

Oral Markers for Systemic Disease

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Introduction

- Early diagnosis is important to prevent complications that can affect a patient's quality of life
- Despite regular checkups and screening programs, many diseases are picked up too late i.e. when morbid symptoms are present.
- Researchers are trying to find biomarkers i.e. genetic material (RNA, DNA) and proteins that reflect physiological processes of disease.
- Blood, CSF and urine are mediums commonly used to detect alternations in molecular molecules.
- Disease marker tests are limited by lack of specificity, sensitivity, absence of inexpensive sample collection methods, and invasiveness.
- Oral biomarkers, through analysis of saliva, offers a non-invasive, accessible, abundance of biomarkers including genetic materials and proteins. Hence, its potential as a diagnostic aid is vast.

Properties of Saliva

- Saliva contains hormones, antibodies, growth factors, microbes and their products. Therefore, the saliva can be used as a reflection of the physiological function of the body
- Concerns with saliva did include low concentration of analytes relative to blood, but new technology is highly sensitive; therefore, this is no longer a concern.
- Table 1 summarizes the advantages of saliva as a diagnostic tool

Table 1

Advantages of salivary testing for diagnosis.

Advantages³, [69](#), [70](#), [71](#)

- Non-invasive, easy to use, inexpensive
 - Safer to administer than serum sampling (no needles)
 - Real-time diagnostic values
 - No need for trained medical staff
 - Multiple samples can be obtained easily
 - Collection and screening can be done at home
 - Minimal risks of cross-contamination
 - More economical sampling, shipping and storage compared to serum
 - Requires less manipulation during diagnostic procedures compared to serum
 - Commercial availability of screening assays
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Javaid et al, 2016

Autoimmune Conditions

Sjogren's Syndrome (SS)

- Salivary secretions of patients exhibit higher levels of antibodies such as IgA, IgG, PGE2, IL-6. This is accompanied by reduced salivary flow which can have several oral manifestations
- Current tests include sialometry, salivary flow rate, serological tests, or minor salivary gland biopsies.
- A recent panel of salivary biomarkers of SS was studied. It was found that 28 proteins were significantly modified by SS. (Starosta et al, 2006).
- Proteomics is also offering new insights into a potential biomarker for SS. pSS has recently been found to be **associated** to pathology, and inflammation of minor salivary glands.

Cystic Fibrosis (CF)

- The salivary profile of patients with CF includes increased levels of Ca, P (may explain why CF patients have more calculus relative to controls), Cl, K, and Na. They are also found to have lower salivary volumes and pH values.

- CF patients have been found to have higher levels of proteins, antioxidants, and uric acid compared to healthy controls. This suggests that salivary changes may be indicators of the chronic oxidative and inflammatory process related to CF.
- These biomarkers could give us more clue about the etiology and monitoring of CF through salivary testing

Cardiovascular Disease

- A significant number of patients suffering from heart disease lack known risk factors such as family history, hypertension, and altered lipid profiles.
- C-reactive protein (CRP) is an inflammatory mediator that is produced in response to acute injury or infection and acts by activating the complement cascade.
- It can contribute to arterogenesis and has been found in arterial plaques.
- Salivary CRP correlate well with plasma CRP; hence obtaining a less invasive CRP measurement could indicate susceptibility to CVD.
- Cardiac troponin (cTn) is another biomarker that detects acute myocardial infarctions (AMI) is elevated when cardiac cells undergo necrosis. The levels of saivary cTn are as sensitive as serum troponin markers in patients undergoing AMIs.
- As CVD is the leading cause of death in Canada, salivary tests offer a practical alternative to serum sampling to help determine at risk populations.

Diabetes

- Very little research has been done on salivary testing for diabetes. It is likely because that pin-prick tests are practical, reliable methods to test blood glucose levels.
- Salivary proteomics offer a less invasive approach for screening
- The protein profiles of patients with diabetes was researched and was found that about 65 of the 487 proteins investigated were higher in diabetic patients than controls
- Proteomics can offer another avenue to diagnose and monitor diabetes

HIV

- HIV virus transmission remains a concern due to its severe complications if left untreated
- 2012: OraSure Technologies Inc developed an at home oral swab test to detect HIV 1 and HIV 2. The swab is placed in the lower buccal vestibule for 2-5 mins to allow for the probe to collect antibodies.
- The swab is then sent to a laboratory where a Western blot analysis. The specificity and sensitivity is 99% and 93% respectively.
- The PPV in higher prevalence areas is 98.7%. This is comparable to blood based testing values.

Oral Cancer

- Squamous cell carcinomas are the most common cancers in the oral cavity.
- The key to early detection of oral squamous cell carcinoma is to decrease the morbidity and mortality related to
- Our current methods rely on visual and tactile oral screening tests. In asymptomatic patients, there is limited evidence to suggest that these will prevent cancer related mortality.
- Salivary proteins are an emerging topic of research in this field. Salivary levels of certain proteins such as CD44 (cell surface glycoprotein involved in cell to cell interaction), Cyfra 21-1, tissue polypeptide antigen (TPS), and Cancer antigen 125 have been suggested as biomarkers for oral cancers.
- No single oral biomarker has been able to detect earlier stages of OSCC with accuracy; instead, panels of biomarkers need to be drawn together to exhibit enough sensitivity to pick up OSCC require a panel of biomarkers to exhibit enough sensitivity to identify OSCC.
- A recent study found that the combination of salivary levels of IL-8 and subcutaneous adipose tissue (SAT) demonstrated the highest sensitivity and specificity to detect OSCC.
- Another significant biomarker is the presence of HPV. A commercial test is available in the US and Canada that identifies people at risk of OSCC as 60% of OSCC tumors are associated with HPV 16.

Conclusion

- Salivary tests offer an accurate, effective, easy-to-use, and cost-effective alternative to identifying biomarkers indicative of systemic diseases.
- These tests offer the potential of screening entire populations for specific diseases in a timely manner.
- As patients visit their dentists more than their physicians, salivary tests can pave the way for chair-side diagnoses and follow up for inquiry of potential systemic disease.
- In order for their acceptance into private practice, these tests need to be streamlined to be more feasible, and accepted by insurance companies. Further studies need to be performed to establish the accuracy and cost effectiveness of these tests.
- It is expected that non-traditional tests, upon validation and standardization will make salivary diagnostics a reality in the future.

References

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