Ayurgenomics in Kayachikitsa: Integrating Molecular Genetics and Clinical Genomics for Precision Ayurveda and Personalised Internal Medicine

Dr. Nishant Kaushik

Associate Professor, Parul Institute of Ayurved & Research, Parul University, Vadodara, Gujarat, India

Corresponding author: dr.nishant16@gmail.com

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Abstract

Background: Ayurveda, the ancient Indian system of medicine, emphasizes individual uniqueness through *Prakriti* stratification (Vata, Pitta, Kapha). Modern medicine is transitioning toward personalized genomics but lacks methods to stratify inter-individual differences in ethnically matched populations.

Objective: To explore Ayurgenomics—a novel integrative framework combining Ayurvedic Prakriti with molecular and clinical genomics—for precision Ayurveda in Kayachikitsa (internal medicine).

Methods: Genome-wide SNP analysis of 262 well-classified individuals across three Prakriti types; exome sequencing of 72 healthy participants; machine learning-based phenotypic trait analysis; and molecular phenotyping (biochemical, haematological, gene expression profiling).

Results: Fifty-two SNPs significantly differentiated Prakriti types ($p \leq 1\times10^{-5}$). Principal component analysis classified individuals irrespective of ancestry. The oxygen sensor gene *EGLN1* emerged as a hub gene linking Dosha Prakriti to high-altitude adaptation and asthma severity. Twenty-eight SNPs from 11 FDA-approved pharmacogenomic genes (e.g., *CYP2C19*, *CYP2C9*, *CFTR*) showed significant differences between Prakriti types.

Conclusion: Ayurgenomics provides a molecular framework for integrating genomics with Ayurvedic principles, enabling predictive, preventive, and personalized internal medicine in Kayachikitsa.

Keywords: Ayurgenomics, Kayachikitsa, Prakriti, molecular genetics, clinical genomics, precision Ayurveda, *EGLN1*, personalized medicine, Trisutra, pharmacogenomics

Introduction

Ayurveda, documented since 1500 BCE, follows a systems approach with parallels to contemporary personalized genomic medicine. Its core tenet—*Trisutra Ayurveda* (Hetu: causes; Linga: features; Aushadha: therapeutics)—offers a predictive and personalized framework for health and disease.[1][2][3]

Modern medicine, despite prolonging human lifespan, has "forgotten the patient and inter-individual variability" even in healthy states. Common diseases like diabetes, asthma, and cardiovascular disorders require lifetime interventions with variable drug responses, necessitating personalized approaches.[2]

Ayurgenomics, emerging at the start of this century, integrates Ayurvedic Prakriti stratification with modern genomics to identify the molecular basis of Dosha constitution. The CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB) pioneered this approach, establishing the **CSIR-TRISUTRA Unit** (Translational Research and Innovative Science through Ayurgenomics) as an interdisciplinary network connecting Ayurveda, modern medicine, and genomic science.[2]

This article examines how Ayurgenomics in Kayachikitsa (Ayurvedic internal medicine) enables precision Ayurveda through integration of molecular genetics and clinical genomics.

Background

Ayurvedic Foundations

Prakriti is an individual's basic constitution determined at birth, governing inter-individual variability in health parameters, disease susceptibility, and response to diet, drugs, and lifestyle. Seven Prakriti types exist based on proportions of three *Doshas*:[2]

Table 1

Dosha	Function	Nature
Vata	Kinetic	Air + space
Pitta	Metabolic	Fire + water
Kapha	Potential (structural)	Water + earth

The three contrasting types with single-Dosha predominance (Vata, Pitta, Kapha) are most vulnerable to diseases.[2]

Tridosha (Vata-Pitta-Kapha) are physiological entities functioning together throughout the body, maintaining equilibrium.[3]

Modern Genomic Medicine

Personalized genomic medicine focuses on genetic, cellular, physiological, and environmental networks to forecast phenotypic repercussions of aberrations. However, no modern methods exist to stratify inter-individual differences within ethnically matched healthy populations.[3][2]

Ayurgenomics Concept

Ayurgenomics links the three Doshas to genetic and physiological individuality, providing insights into Tridosha that may pave the way for precision medicine. The approach enables systematic exploration of Trisutra Ayurveda using genomics and molecular phenotyping.[4][3][2]

Methodology

Study Design

The Ayurgenomics research encompassed five key activities:[5]

1. **Exome sequencing** of 72 healthy participants representing various predominant Prakriti types from North Indian Indo-European population
2. **Consortium formation** creating five genetically consistent cohorts from different ethnic and geo-climatic backgrounds
3. **Protocol standardization** for objective Prakriti evaluation
4. **Prakriti assessment** applied to 7,500+ individuals across five cohorts
5. **Data repository creation** with integrative omics pipelines for genomic correlates

Genome-Wide SNP Analysis

- **Subjects:** 262 well-classified male individuals (screened from 3,416 subjects)[6]
- **Platform:** Affymetrix Genome-Wide Human SNP Array 6.0[6]
- **Population:** Genetically homogeneous Western India population, validated with 297 Indian samples with known ancestry[7][6]

Molecular Phenotyping Parameters

Table 2

Category	Metrics
Anthropometric	Physical attributes (height, weight, body measurements) [5]
Biophysical	Skin types, heart rate variability (HRV) [5]

Physiological	Spirometry (lung capacity), gustometry (taste sensitivity) [5]
Biochemical	Haematological parameters, immunity markers [2]
Genomic	Gene expression levels, SNP profiling [2][6]

Machine Learning Approach

- **Sample:** 147 healthy individuals from three extreme Prakriti types[7]
- **Methods:** Unsupervised clustering + supervised classification models[7]
- **Validation:** North Indian population cohort[7]

Statistical Analysis

- Permutation testing: 10^6 permutations[6]
- Significance threshold: $p \leq 1\times10^{-5}$[6]
- Principal component analysis (PCA) for classification[6]

Main Body

Genomic Correlates of Prakriti

SNP Discovery

Genome-wide analysis revealed **52 SNPs** significantly different between Prakriti types ($p \leq 1\times10^{-5}$) without confounding stratification effects. PCA of these SNPs classified 262 individuals into Vata, Pitta, and Kapha groups irrespective of ancestry.[6]

Validated Gene: *PGM1* (phosphoglucomutase 1) correlates with Pitta phenotype as described in *Charaka Samhita*, confirming genetic basis of traditional phenotypic classification.[6]

Pharmacogenomic Significance

Exome sequencing identified **28 SNPs from 11 FDA-approved pharmacogenomic genes** showing significant Prakriti differences:[5]

Table 3

Gene	Pharmacogenomic Class	Clinical Relevance
CYP2C19	Drug metabolism	Antipsychotics, proton pump inhibitors

CYP2C9	Drug metabolism	Warfarin, NSAIDs
CYP2D6	Drug metabolism	Beta-blockers, antidepressants
CFTR	Ion transport	Cystic fibrosis
CPS1	Urea cycle	Nitric oxide metabolism
HLA-DQB1	Immunity	Drug hypersensitivity
HLA-DRB1	Immunity	Autoimmune disease

These polymorphisms exist in Indian and global populations (1000 Genomes Project).[5]

Molecular Basis of Dosha Prakriti

Gene Expression Differences

Healthy individuals of contrasting Prakriti types exhibit **striking differences** in:

- **Biochemical parameters**[2]
- **Haematological parameters**[2]
- **Gene expression levels** (especially immunity, cell division, blood coagulation genes)[2]

Hub Gene Discovery: *EGLN1*

The Ayurgenomics study identified **EGLN1** (EC 1.14.99.66), an oxygen sensor gene, as a critical hub gene:[1][2]

Table 4

Property	Finding
Function	Oxygen sensing, hypoxic response regulation [2]
Prakriti difference	Significantly different between Vata-Pitta-Kapha types [1]
Adaptation link	High-altitude adaptation [2][1]
Disease relevance	Asthma severity in murine models [2][8]
Molecular correlate	Pitta-Kapha axis identified through inter-individual variability [8]

Modulation of *EGLN1* levels affects hypoxic response and asthma severity, explaining molecular correlates of Pitta-Kapha dosha.[8][2]

Clinical Applications in Kayachikitsa

Predictive Medicine

- **Disease susceptibility prediction:** Identifies genetic predispositions for metabolic, cardiovascular, respiratory diseases[3][2]
- **Progression prediction:** Predicts disease course based on Prakriti-genomic profile[2]

Preventive Medicine

- **Lifestyle customization:** Diet and exercise tailored to genetic-Prakriti constitution[9]
- **Environmental adaptation:** High-altitude sickness susceptibility assessment using *EGLN1* variation[2]

Personalized Therapeutics

Case Study: Adhatoda vasica (Vasa) for Respiratory Illness

Table 5

Aspect	Finding
Ayurvedic description	Balances Pitta-Kapha dosha; used for respiratory illnesses [2]
Molecular mechanism	Anti-hypoxic + anti-inflammatory action [2][8]
Protective effects	Airway inflammation, acute allergic asthma, severe asthma, fibrosis [2]
Novel discovery	Novel HIF-1α inhibitor [8]
COVID-19 relevance	Potential for airway inflammation/fibrosis in COVID-19 patients [2]

This study validated the molecular correlate of Pitta-Kapha axis and explained Vasa's therapeutic mechanism.[8][2]

Drug Discovery Framework

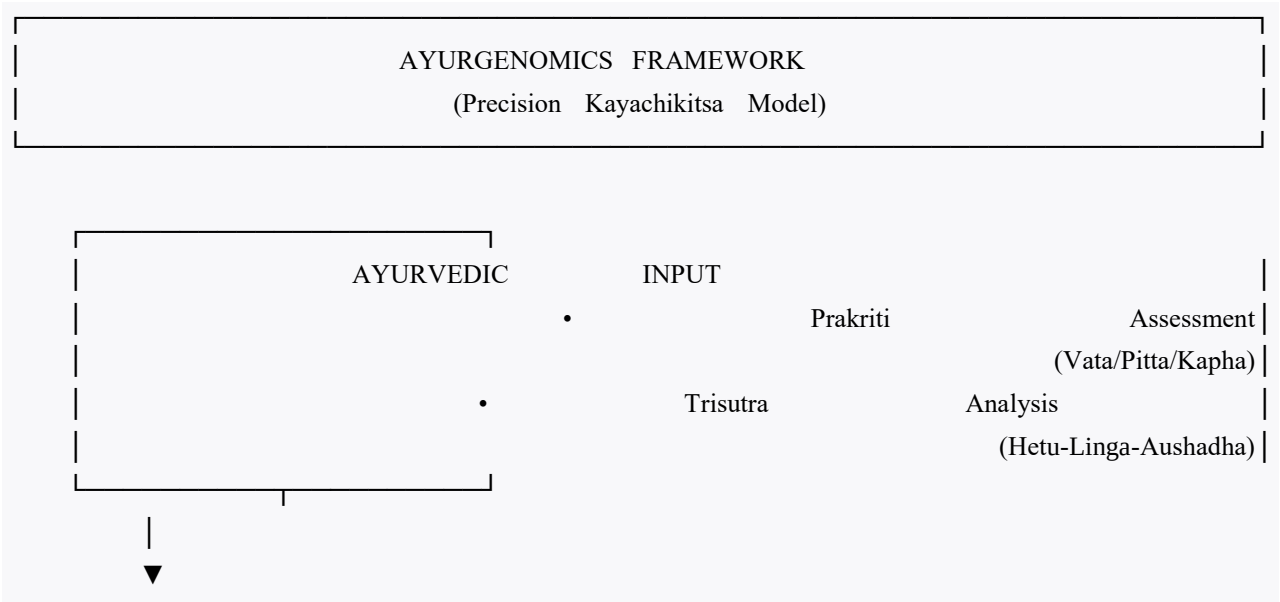
Ayurgenomics enables **Prakriti-based drug discovery** by:

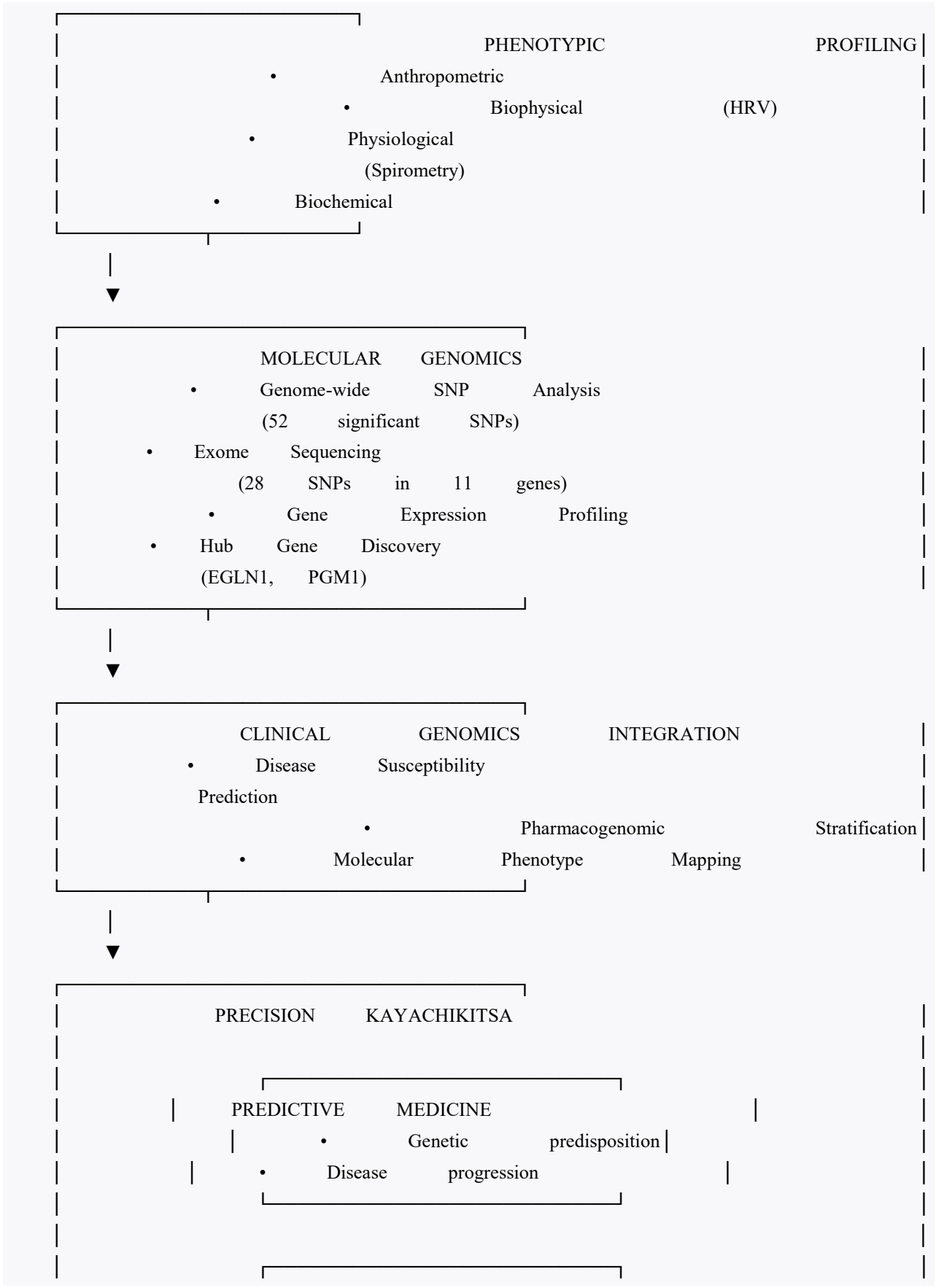
1. Stratifying individuals based on Dosha constitution
2. Identifying genomic correlates of phenotypic traits
3. Discovering actionable therapeutic points in individualized manner[10][1]
4. Accelerating biomarker discovery for precision medicine[4][2]

Table 6: Comparative Features of Ayurvedic and Genomic Personalized Medicine

Dimension	Ayurvedic Approach (Trisutra)	Genomic Approach	Ayurgenomics Integration
Individual stratification	Prakriti (Vata-Pitta-Kapha) [2]	Genetic profile (SNPs, haplotypes) [9]	Prakriti-genomic correlation [2][6]
Disease causation	Hetu (causes: environmental + inherent) [2]	Genetic + environmental networks [3]	Integrated Hetu-genomic model [1]
Disease features	Linga (phenotypic characteristics) [2]	Molecular phenotypes, intermediate patho-phenotypes [1]	Molecular correlates of Linga [2][1]
Therapeutics	Aushadha (herbal/pharmacological) [2]	Pharmacogenomics, targeted therapy [5]	Prakriti-based drug discovery [4][10]
Variability basis	Tridosha imbalance [3]	Genetic polymorphisms [6]	Tridosha-Dosha genetic basis [2][1]
Key biomarker	Dosha predominance [2]	SNP variants, gene expression [6]	*EGLN1*, *PGM1*, 28 pharmacogenomic SNPs [2][1][5]

Figure




PHENOTYPIC PROFILING
• Anthropometric
• Biophysical (HRV)
• Physiological (Spirometry)
• Biochemical
MOLECULAR GENOMICS
• Genome-wide SNP Analysis (52 significant SNPs)
• Exome Sequencing (28 SNPs in 11 genes)
• Gene Expression Profiling
• Hub Gene Discovery (EGLN1, PGM1)
CLINICAL GENOMICS INTEGRATION
• Disease Susceptibility Prediction
• Pharmacogenomic Stratification
• Molecular Phenotype Mapping
PRECISION KAYACHIKITSA
PREDICTIVE MEDICINE
• Genetic predisposition
• Disease progression

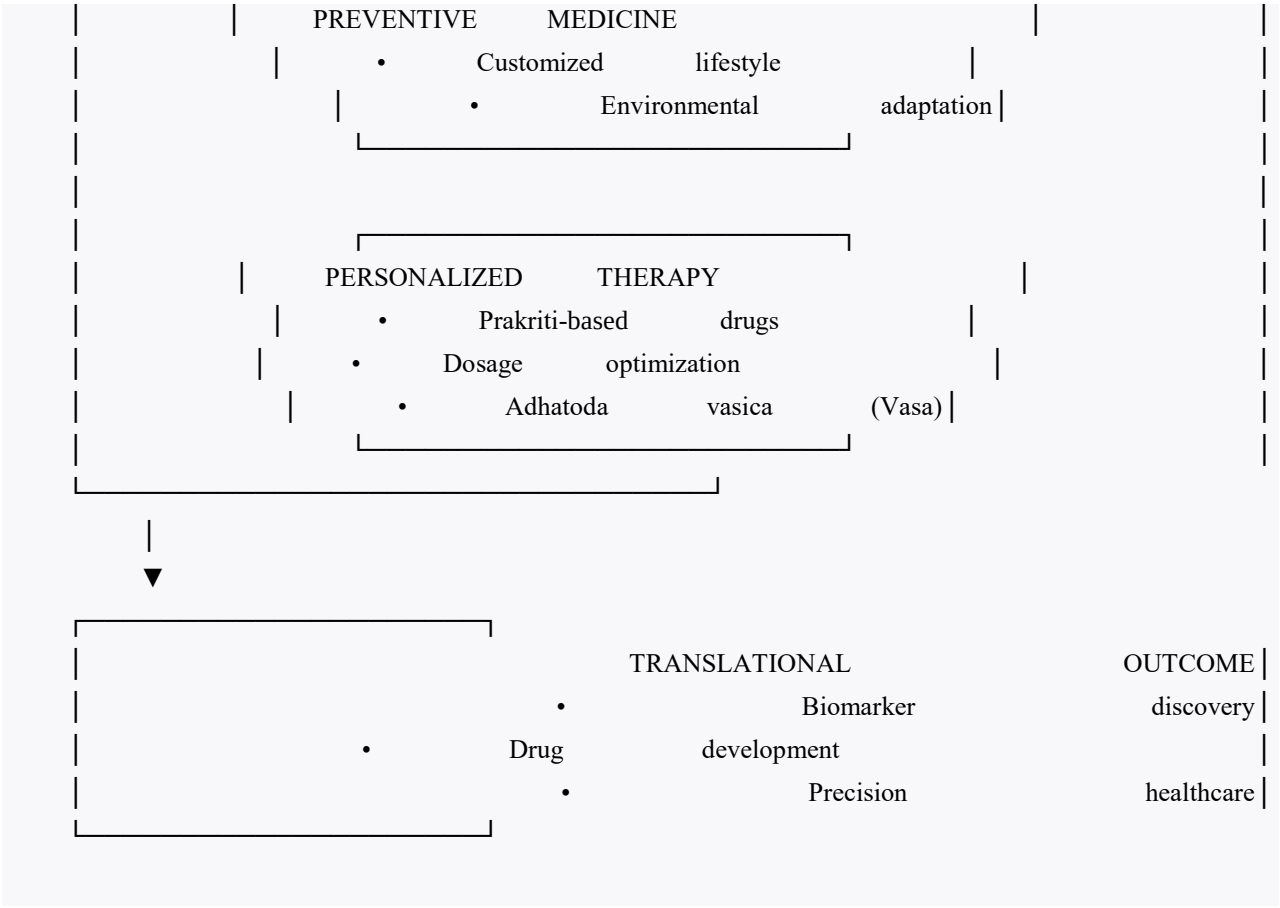


Figure 1: Ayurgenomics Framework for Precision Kayachikitsa

Key Molecular Correlates:

- *EGLN1*: Oxygen sensor → Pitta-Kapha axis → High-altitude adaptation + Asthma severity[1][2]
- *PGM1*: Correlates with Pitta phenotype → Charaka Samhita validation[6]
- 28 SNPs in 11 pharmacogenomic genes → Drug response stratification[5]

Discussion

Scientific Validation of Ayurvedic Principles

Ayurgenomics provides the **first molecular framework** linking Ayurvedic Dosha Prakriti to genomic variation. The discovery that 52 SNPs differentiate Prakriti types without ancestry confounding validates that traditional phenotypic

classification has a genetic basis. This confirms Ayurveda's millennia-old practice of Prakriti-based stratification resonates with modern personalized medicine.[6][2]

The identification of *EGLN1* as a hub gene differentiating Prakriti types demonstrates that **highly connected hub genes** explain inter-individual Dosha differences. This finding bridges ancient Ayurvedic wisdom with contemporary systems biology, showing Tridosha has molecular correlates in oxygen sensing and hypoxic response pathways.[1][2]

Clinical Implications for Kayachikitsa

Precision Internal Medicine

Ayurgenomics transforms Kayachikitsa from empirical practice to evidence-based precision healthcare by enabling:

1. **Individual stratification** within ethnically matched populations—previously impossible in modern medicine[2]
2. **Actionable therapeutic points** identified in individualized manner through Trisutra-guided genomic integration[1]
3. **Pharmacogenomic optimization** using 28 SNP variants in 11 FDA-approved drug metabolism genes[5]

Therapeutic Discovery

The *Adhatoda vasica* (Vasa) study exemplifies Ayurgenomics-enabled drug discovery:

- **Mechanism validation:** Novel HIF-1α inhibitor explains anti-hypoxic/anti-inflammatory effects[8]
- **Prakriti correlation:** Validates molecular correlate of Pitta-Kapha axis[8]
- **Clinical translation:** Potential for COVID-19 airway inflammation and fibrosis[2]

This demonstrates how Ayurgenomics accelerates biomarker discovery for preventive and personalized medicine.[2]

Limitations and Future Directions

Current gaps:

- Diagnostic and therapeutic applications of Ayurgenomics require further research[3]
- Large-scale massive effort needed for clinical implementation[3]
- Epigenetic mechanisms (lifestyle-gene expression interactions) need exploration[9]

Future priorities:

1. **GWAS expansion:** Identify additional biomarkers for disease prevention strategies[9]
2. **Epigenetic studies:** Understand lifestyle influence on gene expression across Prakriti types[9]
3. **SNP analysis scaling:** Implement genome-wide SNP profiling in clinical Kayachikitsa practice[9]

4. **Consortium growth:** Expand CSIR-TRISUTRA network for multi-ethnic validation[5]
5. **Clinical trials:** Test Prakriti-based therapeutics in randomized controlled settings[3]

Policy and Institutional Support

The **Ministry of AYUSH** awarded CSIR-IGIB's Ayurgenomics initiative a **Centre of Excellence Grant** for Applied developments of Ayurveda Prakriti and Genomics, recognizing its transformative potential. The CSIR-TRISUTRA Unit enables cross-talk between Ayurveda, modern medicine, and genomic science, facilitating translational research.[2]

Integration with Global Precision Medicine

Ayurgenomics aligns with global precision medicine initiatives while offering unique advantages:

Table 7

Aspect	Global Precision Medicine	Ayurgenomics
Stratification basis	Genetic profile alone	Genetic + Prakriti + lifestyle [9]
Population applicability	Ancestry-specific	Ancestry-independent (PCA validation) [6]
Preventive framework	Risk prediction	Trisutra-guided holistic prevention [2]
Therapeutic approach	Targeted drugs	Prakriti-based personalized therapeutics [4]

This integration enriches personalized healthcare by honoring both genetic diversity and traditional knowledge.[9]

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Author Note: This article synthesizes research from CSIR-IGIB's Ayurgenomics initiative, the CSIR-TRISUTRA Consortium, and peer-reviewed publications on Prakriti-genomics integration. The framework presented enables translation of Ayurvedic internal medicine into precision healthcare aligned with contemporary genomic science.

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