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Research Article

Microbiomics in the Molecular Era: A Bird's Eye View into the Future of Personalized Medicine

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Abstract

Humans, like all other complex living beings, nurture trillions of microbiological cells within, and on the surface of, their bodies which they acquire from their environment right from their time in the womb, to their entry into their tomb. These living cells are termed as our microbiota, and their totality, when seen in their genotypical and phenotypical entity, is called the microbiome. The current paradigm of personalized medicine is heavily reliant on the variation in human host genomics. Research has proven that human microbiome varies from individual to individual to a much higher degree compared to the host genome, rendering it more individualized. This has behooved engendering a new shift in the personalized medicine modality from its current focus to a multi-omics approach, which encompasses not just microbiomics as one of its principal reinforcers, but also metabolomics and proteomics. The ambitious projects to decode human microbiome and mapping it to various faucets human health and disease with completeness or near completeness, in spite of the mighty volume of their task, which aim for goals much more complicated than the Human Genome Project, throw a light of promise on an already optimistic future of personalized medicine.

Keywords: Microbiota; Microbiogenomics; Personalized Medicine; Human Genome; Bioinformatics; Pharmacogenomics

Introduction

Evolution has rendered humans, taxobiologically, as one of the most complex living entities on earth [1]. Like others of their kind, they survive as holobionts, which are systems of microbiological organisms within a eukaryote [1,2]. A human body, as a holobiont, is composed of different microbial symbionts, apart from itself, in order to subsist as a single ecological unit [1,3]. Microbiotic cells amounting up to 10 to 100 trillion within a single human, form a significant proportion of the total living cells in the body, with a share as high as fifty percent of total cellular count therein [4-6]. The population of our microbial occupants is known as our microbiome [5], Joshua Lederberg [7], the Nobel Prize winner who is credited with coining the term 'microbiome,' used the argot 'to signify the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space and have been all but ignored as determinants of health and disease. Encouraged by the prospects that its study and application produces on humans, microbiome projects worldwide have been started in order to create capacity and resources for the characterization of the human microbiome, determine with exactness the functionalities that the microbiota exhibit and to gauge their impacts on our health [6,8-11].

One of these projects, the Meta-HIT consortium, has compiled an array of more than three million functional genes in the microbiome resident in the human alimentary canal [11,12] as compared to the about twenty-two thousand genes present in the entire human genome [13]. Additionally, individual humans' microbiome has an enormous diversity, when seen against their genomic variation. Each human is about 99.9% identical to another seen in light of the host genome [14] but individual microbiomic similarities are only up to ninety per cent seen in the light of the microbiome of the human gut [15,16]. These observations emphasize that in conjugation with human metabolomic differences [17-19] utilizing the human microbiome - which is much more specific compared to human host genome - can be very positively impactful in the arena of personalized medicine [20-25].

A number of human disorders and diseases have been directly and indirectly associated with the microbiome, that may include the pseudocommensals as well (which are those microbiota that do not replicate in the gut [26] but, from their presence in infected water, supplies and soil, through oro-fecal, dermal and other channels, have had continuously used human body as passage, over the centuries [27,28]. For example, Shukla., *et al.* [29] have enlarged

upon how the gut microbiota may play a role in myalgic encephalomyelitis/chronic fatigue syndrome. The greater uniqueness of individual microbiome (the individual microbiomic fingerprint) can help us tackle these health issues, pharmacogenomically, with greater ease now. The emergence of new genomic technologies and bioinformatics tools, enhancements in the definition of new and existing clinical phenotypes, development of new sequencing techniques, and the presence of advanced statistical tools to analyze a broad range of data associated with human microbiome, which has provided a commanding measure to recognize the influence of microbiome on human health [30-33].

Kilian., *et al.* [31] have suggested for the adoption of an ecological approach to the maintenance of oral health, along with a shift to personalized strategies to refurbish the health of the helpful oral microbiota subsequent to the dysbiosis after treatment of oral ailments like periodontitis. Their research draws attention to not only the immense utility of our microbiome, but also the essentiality of shifting to personalized medicine.

Microbiomics can consort personalized medicine to revolutionize patient treatment modalities [34], in an era when non-communicable disease is a burden compared to waning communicable disease [35-38]. Rapid environmental transformations, in conjugation with human interventions, combined with altered lifestyles may have been the agency of a shift in the biodiversity, metabolite production, and pathophysiological responses of the human gut microbiota, as an evolving and adaptation course [39-41]. This not only increases their individual specificity, giving a boost to personalized medical intercessions, but also their variation within a single individual, enabling us to understand microbiota-disease linkages more precisely [32-45]. In an effort to establish how disease can potentially be prevented through precise targeting of microbiome, Santilli., *et al.* [46] have, in their experiments with acarbose, discovered that small doses of the drug can negatively impact the starch utilization system in bacteroides, leaving the rest of the colon-inhabiting beneficial bacteria and other microbiota unaffected.

Sex specificity of human microbiome [47-52] can help us personalize medicine based on sex. Further, the sex specificity of pathophysiology of non-communicable diseases [53,54] which showcases their personalized characters, can help us target them much better with further research on host/microbiome interaction.

The microbiome has been found to have bearing on the psychological and mental aspects of the hosts. The advancements in the knowledge and research on the pathophysiology of cerebral illness coupled with psychoneuroimmunology [55-57] have kicked off an entirely novel discipline, the "psychobiotics" [55,59-61] which is the study of impact of the ingested microbiota on mental health by the way of their interaction with commensal gut bacteria [59]. The study of the effects of gut microbiota on mental health and psychobiotics, has been characterized as the microbiota-gut-brain axis [59,62-64]. With pharmacogenomics increasingly directing towards the incorporation of, apart from the physical, other personal faucets like psychosomatic [65-67] and emotional traits, borrowing eagerly and effectually from the Sansong's oriental systems of medicine [68,69], the in-depth study of microbiota-gut-brain axis shows immense promise in the maturation of personalized medicine [70-72].

The relation between microbiome and lifestyle choices, and thus pharmacogenomics [73], is a suggestive deliberation. Research has revealed that people who binge drink have fewer good bacteria like *Lactobacillus* and more bad bacteria like *Bacteroides, Actinomyces* and *Neisseria* species [74]. Binge drinking has been associated not only with higher risks of gum disease, but also certain cancers of head and neck, which can be attributed to the change in oral microbial flora in drinkers [75-78]. Alcoholism disrupts the gut microbiome activity which can be linked to liver disease [79], affecting the microbiota-gut-liver axis [80]. Thus, cirrhosis in chronic alcoholics can be from direct damage to liver cells, or from distressing of gut microbiota, influencing neutrophils leading to gut inflammation and liver scarring [81-83]. However, it is possible that these disorders may not be linked to alcohol intake but to a disrupted immune system due to a faltered microbiome [84-86]. Apart from genetic predisposition, alteration in gut microbiota and the resultant gut inflammation plays an important role in the development of colorectal cancer [87-96]. This knowledge not only helps in understanding the role of microbiome in liver disease, but also in personalizing medicine.

There are many more illustrations that show how microbiomics can be a panacea for personalized medicine. But there remain impediments in fully utilizing this approach. Shukla., *et al*. [34] and Qin J., *et al.* [10], have independently hinted towards the enormity of the task of completely decoding the role of microbiome in human pathophysiology.

For the attainment of an implementable worldwide personalized medicine regimen, with one of its major basis as microbiomics, age-, sex-, population-, environment- and diet preference-wise determination of microbial ingredients of humans through their orofecal and skin remnants needs to be carried out on a substantial and pertinent scale, and further research to associate metabolites and microbiomic specificities to disease susceptibility and causations, needs to be carried out. There have already been efforts for headways here. For example, it has been revealed how aspirin in-

take can inhibit the activity of the microbiological constituents of the gut that produce metabolite trimethylamine N-oxide (TMAO) by acting on dietary ingredients like phosphatidylcholine, resulting in the control of hyperactivity of platelets and thrombosis, and reduction of cardiovascular risk, which has been associated with TMAO activity [97-100]. ElRakaiby., *et al.* [101] believe that with a more extensive penetration of sequencing of humans from all over the world, along with more intensive and detailed sequencing from the same individuals over longer durations, biomarkers may be developed which can help diagnose microbiome-driven impacts on health and the necessary evolvement of therapeutics. The assessments of the effect of microbiome and metabolome, in concurrence with the genome and proteome of humans, on diseases like diabetes and cardiovascular events, may thus lead to novel medicinal strategies.

Conclusion

With our microbiome, the genome and the environment constantly interact to influence human pathophysiology. With newfangled biomedical research endeavors and their existential triumphant conclusions, as a future perspective, it is thought that the progno-diagnosis of simple and compound diseases will be personalized and so will be the treatment regime. This will be based on the microbiogenomics and other omics that render an individual, distinct from others. With the evolution of molecular diagnostics, there will be development in the field of microbiomics-based personalized and precision therapy. The resultant positivity in the prediction and medication of disease is to be witnessed in the years to come.

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