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Short Review

Prakriti phenotypes as a stratifier of gut microbiome: A new frontier in personalized medicine?

Apoorva Jnana [a], Thokur Sreepathy Murali [a], Kanive Parashiva Guruprasad [b, d], Kapaettu Satyamoorthy [c, d, *]

[a] Department of Biotechnology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India
[b] Department of Ageing Research, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India
[c] Department of Cell and Molecular Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India
[d] Centre for Ayurvedic Biology, Manipal School of Life Sciences, Manipal Academy of Higher Education, Manipal, 576104, India

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ABSTRACT

Ayurveda has a rich history and its significance woven deeply in the Indian culture. The concept of *prakriti* (a person's "nature" or constitutional type determined by the proportion of three doshas, namely - *vata*, *pitta* and *kapha*) in Ayurveda is deeply rooted in personalized health management. While the attributes of *prakriti* has been established to have a genomic basis, there is dearth of elaborate evidences linking *prakriti* with manifestation of diseases. Next generation sequencing studies have provided a causal link between variation in the gut microbiome and its effect on an individual's fitness. Separately, reports have identified gut microbial patterns associated with several host variables such as geography, age, diet and extreme *prakriti* phenotypes. Recently, few reports have identified a "core gut microbiome" consisting of *Bacteroides, Faecalibacterium, Prevotella* and *Ruminococcus* prevalent across the Indian population; however, a few bacterial genera were specifically enriched in certain *prakritis*. Hence, in this review we aim to analyse the role of *prakriti* variations on dysbiosis of the gut microbiome and concomitantly its effect on human health. We suggest that *prakriti* phenotyping can function as a potential stratifier of the gut microbiome in a given population and may provide evidence for the conceptual framework of personalized medicine in Ayurvedic system of medicine.

1. Introduction

As a discipline of "Upveda", Ayurveda is an ancient knowledge with rich history and significance woven deeply in the Indian culture [1]. It represents the Indian system of 'personalized medicine' whose primary aim is maintenance of health and eradication of disease [2–4]. Ayurveda involves disease prevention and alleviation by largely focusing on the host rather than the disease [5]. A large emphasis is laid on the knowledge of disease manifestation and its progression in relation to the host effects such as their environment factors, life style practices, dietary intake along with herbal and traditional medicines, making it highly personalized to the patient [6]. These treatment practices are analogous to the recent trends in contemporary medicine that place emphasis on disease alleviation *via* lifestyle and dietary changes [7–9].

Intrinsic heterogeneity among individuals of a population can drastically alter the treatment response and disease outcome. There are three essential doshas described in Ayurveda (*vata*, *pitta* and *kapha*) whose balanced and imbalanced states determine health and disease respectively of an individual. *Prakriti* is defined as the constitution of the human body from birth to death in terms of the three doshas and any deviation or imbalance of the three doshas will have pathological consequences (termed as *Vikruti*) [10]. The concept of *prakriti* (a person's "nature" or constitutional type in terms of the three doshas) in Ayurveda and its relationship with genomics was hypothesized over a decade ago and recent studies suggest that the phenotypic classification of India's traditional medicine has a clear genomic and epigenomic basis. This *prakriti*-based maintenance of personalized health essentially embodies the recent concept of personalized medicine [11]. "*Prakriti*" assignment involves phenotyping of an individual based on several

* Corresponding author.
E-mail: ksatyamoorthy@manipal.edu
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characteristics including body frame, food and bowel habits, disease resistance and healing capabilities, memory retention, metabolism, etc. [12]. For instance, there are a few characteristics and diseases explicitly reported to be associated with *vata*, *pitta* or *kapha* phenotypes. *Vata prakriti* individuals tend to show dry skin and hair, lean phenotypes and are susceptible to fatigue, nervous system related disorders, insomnia, among others. *Pitta prakriti* individuals are strong-willed personalities with a tendency to develop inflammation related disorders, ulcers while *kapha prakriti* individuals tend to be heavy with bones, muscle and fat with increased susceptibility to respiratory disorders and obesity associated comorbid conditions [13].

It has long been known that Ayurveda practices include systems based framework analysis for the promotion of health and prevention of diseases. However, several principles and concepts of this ancient knowledge need rigorous scientific evidence and the efforts are ongoing. It is in this context that attempts have been made to decipher relationships between gut microbiome and *prakriti*. In this review, we have attempted to relate recent gut microbiome discoveries with *prakriti* phenotypes to enable clinicians to offer better disease management strategies based on an individual's *prakriti* type.

2. Association of gut microbiome with health and disease

Human microbiome studies have received much attention in recent years, with focus on the intimate association of human health with the gut microbiome [14]. Inoculated at birth, the gut microbiota colonizes the human intestine and gradually begins to play crucial roles that may influence a wide range of host responses including neural, inflammatory and digestive traits [11]. The composition of gut microbiota varies among different individuals reflecting variations of digestion/metabolism capabilities of the individual [15,16]. Dysbiosis of the gut microbiome is associated with large spectrum of diseases ranging from inflammatory bowel disease [17], colorectal cancer [18] to autism [19]. The plasticity of the gut microbiome provides a favourable scientific measure to explain the behaviour of the various *prakriti*s as described in Ayurveda. The growing body of evidence suggests diet as an important external factor that can modulate gut microbiota and in turn affect human health [8,16,20,21], similar to the dietary and lifestyle changes recommended as one of the treatment modalities in Ayurveda. A few studies have suggested a possible stratification of the gut microbiome (either as an enterotype or as a continuum) [22,23] to enable its translation to healthcare applications such as diagnosis, biomarkers for disease progression and several others [24]. However, the need to classify a complex, heterogeneous population into discrete sets of homogeneous entities can lead to erroneous conclusions [25]. We propose that establishing gut microbiome signatures with *prakriti* phenotypes can enable an efficient population stratification method while providing scientific evidence for the personalized medicine concept of Ayurveda.

3. Gut microbiome of the Indian population

Several studies have demonstrated the composition of the gut microbiome of various populations including from USA, Europe and Japan to be primarily enriched in *Bacteroidetes* and *Prevotella* [25,26]. Studies indicate that the changes in the composition, diversity and abundance of gut microbiome are affected by several variables including medication (consumption of antibiotics), blood parameters such as RBC count and haemoglobin concentration, bowel habits, dietary composition, health status, anthropometric features, lifestyle and gender. For instance, while Lopez-Siles et al. [27] found decreased abundance of genus *Faecalibacterium* in subjects with ulcerative colitis, Falony et al. [28] found higher richness and evenness of members of *Clostridia* and hydrogenotrophic methanogens among females, individuals with low birth weight and a longer intestinal transit time. In a country like India, there is a significant diversity in ethnicity, diet, disease susceptibility and several other host variables which may also influence the gut microbiome composition [29]. Hence, studying the Indian gut microbiome and its association with various factors including *prakriti* phenotypes is challenging and may provide more clues towards *prakriti* based disease management.

Recently, there have been a few studies (see Table 1) conducted to test the association of the Indian gut microbiome of healthy adults with various factors such as geography, age, gender, diet and/or *prakriti*. Briefly, Dhakan et al. [30] carried out a gut microbiome study of the Indian population including samples representing northern (LOC1) and southern part (LOC2) of India (n = 110), encompassing wide diversity in lifestyle and dietary habit patterns across the two regions. Using multi-omic approaches including 16S marker-based metagenomics, whole genome metagenomics and mass spectrometry-based profiling, they found significant differences in the composition of the gut microbiome across the two regions. While the gut microbiome from northern Indian population was significantly associated with *Prevotella*, the southern India cohort was associated with *Bacteroides, Faecalibacterium* and *Ruminococcus*. They observed enrichment of metabolic pathways involved in degradation of complex polysaccharides in Indian gut microbiome which concurs with the general dietary patterns in India (plant-based, carbohydrate rich diet). In another study, Das et al. [31] studied the gut microbiome of rural and urban healthy individuals living in sea level and high-altitude areas (n = 84) of Haryana and Leh, Ladakh in northern India *via* 16S marker-based metagenomics. They found *Firmicutes* to be predominant over Bacteroidetes followed by bacteria belonging to phyla Actinobacteria and Proteobacteria. Chauhan et al. [32] used a similar approach to analyse the microbial composition of 135 individuals from a single geographical location in India. They also found higher abundance of *Bacteroidetes* and *Firmicutes*. Taxonomic analyses of the core bacterial groups showed female core gut microbiome to additionally include *Clostridium, Turicibacter* and *Odoribacter* while *Streptococcus, Slackia* and *Collinsella* were additionally found in males. Dubey et al. [33] performed the largest study to date of the Indian gut microbiome profiling 1004 individuals with equal proportions of obese and non-obese individuals uniformly distributed across the major geographical regions of India. They reported an increased abundance of *Prevotella* and *Faecalibacterium* in Indian gut microbiome with 390 species of 990 being shared across individuals from different geographies. Chaudhari et al. [34] analyzed the gut microbiome of 53 individuals from Pune, Maharashtra and reported a similar conclusion as that of Chauhan et al. [32] with higher abundance of Bacteroidetes followed by Firmicutes. The top 3 abundant genera were *Prevotella, Bacteroides* and *Dialister*. Chaudhari et al. [35] analyzed the association of age with gut microbiome by studying 54 genetically linked individuals (encompassing samples from 6 joint families) with similar diet, ethnicity and geographical locations. They observed an increase in the members of Proteobacteria and decrease in genus *Bacteroides* with increasing age. Tandon et al. [36] studied the gut microbiome of 80 individuals residing in Ahmedabad, Gujarat and found the gut microbiome to be dominated by phyla Bacteroidetes and Firmicutes which is in agreement with results obtained from most of the studies conducted earlier.

All these studies, in spite of their inherent differences, have essentially attempted to stratify the gut microbiome composition based on population taking into due consideration the variance caused by geography, diet and age. However, there are some

Table 1
A comparison of the papers published in the last 3 years (2018–2020) with an analysis of the Indian gut microbiome and its associated metadata (such as geography, diet, age and *prakriti*).

Parameters	Chauhan et al. [32]	Das et al. [31]	Tandon et al. [36]	Chaudhari et al. [34]	Dhakan et al. [30]	Chaudhari et al. [35]
Geography	Rural population in Pune (VHDSS)	Rural and urban sea level Ballabhgarh areas, Haryana and rural high altitude areas of Leh, Ladakh	Ahmedabad, Gujarat	Rural population in Pune (VHDSS)	Bhopal (LOC1) and Kerala (LOC2)	Rural population in Pune (VHDSS)
Samples analyzed (male + female)	113 (50 + 63)	84 (45 + 39)	80 (NA)	18 (8 + 10)	110 (58 + 62)	50 (NA)
Sequencing platform	Roche GS FLX	Roche GS FLX	Illumina Miseq	Illumina MiSeq	Illumina NextSeq 500	Illumina MiSeq
Variable region	V2–V6	V1–V5	V3–V4	V3–V4	V3	V3–V4
Core microbiome estimation method	Presence in >50% samples	Presence in >50% samples (abundance $\geq$ 0.01%)	Bootstrapping procedure	NA	MetaHIT algorithm	Presence in >95% samples (abundance $\geq$ 0.1%)
Association parameters	*Prakriti* phenotype	Geography, Diet, Cooking oil	Geography (country), Diet	*Prakriti* phenotype	Geography (country)	Age
Core members described	22	54	52	NA	19[a]	6[b]
Top 2 Phyla	Bacteroidetes and Firmicutes	Firmicutes and Bacteroidetes	Bacteroidetes and Firmicutes	Bacteroidetes and Firmicutes	Bacteroidetes to Firmicutes ratio in LOC1 > LOC2	Bacteroidetes and Firmicutes

[a] For comparison with other studies, the list was curated by maintaining genera identity and only genera found associated with Indian gut microbiome (log odds ratio > 0.5) was considered.
[b] All microbes that passed the "core microbiome" criteria were included irrespective of their individual presence in the sub-cohorts as defined in the study.

differences between the core microbiome (gut microbiota members present across all samples within a study irrespective of the variables) described by these five studies which could be attributed to the following reasons [30–32,35,36]. While the study design for all the reports involved 16S rRNA profiling for taxonomic assignments, the hypervariable regions profiled varied among the five studies. Majority of the studies profiled V3–V4 region while, Das et al. [31] and Chauhan et al. [32] profiled V1–V5 and V2–V6 hypervariable regions respectively.

Dhakan et al. [30] used a stringent classifier to define the core microbiome as proposed by MetaHIT (Metagenomics of the Human Intestinal Tract) [37] and the usage of such stringent analysis parameters could be one of the reasons for the discordance in numbers with the other studies. In addition, the observed variations can be attributed to the dietary preferences of the individuals, the extensive genetic heterogeneity among populations, and the geographical location from where the samples were collected. For instance, though all the studies report a dominance of Bacteroidetes members over Firmicutes, Das et al. [31] reported a higher abundance of Firmicutes compared to Bacteroidetes members. Indian core gut microbiomes from other studies were conducted on a population mainly on a plant-based diet while Das et al. [31] in their study included individuals on animal protein rich diet in addition to fibrous vegetarian diets. This is in concordance with the sub-cohort profile of LOC2 reported by Dhakan et al. [30] who showed a lower Bacteroidetes/Firmicutes ratio in individuals with a similar diet. Dhakan et al. [30] also found clusters within the gut microbiome populations based on dietary habits (predominantly plant based in Northern India and animal based in Southern India). Tandon et al. [36] and Das et al. [31] with similar samples sizes (n = 84 and 80 respectively) identified more bacterial species to be part of the "core microbiome" (>50) which was comparatively different from the other two studies that had a sample size >100. In addition, Chauhan et al. [32] exclusively selected a relatively homogenous population (in terms of ethnicity, language, lifestyle, diet) which was further validated using a panel of SNP markers. Hence, it is possible that similar abundance patterns of gut microbiome were observed between the individuals leading to significantly fewer members constituting the core. It is also quite important to consider that the analysis parameters used for defining the core microbiome is not similar across all the studies.

Das et al. [31] found clear difference in patterns of distribution of core microbiome based on geographical location (lower altitude area of Balabhgarh *vs* high altitude of Leh, Ladakh – both from North India) and dietary patterns. Chauhan et al. [32] and Chaudhari et al. [35] analyzed a similar population subset from Pune (Vadu Health and Demographic Surveillance System (VHDSS) participants) and reported a similar assemblage of core microbiome (Fig. 1) but with varying abundance. This difference in abundance could largely be due to the difference in the definition of "core microbiome" between the two studies. While Chaudhari et al. [35] considered only microbes in >95% of samples with abundance of at least 0.1% for their analysis, Chauhan et al. [32] considered all those microbes present in >50% of samples irrespective of abundance.

Despite the discordance in the microbiome across the studies, we could identify a "core gut microbiome" which can be defined as gut microbes that are prevalent across all geographies irrespective of the dietary patterns, age, *prakriti* or data analysis parameters. Overall, all the five studies identified *Prevotella, Ruminococcus, Faecalibacterium* and *Bacteroides* as part of the "core gut microbiome" in the Indian population (Fig. 2). In spite of the occurrence of "core gut microbiome" in all these studies, some variations were observed with reference to the gut microbiome. Of interest is the association of *Prevotella* with diet. *Prevotella* is usually associated with a plant-based diet [31] and a similar association was seen in other studies as well [32,36]. Chaudhari et al. [35] also cited similar reasons for the abundance of *Prevotella* in their population although no significant association was found between the abundance of *Prevotella* and fibre-rich diet. This is more evident in the study by Dhakan et al. [30] who analyzed two populations with distinct dietary patterns; LOC1 from Bhopal consuming a vegetarian, fibre-rich diet and LOC2 from Kerala consuming a diet rich in meat and fish. *Prevotella* was relatively more abundant in LOC1 in comparison to LOC2. Hence, it is intriguing that Das et al. [31] report higher abundances of *Prevotella* in a population consuming mostly non-vegetarian diet. Further oligotyping of *Prevotella* revealed that the prominent Indian gut microbiomes (independent of location or altitude) were associated with omnivorous diets.

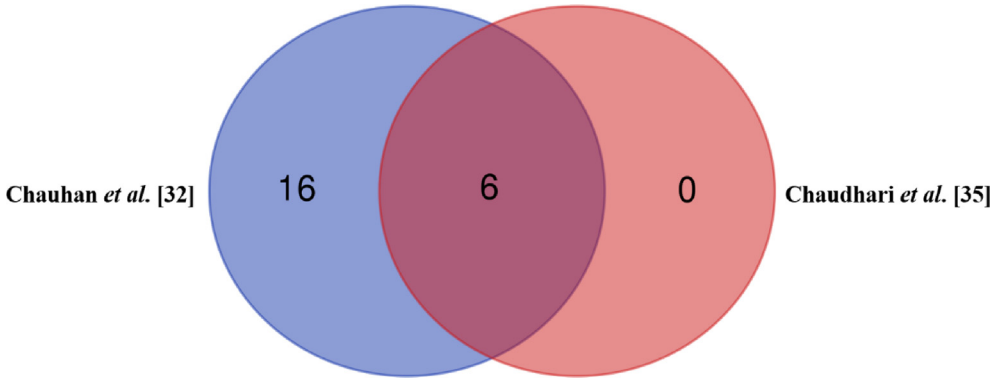

Fig. 1. A comparison of the "core microbiome" by bacterial genera of the Vadu HDSS population surveyed by Chauhan et al. [32] and Chaudhari et al. [35].

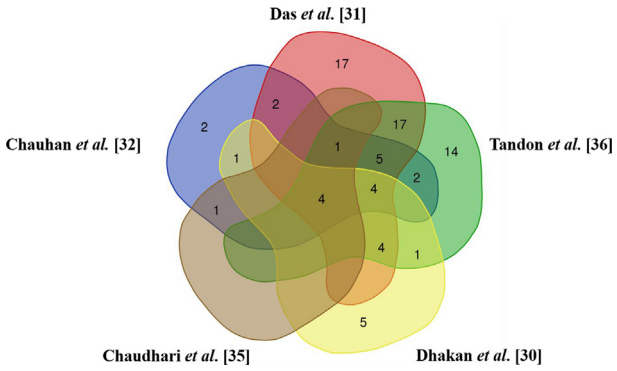

Fig. 2. The "core gut microbiome" derived from the studies by Dhakan et al. [30], Das et al. [31], Chauhan et al. [32], Chaudhari et al. [35] and Tandon et al. [36].

However, it is important to note that the oligotype associations are based on information from the European population and only 7% of the *Prevotella* sequences in the Das et al. [31] study could be oligotyped.

4. Linking *prakriti* with gut microbiome

Earlier studies have established the influence of environment and dietary habits on the composition of the gut microbiome [38]. However, very few have attempted to associate the observed variability in gut microbiome members with *prakriti* types. Chauhan et al. [32] and Chaudhari et al. [34] identified extreme *prakriti* phenotypes (*vata, pitta* and *kapha*) from a population of the VHDSS area in Pune and analyzed for the association between *prakriti* and gut microbiome.

Chauhan et al. [32] studied 135 extreme *prakriti* individuals (48 *kapha prakriti*, 35 *pitta prakriti* and 52 *vata prakriti* individuals) from a single geographical location. They observed dominance of Bacteroidetes and Firmicutes members across all observed *prakriti* phenotypes in both males and females. The core microbiome of females was enriched in phyla Bacteroidetes and Firmicutes while, *Coriobacteriaceae* belonging to Actinobacteria were found to be additionally present in core microbiome of males. On manual curation of the core microbiome members in each group, they identified *prakriti* specific enrichment of bacterial taxa among the different *prakritis* (15 and 2 *prakriti* associated taxon in female and male groups respectively). The gut microbiomes of *pitta* females were enriched in *Blautia luti, Blautia obeum, Blautia torques, Butyricicoccus pullicaecorum, Gemmiger formicilis,* Incertae sedis *mahella* and *Lachnospira eligens,* while that of *pitta* males were enriched in *Roseburia inulinivorans.* Gut microbiome of *kapha* females were characterized by overabundance of *Prevotella copri.* Gut microbiome of *vata* females showed higher abundance of *Bacteroides vulgatus, Blautia stercoris*, *Butyrivibrio crossotus, Clostridium indolis, Eubacterium rectale, Oscillibacter valericigenes* and *Roseburia hominis* while that of *vata* males were associated with *Fusicatenibacter saccharivorans.* Overall, researchers found the male gut microbiome to be more homogenous than the female counterparts. It is worth noting that while the previous studies observed varying trends of bacteria which could be attributed to geographical location and dietary habits, the study by Chauhan et al. [32] was able to offer discriminatory patterns of microbial assemblage within a relatively homogenous cohort in terms of ethnicity, diet, geographic location and socio-cultural lifestyle.

Chaudhari et al. [34] identified 53 individuals (40 *pitta,* 7 *vata* and 6 *kapha prakriti*) of whom, 18 (6 of each *prakriti*) were considered for further analysis. Similar to the results obtained by Chauhan et al. [32], they reported the dominant phyla to be Bacteroidetes and Firmicutes; however, gender-based abundance data was not available. They also found several genera shared between the three *prakriti* phenotypes of which only 5 genera significantly differed in abundance among the three *prakritis*. While, *pitta* individuals were enriched in *Bacteroides* and *Parabacteroides, vata* individuals were enriched in *Desulfovibrio, Slackia* and *Succinivibrio.* No significantly differentially abundant taxa were reported for *kapha* individuals.

Since both studies were performed on the same population, it is unusual to find large differences in the reported gut microbiome composition. The discordance between the two studies at the genera level regarding differentially abundant taxa (Fig. 3) could perhaps be due to several factors such as difference in sample size ($n = 113$ and 18), choice of variable region chosen for analysis in bacterial identification (V2–V6 *vs* V3–V4 regions of 16S) and analysis parameters including the definition of core microbiome.

5. Linking *prakriti* with gut metabolome

While finding unique *prakriti*-specific microbial signatures forms an attractive basis of personalized medicine, mere microbial identity is insufficient to establish a causal link between the *prakriti* phenotype, gut microbiome and disease. As per Ayurveda, *vata* individuals have irregular digestion patterns and are predicted to be enriched with biochemical processes related to energy input/output processes such as membrane transport. Similarly, *pitta* individuals are said to have better metabolism capabilities and are predicted to be enriched with processes related to energy production *via* enzyme mediated metabolic pathways. *Kapha* individuals have the least metabolism capacity among the three

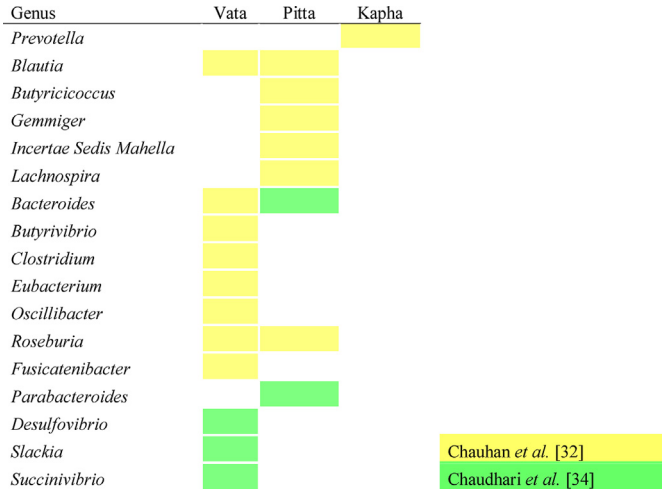

Fig. 3. Comparison of the significantly differentially abundant genera associated with different prakritis from studies by Chauhan et al. [32] and Chaudhari et al. [34].

prakriti types and are mainly concerned with energy storage and hence are predicted to be enriched in energy storage molecules such as lipids and carbohydrates [39]. The gut microbiome has been shown to have an extensive chemical dialogue with its host with immense contributions to several biological functions such as maintenance of homeostasis, digestion/metabolism, detoxification, and several others [40]. Therefore, establishing a link between the functional aspects of gut microbiome/metabolome and the *prakriti* phenotypes can provide compelling scientific evidence to Ayurveda treatment.

Towards this, Mobeen et al. [41] performed a functional profiling of the gut microbiome of 63 females and 50 males sampled by Chauhan et al. [32] using an imputed metagenomic approach with predictive functional profiles derived from KEGG database. High levels of functional redundancy were evident among the three extreme *prakriti* phenotypes irrespective of the gender. This is least surprising considering that all the individuals sampled for the study were healthy adults. While there were varying profiles among the various *prakritis* based on hunger and digestive capabilities, homeostasis/health is maintained among all phenotypes. Majority of the functions were contributed by members of the Bacteroidetes and Firmicutes phyla as reported by Chauhan et al. [32]. There was a slight variation in the contributions of these phyla towards the KEGG functional categories broadly classified as "cellular process", "environmental information processing", "genetic information processing", "metabolism" and "unclassified". In females, the ratio of the total attribution of each phyla (Firmicutes/Bacteroidetes) towards all of these functions on average was 2:1, while in males it was 1:1. Currently, there are conflicting reports on the association of gender with gut microbiome composition (at the phylum level) [42,43]. However, the female gut microbiome has been reported to be associated with a lower abundance of phylum Bacteroidetes and this difference is attributed to hormonal/immunity variations and differences in gut transit time [44,45]. This concept is central to the *prakriti* phenotype based treatment of Ayurveda where treatment is given considering, among other factors, gender and immunity profiles of the patient.

In terms of *prakriti* specific functional profiles, most of the functional signatures of the gut microbiome were found for the female datasets [32]. Disregarding the influence of the classifier, or methods employed, the overall functional signatures identified correlated with the *prakriti* phenotypes. Of note, functional signatures specific to microbiome from *kapha prakriti* females were related to amino acid metabolism and biosynthesis pathway categories. Microbiome from *kapha* individuals were also enriched in pathways involved in replication, translation, repair and stress survival responses which according to the authors corroborate with the higher abundance of potential pathogens detected in *kapha* individuals. Individuals of this prakriti type are also observed to poorly metabolize toxic substances which could be related to the higher abundance of potential pathogens. However, it has been noted that individuals with *kapha* phenotype are disease tolerant with excellent healing capabilities [12].

Functional signatures specific to microbiome of *pitta* females included biosynthesis of various amino acids and were generally enriched in pathways of chloralkane/chloralkene and nitrotoluene degradation. The higher enrichment of "metabolism' related pathways agrees with the fact that *pitta* individuals are classified as those with the highest metabolism capacity. It is pertinent to note here that, enrichment of metabolism genes, albeit of a different category, were also observed in *kapha* individuals. This could suggest an overall functional redundancy among the various *prakritis* while accounting for specific differences among the individuals in terms of the metabolism pathways prioritized in each phenotype.

Vata individuals showed a higher abundance of butyrate-producing microbes which might contribute to the maintenance of lean body phenotype. The authors also suggested that the higher presence of nitrogen metabolism pathways might contribute to maintenance of an adequate number of neurotransmitters to impede the development of neurological disorders in *vata* individuals who are more prone to developing neurological disorders as per the Ayurvedic system.

Overall, this study provides an insight into the functional roles of the gut microbiome in specific extreme *prakritis* which could be correlated with the associated Ayurvedic phenotypes. Further characterization with a larger population is necessary to understand the dominant pathways and functional specialization of the gut metabolome in each *prakriti*. Genetic and epigenetic differences among individuals forms the basis of personalized medicine in Allopathic system of medicine. It involves prescribing individual-specific treatment for patients based on their genetic make-up. The broad equivalent of the "genetic make-up" of the individual in Ayurveda, is the *tridosha* theory and Ayurvedic practitioners prescribe personalized treatment based on the person's *prakriti* which is a mix of the three doshas - *vata, pitta* and *kapha* [11]. This practice is based on the ancient knowledge that has been passed on from one generation to the other along with the written texts, however with limited compelling scientific evidence. Over the years, various studies have established unique genomic [46], epigenetic [47] and biochemical attributes [48] to *prakriti* thus providing scientific evidence for the concept of personalized medicine in Ayurvedic system of medicine. The recent gut microbiome studies bring into focus another facet of the Ayurvedic *prakriti* phenotyping by attesting to functional significance of gut microbiome in different *prakritis* that may significantly contribute to the associated physical and immunological traits. An interdisciplinary study of Ayurveda incorporating genetic, epigenetic, biochemical and microbiome factors can help us to discover novel paradigms in personalized medicine, an imminent need of the modern era.

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Conflicts of interest

None.

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