GENES, POLYMORPHISMS AND THE MAKING OF SOCIETIES

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How Genetic Behavioral Traits Influence Human Cultures

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Universal-Publishers
Boca Raton

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Universal-Publishers
Boca Raton, Florida • USA
2012

ISBN-10: 1-61233-093-2
ISBN-13: 978-1-61233-093-8

www.universal-publishers.com

Cover photo "Los Angeles city" © Konstantin Sutyagin | Dreamstime.com

Cover photo "Li-river, Yangshuo, China" © Nico Smit | Dreamstime.com

Library of Congress Cataloging-in-Publication Data

Kiaris, Hippokratis.
Genes, polymorphisms, and the making of societies : how genetic behavioral traits influence human cultures / Hippokratis Kiaris.
p. cm.
Includes bibliographical references.
ISBN 978-1-61233-093-8 (pbk. : alk. paper) -- ISBN 1-61233-093-2 (pbk. : alk. paper)
1. Human genetics--Social aspects. 2. Human genetics--Variation. 3. Human behavior. 4. Cultural evolution. 5. Genes--Social aspects. 6. Genetic polymorphisms--Social aspects. I. Title.
QH431.K425 2012
599.93'5--dc23

2012006731

To my lovely wife Ioulia,
and to my adorable kids Frosini and Harry,
for their patience and inspiration

Contents

Preface

I am neither a geneticist nor a historian or anthropologist. As a biologist by training, I have received some academic and formal training in genetics. My knowledge—that is, ignorance, actually—in history and cultural anthropology is only empirical and superficial. Therefore, by having this excuse, I hope that I will avoid the rigorous critique from the academic experts in these fields. To such experts, my thoughts may seem naive and oversimplistic, or that I have "reinvented the wheel"—which, intellectually, is even worse. With these reservations constantly accompanying my endeavor, I have continued writing this book.

The issues I attempt to explore all spin around one central question: Why the different populations around the world have developed different and distinct cultures that eventually led to different historical outcomes and different ways, according to which the corresponding societies have been organized, and, in general, distinct ways by which life has been viewed and perceived. These and other relevant questions are examined in view of the different frequencies in various genetic polymorphisms in genes affecting behavior. Furthermore, I attempt to focus on a comparative outline, both cultural and genetic, of peoples and populations from the two major cultural lines and civilizations that have appeared in human history and persist until today: the Eastern (Asian) and Western (European and American). In other words, these questions are reduced to why the Western line of thought has been dominated by Aristotle's *reason* and *logic,* while the Eastern line of thought has been dominated by Confucius's *harmony, collectivism, and context dependency*. The main idea of this book is that the presence of different genes in the corresponding people has actually dictated the acquisition of these distinct cultural and historical lines, and that an alternative outcome might have been unlikely. Based on current trends related to the globalization of cultures and economies, some predictions are finally being made on the development of human cultures and the potential future of human history.

I want to thank Joanne Asala for her great job in editing the text and making it comprehensive and Dr. Jeff Young, my publisher, for his help and valuable suggestions during all stages of preparation of this book. I also want to thank the publishing associates of Universal Publishers, the production editor Christie Mayer for generating the layout of the book, and especially the artistic director, Shereen Siddiqui, for designing the cover. Finally, I want to express my gratitude to my wife Ioulia for her constructive comments, critique and patience for the whole duration of this project.

Part I

Introduction

1. The Concept

The central notion of this book is based on a very simple idea—so simple that it can be considered as self-evident. If the genetic content (status, variability, signature) of individuals, affects—if not dictates—behavior, then shouldn't this content also affect collective decisions and actions, if examined at the level of groups of people that share certain genetic characteristics? Shouldn't people that are genetically similar among each other exhibit similar trends in their decisions that have affected their culture and history? Such groups of people, with a genetically distinct identity, can be considered as entire nations or even what we call races and ethnic groups. No matter how stringent the definition of homogeneity is, especially genetic homogeneity, it is really arbitrary and quantitative. In any case, though, it involves groups of people that genetically are more uniform than people that may belong to other "groups" of people. Therefore, it is conceivable that history, at least the part of it that reflects the outcome of certain decisions and reactions of human individuals, is also affected by the genetic identity of the people involved. In other words, different people would have made different choices that, in turn, would have created a different outcome to their history.

This notion is applicable at the various levels of organization of such groups, from families in which the genetic relations are so apparent, to the anthropological bands and tribes and races—notwithstanding that there is not a scientific consensus regarding what, exactly, the human races are or how many (Molnar, 2005). This term historically was defined by using a combination of both biological and socio-cultural criteria. Regardless of whether Asian people can be classified into five or fifty groups, whether or not they represent a distinct and single "race" or many different races, it is clear that they are in principle more "identical" among each other and distinct as regards their physical characteristics when compared to European people, and vice versa. This is due to the existence of several features among them that largely reflect (and are reflected to) their genetic identity. Not that all Europeans can pass as Europeans by looking only at their physical appearance, or Asians for Asians. Many

cases exist of individuals with intermediate (or mixed) characteristics that point to the fact that there is a continuum in the intensity of these features. Thus, a certain grey zone exists that does not allow drawing strict barriers among different populations. This often involves traits that manifest in lower frequencies in certain groups while they are more common in other groups of people, or features that are stronger in the one group and milder in the other. This can be due to the occasionally extended interbreeding during certain historical periods between people of different ethnic groups, as well as to the even more important fact that there is not a single genetic characteristic present in all people of the same population and absent from all others. Thus, a single (and objective) criterion to classify an individual as a member of a specific race does not exist. It is all a matter of frequencies, ratios, and intensities—but we'll come back to that later. We'll see in some detail in subsequent chapters that characteristics, such as the epicanthic fold or the double eyelid, are considered typical for East Asians and are usually accompanied by light skin color. At the same time, though, we have also seen individuals that belong to Western populations who have considerably darker-than-average color skin types, accompanied by pronounced double eyelids, characteristics that are considered more "typical" for African and East Asian people respectively. Frequently, notwithstanding not exclusively, in the world of show-biz, such exceptions and deviations from the mainstream characteristics are more common than in the average population, which probably implies the attraction these "minority" traits elicit—a fact that possesses apparent implications in providing certain mating advantages!

At this point, it also has to be emphasized that notions related to the genetic classification and the eventual categorization of the various races are obviously wrong scientifically, and are completely outside the intentions of this book. Even when we subsequently describe examples of certain genetic features that superficially may be taken as disadvantages, we have to keep in mind that those should be judged as such only within the certain context that they have appeared and stabilized in a given population. Certain examples point to the fact that even disease-related genes, such as those responsible for the development of sickle cell anemia and Glucose-6-phosphate dehydrogenase (G6PD) deficiency, have an eventual role in conferring resistance against infectious diseases. Thus, what can be viewed as a disadvantage in the first instance is certainly an advantage within a given environment. Many more are the cases of genes that, while

not responsible per se, can modulate the development or the severity of specific diseases and have a different prevalence among people of different origin.

Obviously, since even in cases that involve pathological conditions the distinction between "harmful" and "beneficial" is not clear-cut, when we talk about behavioral traits, the whole picture becomes even more complicated. It is much more complex to classify a characteristic as purely advantageous or disadvantageous for the individual that bears it when we focus on characteristics that affect human behavior and personality. For example, novelty-seeking is a behavioral trait related to the tendency for increased risk-taking and exploratory excitability. This trait, historically, might have produced a positive influence in individuals, since it might have facilitated progress and advancement. It is noteworthy to mention that it has also been related, genetically and behaviorally, with increased incidences of drug addiction. Does this remind you of Western people (or people of European descent) and their civilizations? How about the observation that the specific polymorphism that is related to this trait is quite uncommon in Asians?

As we will see in subsequent chapters, recent complex analyses and genetic modeling suggest that these polymorphisms, such as those related to novelty-seeking, are likely associated with the migratory patterns of human populations, providing a direct hint on how genetics might affect the history of certain people. And not coincidentally, speaking about the migratory pattern of behavior, the easier (or more efficient) adaptation into a new environment is intrinsically linked to novelty-seeking behavior. We will discuss all of these issues in much greater detail in subsequent chapters, along with other analogous traits. Thus, what is positive in a specific view can be negative in another. The level of complexity increases even more by the observation that certain genetic traits, depending on the exact conditions that are being studied, may affect a variety of behavioral trends and patterns, and what we see and record is actually the collective outcome of all these behavioral variables.

Another issue that may arise throughout this book is related to the concept of "free will." In that sense, genetically speaking, the unavoidable question is this: How free is our will if we are actually hardwired, or at least predisposed, against certain behaviors, choices, and reactions that differ among individuals? I admit that I will not attempt to deal with such questions since, after all, these are rather philosophical issues, and it is not my intention to approach them.

However, no matter what the correct answer may be, our only rational option in life, both as individual persons and as members of a larger group or community, is to keep on trying to extract the best out of what we have. Within this context, as individual persons we experience the option for a will that is really free.

Keeping these issues in mind, my whole point is that different people respond or are more likely to respond differently against similar stimuli, and that these responses are likely more common among people that are more similar genetically. The latter is quite likely to occur with people that belong to a group or population with similar (or more homogenous) genetic imprint. Thus, if against the same stimulus or during an encounter, A people are more possible to elicit a type-K response while B people are likely to elicit a type-L response, then A and B people are likely to take consecutively different decisions through historical time: The A people will repeatedly respond with a K-type response while the B people respond with an L-type response. And, importantly, the genetically similar offspring of these people will continue to make similar decisions whenever they face similar challenges, thus exhibiting an apparent consistency in the building of their culture and norms. These decisions eventually will be reflected in their collective history. If, for example, this K-response is to retreat and negotiate when they deal with offensive actions, while the L-response involves confrontation and "fight back" decisions, then it is quite likely that A people will be less prone to warrior-type cultures than B people. We can also imagine that another genetically regulated trait exists that makes A people more cooperative than B people. It is conceivable in that case to expect that the A people will develop cultures and societies at which their individual members will exhibit increased interdependency than the B people. Thus, their cultures will be more "collective," when compared to those of the B people, who in turn will have a tendency toward individualistic cultures. Of course, the unbiased question is whether such genetically regulated traits exist that can affect those types of cultural and historical decisions. This is a main focus of this book, and we will try to address it in subsequent chapters.

Consistent with these notions, it is not only the socio-economical environment, the geography, the natural phenomena, the occurrence of certain disasters and diseases or other exogenous factors that have affected and will continue to affect the history of humans, but also the genetic signature of the people. Therefore, in any attempt to explain human history, the genetic profile of the corre-

sponding people should also be taken into consideration, along with the other conventional parameters. Even if this is not feasible technically as yet, it is rather likely that in the near future it can be. And in that case, we can even go one step further; besides explaining the past, we might also be able to "predict" the future. This may sound like a science-fiction scenario right now, but if we were able to "measure" behavioral tendencies and the genetic structures of given societies, then the prediction of possible outcomes against specific conditions could be made.

That this "runs in the family" does not only refer to diseases or certain physical features, but also to behaviors, our likes and dislikes that, conventionally, we used to attribute only to certain socio-environmental factors—in other words, to the way we "grew up." For example, that ancient Greeks (or, to use a present-day example, the Kennedy family) were deeply political may reflect, at least in part, their genetic signature. A certain predisposition against specific behaviors, such as the tendency of not taking things and conditions as a given, in combination with the desire to lead, may manifest as an attraction to politics.

Not that the environment—in its widest sense—is not playing a major role, of course. On the contrary, actually! However, in order to formulate characters and mentalities (as well as physical characteristics and diseases), the environment needs to interact with the given genetic background, and the result will be as specific as it can be for each individual. Thus, the behavioral pattern that emerges is not the sole result of the environment, but is also greatly affected by the genetic information carried by each and every person as well. This is, of course, a given, a basic and elementary knowledge of biologists. The notion of context dependency ranges from the study of the genetic basis of behavioral traits, and it affects the interpretations of those attempting to understand the response of individuals against certain stimuli, to the elucidation of the effects of the (micro)-environment in cellular differentiation and disease. Or to why the same carcinogens cause cancer in some individuals but not in others. It is increasingly appreciated that the magnitude and the extent of any biological response is greatly influenced by the genes of the individual.

In a reductive approach on addressing how genes affect behavior, the emphasis is given to the prediction of how individuals will respond to a specific (socio-economical) environment, or in other terms, to the building up of "characters" and personalities in their wider sense. It is reasonable, though, to speculate that analogous

mechanisms will also operate at a larger scale as well, at the level of populations, and in that case, the outcome will be reflected not to individuals' decisions, but rather to collective decisions that are capable of affecting history. We can read in J. M. Roberts's classic book *A Short History of the World* (1997) that "[H]uman history began when the inheritance of genetics and behavior which had until then provided the only means of survival was first broken through by conscious choice" and "[I]t (human culture) was increasingly built by deliberate selection…" (p. 2). The question, in that case, is related to how strictly we define the terms "broken through by conscious choice" as well as "deliberate," and on whether all conceivable options indeed carry the same probability for different groups of people…

2. Genes, Polymorphisms, and Genetic Heterogeneity

Individuals are different. They differ in their physical appearance, their specific abilities, their inherent risk to get sick from certain diseases, their characters, and their entire existence. Depending on the particular characteristics we are studying, such differences can be attributed, to some degree, to the individual's DNA, or in other words, to the genes that someone has inherited from his or her mother and father. For some characteristics, the contribution of the genes is absolute and apparent, while for others, the environment may play an equal or even more important role than that of the genes. Thus, while our eye color is solely determined by our genes, our character and behavior are also determined by the conditions we grew up in, our friends, our family, and, in general by the environment, or alternatively, by nurture[1]. Again, even in the case of traits that are so obviously shaped by socio-environmental factors, a not negligible genetic contribution is there. Savings behavior, for example, a trait that is thought to be affected grossly by the environment, was (according to a recent report) found to have a substantial genetic component (Cronqvist & Siegel, 2010). Interestingly, according to this study, the strength of the genetic expression of savings behavior is modulated by whether the subject grew up in a supportive environment, exemplifying the interplay between "nature" and "nurture" in a behavioral trait.

What are these genetic polymorphisms that underline our individual identity? Let's turn to some basic concepts. Simply speaking, the term refers to the existence of different "versions" of the same genes that, while in principle are identical, exhibit a slightly different activity. This is due to slight differences in their structure (primary sequence) or their regulatory regions. The differences can be quantitative (for example, stronger or weaker activity of some enzymes) or qualitative (such as a product with different color). It is noted, though, that most of the time, these qualitative differences can be reduced to differences in the activity (quantity) or the amount of the

pigment for color-related phenotypes, but for our purposes this doesn't make any actual difference.

The variation between individuals in virtually all their physical characteristics is due to such polymorphisms, or in other words, due to the fact that different persons carry different versions (and the combinations) of the genes. This is why two brothers can have different color of hair, two sisters have different skin types, or a father has wet-type earwax while his son has the dry type. It's just because they have inherited different versions of the genes that control these traits. Given that humans have about 22,000 genes, and that many of them are polymorphic, the combinations are practically unlimited. Furthermore, many genes have more than two polymorphic alleles, a fact that increases the possibilities even more. This is the genetic basis of human variation, or vice versa, human individuality.

The reason this variation exists is usually related to the evolutionary and adaptation processes, as well as to phenomena associated to pure randomness. In many cases, the benefits conferred by certain alleles and the resulting characteristics are apparent. For example, in human populations, darker colors in the skin confer increased protection against harmful sunrays. This is the reason that darker skin colors are more common in populations closer to the equator, since people in these places are exposed to more time in the sun. On the other hand, since sunlight is also important for the metabolism of vitamin D, people who have darker skin color (due to increased amounts of melatonin) in geographic areas with little sunlight, such as in the northern climates, often have deficiencies in vitamin D. So, what is an advantage under certain conditions can be a disadvantage under different conditions. Obviously, the specific environmental conditions play an important role in attributing a certain genetic feature with a beneficial or negative character.

In other cases, the advantages are more obscure and hard to identify, such as in the case of the earwax type, for which the dry-type has been proposed to be an adaptation against colder climates. Even the variability in a "minor" characteristic, such as earwax type, can produce benefits affecting the domination of one population over another, reflecting the cumulative power and magnitude that even slight genetic variation may have in whole populations. Of course, new alleles, or different versions of the same genes, do not necessarily need to offer selective advantages in order to be stabilized in a population. Even more importantly, these new genetic variants do not necessarily need to offer such advantages instantly, at the time

they appeared in the individuals. They may just be present in the population, increasing the variability and waiting for the conditions to change so natural selection and evolution can utilize them. Thus, it is not only natural selection that drives evolution. Other complex phenomena, such as genetic drift, may account for this stabilization. Genetic drift essentially incorporates random phenomena that affect the frequency of alleles and are stronger in smaller populations. So, if a new genetic variant appears suddenly in a small and relatively isolated population, it may be stabilized and eventually dominate this population, even if it doesn't affect the individual's survival (Ridley, 2003; Futuyma, 2009).

By an analogous manner, it is known that certain diseases are controlled by specific "sick" versions of genes (more accurately speaking, genes encoding for products related to sickness or disease), while others regulate our predisposition or modulate our possibility (or risk) to get a disease. In other words, their presence operates as a genetic risk factor for certain conditions. The stabilization of these "sick" genes within a population occasionally may also be associated to an advantage contributed by these genes in a certain environmental context. In sickle cell anemia, for example, the allele that is related to the disease, when it is found in heterozygosity (one copy of the sick gene and one copy of the normal or wild type allele in diploid organisms, such as humans), renders individuals more resistant to malaria, and this is the reason it is more common in geographical areas with higher malaria incidence. In other cases, disease-related genes may be stabilized in certain populations due to cultural and other phenomena that are not related directly to the genes' function. One such example is the relatively high prevalence of Usher syndrome in Samaritans that causes congenital deafness. Samaritans are related genetically to Jews in terms of being descendants of a group of Israelite inhabitants. While in ancient times they exceeded a population of one million, today there are just a few hundred, and they are considered as one of the more highly inbred populations of humans. Due to the high degree of inbreeding and their relatively low population numbers, a specific mutation in chromosome 11 that causes Usher syndrome has been stabilized in this population. Thus, individuals that have inherited two copies of this gene from their parents suffer from deafness (Bonné-Tamir et al., 1997).

Whenever an apparent association does not exist between the presence of certain "disease"-related alleles and specific advantages, while cultural and historical parameters cannot explain their presence,

the reasons that account for these alleles not having been eliminated from the general population remain under debate and beyond the scope of this book. In any case, though, it has to be kept constantly in our minds that natural selection, by definition, is a constant process that never ends, and what we see now is only a snapshot of evolution. So, in other words, what we see now is not an evolutionary end-point at which the selection processes have been completed and the best possible outcome produced. There is always the possibility that what we see as a negative trait today will be eliminated in the future or turn out to be advantageous when the conditions change. Or new mutations may appear in specific genes that, due to an advantage they offer, the individuals bearing them may increase in numbers and the corresponding alleles may be stabilized in the population. In that latter case, we may even witness that other alleles located in the vicinity of these advantageous alleles may also be favored, indirectly.

While the whole situation, in terms of genetic contribution, is relatively clear, as regards some well-defined physical conditions and characteristics, in discussing behavioral traits the landscape is by far more elusive, and thus the corresponding scientific controversies more vivid. The explanation is simple, and it is related to both the complexity of these characteristics in terms of how the corresponding genetic loci control the development of behavioral traits, as well as the not precisely understood, and indeed defined, contribution of the environment to behavior. Simply speaking, it is easier to identify the contribution of nutrition as an environmental factor in regulating, besides his genes, someone's height (or for a smoker with a history for lung cancer, the possibility to get the disease) in the presence or absence of specific polymorphic alleles, than understand whether some violent behavior, besides the environment, is also due to the genetics of the individual.

On top of that, the scientific and conceptual limitations are reinforced by the public sensitivity—that is not frequently irrational—against these notions that restrict these studies. Speaking about how society, in terms of a given cultural context, might judge and classify behaviors and behavioral traits, it is also noted that these are not static notions, but are rather dynamic and are highly influenced by the socio-cultural environment and the historical time-point we refer to. These notions are illustrated very nicely by studying how different and occasionally extreme behaviors were considered (or not) to be pathological in different historical periods. Such issues are discussed,

among others, in high detail and depth by Michel Foucault in his classic *History of Madness* (2006). Thus, if even the borderline between normal and pathological is not strict and objective, then it is understandable why the classification of an individual's trait A as A1 or A2 type is also inconclusive at the least.

Despite those—conceptual or not—limitations, a lot of progress has been made and various behavioral traits have been linked to specific genetic variations. Or, vice versa, certain polymorphisms have been linked to an increased probability against specific behaviors. The term "probability" is of particular importance because it indicates that merely having the gene doesn't mean that someone will develop the trait, but rather that he has higher or lower chances to do so. Or, alternatively, among a group of people that carry the gene, only a fraction will develop the trait. These "chances" (reflected by the genetic penetrance of the trait) among others are determined by the interaction of the gene with the environment. In other cases, they are attributed to pure randomness or stochastic phenomena.

Naturally, the precise manifestation of these behaviors, their degree or level of expression, and their exact type are formulated by environmental factors, as well, but undoubtedly, the genes we carry also play a major role in the determination of personality. In several cases, a link between various traits and specific genetic loci has been reported with some being better supported by the experimental evidence than others. Those include, but are not limited to, behaviors such as the exploratory activity, novelty-seeking, tendency for aggression, social behavior, or even risk-taking behavior related to financial decisions. Genetic variations in (brain-) hormones, neurotransmitters, their corresponding receptors, and other proteins related to their metabolism or physiology, are the usual suspects. The role of neurohormones in the decision process has recently been described, among several other interesting examples, by Lehrer in his book *How We Decide* (2009). This observation is not surprising, considering the pleiotropic action of such hormones and their involvement in determining our behavior and responses. As we will discuss in detail in subsequent chapters, an example is offered by the polymorphisms in the serotonin transporter gene. Serotonin, or 5-hydroxytryptamine (5-HT), is a neurotransmitter that is derived by the modification of the amino acid tryptophan. Amino acids are the building blocks of proteins; tryptophan is one among 20 of those. Among other tissues, tryptophan can be found in the central nervous system. It is acting via specific receptors that, in turn, can affect the activity of other

neurotransmitters, such as epinephrine, dopamine, and achetylcholine. Serotonin levels are regulated depending on specific internal and external stimuli, and have been associated with various behaviors and conditions, such as appetite, mood, emotion, and sleep. Proper activity of serotonin is facilitated by serotonin transporter (5-HTTLPR), a protein responsible for the re-uptake of serotonin from the synaptic cleft. Importantly, the gene encoding for this transporter protein is polymorphic. A certain polymorphism in the promoter region of this gene that corresponds to the gene's regulatory region, which determines when it will be activated, results in two versions of the gene: a long version (*l*) and a short version (*s*), with the latter associated with reduced transcriptional activity and, thus, decreased availability of the serotonin transporter. As regards a potential link of 5-HTTLRP and behavior, the long allele has been associated, among other traits, with "happiness," while the short allele with anxiety and impulsivity. It's worth noting that the short version of 5-HTTLRP is found in Asian populations almost twice as much as in Caucasians, with considerable variation among Europeans.

This book attempts to explore various selected behavioral traits in view of their potential contribution in shaping cultures, history, and eventually historical decisions. The genetics of these traits will also be discussed in light of the prevalence of specific polymorphisms in different ethnic groups and how such differences may account for the different characteristics between people of different races, or how they might have affected their culture and history.

The study of various polymorphisms in different human populations is also of great interest to anthropologists; however, such studies usually focus on the distribution of these polymorphisms. By using them as markers, biological anthropologists attempt to identify similarities or divergences between different populations, patterns of migration and intermixing, and other factors related to those characteristics. Besides that function, such "meaningful" polymorphisms may also exhibit occasionally a specific contribution to behavior and may affect differentially some general trends or traits in various distinct populations. This latter notion is the main focus of this book. We will concentrate particularly on the "comparison" between people of Asian and Western origin, since these people exemplify the two major cultural lines of humankind. By analyzing cultural trends and characteristics of Eastern as opposed to Western civilization, we will explore whether they are in line with specific genetic trends de-

scribed for these people, which in turn may indicate the existence of a causal association between genes and cultures.

2.1. Genetic Markers and Analysis

When talking about polymorphisms and different versions of our DNA, it has to be mentioned that it is not all our DNA that corresponds to genes (that, in turn, and as mentioned before, comes into different versions). Actually, the vast portion of our DNA, at the magnitude of about 98%, is "junk." It doesn't have any specific function (as far as we know), but it's still there. And it exhibits even stronger variability, or polymorphic incidence, than the coding DNA between individuals. This is not surprising, considering that it isn't the subject of evolutionary pressure. The two major—and genetically useful—sources of variation in the DNA correspond to small changes in the repetition number of certain core, repetitive sequences, or base substitutions (that occasionally, if they are found within the gene's coding sequence, don't change the corresponding protein). The onset of a mutation in a protein-coding segment of DNA can quite possibly affect the cell's—and, by extrapolation, the individual's—viability. Whether a certain protein has a version with activity one fold or two fold, due to polymorphisms in its genomic sequence, it is quite possible to affect some physiological process, with the one version being "better" than the other, at least within a given environment.

Most of the time, these mutations are eliminated because pure chance in their occurrence is more likely to generate "bad" alleles. Infrequently, these random genetic events are associated with the contribution of a beneficial feature, a sort of advantage, and eventually they will dominate the population if they contribute to the individual's (mating at the end) performance, or the performance of the group as an entity (in cases of group selection). This is the essence of evolution and refers to the cases at which the changes interfere with some kind of activity or overall efficiency.[2] On the other hand, if the mutation has targeted a non-coding segment of our genome, namely our "junk" DNA, it is not going to affect the individual's viability. In these cases, and by mechanisms that do not directly involve selective processes, they can be stabilized in the population and passed into the subsequent generations by following of "unbiased" inheritance. The term "unbiased," in this case, refers to the fact that the chances of inheritance into the subsequent generations of any of the two po-