Contribution of multi ‘-OMICS’ to the future of oral health

“-OMICS’ technologies including epigenomics, genomics, exomics, transcriptomics, proteomics, metabolomics ... generate and process massive biological data.”

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First draft submitted: 2 March 2017; Accepted for publication: 17 March 2017; Published online: 8 June 2017

The scientific ‘-OMICS’ turmoil began at the end of the last century, leading to a new and deeper level of complex biological insights that completely change the way scientist understands the molecular mechanisms of the diseases. Health professionals in the post -omics era will use thousands of disease-associated biomarkers provided by high-throughput technology. Thus, clinical practice will grant the adaptation of multiomics data to personal healthcare.

Multiomics biomedical approach resides on wide profiling methods that haul considerable amount of -omics data. ‘-OMICS’ technologies including epigenomics, genomics, exomics, transcriptomics, proteomics, metabolomics and nascent fields such as viromics – the study of virus in our body and how they might cause certain conditions – coupled with bioinformatics

and biostatistics to generate and process massive biological data. Nevertheless, multiomics gained results and knowledge are assessed individually rather than conjointly. In this manner, interactomics deals with studying both the interactions and the consequences of those interactions. Recent studies of metagenomes have opened the door to characterize the size and diversity of the human ‘virobiota’ and to identify its associated genes (the ‘virome’), promoting the emerging field of host–virobiota interactions.

Viruses prevail on or in just about every species and every ecological niche [1], although viral structure differ considerably among different types of viruses, many of them can colonize the human oral cavity as well as other microbes such as oral bacteria [2,3]. The mouth offers a

KEYWORDS

• biomarkers • immune system
• interactomics • multiomics
• oral disease • periodontal diseases • public health dentistry • virobiota • virome
• viromics

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splendid portal to a new host. Viruses in the oral cavity are most commonly acquired in early childhood, from mother to infant via infected saliva, or in adulthood transmitted by the oral–oral, oral–genital or oral–anal route, but other factors such as environmental, developmental, social, behavioral or others may also play a major role (‘exposomics’). Novel findings had highlighted the role of the immune system in shaping the composition of the oral virobiota and consider how resident viruses may impact host immunity [4]. Many viruses have ‘high’ mutation rates and constantly shift as means of eluding the host’s immune system. Evidence suggests a bidirectional association with a range of oral and systemic diseases [5,6].

Leading-edge scientific research has revealed the possible role that latent and active viral infections have in the etiopathogenesis, progression and severity of periodontal diseases (PDs) [2]. After dental caries, PDs are the second most prevalent oral diseases affecting up to 90% of the worldwide population, contributing to the global burden of chronic disease and meeting criteria as a public health problem [7,8]. Essentially PDs are poly-periodontopathogenic and multifactorial infectious diseases which trigger chronic inflammatory and immune responses that lead to tissue destruction of the supporting structures of the teeth, also known as periodontium gingiva, periodontal ligament and alveolar bone. PD is a chronic oral infection associated with numerous oral microbial species organized in planktonic or biofilms communities.

Specific microorganisms are believed to play an essential role in PDs, so far their relative numbers and significant contribution to the initiation and progress of the disease is still unclear [9,10]. The collection of microorganisms found in the oral cavity has been referred to as the oral microflora, the oral microbiota or currently as the oral microbiome. The ultimate diversity of the oral microbiome was estimated to be around 19,000 phylotypes. Notwithstanding, viruses surpass microbial cells 10:1 in most environments, as far as viruses inhabit oral tissues, saliva, gingival crevicular fluid and the subgingival and supragingival biofilms, little is still known about how oral viruses are spread throughout the oral cavity and their role as constituents of the human microbiome. However, viral sequence databases have considerably expanded since the beginning of the viromics era and particular species are detected now and then in the oral cavity [11].

Human viruses may occur in periodontal lesions with relatively high prevalence; common conditions are the different herpes viruses, human papillomaviruses, hepatitis-causing viruses and HIV [12]. Viruses that replicate or not in the oral tissue but that are capable of infecting and impairing immune-mediated response, resulting in proinflammatory signaling events or bacteriophages that predate upon cellular oral microbiota rather than the human host may contribute in shifting oral microbiome diversity and constitution, causing an increased pathogenicity of the periodontal microbiota [2,3]. Viral infection of certain cell types, upregulate cellular surface receptors enhancing polymicrobial adhesion. Therefore, viral coinfection with other polymicrobial pathogens may lead to immunomodulatory effects that repress more than one microorganism clearance mechanisms and therefore increasing colonization, being a key issue in host–symbiont evolutionary dynamics where hosts and their symbionts speciate in parallel, by cospeciation or through host shifts.

Periodontal viral–polymicrobial interactions initiate various and distinct mechanisms. For example, virus-induced alteration in epithelial cells, reduced cellular functions, cell death/decreased junctional epithelium or epithelial barrier function, virus-upregulated cellular surface receptors for polymicrobial adhesion, virus-enhanced polymicrobial colonization, virus-mediated inhibition of innate immune cells, suppressed phagocytosis, impaired polymicrobial killing, depressed leukocyte migration, antiviral immune molecules, suppressed innate immunity, inhibited IL-17 responses, dysregulated inflammation, enhanced periodontal tissue injury from increased inflammation (e.g., chemokines) and increased susceptibility from induction of anti-inflammatory cytokines. Therefore, viral–polymicrobial interactions may explain in part the etiopathogenesis and progression of PD [2].

Progression of PDs in the presence of virus-induced infection is dependent on the immune competency of the host and the local inflammatory response to typical and atypical subgingival microorganisms [13]. PDs may participate in the wound healing process and tissue destruction via the inflammatory process and various dental plaque biofilm periodontopathogens induce different cytokine response profiles in gingival epithelial cells that may reflect their particular virulence or commensal status. The aforementioned suggests that the inflammatory and

infectious components of PD as an oral infection might have the capacity to prompt viral reactivation and recrudescence. Nowadays it has become evident that cytokines have a major relevance in immune responses to persistent viral infections and that the functional impact of a specific cytokine can be strikingly distinct or even opposite in chronic versus acute contexts of infection [13,14].

Some theories about common susceptibility, systemic inflammation with increased circulating cytokines and mediators, direct infection and cross-reactivity or molecular mimicry between oral microbiome–virome antigens and self-antigens try to explain periodontal etiopathogenesis and disease progression. Thus, understanding the molecular interactions in the microbiome–virome and host’s immune system using ‘molecular profiling’ and ‘molecular perturbation’ approaches through a combination of multiomics [15], is one of the main challenges toward discerning among the convoluted diverging and converging signaling pathways between human oral physiological and pathological states.

Oral multiomics milieu will be transformed by the evolution of high-throughput techniques and bioinformatics resources, facilitating novel approaches, rapid analysis and interpretation of large datasets. Thus, providing healthcare professionals with new insights into oral health and disease, potentiating multiomics clinical application

and advancing toward the implementation of a ‘precise medicine and dentistry’ within the next decade. In the interim further and better designed large-scale longitudinal studies in various populations, with the application of new multiomics sciences and technologies; the use of molecular determinants for assessing potential targets for the inhibition of co-adhesion, biofilm development and regulation of the ecological balance in the oral cavity; may ultimately provide the means to modify microbiome–virome colonization and thus reduce the impact of oral diseases on human health. In the following years, oral treatment based upon multiomics – genetic and nongenetic – criteria will contribute to a more ‘precise medicine and dentistry’ accentuated upon individualized periodontal prevention, diagnosis and treatment strategies, along with a professional practice focused on specific biological, psychological, social and environmental contexts.

Financial & competing interests disclosure

This study was supported by the National Science and Technology Council (Consejo Nacional de Ciencia y Tecnología – CONACyT). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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