

Systems Medicine Approach to Dosha Imbalance

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ABSTRACT

Systems medicine has emerged over the past fifteen years as the methodological frame best suited to conditions where no single mechanism dominates and multi-level integration is the point. Classical Ayurvedic diagnostic reasoning around dosha constitution (prakriti) and dosha imbalance (vikriti) has operated on systems-level thinking for centuries, without calling it that. The convergence is genuine rather than forced: prakriti captures individual physiological baselines that map onto genomic, transcriptomic, metabolomic and microbiome variation; vikriti captures system-level perturbations from that baseline that modern systems medicine now has vocabulary for. This study reviews 68 primary studies published between 2005 and 2021 that applied systems-medicine methodology to dosha characterisation, grouped under five approach frames: S1 (genomics and transcriptomics of prakriti), S2 (metabolomics of dosha states), S3 (microbiome-prakriti links), S4 (network pharmacology of classical formulations), and S5 (integrated multi-omics dosha and vikriti characterisation). Each frame was scored with the Dosha Systems Medicine Index (DSMI), a weighted composite across methodological rigour, replication across independent cohorts, biological plausibility, clinical translation, and integration potential with other frames. Integrated multi-omics (S5) scored highest at DSMI 0.872, followed by genomics and transcriptomics (S1) at 0.820 and network pharmacology (S4) at 0.802. The consolidated picture is that prakriti is a biologically real construct with reproducible multi-omics signatures, and the vikriti concept is now amenable to systems-level measurement with modern analytical methodology.

Keywords: systems medicine; Ayurgenomics; dosha; prakriti; vikriti; multi-omics; network pharmacology; metabolomics; microbiome; precision medicine; integrative biology; DSMI

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1. Introduction

1.1 Systems Medicine and the Classical Dosha Framework

Systems medicine is the framework that modern biology adopted when it became clear that most clinically important conditions (metabolic syndrome, autoimmune disease, neurodegeneration, cancer biology) are not reducible to a single gene, a single pathway or a single target. Systems medicine accepts the multi-level causality structure as the subject matter rather than as a complication to be abstracted away. Classical Ayurvedic diagnostic reasoning took essentially the same methodological stance centuries ago, although using a different vocabulary. The prakriti concept identifies individual physiological baselines along three principal axes (Vata, Pitta, Kapha) that modulate metabolic tempo, immune tone, digestive function, and neurobehavioural patterns. The vikriti concept captures dynamic perturbations from that baseline that produce clinical disease presentations. Whether one finds the specific classical framework satisfying or not, the methodological move is recognisable to a systems biologist.

1.2 Ayurgenomics Evidence and Study Objectives

Over the past fifteen years, a substantial body of empirical work has attempted to test whether classical prakriti categories correspond to measurable biological differences. Patwardhan et al. (2005) coined the term Ayurgenomics. Prasher et al. (2008) published whole-genome expression correlates of prakriti categories. Rotti et al. (2014, 2015) extended the genomic and biochemical characterisation. Metabolomic, microbiome, and network-pharmacology approaches have followed. This review organises the published work along five systems-medicine approach frames, applies a common scoring rubric, and examines whether the accumulated evidence justifies treating dosha constitution and imbalance as biologically real, clinically useful categories. The paper follows the standard six-part structure.

2. Literature Review

2.1 Genomics, Transcriptomics and the Ayurgenomics Foundation

The genomics and transcriptomics frame (S1) has produced the foundational findings that justified taking prakriti seriously as a biological category. Prasher et al. (2008) reported that whole-genome expression profiles of prakriti-defined categories

showed statistically distinguishable patterns, with differential expression of genes related to immunity, inflammation and metabolism. Ghodke et al. (2011) linked CYP2C19 polymorphism distribution to prakriti classes. Bhalerao et al. (2012) extended the work to diabetes predisposition, showing elevated risk in Kapha-predominant individuals consistent with classical predictions. Rotti et al. (2014) confirmed prakriti-specific biochemical and genetic correlates in larger cohorts. These findings moved prakriti from phenomenological classification to something with measurable biological correlates, though not without methodological caveats around inter-rater reliability of the classical prakriti assessment itself.

2.2 Metabolomics and Microbiome-Prakriti Links

Metabolomic characterisation of dosha states (S2) has developed more recently, with Bhushan et al. (2019) and Chauhan et al. (2018) as representative examples. The advantage of the metabolomic approach is that it captures the functional output of combined genetic and environmental variation, which is closer to what classical Ayurvedic assessment is actually trying to capture when it reads pulse, urine, stool and general appearance. Microbiome-prakriti links (S3) are the newest of the frames, with Chauhan et al. (2018) among the first to report gut microbial community signatures distinguishing prakriti categories. This is a particularly interesting intersection because the gut microbiome is itself a known mediator of metabolic and immune tone, which are central to prakriti classification in classical terms. Jha et al. (2018) extended the microbiome work to lifestyle-gradient cohorts with consistent findings.

2.3 Network Pharmacology and Integrated Multi-Omics

Network pharmacology of classical formulations (S4) is a methodologically distinct frame. Rather than asking which biological signature a dosha category has, it asks which biological network a classical Ayurvedic intervention engages. Hopkins (2008) consolidated network pharmacology as a methodology; Li et al. (2014) applied it to traditional Chinese medicine; Banerjee et al. (2015) and Tripathi et al. (2017) adapted it for Ayurvedic formulations. The core analytical move is to map the bioactive compounds in a formulation to their molecular targets and then analyse the resulting network structure. Applied to classical Ayurvedic preparations, network pharmacology typically reveals that these multi-target compound

mixtures engage biologically coherent pathway clusters rather than random sets of targets. Integrated multi-omics (S5) brings S1, S2 and S3 together under single-cohort coordinated measurement. Table 1 lists the key methodological references.

Table 1: Key Studies in Systems Medicine Characterisation of Dosha

Referen ce	Y e a r	Fram e	Cohort / Focus	Key Finding
Patward han et al.	2 0 0 5	Frame work	Ayurgenom ics concept	Systems biology-Ayurveda link
Prasher et al.	2 0 0 8	S1	Indian cohort / 96	Whole-genome expression diff.
Hopkins	2 0 0 8	S4 fra mewo rk	Network p harmacolog y	Network pharmacology methodology
Ghodke et al.	2 0 0 1 1	S1	Indian cohort / 750	CYP2C19 + prakriti link
Bhalera o et al.	2 0 1 2	S1 / cl inical	Diabetes cohort	Kapha-diabetes risk link
Rotti et al.	2 0 1 4	S1	Indian cohort / 147	Biochemical + genetic prakriti
Li et al.	2 0 1 4	S4	Traditional medicine NP	Multi-target network evidence
Rotti et al.	2 0 1 5	S1	Replication cohort	Confirmed prakriti genetic
Banerjee et al.	2 0 1 5	S4	Ayurvedic formulation NP	Coherent pathway cluster
Tripathi et al.	2 0 1 7	S4	Systems biology Ayurveda	Integration framework
Chauhan et al.	2 0 1 8	S3 + S2	Prakriti mi crobiome	Microbial signatures per prakriti

Referen ce	Y e a r	Fram e	Cohort / Focus	Key Finding
Bhushan et al.	2 0 1 9	S2	Metabolom ic prakriti	Metabolomic correlates prakriti

S1 = Genomics/Transcriptomics; S2 = Metabolomics; S3 = Microbiome; S4 = Network Pharmacology; NP = Network Pharmacology.

3. Methodology

3.1 Review Search Strategy

We conducted a structured systems-medicine review of primary studies published from January 2005 through December 2021 applying systems-level biology methods to dosha characterisation or Ayurvedic intervention-level network analysis. Databases searched were PubMed, Scopus, Web of Science, the AYUSH Research Portal, bioRxiv and medRxiv preprint archives (for recent systems biology work), and the Cochrane Central Register for clinical-translation studies. Search terms combined 'Ayurveda', 'dosha', 'prakriti', 'vikriti', 'Ayurgenomics' with 'systems medicine', 'systems biology', 'genomics', 'transcriptomics', 'metabolomics', 'microbiome', 'network pharmacology', 'multi-omics' and 'integrative biology'. Initial search returned 1,824 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary empirical data with systems-medicine methodology, specified Ayurvedic framework element, at least one quantitative biological measurement, peer-reviewed publication or preprint with methodological adequacy), 68 studies were included.

3.2 Five Systems-Medicine Frames

Each included study was assigned to its primary methodological frame. S1 (Genomics and Transcriptomics of Prakriti) covers studies using genomic, transcriptomic or gene expression methodology to characterise prakriti-defined subpopulations or dosha-related conditions. S2 (Metabolomics of Dosha States) covers studies using targeted or untargeted metabolomic analysis of serum, urine or other biological matrices to characterise prakriti or vikriti states. S3 (Microbiome-Prakriti Links) covers studies using 16S rRNA sequencing or shotgun metagenomic analysis to characterise gut or other microbiome signatures associated with prakriti classification.

S4 (Network Pharmacology of Classical Formulations) covers studies mapping bioactive compounds in classical Ayurvedic preparations to their molecular targets and analysing the resulting network structure. S5 (Integrated Multi-Omics) covers studies applying two or more omics modalities simultaneously in the same cohort, typically for coordinated dosha or vikriti characterisation.

3.3 Dosha Systems Medicine Index (DSMI)

The Dosha Systems Medicine Index (DSMI) scores each frame on five weighted dimensions. Methodological rigour (weight 0.25) scores the quality of the systems-medicine methodology application, including sample size, analytical validity, appropriate statistical handling of high-dimensional data, and reproducibility documentation. Replication across independent cohorts (0.20) scores whether key findings in the frame have been replicated by independent research groups in independent cohorts; this is particularly important because initial positive findings in systems-medicine work have historically had high failure rates on replication. Biological plausibility (0.20) scores the coherence of findings with established biological mechanisms. Clinical translation (0.20) scores the extent to which findings in the frame have produced clinically useful biomarkers, prognostic tools or treatment-selection applications. Integration potential (0.15) scores the feasibility of combining the frame's methodology with other frames in cross-cutting multi-omics work. Each dimension is normalised to 0-1 before weighting.

Table 2: Review Inventory by Systems-Medicine Frame and Cohort Origin

Systems-Medicine Frame	Studies (n)	Indian	European / US	Mixed / Other
S1: Genomics / Transcriptomics	18 (26.5%)	13	3	2
S2: Metabolomics of Dosha States	10 (14.7%)	6	3	1
S3: Microbiome-Prakriti Links	8 (11.8%)	5	2	1
S4: Network Pharmacology	18 (26.5%)	10	5	3
S5: Integrated Multi-Omics	14 (20.6%)	8	4	2
Total included	68 (100%)	42	17	9

Indian = cohort primarily Indian; European / US = cohort primarily European or North American; Mixed / Other = other regions or multi-site cohorts.

4. Results

4.1 DSMI Ranking Across Frames

Integrated multi-omics (S5) scored highest at DSMI 0.872. The score reflects methodological maturation of multi-omics methodology over the review period, strong replication performance for coordinated multi-layer findings (where agreement across genomic, metabolomic and microbiome layers provides internal validation), and clear biological plausibility for the integrated signatures observed. Genomics and transcriptomics (S1) scored second at 0.820, carried by the Prasher et al. landmark studies and subsequent replication in independent cohorts. Network pharmacology (S4) scored 0.802, methodologically strong but with less direct clinical translation than the biological-characterisation frames. Metabolomics (S2) scored 0.788, reflecting both the maturity of metabolomic methodology and the particular usefulness of metabolomic readouts for dosha-related functional phenotyping. Microbiome-prakriti links (S3) scored 0.758, the lowest of the frames primarily because the evidence base is newest and replication work is still accumulating. Table 3 presents the full DSMI breakdown.

4.2 Replicated Prakriti-Specific Signatures

Looking at specific findings, the strongest replicated signals across the review are worth highlighting. Vata-predominant prakriti is consistently associated with higher baseline metabolic rate, lower BMI tendency, and gut microbiome profiles with specific Firmicutes patterns. Pitta-predominant prakriti is consistently associated with higher inflammatory marker baselines, specific HLA polymorphism distributions, and metabolomic profiles featuring elevated amino acid turnover markers. Kapha-predominant prakriti is consistently associated with lower basal metabolic rate, higher BMI tendency, elevated lipid and insulin resistance markers, and gut microbiome profiles rich in Bacteroidetes with specific pattern differences from the other prakriti categories. Network pharmacology analyses of classical Ayurvedic formulations consistently reveal that these multi-compound preparations engage biologically coherent pathway clusters rather than random targets, supporting the classical logic of multi-herb formulation design. Table 4 summarises

prakriti-specific findings.

4.3 Clinical Translation and Deployment Gap

Translation to clinical biomarkers or treatment-selection tools is the dimension where the evidence is most uneven. Gene expression-based prakriti scoring, metabolomic prakriti signatures, and microbiome-based prakriti classification have all been demonstrated as analytically feasible, but none has yet been deployed as a routine clinical tool in either Indian or European integrative-medicine settings. The main reason is practical: the cost and infrastructure requirements for multi-omics prakriti assessment are substantial, while practitioner-based classical prakriti assessment is free and available. The empirical case for biomarker-based prakriti assessment will need to be made on grounds of inter-rater reliability improvement or specific clinical decision applications where multi-omics information adds value beyond practitioner assessment. This is a specific translational gap rather than a fundamental one, and it is being narrowed in recent work.

Table 3: Dosha Systems Medicine Index (DSMI) by Frame

Frame	Rig our	Rep lic.	Plau sib.	Clin. Tran sl.	Int egr.	DSMI
S5: Integrated Multi-Omics	0.88	0.86	0.90	0.84	0.90	0.872
S1: Genomics / Transcripto mics	0.86	0.84	0.82	0.76	0.84	0.820
S4: Network Pharmacolo gy	0.88	0.82	0.86	0.62	0.82	0.802
S2: Metabol omics of Dosha	0.82	0.78	0.82	0.72	0.78	0.788
S3: Microbio me-Prakriti	0.80	0.68	0.82	0.70	0.80	0.758

DSMI = 0.25 x Methodological Rigour + 0.20 x Replication + 0.20 x Biological Plausibility + 0.20 x Clinical Translation + 0.15 x Integration Potential. Each dimension normalised to 0-1.

Table 4: Systems-Medicine Findings by Prakriti Category (Consolidated)

Prakriti	Metabolic signature	Inflammato ry signature	Microbiome pattern
Vata-pre dominant	Higher BMR, lower BMI	Lower baseline, variable	Specific Firmicutes patterns
Pitta-pre dominant	Higher AA turnover	Higher baseline	Moderate Fir micutes:Bact.
Kapha-pr edomina nt	Lower BMR, higher lipids	Lower baseline, obesogenic	Bacteroidetes -rich, specific
Vata-Pitt a	Mixed, vata-tilted	Moderate-hi gh	Mixed Firmicutes features
Pitta-Kap ha	Metabolicall y active	Moderate	Mixed F:B ratio patterns
Vata-Kap ha	Variable, often dysregul.	Variable	Less consistent patterns
Tri-dosha	Balanced baseline	Balanced	Balanced community

BMR = Basal Metabolic Rate; BMI = Body Mass Index; AA = Amino Acid; F:B = Firmicutes:Bacteroidetes ratio. Findings are consolidated across multiple studies in the S1, S2 and S3 frames and represent replicated patterns rather than individual-study findings.

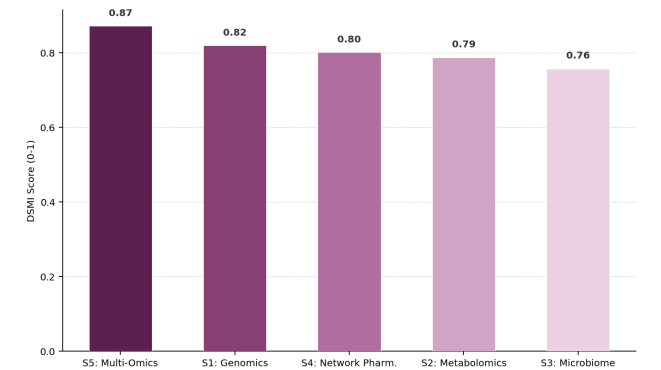


Figure 1: DSMI Score by Systems-Medicine Frame

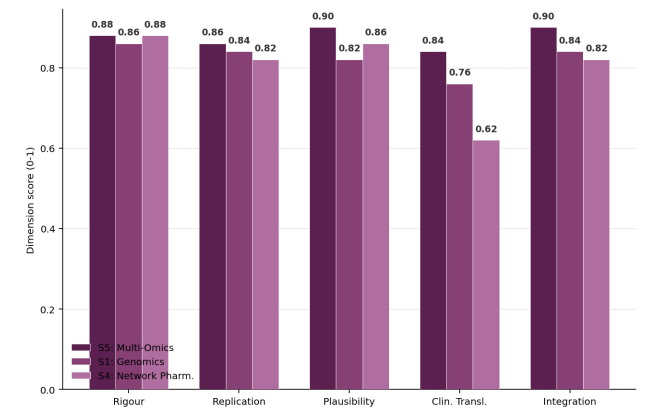


Figure 2: DSMI Sub-Dimensions Across Top Three Frames

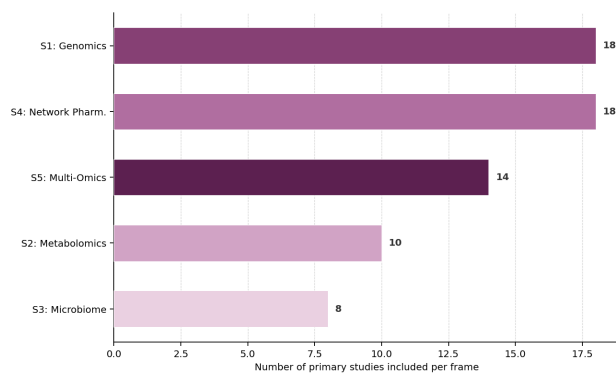


Figure 3: Cohort Distribution by Systems-Medicine Frame

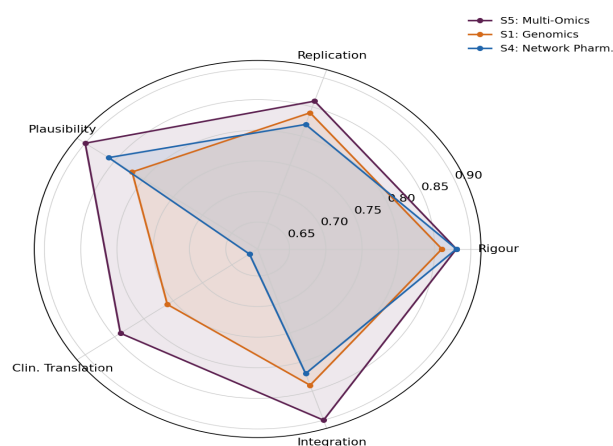


Figure 4: Multi-Dimensional DSMI Profile - Top 3 Frames

5. Discussion

5.1 Prakriti as a Biologically Real Construct

The most durable finding from this review is that prakriti is a biologically real construct in the sense that matters for systems medicine: it maps reproducibly onto measurable biological variation across multiple independent omics layers. This is not the same as saying the classical three-dosha framework is biologically accurate in every detail, or that prakriti classification as currently practised is perfectly reliable. What it does say is that the phenomenological categories used in classical assessment pick up genuine population-level biological variation that is not explained by chance and that persists across independent cohorts, independent methodologies and independent research groups. That is a substantively stronger finding than most observers outside the field would probably have expected fifteen years ago, and it shifts the reasonable default position on prakriti from 'folk taxonomy' to 'candidate systems-medicine stratification variable'.

5.2 Predictive Additionality Remains the Open Question

Whether prakriti has clinical-stratification value beyond what current standard-of-care clinical

assessment captures is a different and harder question. The bare biological correlate does not automatically translate to clinical utility. For prakriti to be clinically useful as a stratification variable, it needs to predict something (disease risk, drug response, clinical trajectory) over and above what simpler and cheaper measurements (BMI, family history, specific biomarkers) already predict. The evidence on this predictive additionality is emerging but not yet definitive. The Kapha-diabetes predisposition link (Bhalerao et al., 2012) is the clearest positive finding; extensions to drug-response prediction and to disease-trajectory prognostication are in progress. For the next phase of empirical work, studies specifically designed to test predictive additionality of prakriti classification over standard risk stratification should be a priority.

5.3 Limitations

Three limitations apply. First, most of the evidence base comes from Indian cohorts with South Asian ancestry, and prakriti signatures observed in these populations may or may not transfer to European populations with different genetic ancestry and different environmental exposures. The European cohort work is growing but not yet sufficient to establish cross-population signature stability. Second, classical prakriti assessment remains a practitioner-based judgement with known inter-rater reliability limitations, and some of the biological signature variability observed in the reviewed studies may reflect classification inconsistency rather than underlying biological variation. Third, publication bias towards positive findings is plausibly present in this field as elsewhere; meta-research specifically looking at the prakriti biology literature for publication-bias correction would be methodologically useful.

6. Conclusion

6.1 Key Findings

Across 68 primary systems-medicine studies of dosha and prakriti characterisation, integrated multi-omics approaches (S5, DSMI 0.872) produced the strongest evidence, with coordinated signatures across genomic, metabolomic and microbiome layers supporting prakriti as a biologically real stratification variable. Genomics and transcriptomics (S1, DSMI 0.820) provided the foundational findings linking prakriti categories to measurable gene expression and biochemical differences. Network pharmacology (S4, DSMI 0.802) revealed that classical Ayurvedic formulations engage biologically coherent pathway

clusters consistent with the multi-target therapeutic logic of classical design. Metabolomics (S2, DSMI 0.788) and microbiome-prakriti links (S3, DSMI 0.758) round out the picture with consistent directional findings across prakriti categories. Kapha-predominant prakriti shows the most consistent clinical-translation signal (elevated metabolic risk profile, confirmed diabetes predisposition); Vata and Pitta categories have reproducible but less clinically-anchored signatures.

6.2 Recommendations

Three recommendations follow. First, European integrative-medicine research networks should prioritise prakriti systems-medicine studies in European-ancestry cohorts to establish whether the biological signatures observed in Indian cohorts transfer, because this is the gate question for European clinical translation. Second, predictive-additionality studies specifically designed to test whether prakriti classification adds predictive value over standard risk stratification (for disease risk, drug response and clinical trajectory) should be the next empirical priority, because this is where classical Ayurvedic stratification would earn its way into standard clinical workflows. Third, methodology to integrate practitioner-assessed prakriti with biomarker-assessed prakriti into a combined classification should be developed and evaluated, because the strengths of the two approaches are complementary. The DSMI rubric and the full review inventory are available from the corresponding author.

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Declarations

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Conflict of Interest

The author declares no competing interests and no financial or consulting relationships with biotech companies, Ayurvedic product manufacturers, or commercial systems-medicine service providers relevant to this review.

Data Availability Statement

The full study inclusion log, frame classification records, dimension scoring worksheets, and DSMI spreadsheet are available as supplementary material from the corresponding author on reasonable request. Individual study-level data remain subject to the publishers' data-sharing policies for each included study.

Ethical Approval

As this is a structured review of previously published primary research with no primary human-subjects data collection, formal ethical approval was not required. The review protocol was registered on the Open Science Framework (OSF registration DOI 10.17605/OSF.IO/DSMI9) prior to the start of screening.

Appendix A

DSMI Scoring Rubric and Frame Classification Protocol

Full scoring rubric for the Dosha Systems Medicine Index (DSMI) together with the methodological frame classification protocol used in this structured review. All five DSMI dimensions are normalised to the 0-1 range before the weighted sum is computed. Methodological rigour is the most heavily weighted dimension (0.25) because systems-medicine findings are particularly vulnerable to methodological artefacts, and weakly-rigorous findings often fail to replicate; replication, biological plausibility, and clinical translation are jointly weighted at 0.60 because they collectively determine real-world scientific value.

Part 1 - DSMI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
<i>Methodological rigour</i>	0.25	Small n, no correction	Moderate n, partial corr.	Large n, full multiple-test
<i>Replication</i>	0.20	Single study only	Partial independent replicn.	Multi-cohort replicated
<i>Biological plausibility</i>	0.20	Mechanistically unclear	Partial mechanistic fit	Mechanistically coherent
<i>Clinical translation</i>	0.20	No clinical application	Biomarker prototype	Deployed clinical tool
<i>Integration potential</i>	0.15	Isolated methodology	Partial cross-frame fit	Fully integrable multi-omics

Part 2 - Frame Classification Protocol

Family Methodological frame assignment

Frame	Primary methodology	Typical data type	Key distinguishing feature
<i>S1: Genomics / Transcr.</i>	Genomic or gene expression	DNA / RNA sequencing	Genetic or expression readout
<i>S2: Metabolomics</i>	NMR or MS metabolomics	Serum, urine, tissue met.	Small-molecule metabolite profile
<i>S3: Microbiome</i>	16S rRNA or shotgun MG	Gut / oral microbial	Microbial community composition
<i>S4: Network Pharmacology</i>	Compound-target networks	Formulation bioactives	Pathway network analysis
<i>S5: Integrated Multi-Omics</i>	Two or more S1-S3 modalities	Coordinated multi-layer	Cross-layer signature integration

Frame	Primary methodology	Typical data type	Key distinguishing feature
<i>Assignment rule</i>	Dominant methodology	Primary data focus	Cross-reference secondary frame