“OMICS” LANGUAGE METAGENOMICS IS IN WAIT FOR PRECISION MEDICINE AS A NEW CLINICAL FRONTIER: FOCUS ON COLORECTAL CANCER

ABSTRACT

With the completion of the Human Genome Project in 2003 and the rapid development in genomics such as the high-throughput genomics technologies we are now in the ‘postgenomics era’. The concept of precision medicine which is an emerging approach evolved over time and was popularized only recently for to disease prevention and treatment considering the genetic makeup and environment of each individual. In principle, “precision medicine” integrate multiple -omics profiles, such as genomics, pharmacogenomics, proteomics, metabolomics, transcriptomics, epigenomics, metagenomics and “exposome” together with lifestyles factors in an effort to improve the prediction, prevention, diagnosis, and treatment of these disorders to make more tailored diagnostic and therapeutic strategies to a particular patient with different monogenic and multifactorial polygenic complex diseases, such as colorectal cancer. Knowing that a significant percentage of many cancers are induced because of microorganisms, future studies in metagenomics will undoubtedly reinforce to explore the role of human microbiota in cancer development contributing significantly in understanding the disease at molecular level.

KEY WORDS

Precision medicine; -omics, metagenomics; colorectal cancer; microbiota

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COMMENTARY

Ever since the international human genome project was completed in 2003, we have been in the post genomic era, marked by the application of genetic knowledge to daily life and development of this project has set the stage for rapid development of “omics” languages -transcriptomics, proteomics, lipidomics, metabolomics, epigenomics, metagenomics thereafter encouraging hopes for scientists better understand the molecular arguments of different multifactorial complex diseases, such as cancer by increasing the ability to measure and manage huge data sets [1]. In this ‘postgenomic’ era rapid developments and advances in high-throughput genomics technologies lay the groundwork for individualized approach for many common complex conditions, such as targeted therapy, screening, prediction and prevention in order to fulfill the promise of precision medicine underpinning more the stratification of molecular-level information [2]. Colorectal cancer (CRC) is a multifactorial polygenic complex disorder that represents the supremacy of healthcare being third most common form of cancer becoming ever-growing and alarming public health problem particularly in western countries with a large economic burden on the health care systems for society [3, 4]. However, wide geographic variation with lower incidence rates are reported in Africa, Asia and South America [5-10] suggesting that besides genetic factors environmental inputs/ behavioural lifestyle risk factors, such nutrition, obesity, diabetes and physical activity could play crucial walk-on in the aetiology of CRC [11-19]. While 75% - 80% of CRCs are considered to be sporadic, familial CRC accounts for about 20% - 25% of which 5% are associated with well-established inherited syndrome such as hereditary nonpolyposis colorectal cancer (HNPPC or Lynch syndrome) and familial adenomatous polyposis (FAP) presenting important challenges to the clinician [20-24]. Sporadic CCR which is the term given to those patients affected with the disease without any obvious reason and family history, however, it involves interaction between age, environment, lifestyle factors, such diet and genetic factors and it is preventable [25-27]. Genetic event frequently occurring, such as inactivation of tumor suppressor genes p53, DCC, DPC4, APC along with activation of the oncogenes such as KRAS and BRAF have been reported in different studies [24]. Moreover, the role of microRNAs on susceptibility in the transformation from benign to malignant in CRC is also described suggesting that microRNAs may be potential early detection biomarkers and therapeutic targets for CRC. [28-30]. Despite genomic inputs as an accumulation of sporadic gene mutations acquired throughout life are important components for identifying “Achilles heel” for the subject affected by sporadic multifactorial complex CRC, it is only one piece of the puzzle [10, 23]. Thereby, the creation of robust data from genomic risk to the “exposome“ together with medical histories, social factors, and life style factors is crucial in understanding of sporadic CRC for precise treatment as an individual approach. In addition to genomic information better comprehension of the role of gut microbiota together with novel gut microbiota biomarkers could provide encouraging direction in early diagnosis, prognosis, prevention and treatment of CRC [31, 32]. Normal colonocytes faced with unfavourable environment can transform into cancer cells through epigenetic reprogramming affecting gene expression which could accelerate proliferation of cancer cells. Accordingly, nutrition is of utmost importance having an impact on epigenetic changes leading to different phenotypes and alters disease susceptibilities in CRC carcinogenesis [26, 33-35]. Close relationship between obesity and CRC was already demonstrated in many studies [36-38].

Since the advent of metagenomics which is one of the fastest growing scientific disciplines [39-41] the recent research studies that link between metabolic diseases and bacterial populations in the gut may be crucial [42]. The composition of the gut microbiome was originally coined by Joshua Lederberg as “the ecological community of symbiotic, and pathogenic microorganisms sharing our body space and describing the collective genome of our indigenous microbes (microflora), and so it is equivalent to the gut metagenome. [43]. Microbiome could be considered an environmental factor modulating the host metabolism and includes more than 100 trillion cells of 400 species (approximately ten times the total number of cells in the human body) [44] and its modulation, perturbation seems to be important for body metabolic disorders such as obesity, T2D and cancer [37, 45, 46]. The human microbiome encompasses the collection of microorganism, including, eukaryotes, archaea, bacteria and viruses. Moreover, it is also important to note that the human microbiome contains 150 times more genes than the human genome [47]. Therefore, Manipulation of the gut microbiota may be an important therapeutic strategy to regulate energy balance in individuals [32]. There are evidence suggest an inverse relationship between the level of dietary fibres, which is source of Short-Chain Fatty Acid (SCFA), and the incidence of human CRC [48-50]. As the main energy sources for the host SCFAs can be used for de novo synthesis of lipids and glucose [51, 52]. Distinct composition of gut microbiota produce different SCFAs and butyrate is one of the SCFA end product of colonic fermentation known to modulate several cellular processes such as cell differentiation, inhibition of cell proliferation in different tumour cell lines [53-56]. Effect of butyrate on epigenetic gene regulation is also demonstrated leading the conclusion that different composition of gut microbiota in obesity, T2D and cancer could affect the epigenetic regulation of genes, such as genes encoding SCFAs receptors FFAR2 and FFAR3 causing changes in gene expression and signalling of FFARs by histone deacetylases (HDACs) inhibition and hyperacetylation [57-60].
The knowledge of the composition of the gut microbiome ecosystem and gut microbial marker, such as the ratio of SCFA are future important key elements of precision medicine, though much more research is needed to achieve more precise diagnosis, therapeutic intervention and might eventually aid in lifestyle interventions for disease prevention and or modulation [61]. Accordingly, dietary interventions such as high dietary fibre intakes which are the important source of SCFAs influencing microbial composition could be considered as an option in the personal nutritional in order to increase, for example, butyrate concentrations and reduce insulin resistance for the engagement against metabolic syndrome such as diabetes and also it could be important avenue in a drug development (example NaB might be a promising molecule) for the prevention and treatment of CRC [55, 58, 62]. However, since every individual is different, gut microbiota should be evaluated at personalized level in context with lifestyle factors for its putative triggering development of CRC.

CONFLICT OF INTEREST
None.

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REFERENCES


