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ROLE OF AYURGENOMICS IN PERSONALIZED MEDICINE

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ABSTRACT

Ayurveda is an ancient Indian system of medicine that uses a systems approach to understand and control health and disease. It has some interesting connections with modern personalised genomic medicine approaches to health and disease management. It is founded on the *trisutra*, which consists of three parts of causes, characteristics, and therapies that are linked by a single organising principle known as *tridosha. Tridosha* is made up of three physiological entities: vata (kinetic), pitta (metabolic), and kapha (potential) that are found throughout the body, function together, respond to the environment, and maintain equilibrium. Each person is born with a unique proportion of *tridosha* that is determined not just by genetics but also by the environment during foetal development. To forecast the phenotypic repercussions of aberrations, modern medicine focuses on genetic, cellular, physiological, and environmental networks. Ayurgenomics is an integrated method that combines *Ayurvedic Prakriti* notions with contemporary genetics research. It links the three doshas of *vata*, *pitta*, and *kapha* to the expression of genetic and physiological individuality. Ayurvedic medicine views each person as unique, and sickness as the result of a complex interaction of internal and external causes. The Ayurgenomics study thus presents a fresh molecular framework for merging genomics investigations with *Ayurvedic* concepts of inter-

individual variability, thereby speeding up the finding of markers for predictive, preventative, and personalised therapy. Using the capabilities of genomics and molecular phenotyping, the Ayurgenomics technique enables for systematic research of *Trisutra Ayurveda*. Ayurgenomics may open the way to achieving preventive and personalised medicine aims more quickly.

KEYWORDS: Ayurgenomics is an integrated method that combines *Ayurvedic Prakriti* notions with contemporary genetics research.

INTRODUCTION

WHAT IS GENETICS AND GENOMICS

Genetics is the science of inheritance, the genes underlying it and their functions. Genetics as a science has existed for the last century, long before the structure of DNA was understood and before molecular access to the genome was available. Genetics involved the study of single genes and their variations as a cause of inherited single-gene (Mendelian) disorders, such as Fragile X syndrome, cystic fibrosis and Huntington's disease. While each of these disorders alone is relatively rare in the population based on the EU definition of rare diseases, it has been estimated that, taken together, approximately 6–8% of the European population will be affected by a rare disorder at some point in their life (European Commission, 2008).

Most common chronic NCDs are multifactorial, caused by numerous variants in the genome that interact with each other and with a range of environmental factors. Moreover, there is a significant genetic component for predisposition to many, if not most, infectious diseases as well. To gain more knowledge about these diseases, researchers work with genomic methods. Genomics involves genome-wide studies, in other words analysing the entire genome and how these genes interact with each other and with environmental factors. Hence, genomic methods allow researchers to explore the causes of common diseases with complex etiology, such as cancer, diabetes or heart disease, which have multifactorial determinants including genes, lifestyle behaviours and other environmental influences.[1]

CONCEPT OF AYURGENOMICS

***A**yurgenomic* is a term that combine *Ayurveda* and Genomics, it refers to an emerging field that integrates *Ayurveda* principal of health and disease with modern genomic science.

The Human Genome Project, which began in 1984, aimed to determine the DNA sequence of the entire human genome. This was a large international collaborative effort that gained momentum in the 1990s and was completed in 2022. The sequencing of the human genome has provided insights into human diseases, allowing researchers to narrow down their search to specific genes and examine their functions interactions, and associations with diseases. This deeper understanding of disease processes at the molecular level has the potential to lead to new therapeutic procedures. Overall, the Human Genome Project has been a significant advancement in molecular biology and has the potential to facilitate medical advances in many areas of clinical interest.[2] Ayurgenomics was established only to understand the principles of Ayurveda using the most recent contemporary methods, paving the door for evidence-based Ayurveda and therefore a greater worldwide recognition. Ayurgenomics creates a new-fangled link between modern and traditional medicine by offering a scientific grasp of fundamental ideas while also infusing Ayurveda's practical prophylactic techniques into modern care. This revolutionary system intends to change the focus from a disease-focused system to a patient-focused wellness system. It is strongly connected to other emerging areas such as personalized, integrative, preventive, lifestyle, and functional medicine. Even before epigenetics and other studies like nutrigenetics, *Ayurveda* understood how nutrition and other lifestyle variables might influence human health. They documented that contemporary medicine is only now a foundation to recognize anticipation is vital for good health. An efficient preventative medical system requires proper exercise, sleep, food, and stress management. Additionally, ayurveda also explains the dose and duration of the drug, which is determined by the patient's *bala, satva, agni, roga bala*, and so on. Ayurgenomics helps to increase the legitimacy of *Ayurveda* and other traditional medicinal systems by expressing their old concepts in terms of current science. Emerging ayurgenomics techniques that employ powerful data analytics and machine learning might greatly simplify the procedure. *Ayurgenomics* medicinal efficacy will have to be tested in strictly managed clinical studies. *Ayurveda* and genetics have a lot to learn from one another. Contemporary science, being an evidence-based medical system, may help *Ayurveda*, and *Ayurveda* must uplift modern medicine, predominantly through its pre-emptive measures.

WHAT IS PRAKRUTI AND ITS IMPORTANCE

PRAKRUTI

In *Brahma Vaivarta Purana, Prakruti* is defined according to the word derivation that is it formed by three letters *Pra*, *Kru* and *Ti*. The letter *Pra* symbolizes *Prakrashta Guna*, the

superior quality- *Sattva, Kru* for moderate *Guna*, the *Rajas* and *Ti* for *Tamas*. *Prakruti* can be understood as *Swabhava* which means one's '*Pratyatmaniyatroop'* i.e an expression of various body functions in the form of morphology, physiology and behavior of an individual. According to Aacharya Sushruta, Prakruti is decided in the very initial stage i.e. during the union of *Shukra* and *Shonit* (sperm and ovum) itself, the dominant *Dosha* form the *Prakruti* of the individual.[3]

TYPES OF PRAKRUTI

In *Ayurvediya* texts *Prakruti* is classified as.

1. *Doshaja /Deha Prakruti*
2. *Manasa Prakruti*

Doshaja or *Deha Prakruti*

Doshaja Prakruti is also known *Sharirika Prakruti/Deha Prakruti*. *Deha Prakruti* is classified on basis of dominance of *Dosha*. There are seven types of *Doshaja Prakruti* according to the predominance of *Dosha*. *Vata, Pitta* and *Shleshma* are *Ekadoshaja* i.e. due to the predominance of one *Dosha*. *Vata-Pittaja, Vata-Shleshmaja,* and *Pitta-Shleshmaja* are *Dwandja* (mixed) i.e. due to the predominance of two *Dosha*. *Sama-Prakruti* occurs due to the predominance of all three *Dosha*. According to *Aacharya Vagbhatta,* individuals of *Sama Prakruti* are *Shreshtha* (excellent) while *Dwandja Prakruti* are *Nindya* (condemned).[4] The person of *Vata, Pitta* and *Kapha* predominance are said *Sadaatur* (always sick).[5]

Manasa Prakruti

On the basis of *Manas Guna (Satva, Raja, and Tama*), there are three types of *Manasa Prakruti*.

1. Satvik.
2. Rajas.
3. *Tamas*.

These three types of *Manas Prakruti* are subdivided into sixteen/eighteen types.[6]

***Satvik Manas Prakruti*:** *Brahma, Mahendra, Varun, Kaubera, Gandharva, Yamya* and *Rishi Satva.*

***Rajasa Manasa Prakruti*:** *Asura, Rakshasa, Paishacha, Preta, Sarpa and Shakuna*.

Tamasa Manasa Prakruti

Pashava, Matsya and Vanaspatya Acharya Kashyap also described *Prajapatya Kaya* under *Satvik* and *Yaksha* under *Rajasa Prakruti*.

Ayurveda's central idea is the Tridosha, a framework for understanding health and illness. In Ayurveda, all of an individual's physical, functional, and behavioural characteristics are part of their individual psychosomatic temperament, or Prakriti. Ayurveda holds that the body, or Purusha, is composed of several elements, such as Dosha, Dhatu, Indriya, Manas, Buddhi, and Atma.[7] Like genetic code, each individual is a unique blend that makes them a unique entity. Consequently, Prakriti (Tridoshas) is determined by a unique combination of these three Doshas. In Ayurveda, Prakriti is said to have been generated at the beginning of human existence and usually does not alter throughout time.

A combination of inherited and acquired elements affect human Prakriti. While Shukra (sperm) and Shonita (ovum) determine the genetic constitution, environmental factors such as age, race, heredity, climate, season, and place determine the acquired constitution.

Table 1: Distinguishing features of three contrasting *Prakriti* types *Vata, Pitta & Kapha* and their disease predisposition as described in the original text.

S. no	Features	*Vata*	*PITTA*	*KAPHA*
1.	Body frame	Thin	Medium	Broad
2	Build & mus-culature	Weakly developed	Moderate	Well developed
3	Skin	Dry & cracked	Soft, thin, tendency for moles, acne & freckles	Smooth, firm clear complexion
4	Hair	Dry, thin, prone to brakes	Thin, oily, early greying	Thick, smooth & firm
5	Weight gain	Recalcitrant	Fluctuating	Tendency to obese
6	Food & bowel habits	Frequent, variable & irregular	Higher capacity for food & water con-sumption	Low digestive capaci-ty & stable food hab-its
7	Movements & physical activities	Excessive & brisk	Moderate	Less mobile
8	Tolerance for seasonal weather	Cold intolerant	Heat intoleran	Endurance for both
9	Disease re-sistance & healing capaci-ty	poor	Good	Excellent
10	Metabolism of toxic substances	Moderate	Quick	Poor

When the relative proportion of *tridosha* in *prakriti* get imbalanced, then abnormalities occur.[7]

Commonly occurring abnormalities due to.

Vitiated V*ata*: dystrophy of nails, derma- tophytosis, sciatica, cramps in the calf muscle, spasticity of thighs, prolapse of rectum, retraction of eyelids, faintness,giddiness, hiccup, asthenia etc.

Vitiated P*itta:* heating, scorching, burn- ing, broiling, local- feto(*charamdalan*), sarcothermia(*angavdaran*), bitter taste, faintness etc.

Vitiated K*apha:* anorexia nervosa, stiffness, loss of strength, increased secretion in throat, erysipelas, lethargy, goitre, obesity, heavy pulse etc**.**[8]

GENOMIC TRAITS ASSOCIATED WITH EACH DOSH

Vata Prakriti*:* Linked to genes regulating nervous system activity, lean body types.

Pitta Prakriti: Association with genes involved in metabolism, heat regulation.

Kapha Prakriti: Tendency toward genes influencing fat storage and immunity.

CONCEPT OF PERSONALIZED MEDICINE

"Every individual is different from another and hence should be considered as a different entity. As many variations are there in the universe, all are seen in human beings".

Charaka Samhita

In Sutra Stana first chapter, Acharya mentions that an exquisite physician should have the knowledge of nomenclature of medicine and its identification along with the ability to treat the disease according to place, time and individual variation. Only then he is regarded as Uttama Bhisha.[9]

In the context of internal administration of Sneha, the dose of Snehapana are three types- Pradhana, Madhyama and Avara; but again, it is specified further that dosage and type of Sneha should be selected according to individual needs.[10] Even after successful administration of Snehana and Swedana, every individual should be assessed properly before the administration of Vamana.

The dose of Vamana Dravya and all the other drugs used for purification therapy is determined according to the individual capability.[11]

All the drugs mentioned in *Samshodha Samshamaniya Adhyaya* should be administered after considering the *Vyadhi*, *Agni* and *Bala*, which varies in every individual.[12]

Ayurveda is a natural health care system that originated in India more than 5000 years ago. It emphasizes the treatment of disease in highly individualized manner as it believes that every individual is unique having different constitution. *Ayurveda* classifies all individuals into different '*Prakriti'* types based on the theory of *tridosha* and each type has varying degree of predisposition to different diseases. This is independent of racial, ethnic, or geographical considerations and may provide appropriate means of classifying phenotypes to be considered collectively for genotyping. Similarly, it classifies the drugs according to the *rasapanchaka* (ayurvedic pharmacology), which states that the drug action is ascribed to certain attributes present in the drug namely *Rasa* (taste), *Guna* (property), *Virya* (potency), *Vipaka* (postdigestive tatse), and Prabhava (effect), while in modern pharmacology the drug action is attributed to the chemical structure of a molecule.[13] The *rasapanchak* modality is able to deliver treatment as it takes into consideration the prakriti of the person as well as the pharmacodynamics and pharmacokinetic properties of a drug unlike a modern treatment that elicits varied response from person to person having same drug for the same disease.

If personalized medicine is to be realized a systematic classification of human population is necessary but modern medicine classifies human population based on ethnicity. Geographic patterns of genetic variation shows that inter-individual variation in drug response is common.[14]

This gap could be effectively filled by Ayurveda and its vision as ayurveda classification is independent of racial, ethnic, or geographical considerations and may provide appropriate means of classifying phenotypes to be considered collectively for genotyping. What is required is a connection of phenotypic features (prakriti) with genotype as personalized medicine aims to design drugs with maximum efficiency and safety for a particular disorder. Ayurvedic system of medicine and other traditional systems of medicine have a personalized approach in treating a patient with centuries of practice, rightly called experiential science.[15] For centuries, Ayurveda has been a source of natural or plant-based medicine in many drug development efforts, although with the hunt for novel chemical entities (Patwardhan and Mashelkar, 2009). Many scientific articles demonstrate the efficacy and promise of Ayurvedic medicines. For example, during the current Covid-19 pandemic, an in-silico evaluation on AYUSH-64 (an Ayurvedic formulation produced and patented by India's

Central Council of Research in Ayurvedic Sciences that has been in clinical use for several decades as an anti-malarial, anti-inflammatory, and anti-pyretic medication) showed that the medicine was a promising candidate for repurposing to COVID-19 treatment (Ram et al., 2022). Additionally, some inimitable insights have been found following systematic investigation of the biological effects of herbs. For example, one of the most notable ayurvedic medicament "reserpine" (active constituent of the herb *"Sarpagandha"* allowed the dissection of the complete dopaminergic pathways and the fusion of psychopharmacology and neurochemistry (Sanjeev Jain, 2009). Ayurveda, in addition to its curative capabilities, provides a predictive, preventative, and personalized strategy to health and illness management that has been thoroughly described in classic literature such as the Charaka and Sushruta Samhita (Patwardhan et al., 2014; Banerjee et al., 2015). This concept paves the way for ayuregenomics drug development.

Conclusion and Future Perspectives

Over 65% of Indians follow "*Ayurveda*," an indigenous Indian system of medicine that is growing generally recognized as an alternative medicine across the globe. Ayurveda follows a personalized strategy for prognostic and preventive elements of medicine. It relates to the inter-individual heterogeneity in vulnerability assessment, and judgment, commonly based on the individual's *Prakriti* types. Modern medicine employs terminologies like gene expression, genome, epigenetics, etc. to define the foundation of our physiology and health in a profoundly reductionist framework. While Ayurveda uses a unique holistic approach that encompasses concepts such as *Prakriti* and *doshas*. Because of a mental bias contrary to folk or traditional medicine, modern medicine has failed to acknowledge many of *Ayurveda*'s effective preventative techniques. Even though traditional medical systems are in still exist and widely practiced in many nations and around the globe, further research into their preventative and rehabilitative treatment programs is required. To date, the focus of the study has been on certain herbal formulations, to isolate a single drug moiety that must subsequently be employed by the pharma industry.

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