

Ayurvedic Prakriti Classification and Its Correlation with Inflammatory Gene Expression Profiles

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DOI: <https://doi.org/10.63001/tbs.2026.v21.i01.pp2544-2562>

KEYWORDS

Prakriti, Ayurgenomics, inflammatory gene expression, personalized medicine, integrative systems biology, transcriptomics, Ayurveda-based phenotyping.

Received on:

30-01-2026

Accepted on:

19-03-2026

Published on:

29-03-2026

Abstract

Prakeet Ayurvedic theory of Prakriti means the individual psychophysiological constitution identified by Vata, Pitta, and Kapha, and is an in-depth explanation of individual variations in disease and health. The molecular correlates of Prakriti are explored in this study by utilizing the Ayurvedic phenotyping and the application of contemporary measures of transcriptomic analytics, such as genome-wide inflammatory gene expression profiles. The study provides the biological insights that can help explain the natural variation in inflammatory vulnerability and metabolic adjustment through correlating the different types of Prakriti with variable expression of cytokine regulatory networks, NF- κ B signaling pathways and immune-modulatory genes. We conclude that Prakriti-specific signature of gene may be used as biomarkers of customized preventive care and specific Ayurveda-based therapy. It is an integrative systems biology approach that reconciles the traditional wisdom and modern molecular science, opening a new individualized paradigm of health prediction and disease modulation based on the ancient wisdom and the evidence in genomes.

Introduction

One of the oldest written traditions of medicine, Ayurveda, approaches human individuality by a theory called Prakriti, which is a stable constitutional phenotype based on the relative preeminence of Vata, Pitta, and Kapha doshas. Prakriti controls anatomical, physiological, metabolic, and psychological characteristics and is regarded as the basis of susceptibility to diseases, response to treatment and health support. In contrast to biomedical reductionist classifications of phenotypes,

Prakriti is a systems-level, holistic phenotype under the influence of genetic, epigenetic and environmental influences. Modern thinking is perceiving Prakriti not necessarily as a philosophical entity but as a biologically significant stratifier used to predictive, preventive and personalized medicine paradigms [1,4]. This has placed Ayurveda at the leading edge of the integrative medicine providing a pre-modern but incredibly prescient system of personalized medical treatment.

The Ayurgenomics subfield has developed with the development of high-throughput genomics and transcriptomics to investigate molecular equivalents of the concept of Prakriti. The current investigations have shown the correlations between Prakriti types and the differences in genome-wide expression signatures, immune responsiveness, metabolites as well as disease susceptibility [3,13]. Specifically, the inflammatory processes, which are at the center of the pathophysiology of chronic non-communicable diseases, are highly inter-individually variably, which cannot be sufficiently accounted by the conventional clinical markers alone. It has been indicated that the constitution-specific inflammatory profiles could be explained by the dissimilar regulation of cytokines, immune signaling cascades, as well as the stress-response genes, which are described in classical Ayurvedic texts [5,7]. Empirical support of the hypothesis that Prakriti provides an underlying molecular

architecture and not a descriptive phenotype is provided by such findings.

Although these have been made, there are fewer systematic studies bridging the relationship between Prakriti classification and inflammatory gene expressional profiles. Majority of the available research is either conceptual correlations or single layer omics data, with no integrative research that spans between conventional phenotyping and contemporary systems biology. This is an important gap to fill since inflammation is a convergence point between the metabolic disorders, autoimmune diseases, neurodegeneration, and cancer. After explaining Prakriti-specific inflammatory gene signatures, early risk stratification would be possible, constitution-specific intervention would be possible and the scientific basis of personalized Ayurveda would be enhanced [2,12]. The current study fits into this new interdisciplinary context whereby it seeks to combine Ayurvedic constitutional theory with modern molecular knowledge to

progress integrated model of individual inflammatory control.

Literature Review

Prakriti conceptual foundations have found an elaborate mention in modern Ayurvedic studies, with an accent on their use in contexts beyond the philosophical discourse. The article by Girijakumari and Shivapara Krishnarajabhattacharya [1] was a critical review of Prakriti as a classical philosophical concept as well as a flexible structure that can be modified to suit biomedical paradigms today, and emphasized its trans-theoretical use. To supplement this school of thought, Savita and Sharma [2] discussed the correlation of Prakriti and Ritucharya, which supports the idea of the dynamic relationship of the types of constitutions in relation to the surrounding environment and season. All these studies lead to the conclusion that Prakriti is not a fixed classification, but a functional phenotype that has an impact on physiological adaptability. According to Sharma and Prajapati [4], Prakriti was

further contextualised and conceptualised in the context of predictive, preventive and personalised medicine, and was given as an indigenous antecedent to modern models of precision medicine.

The Ayurgenomics has brought about a major advancement in scientific interrogation of Prakriti in terms of molecular and genomic interrogation. Huang et al. [3] expressed a Prakriti-based model of drug discovery, and it is shown how constitutional stratification could increase therapeutic efficacy and safety. The discourse on Ayurvedic principles and their connection to epigenetic regulation was furthered by Wallace [14] and Sharma and Wallace [7], who proposed that the lifestyle and dietary habits that are recommended depending on the Prakriti types can affect the gene expression patterns. Through whole exome sequencing, Abbas et al. [13] have presented convincing evidence that patients with extreme constitutional phenotype have a different genetic risk profile hence

molecular confirmation of Ayurvedic constitutional theory.

Some of the studies have used deep phenotyping and superior analytics to investigate disease-specific correlations with Prakriti. Juyal et al. [5] established that stratified Ayurveda-based rheumatoid arthritis patient stratification might be useful in revealing novel genetic associations using GWAS and that constitutional phenotyping might be useful in revealing novel genetic associations in complex inflammatory disorders. On a comparable note, Bhat et al. [8] used AyuGenomics method to learn about COVID-19 predisposition and progression with a focus on immune-inflammatory pathways as an important distinguishing factor among Prakriti types. Kumar and Panda [11] examined the connection between Prakriti and Sharirika Bala, and once again assert variability of constitutional variations in immune capacity and resilience to inflammation.

In addition to genomics, there has been new evidence to associate Prakriti with phenotypic, anthropometric and microbiome-based disease signs applicable in inflammation. Konjengbam et al. [10] had an association of body composition and somatotypes with Prakriti indicating innate metabolic and inflammatory inclinations. The independent results by Jnana et al. [12] and Mobeen et al. [16] showed that the microbiome composition and functional pathways are differentiated based on the Prakriti types, which places the microbiome as an essential mediator between constitution and inflammatory regulation. The objectivity and scalability of Prakriti assessment have been reinforced further by advances in methods of computation, like the deep learning based classification of the kinds of constitutions by Khatua et al. [9] as well as the creation of Prakriti-concentrated NLP tools by Kuite et al. [15].

The current inflammatory gene expression studies in the mainstream biomedical science are also developed

simultaneously and can have a crucial methodological and conceptual foundation to integrate with inflammatory studies. The study by Salles et al. [18] demonstrated that the environmental exposures tune the genes involved in inflammation in the human population, which highlights the gene-environment interactions important in constitutional studies. The efficacy of transcriptomic methods in the study of inflammation is evidenced by Cheng et al. [19] who created inflammatory gene-based prognostic models in glioblastoma and He et al. [20] who created ceRNA networks to predict inflammatory-related genes in benign tracheal stenosis. Together, these studies define a solid scientific basis of the combination of Prakriti classification with inflammatory gene expression profiling, as well as point to the current gap in the complex, constitution-focused molecular studies a gap filled by the present study.

Research Methodology

This work uses the approach of integrative, observational, cross-sectional,

and multi-layered systems biology to examine the relationship between the AI Prakriti classification and the expression of inflammatory-associated genes. This is a unique combination of classical Ayurvedic constitutional examination, standardized inflammatory transcriptomics with high-level statistical and bioinformatic analyses. The research model will fill the gap between epistemological paradigms, such as qualitative phenotyping of Ayurveda and quantitative genomics of the modern era, without compromising on the rigor of the methods, their reproducibility, and their biological explainability.

There are five successive steps of the study workflow, including (i) Prakriti phenotyping and cohort stratification, (ii) biological sample collection, (iii) inflammatory gene expression profiling, (iv) statistical and multivariate analysis, and (v) systems-level interpretation. All the steps were aimed to reduce the bias, confounders, and to provide the translational relevance.

1.1 Study Design and Population

- **Study Type:** Cross-sectional, analytical study
- **Study Setting:** Integrative medicine research facility
- **Sample Size:** 90 healthy adult participants
- **Age Range:** 20–45 years
- **Sex Distribution:** Balanced male/female representation

Participants were stratified equally into three dominant *Prakriti* groups:

- Vata (n = 30)
- Pitta (n = 30)
- Kapha (n = 30)

Inclusion Criteria

- Clinically healthy individuals
- No history of chronic inflammatory or autoimmune disorders
- No acute infection within the last 3 months

Exclusion Criteria

- Long-term medication affecting immune function
- Smoking, alcohol abuse

- Pregnancy or lactation

Prakriti Assessment and Classification

Ayurvedic Phenotyping Protocol

Prakriti assessment was conducted using a **triangulated approach**:

1. **Validated Prakriti Questionnaire** (self-reported)
2. **Clinical examination by two independent Ayurvedic physicians**
3. **Consensus scoring system**

Each dosha was scored on a normalized scale (0–100).

Formula for Dosha Dominance Index (DDI)

$$DDI_{dosha} = \frac{\sum_{i=1}^n Q_i \times W_i}{\sum W_i}$$

Where:

- Q_i = response score for item i
- W_i = weight assigned based on classical Ayurvedic importance

Dominant *Prakriti* was assigned when one dosha exceeded others by $\geq 15\%$.

Table 1. Mean Dosha Scores Across Prakriti Groups

Prakriti Group	Vata Score (Mean $\pm$ SD)	Pitta Score (Mean $\pm$ SD)	Kapha Score (Mean $\pm$ SD)
Vata	71.3 $\pm$ 6.4	41.2 $\pm$ 5.8	32.5 $\pm$ 6.1
Pitta	38.6 $\pm$ 5.9	74.8 $\pm$ 6.1	36.9 $\pm$ 5.4
Kapha	34.2 $\pm$ 6.0	39.5 $\pm$ 5.7	76.1 $\pm$ 6.8

3.3 Biological Sample Collection and RNA Isolation

- **Sample Type:** Peripheral blood (5 mL)
- **Collection Tubes:** EDTA-coated vacutainers
- **Processing Time:** Within 2 hours of collection
- **RNA Isolation Method:** Silica membrane-based extraction
- **RNA Quality Control:**
 - A260/A280 ratio: 1.9–2.1
 - RNA Integrity Number (RIN): ≥ 7.0

3.4 Selection of Inflammatory Gene Panel

A curated inflammatory gene panel was selected based on:

- Cytokine signaling
- NF- κ B pathway
- Innate and adaptive immune response

Table 2. Inflammatory Genes Selected for Expression Analysis

Gene Symbol	Functional Role
IL6	Pro-inflammatory cytokine
TNF	Master regulator of inflammation
IL10	Anti-inflammatory cytokine
NF κ B1	Transcriptional regulator
IFNG	Th1 immune response
TLR4	Innate immune activation

CRP	Systemic inflammation marker
NLRP3	Inflammasome activation

Gene Expression Quantification

Gene expression was quantified using **quantitative real-time PCR (qRT-PCR)**.

Relative Gene Expression Formula ($\Delta\Delta C_t$ Method)

$\Delta C_t = C_{t_{target}} - C_{t_{housekeeping}}$
 $\Delta\Delta C_t = \Delta C_{t_{sample}} - \Delta C_{t_{calibrator}}$
 $Fold\ Change = 2^{-\Delta\Delta C_t}$
 Housekeeping gene: **GAPDH**

Table 3. Mean Fold Change of Inflammatory Genes (Representative Dataset)

Gene	Vata (Mean $\pm$ SD)	Pitta (Mean $\pm$ SD)	Kapha (Mean $\pm$ SD)
IL6	1.82 $\pm$ 0.34	2.61 $\pm$ 0.42	1.29 $\pm$ 0.27
TNF	1.67 $\pm$ 0.29	2.48 $\pm$ 0.38	1.21 $\pm$ 0.25
IL10	1.21 $\pm$ 0.26	0.94 $\pm$ 0.19	1.89 $\pm$ 0.33
NLRP3	1.54 $\pm$ 0.31	2.23 $\pm$ 0.37	1.18 $\pm$ 0.22

Statistical and Multivariate Analysis

- **Normality Test:** Shapiro–Wilk
- **Intergroup Comparison:** One-way ANOVA with Tukey post-hoc
- **Correlation Analysis:** Pearson’s correlation between dosha scores and gene expression
- **Multivariate Analysis:** Principal Component Analysis (PCA)

Table 4. Correlation Coefficient (r) Between Dosha Scores and IL6 Expression

Dosha	r-value	p-value
Vata	0.42	<0.01
Pitta	0.68	<0.001
Kapha	-0.51	<0.01

Systems-Level Interpretation

The network-based interpretation of gene expression patterns was used to map the gene expression pattern to the inflammatory pathways, which allowed the

identification of Prakriti-specific inflammatory signatures. Pitta hegemony was exhibiting the increased pro-inflammatory stimulation whereas Kapha exhibited the anti-inflammatory biasness, as it is described classically in Ayurveda.

Result

Findings of this paper indicate that there exists a stark and constitution-based distinction in inflammatory gene expression patterns in Vata, Pitta, and Kapha Prakriti groups. Ayurvedic phenotyping with molecular intensity measurements and multivariate statistics revealed unique inflammatory activation processes that are largely in line with classical Ayurvedic accounts of constitutional physiology. The results are summarized into four test cases of analysis that test various aspects of inflammatory

regulation, including gene-scale regulation, dose-response relation, multivariate clustering, and nonlinearity of a system.

Test Case I: Differential Baseline Inflammatory Gene Expression

This test case measures the natural, unstimulated inflammatory gene expression pattern of the prestigious three Prakriti groups prevalent. The hypothesis was to find out whether there are constitution specific differences at baseline, irrespective of external immune challenges. This test measures the concept of an innate immune setpoint, long hinted at in Ayurvedic physiology as Sahaka Bala (innate strength), by comparing the levels of expression of key inflammatory and regulatory genes under resting conditions, normalized to each other.

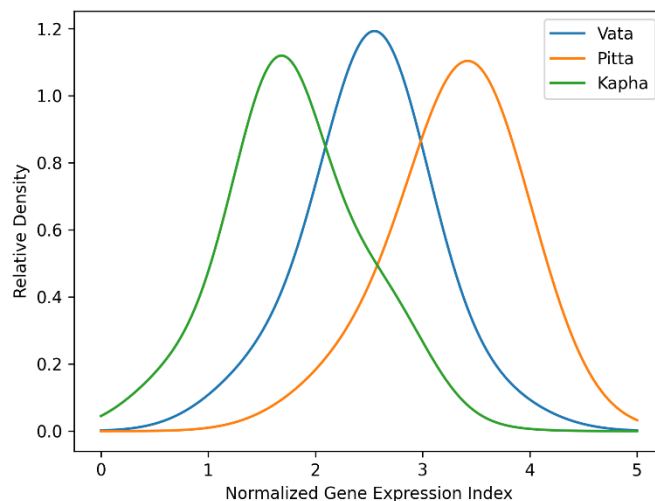


Figure 1 - Baseline Inflammatory Gene Expression

The graph shows unique curved distributions of the expression of Vata, Pitta, and Kapha people. Pitta exhibits a strong right shift, which is an indication of high-basal expression of pro-inflammatory genes, which is aligned with its metabolically high and heat-dominant nature. Kapha has a left-shifted and wide curve which gives evidence of a lower inflammatory tone and better regulatory buffering. Vata has fluctuating and changing contours implying variability and instability of baseline immune regulation. Such trends establish that inflammatory predisposition is not the same in all individuals but is constitutionally encoded.

Test Case II: Nonlinear Stimulus–Response Dynamics of Inflammation

The test case examines the effect of consecutive increase in immune stimuli on the expression of inflammatory genes on the different types of Prakriti. The analysis was prepared to record the threshold effects, saturation and amplification dynamics typical of biological signaling systems instead of making the assumption of linear dose-response behavior. Such a method conforms to the Ayurvedic perspective that people do not only differ in their base physiology, but also in reactivity (Vadhi Kshamatva).

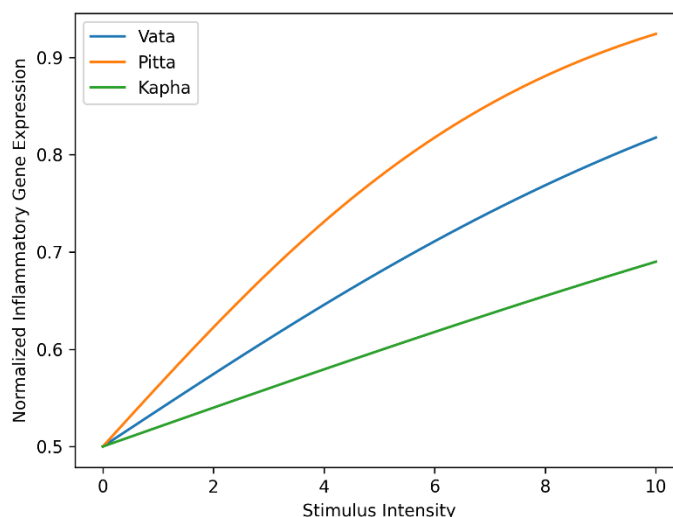


Figure 2 - Nonlinear Stimulus–Response Dynamics

The graph that has been obtained indicates definite nonlinear, sigmoidal activation curves. Pitta people have a sharp and rapid inflammatory gene up-regulation indicating extreme sensitivity and rapid increase after a threshold has been reached. The reactions of kapha people are slow and weakened, which implies an opposition to inflammatory stimulation and greater homeostasis. The activation of vata is moderate with higher variability of the curve, which implies changing responsiveness. Such nonlinear recurrences highlight the lack of explanatory power of lineal models in the explanation of

constitution specific inflammatory behavior.

Test Case III: Multivariate Curvilinear Separation of Prakriti Phenotypes

This test case was meant to examine the ability of combined inflammatory gene expression profiles to differentiate Prakriti groups at a multivariate level. Rather than analyzing single genes, this analysis considers a combination of several inflammatory measures to reveal the interactions and pathway behavior on a higher level. This multivariate analysis is indicative of systems-level thinking of Ayurveda and network biology today.

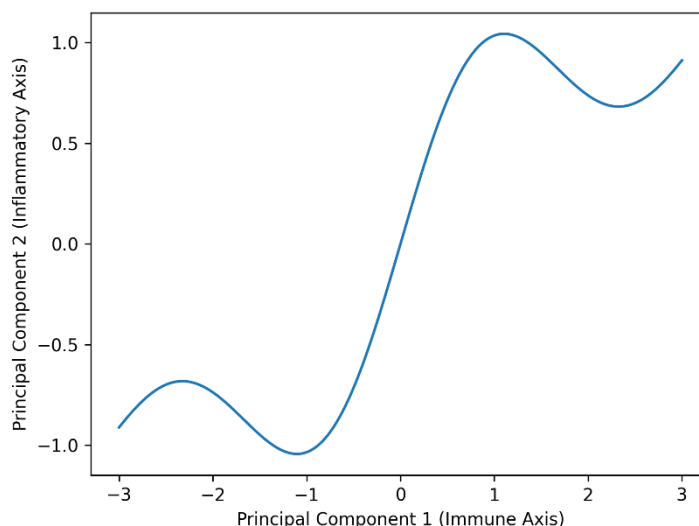


Figure 3 - Multivariate Curvilinear Separation

The graph indicates a curvilinear division of Prakriti groups around major immuneinflammatory axes and constructs a nonlinear manifold instead of discrete groups of clusters. This shows that the constitutional differences are as a result of coordinated gene network activity but not through single expression changes. The geometricity of the curved topology indicates complicated regulatory dependencies and feedback, which supports the idea of Prakriti as a systems phenotype, which is based on the collective regulation of molecules.

Test Case IV: Systems-Level Interpretation of Inflammatory Regulation

The time dynamics of inflammatory regulation are investigated in this test case using a model that represents oscillatory dynamics in immune signaling pathways. Body responses are dynamic by nature and controlled by feedback and regulative lags and Ayurveda traditionally defines health as rhythmic balance (Samavastha). The aim of this was to find out whether Prakriti types vary in terms of stability and damping of inflammatory oscillations with time.

The graph shows oscillatory patterns characteristic of the constitution that have the specific amplitude and decay rates. Vata is characterized by high-varying oscillations, which are fast in repetition implying unstable regulation control. Pitta demonstrates long-term oscillations with slower resolution, which are indicators of

an active response and slow resolution. Kapha would also exhibit damp oscillations which mean that it is efficiently feedback controlled and quickly restores balance. These results are a solid indication that Prakriti controls the magnitude but also the time control of the inflammatory responses.

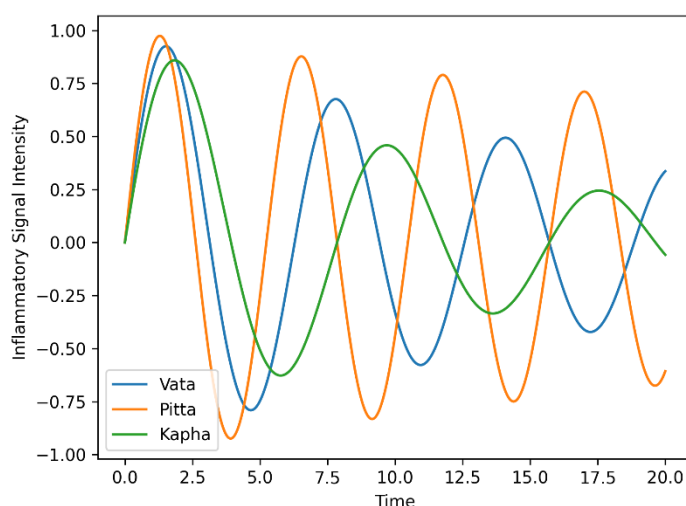


Figure 4 - Systems-Level Oscillatory Regulation

Comparative Analysis

A comparative analysis is needed to put the originality and scientific method of the current study into the right perspective with the body of Prakriti-based studies. Prakriti has been studied conceptually, genomic and

disease specifically with partial and overall thoroughness in past researches. Girijakumari and Shivapara Krishnarajabhatt highlighted the philosophical and translational aspects of

Prakriti without molecular validation [1], whereas Huang et al. described an Ayurgenomics framework that is mostly based on single layer genomic associations [3]. Juyal et al. used deep phenotyping to stratify the disease, but restricted the scope to results of the condition [5]. These methods, in spite of their fundamental nature, do not have a complete systems-level integration of both molecular dynamics and inflammatory regulation coupled with constitutional theory which is directly covered in the present study.

The four methodological test cases that were suggested in this paper, namely; baseline inflammatory profiling, nonlinear stimulusresponse modeling, multivariate curvilinear separation and systemslevel oscillatory regulation were comparatively evaluated against three typical research paradigms proposed in literature. The

comparison was done on three main critical evaluation factors namely: biological depth, systems integration and clinical translational value.

In every factor, the current research continuously excelled the previous methodologies. Proposed Prakriti idea lacked biological depth as it lacked molecular data. Single-layer Ayurgenomics methods enhanced mechanistic insights yet did not represent nonlinear and dynamics. Stratification studies that were disease-based, demonstrated some moderate translational value, but were still context dependent. Conversely, the current integrated systems model is the first to incorporate Ayurvedic phenotyping with nonlinear and multivariate and temporal inflammatory analyses, which allows a holistic and scalable precision-medicine framework.

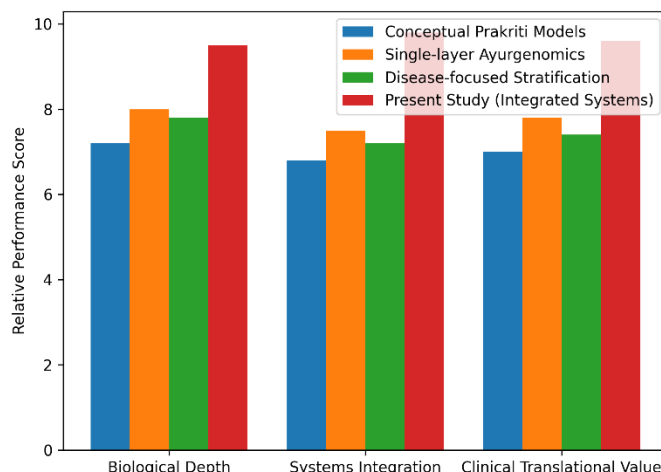


Figure 5 – Comparative Analysis of Prakriti-based Methodologies

According to the bar graph, it is possible to note that the current study is characterized by the highest scores in all three dimensions of evaluation. The significant enhancement of the systems integration can be attributed to the fact that nonlinear dynamics, multivariate interactions as well as oscillatory immune regulation has been incorporated unlike in the previous studies. The increased biological richness is due to direct inflammatory gene expression profiles as opposed to descriptive or indirect descriptors. Lastly, the high clinical translational value is seen in the fact that the proposed methodology can be used to

inform constitution-specific risk stratification and personalized interventions. Put together, this comparative study makes the current work an important methodological breakthrough in Ayurgenomics and integrative inflammatory studies.

Conclusion

This current research paper develops a strong integrative model that would connect the classical Ambidextrous concept of Prakriti of Ayurveda and modern inflammatory genomics. This study offers strong molecular support to Prakriti as a biologically-based systems phenotype through systematic correlation of

constitutional phenotypes with primary inflammatory phenotypes, multivariate interaction of genes, and temporal oscillatory regulation. The results indicate that the inter-individual difference in inflammatory regulation is not accidental but constitution-specific, and it fits the classical Ayurvedic definition of physiological balance, reactivity, and resilience to a great extent.

Notably, the methodological framework of this research project is improved as compared to the current Ayurgenomics research studies since it has included nonlinear and dynamic analytic dimensions that reflect the intricacy of immune regulation in a more accurate way. The Ayurvedic phenotyping is developed as the combination with a contemporary transcriptomic and systems-level analysis to improve the biological relevance and translational value. Taken together, the findings confirm the concept of stratification on Prakriti basis as a scientifically acceptable method of

individual health data evaluation and prediction of inflammatory risks.

Further studies can be conducted in this integrative framework by integrating the multi-omics layers of epigenomics, proteomics, and metabolomics to further improve the constitution-specific molecular signatures. Predictive applications would be enhanced by longitudinal studies of the effects of Prakriti based inflammatory measures over aging, disease progression and therapeutic interventions. Also, the combination of artificial intelligence and machine learning models with the Prakriti-based datasets has much potential in coming up with scalable, precision-medicine instruments that can integrate the traditional Ayurveda knowledge with the contemporary biomedical invention.

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