TRANSLATIONAL RESEARCH IN AYURVEDA WITH SPECIAL REFERENCE TO PREVENTION OF LIFESTYLE DISORDERS WITH AN EMPHASIS ON THE CONCEPT OF EPIGENETICS

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ABSTRACT

Epigenetics is the study of the process by which genetic information is translated into the substance and behaviour of an organism: specifically, the study of the way in which the expression of heritable traits is modified by environmental influences or other mechanisms without a change to the DNA sequence. Epigenetics is the study of changing genetics without actually touching the genes. The cells of our body can behave and respond differently based on particular environmental factors. Research has shown that cells have dynamic intelligence and that the environment can turn certain genes on or off. For example, if an environmental factor that turns on a gene that is linked to a disease process is eliminated and replaced with a healthier environment, then the predisposition for that genetic disease will not be supported and is less likely to manifest.New research has revealed that cells are responsive to the internal environment of our thoughts, beliefs and feelings as well as the physical environment. This research states that, genetics are controlled by the perception of the environment rather than genes themselves. With the science of epigenetics we can begin to map out genes that keep us in a healthy state and eliminate those bad genes that have been plaguing humans over the course of time. There is real possibility to map cures for certain cancers, autoimmune disorders, and many other debilitating diseases.Ayurveda relates to the concept of epigenetics in distinct ways. The first way relates the Ayurvedic concept of Prakruti vs. Vikruiti with that of genetics vs epigenetics. Role of nature and lifestyle routines in relation to epigenetic research is being understood. Not only what we eat but everything we take in through the five senses affects our health and our susceptibility to disease. Both Epigenetics and Ayurveda have shown that a person's experience at the physical, mental and cellular level can directly affect the quality of that person's life experience. This paper highlights the recent findings of research and scope of further research in the field of epigenetics translating the concepts of Swasthavritta

***Keywords**: Epigenetics, Swasthavritta, lifestyle, Ayurveda*

INTRODUCTION

Epigenetics literally means Epi - "above" and genetic - "origin" i.e. above the origin. So epigenetics is the study of the process by which genetic information is translated into the substance and behaviour of an organism: specifically, the study of the way in which the expression of heritable traits is modified by environmental influences or other mechanisms without a change to the DNA sequence. Simply it means that the cells of our body can behave and respond differently based on particular environmental factors. Whatever the function of the cell there is a surface receptor that bonds with an extracellular molecule to trigger the cell into behaving a certain way. Here are four key things to know about Epigenetics[1]:

1. Epigenetics Controls Genes. Certain factors in life can cause genes to be turned on or off. Genes may lie dormant in the body or become altered by epigenetic factors that will cause genes to express in a certain way.
2. Epigenetics is everywhere. Everything we eat, touch, smell, hear, or feel can cause chemical modification in our body altering our genes. Even how we sleep, how we exercise and how we age will affect how our body transcribes the genes. Certain diseases are brought on by a malfunction of genes from a healthy state to a disease state.
3. Epigenetics makes us unique. Epigenetic factors can be passed down from generation to generation but also; epigenetics is responsible for the little things that make us all unique.
4. Epigenetics is reversible. With over 20,000 genes in our body the different combinations are enormous. With the science of epigenetics we can begin to map out genes that keep us in a healthy state and eliminate those bad genes that have been plaguing humans over the course of time. There is real possibility to map cures for certain cancers, autoimmune disorders, and many other debilitating diseases.

The incidence of lifestyle diseases like hypertension, diabetes mellitus, dyslipidemia, and overweight/obesity associated with cardiovascular diseases is high on the rise. Cardio vascular disorders continue to be the major cause of mortality representing about 30% of all deaths worldwide. With rapid economic development and increasing westernization of lifestyle in the past few decades, prevalence of these diseases has reached alarming proportions among Indians in the recent years[2].

Translational research applies findings from basic science to enhance human health and well-being. In the context of medical research, findings in basic research are to be translated into medical practice that will lead to meaningful health outcomes. There is a lot of scope in research translating the concept of Swasthavritta in the light of epigenetics into clinical research outcomes.

PREVENTION AND MANAGEMENT OF LIFESTYLE DISORDERS IN AYURVEDA:

In the management of lifestyle diseases, Ayurveda offers various regimens including *Dinacharya* (daily regimen), *Ritucharya* (seasonal regimen), *Panchakarma* (five detoxification and bio-purification therapies), and *Rasayana* (rejuvenation) therapies. The Sadvritta (ideal routines) and *Aachara Rasayana*(code of conduct) are utmost important to maintain a healthy and happy psychological perspective. The inclusive utilization of all these treatment modalities has a great effect on lifestyle disorders. Moreover, the application of organ-specific *Rasayana* herbs also provides enough scope not only for prevention of disease, but also for the promotion of health and cure of disease too[3].

According S.L. Martin,genes regulate 25% of longevity, whereas 75% is determined by lifestyle factors such as sleep habits, alcohol beverage consumption, stress levels, exercise, and diet[4].Basically, a particular lifestyle of person is a cumulative product of his/her physical capacity co-ordinated with psychological functioning, displayed in the form of habits, behavior, dietary and living pattern based on his own training sought from childhood, and mimicries he gained from his immediate companions including parents, siblings, peers, etc. Thus, it involves a pure psychological and innate control over the physical and sensory activities. When this initiation, control, and co-ordination are disturbed, it leads to the derangement of lifestyle and results in any lifestyle disorder. Ayurveda narrated this phenomenon as '*Prajnaparadha*'[5] (intellectual blasphemy) which is one of the three basic causes of any disease. There are ample improper actions as an impact of *Prajnaparadha* which are root causes of various diseases, e.g., habit of suppression of any natural urge is a result of *Prajnaparadha* and enlisted as a cause of nearly 50% of the diseases. Reversal of any neurotransmission or improper removal of the waste products formed during metabolism leading to accumulation of toxins is the basic cause of a disease. Therefore, the habit of suppression of urge in improper lifestyle can be considered as one of the root causes of lifestyle diseases.

A lifestyle of an individual is the outcome or composed of physical traits, capacity, habits, dietary style, living condition, psychological functions, likes and dislikes, etc. Many of these traits are observed / nurtured from the parent, siblings and the surroundings. So, the physical activities are influenced by psychological feeling. The psychology controls all bodily activities. When the psychological initiation and control is disturbed, it results with lifestyle diseases and disorders. It is referred as Prajnaparadha in Ayurveda, one of the three major causes of diseases.Around 50 to 60 percent of lifestyle diseases are cured easily and effortlessly with Ayurvedic diet and lifestyle recommendations. Also, a few alarming diseases like osteoporosis (loss of bone density), type I diabetes – an insulin dependent condition, cardiac / cardio vascular diseases, neurological disorders, etc can be improved to a great extent. While many of the lifestyle diseases are the outcome of poor immunity, the concept of Ayurveda is solely based on eliminating diseases by building up Ojus.

Ayurveda suggests simple lifestyle routines for a healthy and disease free life. Lifestyle diseases have a unique approach in Ayurveda, called 'Swasthavritta.' It refers to abiding naturally to one's own nature. In simple words, it is following the healthy regime for healthy life with appropriate activities. Swasthavritta focuses on individual hygiene and public health.
The optimal health can be achieved to curb down the lifestyle diseases include Dinacharya, daily routine and Ritucharya, seasonal routine, Panchakarma, the detox treatment to remove the toxins and toxic effects from the body, Rasayana – rejuvenation therapy – Massage and spa therapy for pain relief, soothing the nerves, stress relief, rejuvenation, etc.

Aachara Rasayana – Personal hygiene, behavior, conduct, etc. A few lifestyle diseases can be effortlessly curbed down by meditation and yoga. For instance, the degenerative disorder, loss of bone density or osteoporosis can be improved with yoga. Ayurveda connects the body with mind, heals from internally. It helps you connect with you through spiritual health. Ayurveda for lifestyle diseases is combined of food and lifestyle modifications, herbal remedies, physical activities, rejuvenation therapies, meditation and yoga.

Increasing evidence shows that environmental and lifestyle factors may influence epigenetic mechanisms, such as DNA methylation, histone acetylation and micro RNA expression.
Several lifestyle factors have been identified that might modify epigenetic patterns, such as diet, obesity, physical activity, tobacco smoking, alcohol consumption, environmental pollutants, psychological stress, and working on night shifts. It has been stated many times throughout the medical world that 95% of disease are not inherited. This means the lifestyle choices people make everyday have a direct impact on the susceptibility to disease. For example, one study shows that mice that are predisposed genetically to cardiac and diabetic disorders can give off normal offspring when they are fed the proper diet. In short, epigenetic factors, proper use of the senses, can supersede genetic factors [6].

Foods

A possible role for nutrition in modifying epigenetic mechanisms has been examined in multiple investigations. For example, a diet rich in polyunsaturated fatty acids could generate mutagenic free radicals and oxidative stress [7] which has been directly linked to epigenetic alterations [8, 9]. Modulation of gene methylation has been observed in human endothelial cells incubated with arachidonic acid promoting up-regulation of proangiogenic mechanisms [10]. Conversely, polyunsaturated fatty acids may have a suppressive function in tumorigenic processes through dampening of inflammation and NF-kappaB pathway [11]. Moreover, diets rich in fruits and vegetables, which contain many natural antioxidants, can yield anticancer protection [12,13] have extensively reviewed the potential epigenetic effects of several nutritional components, mostly derived from vegetables. For instance, a study in healthy human subjects fed with a single serving of broccoli sprouts showed inhibition of histone deacetylase activity in circulating peripheral blood mononuclear cells 3–6 hours after consumption, with concurrent induction of histone H3 and H4 acetylation [14]. An in-vitro study on human tumor colon cell lines revealed that high doses of diallyl-disulfide from garlic increased histone H3 and H4 acetylation[15]

In epigenetic research, scientists are researching how different factors are changing the potential for disease states without changing DNA sequencing. Three main mechanisms are DNA methylation, histone modification and RNA alteration. These changes are all potentially reversible. Modern science is proving that the path of personalized therapy can affect disease screening and prevention strategies.

RNA Alteration

RNA, particularly microRNA's, has its roots at the post transcriptional level. Micro RNA's are non-coding RNA that regulates gene expression. Theses microRNA's are primarily responsible for normalizing cell function. They are a "blueprint" for the cell to form in a certain way. MicroRNA can also be affected by environmental factors that can alter the blueprint for the cell thus making it behave differently than intended. These RNA have the ability to turn on and off their DNA making them functional or dormant depending on the signals[16]

Prakruti vs. Vikruti and epigenetics

Our Prakruti in Ayurveda roughly resembles our DNA, or our genes, in western medicine. Each us of is born with a unique constitutional balance. Prakruti is determined by our parents' nature, as well as the circumstances of our birth. Our mother's emotional and physical state, the season, and location of our birthplace are all determining factors in our prakruti. According to Ayurveda this happen at the moment of conception and the lifestyle of our mother will play a role in the development of the offspring but the seeds of karma are also a factor in determining the tendency of the offspring [17]. So if our Prakruti is roughly related to our genes then our Vikruti is roughly related to our phenotype in Epigenetics[18]. Our Vikruiti is defined as the nature of the imbalance. It is our current state. Prakruti is determined at the moment of conception and our Vikruti is the present state of the person. To get from point A (Prakruti) to point B (Vikruti) there can be any number of changes and those changes relate to epigenetic factors that include sensory input from the outside world. This includes diet, lifestyle, visual input, sensory stimulation, emotions, as well as many other environmental factors.

Western science looks at this a little differently. Western science believes that the offspring is a combination of the genes of the mother and the genes of the father. This creates a unique DNA of a child that will be different than any other person on the planet, the only exception being genetic twins. This has been the basis for Personalized Preventative Medicine (PPM) in the modern world. Ayurveda is filling the gap for personalized medicine as it relates to the individual in accordance with diet and lifestyle, season, time of life, and individual tendencies. Personalized Preventative Medicine PPM has been at the forefront of study in recent times. Modern science is realizing that epigenetic factors (i.e. diet, lifestyle, season, time of life, and individual tendencies) are directly influencing drug response. Ayurveda commonly describes its medicine in terms of its rasa, virya, vipaka, and prabhav. This will have a unique effect for each person as it relates to their prakruti or individual constitution. As modern science is learning drug reactions are found on an individual basis independent from that of any ethnic, racial or geographic grouping.

Dinacharya and epigenetics

In Sanskrit Dina means "daily" and Charya means "following or moving". Ayurveda recommends that in order to be in an optimal state of health we should tune our bodies into the cycle of nature which in turn regulates the various other rhythms of our body. As modern society has taken hold of our lifestyle, our ability to live within the rhythms of nature has become increasingly difficult.Ayurveda suggests that we live by the light of the sun. It is best to wake up in the dawn hours (Brahma Muhurta).It is best to take this time to eliminate and cleanse the body, perform self-care including abhyanga, do physical exercise to further cleanse the body, take time for proper meditation and take nourishment of proper foods. All of these tasks shall keep a body free of disease. If these natural rhythms are allowed to fall by the wayside, change in our body chemistry can be seen. A study done on shift workers indicates their circadian rhythm disruption and its link with breast cancer. This study pointed out that as our circadian rhythms get more and more out of kilter with nature, there is an increasing likelihood that certain genes will have the ability to mutate into cancer causing cells[19].

THREE CAUSES OF DISEASE

Ayurveda believes that the three cause of disease have a direct correlation with our influence from our personal choices and our environment. These three causes – Prajnaparadha, Asatmendriyartha Samyoga, and Parinama are three factors that, when not taken into consideration, will be the cause for dis-ease in life. According to Ayurveda treatment of the disease does not treat the symptoms but brings the person back to their true nature. The body will then be able to rid itself of the disease. The Caraka Samhita states, "So the unwholesome conjunction of the sense organs with their objects, intellectual blasphemy (prajnaparadha) and transformation (parinama) – these are the threefold cause of diseases. Proper utilization of the objects, action and time is beneficial to the maintenance of normal health."

Prajnaparadha

Prajnaparadha is translated to mean – "intellectual blasphemy." In short, we know that when we truly listen to our inner self, we can make decisions that reflect a state of balance. When our ego gets in the way we can potentially make choices that go against the health of our entire being. This idea of prajanparadha (intellectual blasphemy) can be seen through the lens of epigenetics. If our choices of the present moment are carried with us as we age it's fair to say that, epigenetically speaking, we are also passing down those choices to our offspring. Here are two studies that show how small insignificant choices can have dreadful long term results, not only for us but our offspring as well.

The first study, and probably one of the most significant studies on epigenetics, relates the choices of the mother agouti mouse directly to the health of her offspring. This study used mice that carried the particular agouti gene scientists could track to see if they could change the genetic legacy of the offspring. When agouti mice breed the offspring are identical to the parents. These

yellow fat mice look different than other mice because they carry this agouti gene that makes the rodent's appetite enormous and renders them prone to cancer and diabetes. The experiment was simple – they changed the mother's diet. In one generation – the mother's offspring were small, slender, brown, normal looking mice. All they did was change the mom's diet. The diet was rich in methyl donors which are found in many healthy foods including onions, garlic and beets. These "good" methyl clusters attached to the agouti gene essentially turning it off so that the developing embryos did not have an open methyl to activate the agouti gene. These offspring did not display susceptibility to cancer and diabetes and lived to a very old age. The DNA of the offspring was not altered and the effects of the agouti gene had virtually been eradicated[19]. This study is remarkable in many ways. Not only does it show that epigenetically we have a great deal of influence over our lives and the lives of our offspring, it also shows that our small, somewhat insignificant everyday choices (i.e. what we eat) have an enormous impact on our well being and the health of our progeny. These choices are all about prajnaparadha.

Our choices are not just having an effect on the physical body. Epigenetic studies have correlated their findings to that of the brain – primarily in relation to stress. Many studies have shown that stress in early life experiences can alter the neuroendocrine system. These alterations can impact the response to stress a person carries throughout life. Studies in both rats and people have shown that early life stressors to infants will cause DNA methylation thereby affecting oxytocin receptor expression as well as anxiety responsivity. "The fetal and early postnatal periods are times of dynamic physiologic change and developing organs and tissues are extraordinarily vulnerable to environmental influences. During sensitive periods of development adverse events such as stress or maltreatment can more readily trigger epigenetic alterations which can adversely affect physiological function and behaviour through adulthood[20]. Cognitive and physiological response to stressors is highly influenced by genetics, early-life environment and trauma. Thus, resilience and susceptibility to stress are dictated by a variety of factors that ultimately determine whether neuroplastic adaptations can effectively promote coping or lead to loss of appropriate stress control and perhaps pathology [21].The vast evidence shows that epigenetic modifications within relevant brain regions will influence behavior, physiological outcomes and disease risk.

Asatmendriyartha Samyoga

Asatmendriyartha Samyoga means improper use of the senses. Our five senses carry a delicate balance between delight and damage. When we repeatedly hyperstimulate our senses we can damage our senses. Epigeneticists are researching the misuse of the senses on a molecular level. They are finding that epigenetic factors are proving to be instrumental in the spread of common diseases. The increased human lifespan of centenarian individuals compared to people with average lifespan is directly related to vastly different diets. In the AstangaHrdayam, it talks directly about the use of the senses in relation to disease. "He, who indulges daily in healthy food and activities, who discriminates (the good and bad of everything and then act wisely), who is not attached (too much), to the objects of the senses, who develops the habit of charity, of considering all as equal (regarding kindness), of truthfulness, of pardoning and keeping company of good

persons only, becomes free from all diseases [22]. This quote sums up the idea of AsatmendriyarthaSamyoga. All good things in moderation and giving of oneself for the benefit of the greater good seems to be an everlasting truth to the endurance of humanity.

Parinama

Parinama means "evolution over time". According to The Principles of Ayurvedic Medicine, there are two types of time – one being linear and the other being biological. Linear time is static. Biological time can be manipulated based on the movement of our bodies and our minds. Being in the present moment is the key to spiritual awakening. When our bodies are in constant motion and our mind is in constant thought, time will speed along until disease sets in. When we consciously slow down our motion (Vata) we can begin to understand the concept of parinama. Epigenetic research is studying the effect of parinama through the study of applied consciousness. The total number of altered methylation sites, where the sensor proteins latch onto, increase as we age. Methylation changes can then lead to altered gene expression which contributes to the delayed onset of age related diseases [23]. As more of the population is living longer, there has been an increase in age related diseases. Environmental variables in the epigenetic processes that involve alterations of gene expression without a change in DNA sequence can determine different aspects of aging, as well as pathogenesis of age-related diseases. Epigenetics plays a role in the aging processes and healthy life extension. The time for the body to relax is essential for repair so the body will continue to last well into the Vata time of life. As we flow into the Vata time of life, our body naturally begins to break down. If one is conscious of this we can work to alleviate the dosha with diet and lifestyle practices thereby promoting a greater likelihood of good health as we age. Parinama can then help us mindfully flow into the golden years of our lives.

CONCLUSION

It is clear that there are many similarities between Ayurveda and Epigenetics. Both Epigenetics and Ayurveda have shown that a person's experience at the physical, mental and cellular level can directly affect the quality of that person's life experience. We can also see that those experiences are easily transferred down from generation to generation. Epigenetics has been around 20 years. Ayurveda has been around 5000 years. Both have come to very similar conclusions. Epigenetic research confirms traditional ancient knowledge that diet, lifestyle and mindfulness can all be used to fight disease and promote health. We are here on this planet to optimize the expression of our genes in a way that supports evolution and growth both individually and collectively. If we follow Swasthavritta properly we can change the expression of our genes in a positive way there by promoting optimal health and preventing the diseases especially lifestyle disorders. There is a good scope for intense translational research where the principles like Dinacharya, Ritucharya, Ahara, Vihara, AcharaRasayana, Sadvritta can be clinically revalidated with the help of concept of epigenetics.Ayurveda's holistic approach to treating the mind, body and soul as a complete person has the potential to solve some of the world's most pressing health problems. Modern medicine

has seen this need for personalized medicine and Ayurveda offers the path which plays a key role towards disease prevention through diet and lifestyle. By taking the knowledge of modern science and combining it with the roots of Ayurveda, there is an opportunity to change the course of some of the most plaguing disorders of the modern world today.

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