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AYURGENOMICS – THE NEXT GENERATION INTEGRATIVE APPROACH TOWARDS PERSONALIZED MEDICINE

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ABSTRACT
Ayurveda the science of Life, aims at promoting the Health and treating the Diseased. It contains some fundamental principles like Prakruti, Tridosha, Panchamahabhuta, Panchakarma and others. Though these principles are widely used in the clinical practice by an Ayurvedic Physician for treatment, they are not completely explored. The mode of action of Panchakarma (the five bio Purification therapies) are very less understood though they are extensively used in treating almost all diseases. Understanding the Basic principles of Ayurveda through some modern parameters is the need of the hour. Prakruti is the discreet phenotype and they are determined on the basis of physical, psychological, physiological and Behavioural traits, and independent of social, ethnic and geographical variables. Since Prakrutis underlie an individual's predisposition to disease as well as response to treatment, it is imperative in Ayurvedic practice to identify the Prakruti of a patient before treatment. According to Genomics, individual's basic constitution is decided by its genetic makeup which indirectly reflects the levels of various biochemical parameters influencing the health and disease. Genomics has ushered in an era of predictive, preventive and personalized medicine wherein it is hoped that not too far in the future there would be a paradigm shift in the practice of medicine from a generalized symptomatic approach to an individualized approach based on his or her genetic makeup.

KEYWORDS: Ayurveda, Genes, Panchakarma, Prakruti, Gut microbiome.

Ayurveda, the traditional healthcare system of India is based on certain principles like Panchamahabhuta, Tridosha, Prakruti, Panchakarma, Rasayana etc.

The three doshas refer broadly to the functions of motion, digestion and cumulation. Though all three doshas exist in every human being one is dominant based on which an individual's Prakruti is determined. Prakruti is the discreet phenotype and they are determined on the basis of physical, psychological, physiological and Behavioural traits, and independent of social, ethnic and geographical variables.[1] Since Prakrutis underlie an individual's predisposition to disease as well as response to treatment, it is imperative in Ayurvedic practice to identify the Prakruti of a patient before treatment.[2] Though the principles of phenotypes in health and disease state are extremely well described in the Ayurvedic texts, still its potential has not been appreciated by modern researchers as they are not readily decipherable.[3] According to Genomics, individual's basic constitution is decided by its genetic makeup which indirectly reflects the levels of various biochemical parameters influencing the health and disease. Genomics has ushered in an era of predictive, preventive and personalized medicine wherein it is hoped that not too far in the future there would be a paradigm shift in the practice of medicine from a generalized symptomatic approach to an individualized approach based on his or her genetic makeup. Several approaches are being attempted to identify genetic variations that are responsible for susceptibility to diseases and differential response to drugs, however, have met with only a limited success.[4]

Concept of Prakruti in Ayurveda and its relationship with genomics was hypothesized over a decade ago. Subsequent studies have attempted to correlate Prakruti classification with genetic information and association of single nucleotide polymorphisms (SNPs) in HLA-DRB1, CYP2C19, EGLN1, inflammatory and oxidative stress related genes, CD markers for various blood cells, DNA methylation alterations and risk factors of cardiovascular or inflammatory diseases have been reported.[5]

The application of Ayurgenomics can also be extended to understand other philosophies of Ayurveda also, like Panchakarma, Rasayana etc.

Ayurveda emphasizes on prevention and health promotion, and provides treatment for diseases.

Panchakarma (Pancha means five, Karma means therapy) or Shodhana presents a unique approach of Ayurveda with specially designed five procedures of internal purification of the body through the nearest possible route.

According to Ayurvedic theory, physical and mental traits are classified as three Doshas - Vata, Pitta and Kapha. Each individual has all three Doshas with one predominant. If an imbalance occurs in these doshas, diseases/conditions appear. Panchakarma balances the doshas, bringing them back to equilibrium and the individual back to good health.

The five detoxification therapies are
1. Vamana (Emesis or therapeutic vomiting)
2. Virechana (Purgation)
3. Basti (enema with medicated herbal decoctions and medicated oil)
4. Nasya (nasal administration of medicines) and
5. Raktamokshana (Bloodletting)

In all the above-mentioned procedures, detoxification of the body is done by eliminating the vitiated doshas in different routes after the administration of herbal medicines.

Ayurveda claims that, if the diseases do not respond to internal medications or external therapies then Panchakarma or Shodhana is to be administered. Charaka also mentions that the diseases treated with Shodhana will not re-occur. There are specific Panchakarma treatments mentioned for specific disease based on the Prakruti of the patient, age of the person, dosha involved in the disease, chronicity, the ritu (season/environment), and the psychological status of the person.

The benefits attributed to Shodhana includes both physical and psychological.

Example
Sthoulya (obesity) is one among the major diseases that is categorised under *Santarpanottha vyadhis* (diseases due to over nourishment). *Sthoulya* can lead to the development of many other disorders in its course and can lead to morbidity and mortality. The main line of treatment explained for *Sthoulya* is *Apatarpana*, wherein *Ushna*, *Teekshna*, *Kaphahara* and *Medohara dravyas* are administered. In *Sthoulya*, therapeutic procedures form the main line of treatment in parallel with internal medications. Among these Vamana, Virechana and Lekhana basti are some of the prime *Shodhana* therapies explained.

After the administration of Virechana or Basti with herbal medications, elimination of the imbalanced doshas take place and the body restores its normalcy. Now how do we explain the action of these medicines used? What are the doshas that are eliminated from the body? What are the changes that can be seen at different levels (physical/psychological/ biochemical/gut microbiome/ genetic). Answers for such questions are yet to be found by integrating contemporary modern parameters with Ayurveda.

Although the efficacies of Panchakarma treatments are very well established, there are no systematic studies to understand the mechanism of action of Panchakarma therapies using modern parameters. One such attempt would be to understand the changes in the Gut microbiome (by doing 16SrRNA sequencing of the samples) of obese individuals after administration of Panchakarma therapies, which can explain one of the modes of action of these therapies.

Recent studies have revealed that human gut has billions of bacteria that can modulate many diseases including obesity, Irritable Bowel Syndrome, Diabetes, etc. The link between these microbes and our health is the focus of a number of research initiatives worldwide and new insights are emerging rapidly from these studies. Obesity is associated with changes in the composition of the intestinal microbiota and the microbiome among the obese seems to be more efficient in harvesting energy from the diet. The recent advances in Next Generation Sequencing (NGS) and metagenomic approach have greatly facilitated the study of gut microbiota.

There are a very few studies conducted in understanding the Ayurvedic principles using modern parameters. One of the studies by Thatte et al., mention that – the study documents that a therapeutic course of Basti modulates immune responses by regulating pro-inflammatory cytokines, immunoglobulins and functional properties of T-cells. These changes are associated with a reduction in the body weight which is maintained even after three months of treatment. The study also documents the safety of Basti procedure.[6]

There are also studies conducted to understand the association of some genes with particular diseases. The article published in Nature India revealed that the disease profiles were most pronounced in the vata subgroup, tallying with the Ayurveda principle that vata people were susceptible to arthritis. Narrowing down to the vata group led to two new associated genes — CD40 and PON2. CD40 is linked to higher rate of joint destruction, also seen in the vata sub-group. Overall, the study found 12 candidate genes from the three sub-groups.

The scientists also found that genes linked to inflammatory pathways influenced arthritis in the vata group but in another sub-group (pitta), genes involved With oxidative stress showed up. This meant different gene interactions and mechanisms led to the arthritis condition, and in turn needed different treatment approaches, Thelma reported.

The theory of possible presence of novel genes in the Ind ian population got a further boost when a separate group of geneticists reported a novel gene ARL15in a north Ind ian population linked to rheumatoid arthritis.[7]

Such Trans Disciplinary researches can throw further light in understanding the Philosophies/principles of Ayurveda and the vision of personalized medicine can be achieved.

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