

Exploring the role of epigenetics in therapeutic and research – A boost to *Ayurveda*

The genetic factor is the most significant of the numerous etiological determinants for diseases. The disease with the environment as well as chromosomes or genetic material that is inherited by parents or grandparents is termed a genetic disorder. In such diseases, environmental and genetic heterogeneity convergence culminates in etiologic heterogeneity, which varies from individual to individual due to environmental influences. Etiologic heterogeneity is a phenomenon that emerges in the general population when multiple subgroups of disease cases coexist. Thus, genetic and epigenetic factors play an important role in preserving health and manifesting diseases.

Despite the inherent variety in disease pathophysiology, contemporary phenotype definitions rely heavily on empirical, measurable parameters. *Prakriti* (somatic constitution) is a distinct phenotype and is established on the basis of a person's physical, psychological, physiological, and behavioral characteristics.^[1] These characteristics are determined irrespective of social, ethnic, and geographical factors. Decades of research imply that phenotypic appearance is the culmination of vast complexity caused by the underlying orchestration of several biological components such as DNA, RNA, protein, and metabolites involved in diverse cellular activities that are receptive to the environment.

A study of the entire human genome has unearthed 52 *Prakriti*-specific single-nucleotide polymorphisms that can be used to delineate between the three primary *Prakriti* types of individuals.^[2] It has already been established that in a homogenous cohort of rheumatoid arthritis patients, genes associated with oxidative stress are associated with the *Pitta*-predominant subgroup, whereas genes associated with inflammation are associated with *Vata*-predominant *Prakriti* patients.^[3] It is becoming increasingly vital to understand the mechanisms of gene expression and the influences of other genes, proteins, and the environment to create preventative, diagnostic, and therapeutic treatments. There are multiple DNA repair pathways that function to repair this damage, and the genes within this system are prime biological possibilities for elucidating why some smokers acquire lung malignancies while others do not.^[4]

The diseases are classified under *Adibala Pravritta Roga* (diseases caused by hereditary anomalies) and *Dosha Bala Pravritta Roga* (diseases caused by vitiated *Dosha*) in Ayurvedic classics like *Kushtha* (various skin diseases), *Arsha* (hemorrhoids), and *Shwitra* (vitiligo); can have both genetic and epigenetic factors.^[5] In addition, epigenetic inheritance is an addition to these facts which mentions that

inheritance can occur not only through the DNA code that passes from parent to offspring but also through the parent's experiences, in the form of epigenetic tags, which can be passed down to future generations.^[6] Thus, the disease manifestation, severity, and chronicity are depended on multiple factors, which may be the reason why a similar disease appears with various presentations in different individuals. These facts substantiate the principle of *Ayurveda* of planning and application of the treatment with an individualized approach. Adopting the principles of predictive, preventative, personalized, and participatory (P4) Medicine, as per the *Ayurveda* may transform the current model of health care from a disease-focused to an individual status of disease-focused one. In order to bring such revolution in health care, it will be necessary to anticipate an individual's susceptibility to a disease, stratify patients to facilitate prospective individualized medication treatment strategies and discover and create novel drug targets. This approach can shorten the duration of disease and its health cost and ultimately reduce the overall health-care burden.

Further, to generate evidence-based data for these facts, planning clinical trials to establish the role of treatment protocols based on individual patient requirements are must. The fundamental tetrapod of any research plan consists of population, intervention, comparator, and outcomes. Defining each of these components in a clinical trial has a direct impact on the outcomes of the clinical trial. A vague definition of patients included under diagnostic and inclusion criteria of the clinical trial can end up in ill-defined outcomes and sometimes may also be not relevant to the objectives of the clinical trial. For generating evidence for the personalized approach of the outcomes of the clinical trial, planning clinical trials using contemporary screening, inclusion, and assessment criteria with a negligible thought of principles of *Ayurveda* diagnostic and treatment approach will never provide fruitful data and outcomes. This may be one of the reasons that the majority of trials at the present in *Ayurveda* yield negligible or insignificant statistical findings for the evaluation parameters. The most likely explanation for this is a concealed heterogeneity in the population (based on the *Prakriti* and *Vikriti* (morbidity) assessment), which may appear homogeneous in contemporary wisdom (based on the laboratory-confirmed cases). This can end up in a condition similar to that competition, where the judgment of someone's singing ability is based on how well he can swim.

Diseases in *Ayurveda* are classified according to their effects on *Dosha* (regulatory functional factors of the

body), *Dhatu* (major structural components of the body), *Srotasa* (channels of circulation), and *Agni* (digestive/metabolic factors) and forms the basis for assessing the patient's symptoms to diagnose them. Disease symptoms are the end result of an evolutionary process that is influenced by the body's genotype and phenotype. This is because, the presentation of the disease, its severity, therapeutic recommendations, and treatment outcome in individuals, will depend upon the metabolic profiles, disease predisposition, and natural history in individuals with respective genotypes and phenotypes. Thus, Ayurvedic medications or therapy techniques are not created for specific diseases, but rather for subgroups of diseases, and dose, frequency, and dosage form depend on many factors. If we screen the patient on the basis of types and stages or phases of the disease and design interventions accordingly, the efficiency of the treatment is expected to be high.

The primary constraint of these kinds of research is that it will necessitate an extended period and a lot of resources to execute it. Further, it will require a team of people with a diverse variety of skill sets. Thereby, this could not be feasible on a small scale. We have one of the world's oldest medical systems, however, the current generation values sensory experience above all else. These initiatives will explicate traditional medicines and reinstate the confidence of *Ayurveda*'s new recruits. Hence, there should be such trials more frequently to unveil the diverse action spectrum of *Ayurveda* drugs. Ultimately, this will boost the relevancy of the science.

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