics to aid in the diagnosis of oral and systemic diseases. Advancements in proteomics and nanotechnology are paving the way for diagnostic tests that will be capable of rapid multi-analyte detection in both laboratory and non-laboratory settings. Salivary protein researches have shown that in addition to the major salivary protein families, saliva contains hundreds of minor proteins or peptides that are present in low concentrations but may play an important role on the discrimination of diseases. This review presents an overview of the value of saliva as a credible diagnostic tool, the discovery of salivary bio-markers and the development of salivary diagnostics now and in the future.

Keywords: Saliva, Diagnosis, Systemic disease, Drug, Hormones.

Introduction

In most cases, the earlier the disease is diagnosed, the more likely it is to be successfully cured or well controlled. Managing a disease, especially in the early stage, may dramatically reduce the severity of its impact on the patient's life or prevent and/or delay subsequent complications. People are aware of the importance of regular health check-ups; however, most systemic diseases are not diagnosed until morbid symptoms become apparent in the late phase. To overcome this challenge, medical researchers are devoted to finding molecular disease biomarkers that reveal a hidden lethal threat before the disease becomes complicated. These markers could be DNA, RNA or protein molecules that act as indicators reflecting particular physiological states. In the past decade, scientists have demonstrated that human genetic alterations can be detected both intracellularly and extracellularly by molecular diagnostics.¹ In addition; abnormal nucleic acids and/or proteins have been identified in patient's bodily fluids such as blood, urine and cerebrospinal fluid, and have been demonstrated to be effective bio-markers for diagnostic use.

Saliva is a complex secretion. 93% by volume is secreted by the major salivary glands and the remaining 7% by the minor glands. Early detection of disease plays a crucial role in successful therapy. It reflects the spectrum of health and disease states. Like blood, saliva is a complex fluid

containing a variety of enzymes, hormones, antibodies, antimicrobial constituents and growth factors. Many of these enter saliva from the blood by passing through the spaces between cells by transcellular (passive intracellular diffusion and active transport) or paracellular routes (extracellular ultra-filtration). Therefore, most compounds found in blood are also present in saliva, thus saliva is functionally equivalent to serum in reflecting the physiological state of the body, including emotional, hormonal, nutritional, and metabolic variations. Hence the analysis of saliva, like blood-based analyses, has two purposes: first, to identify individuals with disease and second, to follow the progress of the affected individual under treatment.²

Saliva as a Diagnostic Fluid

Saliva is an oral fluid that contains an abundance of proteins and genetic molecules. As a diagnostic fluid, saliva offers distinctive advantages over serum because it can be collected non-invasively by individuals with modest training. Furthermore, saliva may provide a cost-effective approach for the screening of large populations. There is minimal risk of contracting infections during saliva collection and saliva can be used in clinically challenging situations, such as obtaining samples from children or handicapped or anxious patients, in whom blood sampling could be a difficult act to perform. It clearly meets the demands for an inexpensive, noninvasive and easy-to-use screening method. As a diagnostic specimen in the clinic, saliva has many advantages in terms of collection, storage, shipping and voluminous sampling; all of these processes can be carried out very economically compared with serum or urine. Saliva is also easier to handle during diagnostic procedures than blood because it does not clot, thus reducing the number of manipulations required. Moreover, for healthcare professionals, a salivary test is safer than using serum, which is more likely to expose operators to blood-borne diseases. For the patients or examines, the noninvasive collection approach could dramatically reduce anxiety and discomfort and increase their willingness to undergo health inspections that will greatly increase the opportunity to monitor their general health over time and to diagnose morbidities in the early stage.³

Salivary Diagnostics

Saliva can be used for interpreting hereditary disorders, autoimmune diseases, periodontal diseases, dental caries, malignant and infectious diseases, endocrine disorders, as well as in the assessment of therapeutic levels of drugs and the monitoring of illicit

drug use.

The greatest challenge of salivary diagnostics is to identify disease diagnostic markers and successfully translate these research efforts from the laboratory into the clinic. The proteome is the protein complement of the genome and proteomics is analysis of the portion of the genome that is expressed. The proteomes in bodily fluids are valuable due to their high clinical potential as sources of disease markers. In principle, a global analysis of the human salivary proteomes can provide a comprehensive spectrum of oral and general health. Besides proteomes, the salivary transcriptomic technology has further advanced the diagnostic potential of saliva for medical applications. Salivary transcriptomes are RNA molecules that are unusually stable in saliva. They include mRNA molecules that cells use to convey the instructions carried by DNA for subsequent protein production.³

Applications of Salivary Diagnostics

1. Specific markers available in saliva for periodontal diseases are IgA, IgM, IgG and non-specific markers are mucin, lactoferrin, salivary ions and salivary volatiles.
2. Gland-specific saliva is used for diagnosis of pathology specific to one of the major salivary glands. Whole saliva is most frequently used for diagnosis of systemic diseases.
3. Monitoring chemical treatments to control dental caries, owing to the possibility of detecting the presence of *Streptococcus mutans* and *Lactobacillus* species, as well as lactic acid, which causes the sub-surface demineralization that causes the onset of the caries lesion.
4. Presence of thiocyanate in the saliva is an excellent indicator of active or passive smoking.⁴
5. Three tumor markers (Cyfra 21-1, tissue polypeptide antigen, and cancer antigen CA125) are significantly elevated in saliva when compared to sera of patients suffering from oral squamous cell carcinoma. Gene methylation in saliva is a promising biomarker for the follow-up and early detection of still curable relapses of head and neck squamous cell carcinoma patients.⁵
6. Five salivary proteins (M2BP, MRP14, profilin, CD59 and catalase) were shown to be able to discriminate oral cancer with greater than 90% clinical accuracy.
7. Measurement of salivary CA125 and epidermal growth factor may have diagnostic potential for ovarian cancer and breast cancer respectively.
8. Measurement of salivary sialic acid

- appears to be promising in the detection of lung cancer.
9. Saliva can also be used to detect pancreatic cancer and type II diabetes.
 10. Sjögren's syndrome (SS) is associated with changes in specific salivary constituents such as an increase in inflammatory proteins (e.g. α -enolase, carbonic anhydrase I and II, salivary α -amylase fragments) and decrease in acinar proteins (e.g., lysozyme C, polymeric immunoglobulin receptor, calgranulin A) compared with the profile in non-SS individuals.
 11. Markers in saliva may be useful in postoperative follow up among patients undergoing cardiovascular surgery. Determinations of total serum amylase and salivary amylase activity have been made before and 6 hours after cardiovascular surgery. The results indicate that if salivary amylase levels are low in preoperative patients with ruptured aortic aneurysm, there is an associated increase in mortality.²
 12. Measurement of antibodies to HIV in saliva has been shown to be as accurate as measurement in serum and the salivary assay has been commercialized as a product called OraQuick.
 13. PCR can be used to measure the shedding of cytomegalovirus and herpes viruses in the saliva of HIV infected patients.
 14. PCR can facilitate diagnosis of human rabies using saliva.
 15. Measurement of Hepatitis C virus. There are commercial kits for determining antibodies to hepatitis B and C viruses that are 100% sensitive and specific.
 16. Detection of antibodies to rubella, parotitis and rubeola viruses.
 17. In neonates, the presence of IgA is an excellent marker of rotavirus infection.⁴
 18. PCR detection of *Helicobacter pylori* infection (critical pathogen associated with peptic ulcer). *Helicobacter pylori* antibodies detection in saliva may be valuable for predicting risk for gastric adenocarcinoma.²
 19. The determination of certain drugs in saliva depends on their concentration in the blood and their diffusion capacity, liposolubility and molecular size. Saliva has been used to monitor the levels of lithium, carbamazepine, barbiturates, benzodiazepines, phenytoin, theophylline and cyclosporine.
 20. Cystic fibrosis is linked to raised sodium, chloride, calcium, phosphate, lipid and protein contents in the submaxillary saliva.
 21. Helpful in providing objective outcome measures during psychiatric therapy. Can be used to monitor therapeutic responses in the treatment of anxiety by measuring salivary levels of 3-methoxy-4-hydroxyphenylglycol.²
 22. Cortisol, dehydroepiandrosterone, estradiol, progesterone and testosterone levels can be determined. Useful in

evaluations of mood and cognitive emotional behavior to predict sexual activity in adolescent males to study child health and development in considerations of premenstrual depression and to screen for Cushing's syndrome.²

23. Intercept, Salivascreen Professional, Rapid HIV -1/2 Antibody Test, Ora Quick Advance, ZRT Saliva Test, Orasure HIV 1 Western Blot and Q.E.D Saliva Alcohol Test are some of the commercial products based on salivary diagnostics.

Conclusion

With the additional advantages of an easy, safe, cost-effective and non-invasive diagnostic approach, saliva shows high potential for monitoring general health and disease with enormous translational values, and unparalleled opportunities for clinical applications.

References

1. Li Y, St John M, Zhou X, Kim Y, Sinha U, Jordan R et al. Salivary Transcriptome Diagnostics for Oral Cancer Detection. *Clin Cancer Res* 2004; 10: 8442-8450.
2. Streckfus CF, Bigler LR. Saliva as a diagnostic fluid. *Oral Diseases* 2002; 8: 6976.
3. Lee YH, Wong DT. Saliva: an emerging biofluid for early detection of diseases. *Am J Dent* 2009; 22: 241-8.
4. Llena-Puy C. The role of saliva in maintaining oral health and as an aid to diagnosis. *Med Oral Patol Oral Cir Bucal* 2006; 11: E449-55.
5. Righini CA, Fraipont F, Timsit J, Faure C, Brambilla E, Rey E et al. Tumor-Specific Methylation in Saliva: A Promising Biomarker for Early Detection of Head and Neck Cancer Recurrence. *Clin Cancer Res* 2007; 13: 1179-1185.

Address for Correspondence

Dr. Shipra Gupta, Asso. Professor, Dept. of Periodontics; Dr. Harvansh Singh Judge Institute of Dental Sciences & Hospital, Panjab University, Chandigarh, teena1472@yahoo.in

IDA Faridabad Full Day Picnic in Camp Wild Village-Dhauj

IDA Faridabad branch has organized a full day picnic in camp wild village Dhauj on 20 October 2013. The whole picnic was well organized by contribution of president Dr.

Kulbhushan Sharma (Secretary), Dr. Rajeev Arora (Treasurer), Dr. Prabhjeet Singh Rana & immediate past-president Dr. Inderjeet Singh Rana. Around 20 families including singles, kids,

couples all enjoyed d picnic wd lots of activities. It was an exciting, enjoyable n different experience for all the IDA members & their families.

