ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4 ,2022

The Future of Periodontics Research is Proteomics

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ABSTRACT:

Background: Inflammatory conditions like periodontitis are brought on by the interaction of the host factors and infectious pathogens. The onset, development, and severity of periodontal diseases are significantly influenced by a variety of protein molecules. The investigation of proteins as indicators in periodontal diseases has gained attention in recent years. Multiple bacterial- and host-derived mediators (e.g., collagen-degrading enzymes, elastase-like enzymes, etc.) produced in saliva and gingival crevicular fluid in periodontitis can be used as diagnostic markers for the condition. The identification of possible novel medications for the treatment of periodontal diseases is another significant advancement in the study of human genes and proteins. Therefore, the diagnosis, prevention, and treatment of periodontal disorders can benefit from knowledge of the proteins implicated in their aetiology.

Keywords*:* Genome, Porphyromonas gingivalis, Proteome, Biomarker

INTRODUCTION:

The "working horses" of a cell are thought to be proteins, the building blocks of life, because they are essential to practically all biological metabolic functions, such as structural support, catalysis, and signal transmission. The Greek word "Proteios," which means "keeping the first place," is where the term "protein" originated. In the year 1838, Jons Jakob Berzelius first used this name. Mark Wilkinsoriginally used the term "proteome" in 1986. It is a combination of the words "protein" and "genome." The term "proteome" refers to the entire

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set of proteins present in a cell, including any variations that have occurred over time or in response to certain needs or pressures that a cell or organism may experience. The word "proteomics" was developed to draw comparisons with genomics, the study of genes and their activities. The study of all the proteins that an organism expresses in a specific environment and at a particular stage of the cell cycle is known as proteomics. Their relative abundance, distribution, functions, interactions with other macromolecules, and post-translational changes are also included.

The existence of thousands of proteins, each folded into a unique three-dimensional form that allows it to interact with one or more of a very heterogeneous array of chemicals, explains why proteins are essential to almost all biological activities. By examining the various patterns of protein content & activity and how these variations arise during development or in response to disease processes, proteomics research has improved our understanding of cellular function.Proteomics has also provided a new glimmer of hope for the discovery of novel therapeutic targets and the creation of novel diagnostic markers.

Post-genomic research

The full genome of a cell is included in genomics, however proteomics, which has a significant advantage over genomics, directly employs the entire gene products of a cell in a given state, including all of its cellular activities and interactions with other macromolecules. Researchers are particularly interested in investigating proteomics since it provides a deeper grasp of an organism than genetics does. First, because mRNA degrades quickly or is translated improperly, the translation of a gene into the ensuing proteins only provides an approximate estimate. Furthermore, a number of proteins experience post-translational changes (i.e. phosphorylation, acetylation, glycosylation). Their actions may be significantly impacted by this. These post-translational alterations are studied using the sciences of phosphoproteomics and glycoproteomics. Thirdly, more than one protein can be produced from a single transcript by alternative splicing and post-translational modifications. Finally, many proteins only function when they are present in complexes with other macromolecules.

Periodontal difficulties

Mark Wilkins suggested in 1994 that rather of studying one protein at a time, one could instead analyse the protein expression of the entire genome. [4] The proteome's complexity, however, appears to be the main impediment to implementing Wilkin's proposal. A protein's function may also be influenced by its position in the cell and its connection with other proteins, both of which may change in a fraction of a second, in addition to its quantity and any post-translational modifications. Due to the lack of methods like the polymerase chain reaction, which we use for the amplification of nucleic acid sequences, we are also fully dependent on the samples for the isolation of proteins.

The periodontium is a complicated tissue, and in order to fully comprehend it, a deeper understanding of the entire set of cellular and matrix proteins is critically necessary for

ISSN PRINT 2319 1775 Online 2320 7876

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cutting-edge developments. After doing an introspective investigation on cemental subtypes, Bosshardt came to the conclusion that some of these subtypes resemble alveolar bone structurally. [5] It is yet unclear whether specific proteins are present in these structures and how they are altered after translation, making it very challenging to pinpoint the precise process governing the growth, creation, and remodelling of cemental subtypes. Therefore, it is evident that proteomics is a challenging field. Only after the development of new mass spectrometry techniques in the mid-1990s was it possible to attempt to examine the proteome.

Technology enables proteomics

Proteomics is a technology-based science that involves fractionating and separating a vast number of proteins produced from cells or tissues, which are then evaluated by mass spectrometry, before being identified and characterised with the use of bio-informatics techniques. The following is a quick explanation of these steps:

Tissue and cell separation

Fractionating the cells and matrix is the first step necessary before doing a protein analysis on the dissected periodontal tissues. The main challenge to efficient fractionation appears to be the creation of a perfect homogenate in which all organelles and other cellular components are released as a free suspension. Since it is nearly hard to fractionate mineralized tissues or tissue in between mineralized tissues (like the periodontal ligament) without contaminating the adjacent tissues, they have an additional constraint. A variety of factors, such as post-translational changes and the localisation of sub-cellular organelles, can result in fractionation.

Separation of proteins

It is carried out at the protein or peptide level and requires separating the very many proteins present in cells or tissues before they are analysed by mass spectrometry, which is then followed by recognition and characterisation with bioinformatics techniques. Two-dimensional polyacrylamide gel electrophoresis, in which proteins are separated in two successive phases based on molecular weight and isoelectric points, is still a crucial method for the investigation of complicated protein mixtures originating from biological samples. For the separation of proteins and peptides, capillary electrophoresis is thought to be an alternative to chromatography and two-dimensional gel electrophoresis.

Spectrometry by mass

Mass spectrometers were a breakthrough in proteomic research because they can detect and describe small amounts of proteins in biological materials with fentomole sensitivity. In order to analyse an unknown mixture, proteins must first be extracted from the biological sample, then the proteins must be tryptically digested into peptides, and finally the peptides must be analysed using a mass spectrometer.

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Measurement and sequence analysis

The use of various fluorescent dyes in a single gel is a simpler method for quantifying various sets of proteins or peptides than using two-dimensional electrophoresis, which is technically difficult (i.e. two dimensional difference gel electrophoresis). [8] Different peptides have peculiar signal intensities during mass spectrometric analysis that change depending on the physical and chemical characteristics of the analyte and the solvent.As a result, signals generated by two peptides, even if they come from the same protein, will have distinctive intensities that allow for their identification. Tandem mass spectrometry is a different method that is employed for protein recognition, structural elucidation, and post-translational modification characterisation. It makes it easier to sequence peptides found in complicated mixes or proteins with amino terminal blocks. The Edman degradation technique, in contrast, is useful for N-terminal sequencing of huge quantities of reasonably pure peptides.

Modern periodontics and proteomics

Proteomics sheds new light on the intricate interactions between periodontal pathogens and their hosts in both health and disease as well as the function of periodontal ligament fibroblasts and other disease-related protein markers that provide an understanding of the physiology of the periodontal ligament.

Periodontal pathogens' function: The oral ecology is a diverse collection of microbial communities that engage in intricate interactions with the host both in a healthy condition and during sickness. Proteomics offers a whole new technique to comprehend the changes taking place as oral microbes adjust to environmental changes in their natural habitat in the mouth.

Periodontal ligament (PDL) fibroblasts' function: Analysis of the complete PDL fibroblast proteome is crucial for comprehending PDL physiology and disease-related protein markers. The protein expression of PDL fibroblast has been studied using immunological approaches, although these studies are only applicable to already characterised proteins for which antibodies are accessible. PDL fibroblasts have produced a total of 117 proteins, which can be used as a reference in fundamental and clinical research.

Periodontogenic microorganisms underwent proteomic analysis

Porphyromonas gingivalis proteomics within a model of the oral microbial community

Oral microbial communities are thought to be complex dynamical biofilms that form as a result of various microbes colonising the mouth. P. gingivalis and other pathogenic anaerobic gramme negative microbes are colonised as a result of the subgingival biofilm's expansion. [1] The most amazing characteristic of P. gingivalis is that it only manifests its pathogenecity in mixed microbial populations. The pioneering microorganisms give substrate and metabolic support, which ultimately aid in the establishment of following organisms. Thus, interspecies communication and signalling molecules like short-range soluble mediators, AI-2, or dietary stimuli result in the formation of a complex consortium. [10] Streptococcus gordonii and

ISSN PRINT 2319 1775 Online 2320 7876

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other closely related oral streptococci can form consortia with P. gingivalis that can be either single species or mixed species. The unique location of P. gingivalis in plaque regions high in streptococcus makes this extremely clear. [9] Due to the aerated environment, Fusobacterium nucleatum predominates in the supragingival plaque, leading to the establishment of more complex multispecies communities. [3] Additionally, oral streptococci and P. gingivalis can coaggregate with F. nucleatum.

Biological significance

The main challenge is how to interpret the data in a physiologically meaningful way. Proteomic analysis has the ability to reveal many proteins that are differently regulated. It is possible to evaluate the significance of individually regulated proteins in the context of the overall expression pattern due to the relatively modest size of bacterial genomes. Proteomic examination of organisms like P. gingivalis revealed a significant increase in several Clp family proteins, including ClpC, ClpP, and ClpX. Additionally, in Listeria, the production of additional virulence factors is regulated by proteins, and the ClpC ATPase is necessary for adherence and invasion of host cells. ClpC also aids Listeria's early egress from the macrophage's phagosomal compartment. 17 As a result, it has been hypothesised that the Clp proteins may be crucial for P. gingivalis invasion and intracellular survival.

Proteomic methods generate periodontal disease biomarkers

To obtain insight into the physiological and pathological processes pertinent to oral health and to identify useful biomarkers for oral illnesses, one must have a thorough grasp of the human salivary proteome. Periodontopathic bacteria produce virulence factors that can directly degrade host tissue or trigger a host response that causes host cells to release biological mediators. When a response is overreacted, these mediators cause host tissue to be destroyed. [2, 3] Enzymes, proteins, and other inflammatory mediators produced by the host and the bacteria seem to hold promise as salivary diagnostic biomarkers for periodontal disorders. The innate host defence is triggered by bacterial lipopolysaccharide and other microbes (including bacterial DNA), which attracts neutrophils, monocytes, and activated macrophages to the location. Numerous cytokines, including prostaglandins (PGE2), tumour necrosis factor (TNF), and interleukins IL-1 & IL-6, are then released by these host cells, which accelerate the inflammatory process. Alveolar bone and polymorphonuclear leukocytes therefore produce matrix metalloproteinases (MMPs), which break down collagen. Osteocalcin and pyridinoline cross-linked carboxyterminal telopeptide are then released into the vicinity and transferred into the periodontal pocket by gingival crevicular fluid. [4,5]

Additionally, gingival crevicular fluid (GCF), which contains proteins released from serum or inflammatory areas, reflects the health of the gingiva. The GCF of the classified periodontitis patients compared to the healthy individuals was used in a study to identify potential protein biomarkers for periodontitis in the GCF proteome. For the first time, azurocidin was identified as an upregulated protein in the periodontitis patients and was verified for its

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increased expression during periodontitis by ELISA (Enzyme linked immunosorbent assay). Azurocidin was also discovered to play a protective effect in the preservation of alveolar bone during the early stages of periodontitis by preventing the development of bone marrow-derived macrophages into osteoclasts.

Therapeutic applications

In the upcoming years, periodontal surveillance and disease diagnosis will be substantially advanced by the use of quick point-of-care oral diagnostics. [8] By managing complicated oral fluids like saliva and gingival crevicular fluid, new technologies like lab-on-a-chip and microfluidic devices offer the ability to assess a patient's periodontal disease risk profile, current disease activity, and responsiveness to therapeutic interventions.

In a chronic infectious condition like periodontitis, this strategy should operate as a stimulus for clinical decision-making and monitoring of episodic disease development.Although the use of salivary diagnostics to diagnose periodontal disease appears to have a bright future, these methods may face challenges in the clinical world. These cutting-edge periodontal diagnostic techniques need to be examined in sizable patient populations in order to be verified and compared to the disease's current gold standards, such as alveolar bone levels and clinical attachment levels.

CONCLUSION

The detection and treatment of periodontal diseases will advance with the use of proteomics and gene expression. New therapeutic prospects will be made possible by developments in biopharmaceuticals, medication delivery, gene therapy, and tissue engineering.Its use in dentistry, however, will rely on how oral health care professionals integrate it into their practises because it calls for in-depth understanding of human genetics as well as the use of novel diagnostic and therapeutic technology.

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