



Genesis of Personalized Medicine: Relevance of Ayurveda in the Present Millennium

Chakraborty S and Chakraborty R*

Omics Laboratory, Department of Biotechnology, University of North Bengal, Raja Ramohunpur District, Darjeeling, Pin 734013, West Bengal, India

*Corresponding author: Dr. Ranadhir Chakraborty, Omics Laboratory, Department of Biotechnology, University of North Bengal, Raja Ramohunpur, District, Darjeeling, Pin 734013, West Bengal, India, Tel: +919434872273; E-mail: rcnbusiliguri@gmail.com

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Abstract

Deciphering human genome has ushered modern bio-medical science towards a future hope of revitalizing current symptomatic or prophylactic treatment methods into personalized and predictive medicine depending upon an individual's genetic makeup. Genetic variations related to a person's response towards drugs, differential susceptibility to disease and reciprocity of phenotypic attributes related to environment, ethno-racial origin and diseases to genotypes have not been meticulously apprehended yet. Ayurveda, an age-old health science resonated unequivocally with ancient system of classifying a person on the basis of "Prakriti" or unchangeable constitution type might be an advantageous inclination towards personalized medicine, bearing testable molecular and genetic correlates. Several genomic and metabolomic studies augmented the possibilities of yet undisclosed molecular and genetic basis of Ayurveda, which could further be integrated or complemented to current medical diagnosis and treatment. Further deep dive into the extremes of utilizable science and technology of this holistic practice remained quintessential for better enlightenment of future bio-medical science to fight all fiends of ailments.

Keywords: Personalized medicine; Ayurveda; Prakriti classification; Tridosha; Genetic polymorphism; Ayurgenomics

Introduction

A rainbow is not just an assortment of seven specific colours, but it contains numerous wave lengths of different coloured light waves stratified into seven distinct arrays. Magnum opus of mapping human genome told us about the innumerable possibilities of variations those exist in genome of one single species dwelling for a tiny period since life began. With more and more perfections in molecular methods, there has been flooding of scientific data in the last twenty years. Advent of molecular and genetic medicine paves a way in fulfilling the need of understanding ailments at a cellular and molecular level to devise an individualistically themed tool for diagnosis, prognosis, prevention or treatment of a situation that lies contrary to the state of well-being. It is very difficult to accommodate updated information about the disease mechanisms in the existing disease classification systems based on signs and symptoms. Often several disease subtypes having distinctive causes at molecular level have been clubbed as a single disease. On the contrary, there is a void in linking many different diseases which share a common molecular cause. Yet we possess a somewhat inadequate perception of what it all signifies. The most imperative shortcoming that hinders the pace of development of molecular medicine is still the proper scientific understanding. Scientific materialists are yet to build up a consensus about certain common conditions, influenced by environmental and social factors coupled to expression of several genes, for patient management either for wellness or to treat their illnesses. Understanding molecular genetic patterns of an individual looking for a cure through these sophisticated tools are however understood to be very expensive in practice under the roof of a modern health-care management system and pretty difficult to match with a reference frame due to the multitude of

diversities in human genome as well as in manifestations (complex phenotypes).

Recalibrating a person's pathological condition into an ideal "well-being" becomes multifactorial and immensely complex. The complexity usually begins with the imbalance between the need of a personalized medication or therapy and the holistic approach. So, it has become imperative to clarify higher freedom of living systems. Hence, in the energy-time uncertainty relation, bringing in a multiplier freedom factor with the Planck's constant would yield very high value for biological systems in contrast to the value (unity) obtained for physical systems. The basic features of life could then be explained by studying the dynamics of such a system. Indian medical science (Ayurveda) meaning 'knowledge of life' or 'knowledge of longevity' defines life as a dynamical system where harmony between chemical and physical processes lead to 'healthy' state of an individual and emergence of discordant notes brings illness. Since 3500 years or more, Ayurveda (doctrine of Sanskrit scripted resolutions) addressed the issue of wellness of the human population on the basis of chemical and physical processes called "Prakriti" [1-6]. This 'prakriti' is the summed-up phenotype- a basic constitution type of every individual that covers multiple attributes like physical built up, parental lineage, likeability, diet and life style, environmental influences and proneness to diseases. "Prakriti" of any individual is determined by thorough evaluation of balance among three components, Vata, Pitta and Kapha collectively termed as "Tridosha" which work in harmony to maintain an individual's well-being and governs defined physiological and phenotypical manifestations [1-6]. Just like the array of seven colors of rainbow, Ayurveda constituted seven possible "Prakriti" depending upon the consequence of individual or combinatorial proportions of "Tridosha" in each person to suit him/her in any one class among Vata, Pitta, Kapha, Vata-Pitta, Pitta-Kapha, Vata-Kapha and Vata-Pitta-Kapha [1,3,5]. This stratification is free of any ethnic, racial, gender or geographical boundaries hence can be applied on entire human

population to scientifically probe the existence of any possible genetic or molecular correlation with the distinguishable phenotypes of people belonging to seven different “Prakriti” classes [7,8]. Ayurveda conceives a four-dimensional definition of health (a far more smarter definition than the definition put forward by ‘modern medicine’) because a balanced condition of somatic and psychic humors (‘doshas’), digestive capacity (‘agni’), body tissues (‘dhatu’), excretions (‘mala’), kriya (physiological activity) and soundness of soul (‘atma’), sensory organs (‘indriya’), mind (‘mana’) actually defines health (‘Ayus’). As per this perspective, Ayurveda is concerned with measures to protect health (‘ayus’) which includes healthy living along with therapeutic measures that relate to physical, mental, social and spiritual harmony [9-11]. Understanding the inner harmony of nature (‘prakriti’) is the philosophical basis of age-old, yet ever-green, medical science of India. Einstein in an article of scientific faith says, “Without the belief in the inner harmony of our world there could be no science. This belief is and always will remain the fundamental motive for all scientific creation”. So, the path of unification of personalized medicine and Ayurveda can be found in the fundamental principles. Like personalized medicine, Ayurveda is not a ‘one-size-fit-all’ system and its regimens are tailored to each individual’s unique body constitution [12,13]. The focus of Ayurveda is on both patient and disease. Therefore, Ayurveda may hold a few keys to unlock some simple solutions those can be complemented or integrated [14] judiciously to make minimize the complexity.

Discussion

To validate genetic and molecular basis of “Prakriti” classification, a few dedicated attempts were made. Some reported studies tried to draw attention by pointing out association of both specific genes and genomic variations with the different phenotypes representative of different “Prakriti” types. As much as 251 genes were already found to be differentially expressed between “Prakriti” groups [2]. Probable correlation among genotypic and expression differences versus “Prakriti” phenotypes were postulated by studying gene polymorphisms of *CYP2C19*, *HLA-DRB1* and *EGLN1* genes [1-3,5,6,11,15,16]. Identifiable differences in allele frequencies of common variations in 14 Single Nucleotide Polymorphisms of five genes (*FAS*, *AKT3*, *FBN2*, *EGLN1* and *RAD51*) were postulated to be a probable predictive marker for differential responsiveness of people belonging to different groups towards environment, drugs and diseases [2,5]. Differences were pointed out in transcription profiles of pooled RNA from different “Prakriti” groups to distinguish core biological processes between the groups [5]. Some earlier studies were also attempted to draw viable psychological and biochemical differences within the groups [1,3,17-19]. Initial Ayurgenomics studies generated valid reasons to initiate further research to establish possible genetic and molecular basis of this classification system adopted by Ayurveda [6,20] in order to make testable predictions for placement of a specific individual correctly to a specific “Prakriti” type as a step forward towards personalized medicine. USFDA reports positively identified the concept of personalized medicine as age old [21], which can be rooted back to the core concept of Ayurveda, where treatments were designed in a different way for each and every individual, uniquely customized for the very person to be treated [12,14,17]. Evaluation of a person’s “Prakriti” remained the primary step of this customization. Diagnosis in Ayurvedic medicine is based on two-fold approach; (i) examination of the patient-ascertaining the constitution of the individual and status of health and vitality; and (ii) examination of disease-defining the stage of the disease based on its acute and chronic

state. Types of treatment followed in ayurveda includes; (i) avoidance of disease causing and aggravating factors (‘Nidan parivarjas’); (ii) purification treatment (‘Shodhana’ therapy); (iii) palliative treatment (‘Shamana’ therapy); (iv) prescription of diet and activity (‘Pathya vyavastha’); (v) psychotherapy (‘Satvavajaya’); and rejuvenating protocols (‘Rasayan’ therapy) [18]. Ayurveda uses whole crude plant, metal and mineral drug having a mixture of many ingredients [7,22]. It uses plant drugs either in single form or in complex compound formulations of many herbs and plants mixed together [8,22].

We could not even possibly touch the tip of the iceberg of promises those remained hidden in this ancient science with revelations of this primary reports suggestive of scientific foundation flowing underneath the “clinic to laboratory” or reverse-pharmacology [9] based healing practices under the name of Ayurveda, usually met with scepticism by scientific materialists [13,14]. If we could make ourselves valiant enough to research beyond our comfort zone and begin analyzing and justifying the actions and promises of Ayurveda under the strictest monitoring of current science, we might soon be able to detect certain diseases, even at a very early stage, which is unrecognizable in current diagnostic practices. At the current age of unimaginable increase in costs of drug development, uncontrollable rise in phenomenon of multiple drug resistance and diminishing numbers of molecules discovered efficacious without producing severe adverse drug reactions [19,22]; Ayurveda surely stands a chance to be explored in every possible way by patrons of current science, particularly those who possess a broad holistic and optimistic view to fight health problems both persistent and unforeseen by diving deep into molecular and genetic level, and hope to cure it.

As in our lab, we try to find insights on plethora of antibiotic resistance by several pathogenic and non-pathogenic bacteria [23] and probable measures to keep them at bay; we came across using last resort antibiotic drugs to crude herbal preparations, only to found promising results shown by the Ayurvedic formulation, eloquently documented in ancient literature. Applying simple biotechnological approaches in combination to Ayurveda, we have been able to decipher mechanisms of action of plant drugs in single form [24-27] or poly herbal fermented preparation, which not only became able to inhibit biofilm formation of *Pseudomonas aeruginosa*, or restrict quorum sensing of *Chomobacterium violaceum*, but also significantly inhibited several natural isolates found to possess resistance towards different classes of conventional antibiotic drugs. Attempts have been made to check the activity of this Ayurveda based drug against various kinds of enteropathogenic metallo beta lactamase producing organisms, and to identify probable mechanisms of action(s) with the help of standard scientific methodology currently adapted in pharmaceutical industry and laboratories across the globe. Research findings are to be published afterwards - as soon as proper scientific basis could be found in unfolding the molecular pathway of drug action and collation of pharmacodynamic and pharmacokinetic data for any possible complementation of current conventional antibiotic therapy.

Conclusion and Future Prospectives

This silver linings at the time of numerous health hazards reaching a new high [21], every now and then; is reminiscent of one dire need of the hour, to explore the extremes of Ayurveda with every available tools of modern science, mostly genetics, molecular biology, drug discovery, bioinformatics, analytical chemistry, pharmacogenomics and clinical practice and diagnostics to utilize every possible health

benefits hidden benevolently since ages faced by ignorance and scepticism of modern science embedded in scientific materialism.

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