

Future of Oral Proteomics.

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The human body contains billions of proteins and peptides that perform various functions to maintain body homeostasis and a functional repair system. These proteins and peptides also assist in monitoring the normal and any diseased condition of the body. Analysing blood parameters for the detection of pathological lesions involves invasive techniques. The method to obtain blood is not suitable for use in immunocompromised and vulnerable patients, patients with terminal illness and patients with clotting disorders such as hemophilia. Moreover, blood investigations do not detect all specific proteins or antigens related to pathological conditions.

Recently, the biomonitoring of the human body has developed an essential system to investigate any significant changes in body physiology. This allows for the management of the condition in a timely manner and according to the body's requirement. Therefore this system is more advanced, diagnostic and effective than advanced-stage management such as invasive surgeries. The term 'Proteomics' was coined in 1997 and deals with the large-scale study of proteins.¹ The oral cavity comprises the tongue, salivary glands, teeth, gingiva, and the surrounding tissues. These structures produce certain proteins that may be useful in the detection or monitoring of diseases in the early stages via proteome analysis. For instance, human saliva contains millions of proteins and peptides that can allow the identification of different oral conditions such as dental caries, periodontitis, gingivitis, oral cancer, fungal diseases. Also, it provides a microbe profiling and a virus screening in different pathological conditions.²

Saliva also contains exosomes which are small cell-secreted vesicles. Exosomes retain cytoplasmic contents and possess characteristic surface markers such as CD63, CD9 and CD81. Non-invasive isolation of exosomes from saliva samples and their specific protein and nucleotide contents that are expressed as biomarkers can be used for diagnostic purposes. Furthermore, exosomes have also been recognised as useful for immunotherapy and vaccination modalities. In the last two decades many researchers have identified proteomes that were extracted from oral tissues and fluids with the help of 2-D gel electrophoresis, mass spectrometry (MS), liquid chromatography (LC), western blotting (WB), enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) and matrix assisted laser desorption/ionization (MALDI).⁵ Khurshid *et al.*,³ elucidated the whole mouth saliva (WMS) proteins and analysed them by two-dimensional (2D) gel electrophoresis. Many researchers have reported a proteomic analysis of dental pulp, saliva, enamel, dentine, cementum, periodontium, and oral stem cells. Subsequently, they generated a protein bank

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for future use as a Point-of-Care (PoC) concept or merely on oral biosensor technology.^{1,2} The use of wearable devices such as watches, glasses, bracelets or skin tattoos is very common, that allow monitoring of the pulse /heart rate, movement, and steps taken by the body. The oral cavity also needs some sticker or adhesive tape-based biosensor to perform dynamic real-time monitoring 24/7 of a specific site or tissue. For this many funding organizations (NIH & NIDCR) have started allocating funds for the development of dynamic, real-time, non-invasive monitoring of physiological processes in the human body by using oral biosensors.

Proteomic analysis of human tooth pulp explored 342 proteins that perform various function in the body such as catalytic activity, osmotic regulation, transportation, protease activity, and immune response. This was evaluated in a study by 2-dimensional gel electrophoresis which was further analyzed by nano-liquid chromatography tandem mass spectrometry (nLC-MS) with a comprehensive data in the field of dentistry.⁴ The latest research identified unique proteins from the pulp-dentine complex and the information gathered from protein analysis is useful for future development of efficient treatment modalities. Dental caries is considered as a common disease of oral cavity. This dental decay is most commonly caused by *Streptococcus mutans* that initially affects the enamel surface and gradually involves the dentine and the pulp chamber.

The role of salivary proteins and enzymes such as lysozyme, histatins, proline rich peptides (PRPs), α -amylase and glycoproteins were identified by the sensitive proteomic science. It provides an unknown mechanism of action in enamel demineralization/ remineralization. The salivary proteins and peptides depict the qualitative changes in the oral cavity and the body as a whole.

The current concept of classical dentistry is to provide

a predictive, preventive, personalised, and non-invasive dental treatment to a patient. This embraces advancement in diagnostic and customised dentistry. One Brazilian group of researchers identified Zika virus proteins from pregnant women saliva with the help of mass-spectrometry. This might bring a confirmatory approach for the development of wearable oral biodevices to detect oral biomarkers.⁵ Another study reported the proteomics of gingival crevicular fluid (GCF) biomarkers from diseased periodontal patients. It revealed the eight most essential proteins including superoxide dismutase-1 (SOD1), apolipoprotein A-I (ApoA-I) and dermcidin (DCD).⁶

Acquired enamel pellicle (AEP) is a protein-rich layer on tooth enamel which plays an important role in the maintenance of tooth integrity. Siqueira et al identified 130 pellicle proteins through liquid chromatography (LC-MS/MS) analysis.⁷ Proteomic analysis of oral squamous cell carcinoma (OSCC) identified three biomarkers which are related to the patient outcome-associated proteins. This identification might provide a significant development of clinical assays for prognosis and treatment planning of OSCC.⁸

There are a few databases reported in last few years like MVsCarta (A protein database of matrix vesicles to aid understanding of biomineralization), salivary proteome database (Available at: http://www.skbucla.edu/cgi-bin/hspmscgi-bin/welcome_c.cgi/) supported by National Institute of Dental and Craniofacial Research (NIDCR).

Hence, the future of proteomics science in dentistry is going to be ground breaking by identifying the unknown functions and pathophysiology of oral tissues. The development of a large protein data bank would involve non-invasive diagnostic parameters and a new drugs therapy system. In addition, this would provide a cutting-edge treatment plan for various pathological conditions.

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