



Microbial signatures as a predictive tool in health and disease

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Abstract

This article is a comprehensive review of literature on the use of microbial signatures as a predictive tool in various aspects of science and its applications in daily life.

Keywords

Microbial Signatures, Predictive tool

Introduction

Trillions of symbiotic microbes live on and play a vital role in the health spectrum and pathogenesis of disease in the human beings. The microbial communities inside the human hosts are as unique as the lines on fingers of each individual.

These specific microbial signatures, have the propensity to be used in the development of predictive models for various disease's aetiologies and therapeutic approaches. They have the implications in diverse disease by modulation of microbiota including Irritable Bowel Disease (IBD), obesity, diabetes, malnutrition oral-dental infective states, and cancers. They have generated ample curiosity in development of pre-biotic, pro-biotic and targeted antibiotics.¹

We are more microbial than human. Microbes outnumber the human cells in a ratio of 5:1 to 3:1. It has been estimated that there are 37.2 trillion cells in the human body and approximately 100 trillion microbes inhabit the human microbiome.¹

Microbiota refers to Microbes that live in specific location or environment (eg. The human body, gut, skin, soil Microbes). Microbiome is the collective genomes of the complete microbiota present in the human body.



The National Institute of Health (NIH) had initiated a project on 13th June 2012 to understand the pathways of human genome and normal human microbiota; Human Microbiome Project (HMP) portal data provides access to various human microbial data-sets. These data-sets can be used in examining influence of specific microbiomes in a range of clinical conditions like IBD, Periodontitis, diabetes, obesity, cancer as mentioned above.¹

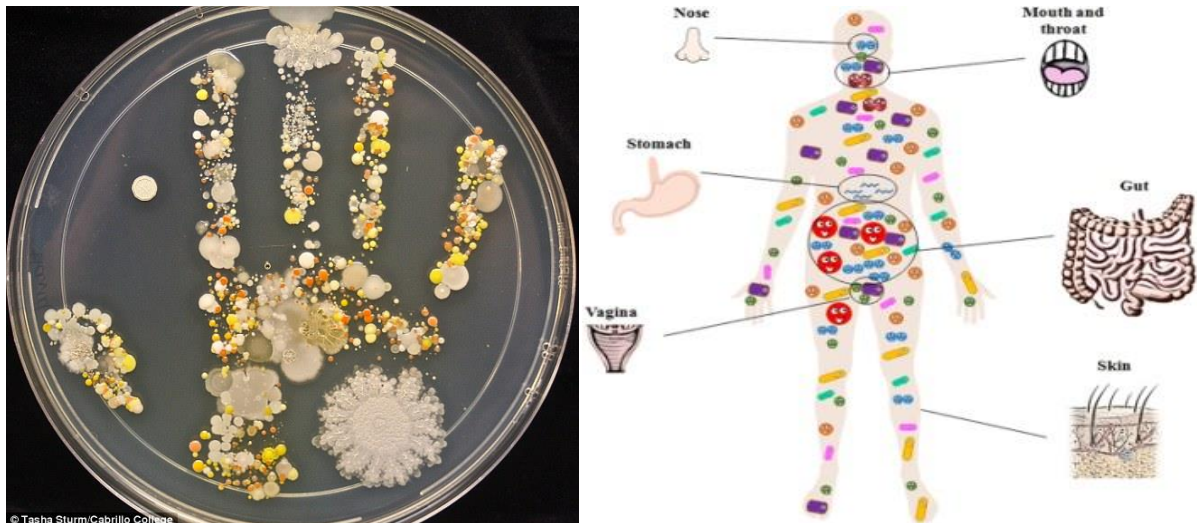


Fig. 1 Uniqueness of human microbial signatures

The amalgamation of Artificial Intelligence (AI) with data-sets has generated abundant interest and has provided an insight into the precision medicine and non-invasive diagnostics using microbiome.²

Metagenomics involves study of the collection of genome-derived from a specific sample or community.

Microbial diversity

These studies have shown that human microbial community is highly variable between different individuals while the individuals have unique microbial fingerprints.

Microbial dispersion can take place from their microbiome to the environment with skin, mucosal membranes, bacteria laden dust particles and bio-aerosol emissions can take place by breath, skin, clothing's and hair. It has been approximated that the humans shed 30 million bacterial cells into their vicinity per hour as "personal cloud" of microbes. It is proposed that the individuals "mark their territory" as done by the tigers & lions in the forest.^{3,4}



The diverse nature of human microbiome was first observed and noted by Antonie van Leeuwenhoek, a Dutch merchant in early 1680s. The Nobel Laureate and Microbiologist Joshua Lederberg is credited with coining the term “microbiome” in 2001.

Many human diseases are caused by single species or strain, such as Tuberculosis by *M. tuberculosis*, tetanus by *Clostridium tetani* & Diphtheria is caused by *Corynebacterium diphtheriae*. In causation of disease, “biomarkers”, a specific taxa associated with most phenotype play a crucial role. A set of bio-makers may include, e.g., phylum Bacteroidetes, Genus *Shigella* and species *Helicobacter pylori* in a hypothetical enteric disease. This set of bio-makers and their association with host phenotype is referred to as microbial Signatures.³

If the house is a microbiome, the persons living in it are the microbiota. It subserves as the microbial organ in the human body. There are interwoven major regions of human body where bacteria, viruses, fungi and protists live in or on. The various microbiota present in body include those present in the oral cavity, eye (ocular), gut, skin & genitalia. Gut microbiome is very enormous and probably better understood. It is postulated that there exists a well-defined bio chemical signalling system that has a profound effect on cognition and behaviour of a person.⁴

Microbiota: The microbial organ

Oral microbiota

Ocular microbiota

Gut microbiota

Skin microbiota

Genital microbiota

Gut – Brain Axis: Biochemical signalling affects Cognition & behaviour.



Major Anatomical Distribution Sites of Microbiota

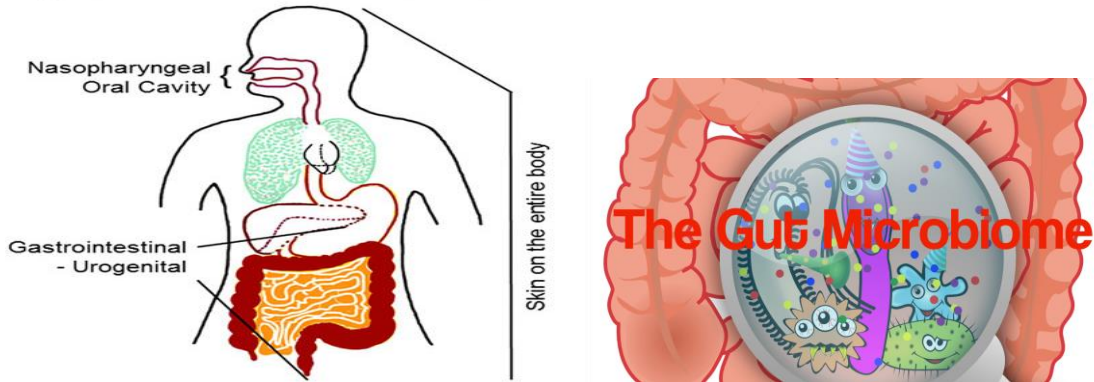


Fig. 2 Interconnected Major regions of the human body where bacteria, viruses, fungi, and protists live in or on.

Bacteriology of Gut Microbiota

The healthy gut microbiota is composed of four predominant phyla, Firmicutes, Bacteriodetes, Proteobacteria and Actinobacteria.

Phylum	Species
Firmicutes	Faecalibacterium Cl. difficile S. aureus Veillonella
Bacteriodetes	B. fragilis
Proteobacteria	Escherichia coli Campylobacter
Actinobacteria	Corynebacterium Propionibacterium Bifidobacterium

Table: 1 Bacteriology of Gut Microbiota



Role of Microbiota:

The role and relevance of microbiota cannot be over-emphasized. Functionally, it is involved in chemical transformation and metabolism of xenobiotics in the pharmaceuticals, food additives, in immune system for its induction of short-chain fatty acids (SCFA), which are closely associated with regulation of gene expression and act as energy source for colonocytes. It is pertinent that as compared to 20,000 or so human genes, the staggering number of microbial genes ranging from 3.5 million to 20 million is sheer perplexing.^{3,4}

Diet and microbiota:

Diet has a vital role in altering or maintaining commensal homeostasis with in GI microbiota food-drug (Tailor made diet plan) is an emergent field of neuro-regenerative nutrition in conditions like autism & schizophrenia. Diet augments the drug responses and tolerances.

Microbial Signatures and Breast cancer:

Diversity of the microbiome is a striking feature of four major types of breast cancer, Endocrine receptor positives (ER), Her-2 positive, Triple positive, Triple negative. Whole genome and transcriptome amplification is being used in their detection.³

Microbiome in precision medicine:

This futuristic modality helps to understand individual response to a therapy especially in reducing non-responder rates and complications, healthy microbiomes provide nutrients, while destructive ones produce toxins and indicate a disease process.

Microbiome and International Space Station (ISS):

It is beyond common domain but provides an interesting terrain to cross-over. Actinobacteria are predominate in the ISS, while Proteobacteria are common at earth-based space stations. Microbes have the propensity to spill-over into space during visits by the astronauts leaving behind their microbial signature for future and intrepid space missions to discover.^{3,4}

Oral Microbiome:

Sporadic reports suggest that chronic periodontitis may be a risk, factor for Alzheimer's Disease (AD), Parkinsonian Disease (PD) & Rheumatoid Arthritis (RA). Increased



translocation of bacteria / toxins from mouth and gut into blood stream appears to be possible mechanism of occurrence (Leaky gut).

Circadian Rhythm, Metabolism & Microbiome:

These are intertwined, where central and hepatic circadian clock and the host metabolic functions are regulated by microbe derived metabolites.

■ Circadian rhythm and diseases

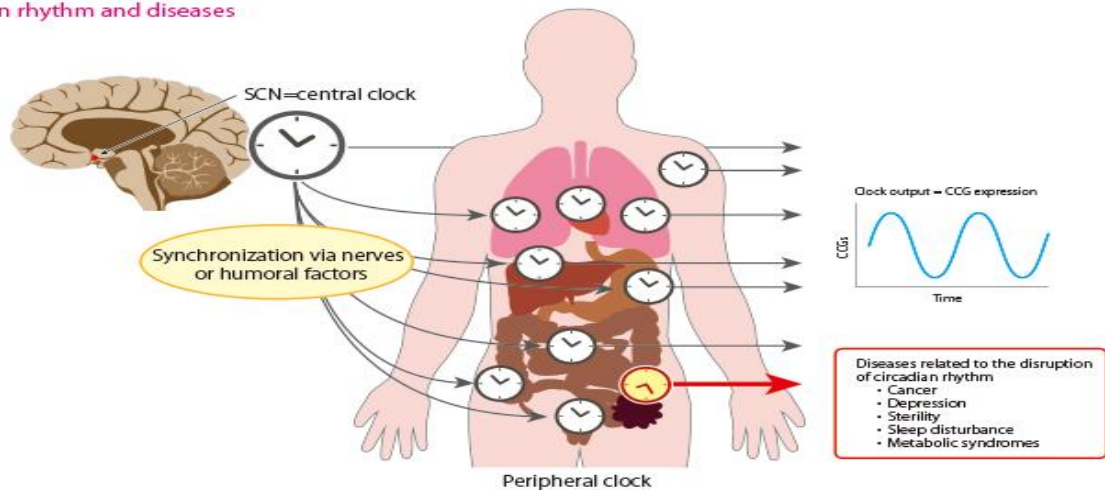


Fig- 3: Circadian Rhythm, Metabolism & Microbiome

Forensics of microbiome profiling:

The scientific community is particularly engaged in harnessing use and application of microbiome profiles in identification of an individual or criminals using their body fluid analysis at the crime scene, that promises to take crime detection to enviable heights.³

Microbiome in GI therapeutics:

Faecal derived and orally administered capsule containing bacterial spore in clostridium difficile and other G1 infections offers a novel approach to microbiota modulations in therapeutics. This is in addition to pre-biotics, pro-biotics already in vogue in various clinical conditions.



Technologies and bio-informatics approaches in detection and microbiome research:

Overcoming the high variability in microbial community is the prime difficulty in detection of microbial signature. Various novel and potent technologies and techniques are being employed for detection of microbiome with high specificity and precision:

Targeted 16 S-RNA gene sequencing

Shotgun meta-genomic sequencing

Pyrosequencing

Pmq-PCR

Micro array

Nanotechnology

All these techniques alone or in combination provide a new dimension and solutions for microbiome-based diagnostics and personalized medicine. 5, 6

New technologies in microbiome

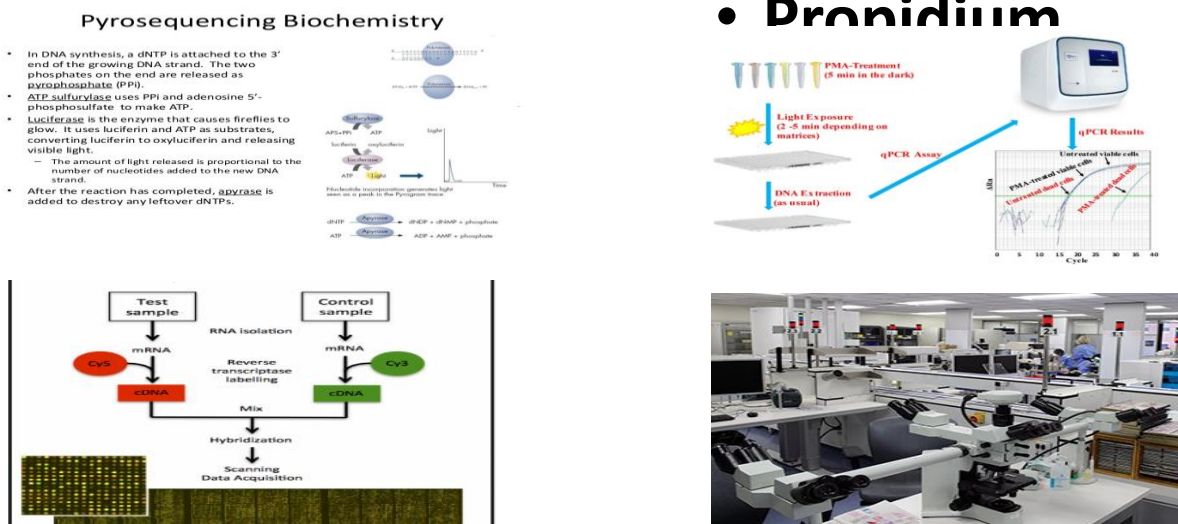


Fig- 4: New technologies in microbiome research



Conclusions:

With the advent of Artificial Intelligence (AI) and optimal use of nanotechnology along with targeted sequencing (16 SRNA gene) and shot gun metagenomic sequencing (whole DNA sequenced) the distant dream of developing a predictive model (glmm Tree) based on generalized mixed model frame work in-phylogeny induced correlation is fast becoming a reality. Microbial signatures are indeed the precision medicine of future!

References:

1. Bang S., Yoo D., Kim S.T. et al. Establishment and evaluation of prediction model for multiple disease classification based on gut microbial data, Sci Rep 9, 10189 (2019)
2. Anna Paola Carrieri, Hiina Haiminen. Explainable AI reveals changes in skin microbiome composition linked to phenotype differences. Scientific Reports, 11, Article number 4565 (2021)
3. Desikan P. Our microbial Signatures. IJMM 35(4): 443, Oct. 2017.
4. Marcus J. Claesson et. al. A clinician's guide to microbiome analysis. Nature Reviews Gastroenterology & Hepatology 14, 585-595 (2017)
5. Celia Fuentes-Chust et.al. The microbiome meets Nanotechnology: Opportunities and challenges in developing new diagnostic devices. Wiley online Library. Vol 33, issue 18 (2021)
6. Gabriele Berg et.al. Microbiome detention revisited: old concepts and new challenges. Microbiome 8, Article 8 (2020)

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