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AYURGENOMICS: BRIDGING AYURVEDIC CONSTITUTIONAL BIOLOGY WITH MULTI-OMICS AND PRECISION MEDICINE—A NARRATIVE REVIEW

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ABSTRACT **Background** Ayurgenomics is an emerging interdisciplinary field that integrates the traditional Ayurvedic concept of Prakriti with modern omics science, including genomics, transcriptomics, proteomics, and metabolomics. Based on the balance of the three doshas —Vata, Pitta, and Kapha—Prakriti explains individual variations in physiology, disease susceptibility, and therapeutic response, providing a culturally rooted framework for personalized healthcare.**Methods:** A comprehensive review of the published literature from 2002 to 2025 was conducted, with particular emphasis on landmark studies from the CSIR–Institute of Genomics and Integrative Biology (CSIR-IGIB) and other international research groups. The reviewed studies investigated the associations between Prakriti and genomic variation, gene expression, epigenetic regulation, pharmacogenomics, and disease susceptibility.**Results:** Multiple studies have demonstrated that distinct Prakriti types exhibit characteristic patterns of gene expression, protein profiles, genetic polymorphisms, and drug metabolism. Significant differences were observed in the immune function and high-altitude adaptation. Kapha individuals showed enhanced natural killer cell activity, Pitta individuals exhibited increased oxidative stress markers, and Vata individuals demonstrated heightened inflammatory responses in this study.Epigenetic studies have identified Prakriti-specific DNA methylation patterns, including CDH22 methylation, associated with increased body mass index in Kapha individuals. The TRISUTRA project translated these findings into population-based healthcare by studying more than 7,500 individuals representing diverse Indian ethnic groups. Applications include Prakriti-guided pharmacogenomics involving CYP450 enzymes, validation of Ayurvedic formulations such as AYUSH-64, Adhatoda vasica, and Cissampelos pareira, and prediction of disease susceptibility for conditions such as diabetes mellitus, hyperlipidemia, rheumatoid arthritis, and obesity.**Conclusion:** Ayurgenomics is a scientifically supported, cost-effective, and culturally relevant approach to personalized medicine that aligns closely with the principles of P5 medicine. Broader clinical implementation will require standardized Prakriti assessment tools, large-scale multi-ethnic validation studies, and the ethical protection of traditional knowledge systems.

KEYWORDS : Ayurgenomics; Prakriti; Tridosha; Personalized Medicine; Pharmacogenomics; CYP2C19; EGLN1; HLA-DRB1; Multi-omics; TRISUTRA; Precision Medicine; Integrative Medicine; Epigenetics.

INTRODUCTION

The main idea of precision medicine is to provide the right treatment to the right patient at the right time. This approach depends on understanding and utilizing the biological differences among individuals. Although advances such as genome-wide association studies (GWAS), polygenic risk scores, and pharmacogenomics have significantly improved our understanding of inherited disease susceptibility and individual variations in drug response, their translation into routine clinical practice remains limited. High implementation costs, the requirement for specialized infrastructure, and incomplete understanding of gene–environment interactions continue to hinder their widespread application.

Ayurveda, one of the world's oldest systems of medicine, originated in the Indian subcontinent over 3,000 years ago and addressed the challenge of individual variability long before the advent of modern genomics. It introduces the concept of *Prakriti,* which describes an individual's unique physical, physiological, and psychological constitution established at birth by the relative balance of the three fundamental *Doshas—Vata, Pitta,* and Kapha. Prakriti influences disease susceptibility, therapeutic response, dietary requirements, metabolic characteristics, and overall physiological function throughout life. Importantly, it represents a comprehensive constitutional framework that parallels the individual biological variations investigated by contemporary genomic science[1].

Ayurgenomics is an emerging interdisciplinary field that integrates Ayurvedic constitutional principles with contemporary genomics. The concept was pioneered in 2002 by researchers at the CSIR–Institute of Genomics and Integrative Biology (CSIR-IGIB), New Delhi, under the leadership of Prof. Samir K. Brahmachari. Over the past two decades, extensive scientific investigations have demonstrated significant associations between Prakriti types and distinct genomic characteristics, including differential gene expression profiles, human leukocyte antigen (HLA) polymorphisms, single nucleotide polymorphism (SNP) signatures, epigenetic modifications, and pharmacogenomic variations. These findings provide strong biological evidence supporting the ancient Ayurvedic system of constitutional phenotyping.

This review summarizes the current scientific evidence supporting Ayurgenomics, including its conceptual foundations, genomic and clinical applications, pharmacogenomic relevance, and future potential. Furthermore, it examines how Ayurgenomics can contribute to the global P5 Medicine framework—Predictive, Preventive, Personalized, Participatory, and Precision medicine—thereby bridging traditional medical knowledge with contemporary precision healthcare[2].

Methodology:

This narrative review summarizes published literature on Ayurgenomics from 2002 to 2025. Literature was identified from databases including PubMed, Scopus, Web of Science, and Google Scholar using keywords such as 'Ayurgenomics',

'Prakriti', 'precision medicine', 'pharmacogenomics', 'epigenetics', and 'multi-omics'. Priority was given to peer-reviewed studies, landmark publications, and clinically relevant investigations."

Conceptual Foundations: *Prakriti* and *Tridosha* Framework. The Three *Doshas* as Organising Principles

In Ayurvedic science, the three doshas act as the basic organizing forces behind all bodily functions. *Vata* is responsible for movement, including nerve signaling, creativity, waste removal, and muscle and bone function. *Pitta* controls transformation processes, including digestion, metabolism, body heat production, mental clarity, and immune response. Kapha provides stability and supports the body's structure, growth, bodily fluids, immune strength, and tissue building. Each *Dosha* corresponds to specific bodily functions that can be linked to particular genetic pathways at the molecular level. Everyone is born with a unique and fairly consistent balance of doshas, known as *Prakriti*[3].

While some people have a dominant single *Dosha* (*Eka* type), most people have a combination of two *(Dwandwa*) or all three (*Sama)Doshas*. *Prakriti* influences a person's physical traits, body processes, mental tendencies, and likelihood of developing certain diseases throughout life. This creates a comprehensive, all-encompassing, and noninvasive method for understanding a person's constitution.

Prakriti vs. Contemporary Phenotyping:

Modern genomics categorizes people based on biochemical markers, imaging, and genetic data—methods that are often costly, require specialized equipment, and are not always widely available.

Assessing *Prakriti,* on the other hand, is forward-looking, observational, non-invasive, and highly affordable[4]. Most importantly, it considers factors such as the environment (*Deshanupatini*), family background *(Kulanupatini*), and ethnic heritage (*Jatiprasakta)*, which are the same variables studied in population studies, as well as how genes interact with the environment. This connection shows that *Prakriti* is a meaningful and scientifically useful framework for understanding a person's constitution[5].

Table1 .Functional Attributes and Multi-Omics Profiles of the Three *Prakriti* Types[6]

Physical Build	**Lean, dry skin, variable appetite**	**Medium build, warm body, sharp appetite**	**Robust build, steady energy, slow digestion**
BMI	Lowest	Medium	Highest
Metabolism	Variable	Fast	Slow
Dosha Function	Neural signals, body movement, creativity, waste removal	Digestion, metabolism, clarity, vision	Stability, growth, lubrication, calmness
Genomic Pathway	Cell cycle, transport & signalling genes	Enzymatic, oxidative stress & metabolic genes	Lipid metabolism & synthetic pathway genes
Immune Profile	Stress pathway genes ↑; innate immune over-reactivity	Oxidative stress genes ↑; high metabolic & ROS activity	NK-cell & antiviral pathways ↑; strong innate + adaptive immunity
Blood Coagulation	Faster	Normal	Slower (fibrinolysis ↓)
Cholesterol	Low	Moderate	LDL ↑, HDL ↓
Haemoglobin	Medium	Higher	Lower
CYP2C19 Expression	Variable (Intermediate metaboliser)	High ↑ (Fast metaboliser)	Low ↓ (Slow metaboliser)
Disease Risk	Anxiety, neurodegeneration, pain, osteoporosis, dryness	Inflammation, acidity, ulcers, skin disorders, autoimmune	Obesity, diabetes, CVD, congestion, lethargy

Scientific Evidence: Genomic Correlates of Prakriti

Research Evolution at CSIR-IGIB (2002–2025)

The scientific development of Ayurgenomics is closely tied to the research program at CSIR-IGIB[7].

Table 2. Research Evolution of Ayurgenomics (2002–2025): Key Milestones

2002	**Inception**	**The CSIR-IGIB initiative was launched and began multi-omics research on Ayurvedic Prakriti phenotypes.**
2005	Immunogenetics	A correlation between HLA-DRB1 alleles and prakriti types was established (Bhushan et al., 2005). HLA-DRB1*02 absent in Vata; HLA-DRB1*13 absent in Kapha; HLA-DRB1*10 higher in Kapha.
2008	Transcriptomics	Identification of genome-wide expression differences across Prakriti groups. Prasher et al. provided the first molecular evidence of distinct biochemical and transcriptomic profiles. (J Transl Med, 2008)
2011	Adaptation Biology	Discovered EGLN1 oxygen-sensor gene variants linked to high-altitude adaptation across Prakriti types; validated across 24 Indian populations (Aggarwal et al., PNAS, 2010).
2015	Epigenetics & SNPs	We created a 52-SNP panel (Govindaraj et al., 2015) revealing distinct SNP distributions and DNA methylation signatures. CDH22 methylation is linked to Kapha-associated BMI.
2016	Pharmacogenomics	Mapped CYP2C19 drug metabolism variability to Ayurvedic constitution types (Ghodke et al., 2011). Pitta = fast metabolizer; Kapha = slow metabolizer with ADR risk.
2020 +	Implementation	Clinical translation initiated: AYUSH deployment, Trisutra-based personalized systems integration, public health applications; >7,500 individuals enrolled in the TRISUTRA consortium.

Transcriptomic Evidence

The first molecular evidence supporting Ayurgenomics was published by Prasher et al.(2008) in the Journal of Translational Medicine. This important study used whole-genome expression profiling to show that healthy individuals categorized as *Vata*, *Pitta*, or *Kapha* have significant differences in biochemical parameters and gene expression across genomes. Key findings included increased activity of immune and inflammatory genes in *Pitta*, lipid synthesis genes in *Kapha,* and cell cycle and transport genes in Vata. This study showed that *Prakriti*-based classification identifies meaningful and distinct molecular subgroups in healthy populations. Further transcriptomic studies have clarified the immune system differences associated with each *Prakriti* type[8].

Pitta individuals had higher levels of oxidative stress-related genes and reactive oxygen species, matching the Ayurvedic description of *Pitta* as heat- and metabolism-dominant. *Kapha* individuals showed increased activity in antiviral and natural killer cell pathways, resulting in better immune

resilience. Vata individuals have higher expression of inflammatory cytokine pathways and overactive innate immunity, explaining their increased risk of autoimmune and neuroinflammatory conditions[9].

HLA Allele Distributions and 52-SNP Classification

Genetic studies have shown that HLA-DRB1 allele distributions vary significantly among *Prakriti* types. For instance, HLA-DRB1*02 is absent in *Vata* individuals but is present in *Pitta* and *Kapha individuals*. HLA-DRB1*13 was absent in *Kapha*, whereas HLA-DRB1*10 was more common in Kapha. These patterns serve as genetic markers for *Dosha* classification and have implications for modeling immune disease susceptibility[10].

A major genome-wide SNP study by Govindaraj et al.(2015) used the Affymetrix 6.0 platform on 262 carefully classified individuals (selected from 3,416 screened people) and found 52 SNPs that were significantly different across *Prakriti* types ($p \leq 1 \times 10^{-5}$). Principal component analysis (PCA) of these 52 SNPs correctly classified all 262 individuals into their respective *prakriti* groups, regardless of their ancestral background. This was validated in 297 Indian population samples. This study provides strong evidence that *Prakriti* represents heritable biological differences[11].

Table 3. *Prakriti*–Genotype Correlations: HLA Alleles, 52-SNP Panel, EGLN1, and CYP2C19

HLA-DRB1*02	Absent	Present	Present — serves as a distinguishing marker; absent in Vata
HLA-DRB1*13	Present	Present	Absent — absent in Kapha
HLA-DRB1*10	Present	Present	Higher frequency in Kapha — significantly more common
52-SNP Classification	Classifiable	Classifiable	Classifiable — PCA-validated molecular tool for Prakriti typing (Govindaraj et al., 2015)
EGLN1 rs479200 (TT)	Moderate frequency	Lowest / near-absent	Highest in Kapha — protective variant for high-altitude adaptation
CYP2C19 Expression	Moderate (Variable)	High ↑ (Fast metaboliser)	Low ↓ (Slow metaboliser) — ADR risk; drugs persist longer

EGLN1 and High-Altitude Adaptation

One of the most clinically relevant findings in Ayurgenomics is the link between the EGLN1 oxygen-sensing gene and Prakriti-specific adaptation to high altitudes.

The protective EGLN1 variant rs479200 (TT) was most common in Kapha individuals, moderate in *Vata*, and nearly absent in *Pitta*. *Individuals of the Pitta genus*, lacking this variant, show poor hypoxic adaptation and a higher risk of altitude sickness. This finding was confirmed across 24 Indian populations at different altitudes and supported by mouse models of hypoxic response and asthma severity (Aggarwal et al., *PNAS*, 2010)[12].This example highlights Ayurgenomics' ability to generate genetic insights from constitutional traits.

Epigenetic Correlates

New epigenomic evidence further supports the connection between *Prakriti* and biological traits. Each *Prakriti* type exhibits unique DNA methylation patterns. Notably, the CDH22 gene has distinct methylation in *Kapha* individuals, linked to higher BMI and fat cell development, in line with *Kapha's* tendency towards metabolic buildup. In patients with asthma treated with Ayurvedic therapies, genome-wide methylation analysis found changes in 4,820 gene sites. After treatment, the gene expression patterns approached those of healthy controls, showing that Ayurvedic approaches can meaningfully alter the epigenome. The three-*Dosha* system also aligns with distinct epigenetic regulatory mechanisms: *Pitta*-related interventions activate and balance metabolic and hormonal genes, *Vata*-related approaches quickly reduce inflammation, and *Kapha*-related strategies regulate lipid metabolism[13].

Table 4. Genomic Pathway and Cellular Profiles by Prakriti Type

Vata	Inflammatory cytokine pathways ↑	Innate immune over-reactivity	Reactive, sensitive immunity; prone to autoimmune inflammation
Pitta	Oxidative stress genes ↑	High metabolic & ROS activity	Heat/metabolism-driven inflammation; stress-responsive constitution
Kapha	Antiviral & NK-cell pathways ↑	Strong innate + adaptive immunity	Immunologically resilient, disease-resistant constitution

Pharmacogenomics: *Prakriti*-Guided Drug Response

One of the most applicable areas of Ayurgenomics is pharmacogenomics, which explores how genetic differences affect the response to drugs. The CYP2C19 enzyme, part of the cytochrome P450 family responsible for metabolizing many important drugs (such as antidepressants, antiplatelets, and proton-pump inhibitors), shows strong correlations with *Prakriti*.

Individuals with the Pitta type have approximately twice the baseline CYP2C19 activity, which means that drugs are broken down quickly, potentially reducing their effectiveness and requiring higher doses. *Kapha* individuals show significantly reduced CYP2C19 activity, which prolongs the drug action and increases the risk of side effects and toxicity. Vata individuals have intermediate and variable metabolism, requiring personalized monitoring.

This framework extends beyond CYP2C19. Genomic validation has enabled precision dosing based on *Prakriti*, with applications in antimicrobial therapy, pain management, psychiatric medications, and nutraceuticals. Three Ayurvedic formulations have been scientifically validated: AYUSH-64 (anti-malarial and anti-inflammatory; repurposed for treating COVID-19, Ram et al.2022); Adhatoda vasica (treats asthma and viral infections by modulating cellular hypoxia, Gheware et al.2021); and Cissampelos pareira (helps with antiviral effects and estrogen receptor modulation, Haider et al.2021).

Table 5. Pharmacogenomics by Prakriti: CYP2C19 Activity and Validated Formulations—Ghodke *et al. (2011); Ram et al. (2022); Gheware et al. (2021); Haider et al. (2021).*

CYP2C19 Activity	Intermediate	Upregulated (2× higher)	Downregulated (slower metabolism)
Metaboliser Phenotype	Variable	Rapid / Ultra-rapid	Poor / Slow
Drug Risk Profile	Unpredictable; requires monitoring	Reduced efficacy without dose adjustment	Drug accumulation; Adverse Drug Reactions (ADR), toxicity
Validated Herbal Formulation	—	Adhatoda vasica (asthma/viral inhibition)	AYUSH-64 (anti-malarial/anti-inflammatory; COVID-19)

Additional Validated Agent	—	Cissampelos pareira (antiviral, estrogen receptor modulation)	Prakriti-guided dosing reduces ADR and enhances efficacy

Clinical Case Studies and Disease–*Prakriti* Associations

Clinical and genomic studies have confirmed disease–*Prakriti* associations described in classical Ayurvedic texts.

Table 6. Clinical Disease–*Prakriti* Associations and Molecular Mechanisms

Type 2 Diabetes	**Kapha, Vata-Kapha**	**Weight gain, sluggish metabolism**	**Insulin resistance genes, elevated blood sugar, high inflammatory markers, higher BMI**
Dyslipidaemia	Kapha, Vata-Kapha	Higher lipid abnormalities	Abnormal lipid metabolism markers; LDL ↑, HDL ↓
Obesity / High BMI	Kapha	CDH22 methylation associated with BMI	Epigenetic changes in CDH22; adipogenesis-linked SNPs
Thrombosis & Bleeding Disorders	Varies by Prakriti	Unique genetic link: EGLN1–VWF	EGLN1 variants, Von Willebrand factor (VWF) protein; altitude-linked coagulation changes
Rheumatoid Arthritis (RA)	Kapha, Vata-Kapha	High inflammatory markers	Elevated cytokines; inflammatory gene upregulation
Altitude Sickness	Pitta (highest risk)	Absent/low EGLN1 protective variant	rs479200 (TT) near-absent in Pitta; impaired hypoxic adaptation

Table 6 summarizes the key findings across major chronic and complex disease categories, connecting Prakriti types with molecular mechanisms and clinical markers.

The rising burden of chronic diseases, especially metabolic syndrome, cardiovascular diseases, and autoimmune conditions, has made Ayurgenomics a promising tool for early risk assessment. *Prakriti*-based profiling is a low-cost, noninvasive screening method that is culturally relevant and genetically informed. This is especially important for the 1.4 billion people in India and the global South Asian population[14].

DISCUSSION

The Trisutra-Based Personalised Healthcare Model

The *Trisutra* framework—*Aushadhi* (constitution-specific medicines), *Ahara* (genomically validated diet), and Vihara (personalized lifestyle practices)—represents the integration of Ayurgenomics into holistic health care.

Genomic analysis helps identify the biological basis of *Prakriti* and individual susceptibility, while combining phenotypic traits with genomic markers provides a clear understanding of metabolic tendencies and the early signs of imbalance.

The CSIR Ayurgenomics Unit's *TRISUTRA* consortium has institutionalized this model at the population level, enrolling over 7,500 healthy individuals across five diverse Indian cohort sites.

The consortium has developed (1) standardized *Prakriti* assessment protocols that combine clinical questionnaires and physical examinations; (2) integrated multi-omics pipelines linking Prakriti phenotype to DNA, RNA, plasma, and metabolome data; (3) pharmacogenomic analyses of gene variants across FDA-approved drug targets; and (4) a comprehensive biorepository supporting long-term studies of Prakriti and health relationships[15].

Alignment with P5 Medicine

The P5 medicine framework— predictive, preventive, personalized, participatory, and precision —represents the ideal goal of modern global health science. Ayurgenomics aligns well with each of these pillars. Using *Prakriti*-based genomic profiling, we can predict disease risk many years before symptoms appear (predictive)[16]. The *Trisutra* model, which focuses on diet, lifestyle, and seasonal adjustments, reflects a preventive approach (Preventive). Tailored assessments of *Prakriti* and constitution-specific treatments deliver personalized care at a deep level (Personalised). Ayurveda's tradition of community involvement and self-care supports participatory health engagement (Participatory). Additionally, multi-omics validation ensures the scientific accuracy expected in precision medicine (Precision)[17].

India's efforts to promote evidence-based Ayurveda globally have increased recognition and investment, making Ayurgenomics a key part of the country's vision for leading scientifically validated traditional medicine. This impact extends from Asia to South Asian communities worldwide, offering a health model that is culturally relevant and works alongside, rather than against, conventional genomic medicine[18].

Challenges in Mainstream Adoption

Standardisation Issues

The main challenge in Ayurgenomics is the standardization of *Prakriti* assessment. Different practitioners use inconsistent methods; there are no standard reference values for *Dosha* dominance, and objective biomarker panels are needed to confirm *Prakriti* types. This makes it difficult to compare studies. The development and validation of a digital, clinician-independent tool for *Prakriti* assessment is a top priority[19].

Clinical Trial Limitations

Most *Prakriti*-based genomic studies have been conducted on small, mainly Indian populations. Larger, multi-ethnic, and international randomized controlled trials are needed to determine the applicability of these findings and to replicate the results. Genetic differences across populations mean that some *Prakriti*-genomic linkages might only apply to certain groups[20].

Integration Barriers

However, compatibility with existing healthcare systems, a lack of practitioners skilled in both Ayurveda and genomics, and the absence of shared digital health platforms create obstacles to clinical integration[21]. Investing in training programs and genomic registry systems is essential.

Scientific Validation and Knowledge Integrity

To address these lingering doubts, long-term studies demonstrating the effectiveness of *Prakriti*-based treatments are necessary. It is also important to maintain the integrity of traditional knowledge during validation to prevent biopiracy and ensure fair benefits for indigenous communities through frameworks such as the Nagoya Protocol and the Traditional Knowledge Digital Library (TKDL)[22].

Future Directions and Vision 2030

Ayurgenomics is at a turning point. Several key areas of research will shape its future:

Artificial Intelligence: Machine learning models trained on *prakriti-based* multi-omics data will help discover complex biomarkers, improve phenotyping, and develop scalable digital tools for population-wide *prakriti* assessment.

Epigenomics: Studying methylome-wide and histone modification patterns across *Prakriti* groups, including therapeutic reversal studies, will elucidate the epigenetic factors that influence constitutional biology and treatment outcomes.

Microbiome Integration: *Prakriti*-related dietary and lifestyle habits likely affect the gut microbiome, which, in turn, influences drug metabolism, immunity, and metabolic health. Systematic studies on the link between *Prakriti* and the microbiome are crucial. Global Multi-Ethnic Trials: Including *Prakriti* as a factor in international randomized trials—especially for metabolic diseases, pharmacogenomics, and lifestyle medicine—will generate high-quality evidence needed for wider acceptance.

Vision 2030: A world where everyone has access to personal health insights combining their genetic makeup with their constitutional assessment, receiving customized guidance for diet, lifestyle, and treatment to improve their well-being and prevent disease. Ayurgenomics is not only the future but also the ongoing evolution of healthcare.

CONCLUSION

Ayurgenomics has evolved from a bold idea into a scientifically supported field with clear and clinically applicable findings. Two decades of research from CSIR-IGIB and partner institutions have shown that *Prakriti*-based classification captures measurable, heritable, and clinically relevant biological differences, which are reflected in gene expression, HLA alleles, 52-SNP fingerprints, CYP450 pharmacogenomics, EGLN1 adaptation, and epigenetic markers.

The *TRISUTRA* consortium's large-scale implementation, the integrative logic of the *Trisutra* treatment model, and its alignment with P5 medicine principles position this field as a legitimate, complementary part of global precision medicine[23]. The remaining goals are standardization, replication, interdisciplinary training, and ethical governance.

In an era where genomic medicine is often limited to well-funded healthcare systems, Ayurgenomics provides an alternative: a personalized medicine approach that is both ancient and modern, local and universal, scientifically sound, and culturally relevant—rooted in the whole human being.

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