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Review Article

Impact of Sequencing Genomes in Search of Human Consciousness

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Abstract

The purpose of this article is to motivate and inspire my students to search for Human consciousness. Would genome sequencing answer some of the most fundamental questions we have asked ourselves since the dawn of human civilization? What does it mean to be human? What is the nature of our memory, our consciousness, and our development from single cell to a complete human being? What is the biochemical basis of our senses, the process of our aging? And what is the scientific basis of our similarity and dissimilarity. Similarity that all living creatures from a tiny blade of grass to the mighty elephant including man mouse monkey, mosquito and microbes are all made of the same chemical building blocks, the four nucleotides AT and GC and yet we are so diverse that no two individuals are alike even identical twins are not identical they grow up to become to separate individuals. Our genome carries the complete catalog of all our genes. Genes code for proteins. Does protein-protein interaction give human consciousness? To answer these questions, we must search in our genome. Since all human organs could be replaced by implantations except Brain, we must search our Brain as the site of our consciousness. Of all the living species on Earth, Chimps are closest to humans. We share 98.9% of our genome with Chimps. Within 1.1% of our genome lies the seat of our consciousness which gives humans exceptional ability to land men on Moon and bring them back safely to Earth. Are there specific genes whose proteins carry instructions to create human consciousness? Is there a master gene, which controls the function of all 24,000 genes in human genome? Is cerebral cortex or Hippocampus prime site of human consciousness? Once identified the genes whose proteins create human consciousness, using genetic toolkit we should be able to cut, paste, copy, and sequence its genome. If human consciousness is in the brain, could we design drugs to control human consciousness? By designing AZQ (US Patent 4,233,215), I have demonstrated that I could punch a hole in the Iron curtain called the Blood Brain Barrier (BBB), the fatty layer that protect the human brain from exposure to all toxic chemicals. Could we create a superior mind? A sound mind is free from all genetic defects. It asks what the fate of humanity on Earth is. What is the purpose of human Life on Earth? Do us a future and a plan to escape Earth before the Sun dies. The answer is that we do have a purpose not only to survive but also to protect, preserve and spread human intelligence in every corner of the Universe.

Keywords: Genes; Conscientiousness; Nucleotides; Glioblastoma; Sequencing; AZQ

A Note to my Readers

The Impact of Sequencing Human Genomes are a series of lectures to be delivered to the scholars of the National Youth League Forum (NYLF). These scholars are selected from around the country organized by the "Leadership in Medicine Program," The NYLF scholars are the very best and brightest students selected from all over the USA and the world brought to Washington by Envision, an outstanding organization that provides future leaders of the world. Part of the following lecture was delivered to the scholars of (NYLF) at the Gaston Hall of the Georgetown University, Washington, D.C. Some of the previous lectures are published in the scientific journals and are also available on the following website: https://www.facebook.com/hameed.khan.7773/notes

Historical Background

Since the dawn of human civilization, we have been asking ourselves an important question that is what makes us humans and what it means to be human. Are humans unique? Is humanness requiring our ability to communicate with each other? Do other species communicate? As far as we know, there are three million known and ten times as many unknown species exist on Earth; some way, they communicate with each other. It is obvious that like humans, all living creatures on Earth communicate with each other whether they are microbes, or mouse, or mosquitoes, or monkeys. How different are we from other species? Over eons, like us other species must have developed some means of communications. Why are humans so very different? Is it because we communicate with each other by languages and gestures? Is it what means to be humans? In this article, we will explore our human mind, human body, human genome, and human society to answer the question what makes us so unique. How we evolve, how we interact and how we communicate with each other? We need to examine the nature and function of our brain because our brain is the seat of our consciousness, the center of our Altruisms and our Free Will. We must examine humans as thinking, evolving species as cultural, social, and technical being.

I have divided this article in three parts:

First, I will provide historical background to explain who are we, where have we all come from and what was it that made us this way and how we use language as a means of communication?

Second, I will describe how we sequenced our genome. The greatest book of human life on Earth. Everything about our humanness is written in our genome. It provides catalogs of all our genes. We identify good and bad genes. How we use the product of good genes to keep us healthy and how we design drugs to shut off bad genes to treat diseases. We suspect that it is the interactions of genes-gene or protein-protein within our brain that make us humans. Is our humanness related to our means of communication vocally by using words, sentences or by hand gestures?

Third, I will address the ethical problems.

Now, we have sequenced human genome and read the entire book of life. We have identified our ability to speak which is due to the evolution of FOXP2 genes, which code for proteins that control our speaking traits. These proteins make our vocal cord and voice box. We have already developed Recombinant Technology to transfer and combine human genes into non-human species including bacteria to produce useful proteins. To compare the vocal ability of modern humans with our past ancestors, scientists at the Max Plank Institute in Germany have sequenced the genome of Neanderthal, a sub-human species that died out over 28,000 years ago. The tissues sample extracted from the Neanderthal fossil obtained near the Rock of Gibraltar has provided enough genetic material, DNA, to read its entire genome or its complete book of life. By comparing Neanderthal Genome with the modern Human Genome, we could see what other genes besides FOXP2 genes that are present in us, which gives us the ability to speak verbally like modern humans. Using its sequence, should we bring back Neanderthal? Could we insert those missing genes in Neanderthal genome and make them equal to us. With the current technology, we could do it. Should we, do it? If we succeed in implanting verbal ability in Neanderthal genome, it will create some serious ethical moral problems such as where should we keep the genetically modified Neanderthals, in your neighborhood-housing complex, or in the Zoo? In this section, I will describe what are the ethical, moral, religious problems we are likely to face in future.

Let me begin with the historical background. According to cosmologist, 13.72 billion years ago, our Universe was a single mass of energy. May be God had said, let there be light and there was light. The Universe exploded with a Titanic force spreading its content in every direction. The echo of that explosion, the background radiations, is still observable and coming from every direction. As the Universe expands, its content, the plasma, cooled and formed subatomic particles such as electron, proton, and neutron. Over eons, the subatomic particles cooled to form molecules leading to matter, which coalesced by gravitational forces to form galaxies. There are about 100 billion galaxies in the visible part of our Universe. The galaxy in which we live, we called it the Milky Way Galaxy. There are at least four hundred billion stars like our Sun in the Milky Way Galaxy alone. Our Sun has 8 planets and about 160 moons revolving around our Sun forming our Solar System. Our Earth is revolving around its own axis and complete one circle in 24 hours. Our Earth is revolving around our Sun and complete one circle in 365 days and our Solar System is revolving around the Milky Way Galaxy completing each circle in 250,000 light years (light travels at about 6 trillion miles in one year making a light year). Our Earth is the third planet from the Sun. Our Solar System was formed about four and a half billion years ago by condensation or accretion of dust and material from the super nova explosion on the third arm of our Milky Way Galaxy. Early Earth was hot and molten lava made of 110 stable elements. It had no water and no Oxygen. All the water on Earth was brought by the intense bombardment of icy comets. Today, seventy percent of our Earth is covered with water. Early Earth was made of Nitrogen, Carbon dioxide, Methane, and mud water. There was no life, but life-supporting ingredients did exist. A million-lightning strike Earth each day. At some remote corner, lightning struck at a cloud of gases on a phosphate rock containing Carbon dioxide, Nitrogen, Methane, and water forming the life giving four organic molecules called nucleotides and they are Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). Three out of these four nucleotides, codes for an amino acid called Codon. Hundreds of codons join to make the essential building

blocks called the life-giving proteins. All living creatures on Earth are made of four nucleotides, which give 64 combinations which code for all twenty amino acids.

In 1953, Stanley Miller in Chicago University demonstrated in the lab how life-giving amino acids were formed by simply sparking electric current in a flask containing Nitrogen, Carbon dioxide, methane, and water. Within days, he was able extract amino acids from the mixture of the gases in the flask. On early Earth, similar building block of life was formed by thunder and lightning. These nucleotides combine and recombine resulting in the formation of the first life giving molecule, the Ribonucleic Acid (RNA). Our journey began in the RNA world. RNA can copy itself. Self-replicating RNA molecules proliferated before the evolution of DNA and proteins. Our planet was filled with anaerobic gases, hostile to life, such as Nitrogen and Carbon dioxide. The earliest life forms we know of were microscopic organisms (microbes) that left signs of their presence in rocks of about 3.7 billion years old. Prokaryotes were the earliest life forms, simple creatures that fed on carbon compounds that were accumulated in Earth's early oceans. Slowly, other organisms evolved that used the Sun's energy, along with compounds such as sulfides, to generate their own energy. Cyanobacteria converted to blue green algae, which turned it into an internal solar power plant. They developed the Photosynthetic apparatus. Land plants evolved from ocean plants. That is, from algae. Plants are thought to have made the leap from the oceans onto dry land about 450 million years ago. Early Earth must have been carpeted by blue green algae. Its job is to conduct photosynthesis that is to absorb Carbon dioxide, convert it to its food Carbohydrate, and release Oxygen as its byproduct. Microbial plant life first appeared. Then around 350 million years ago, many kinds of small plants started evolving into trees. These made the first great forests of the world. Over billions of years, the forest absorbed Carbon dioxide and pumped Oxygen in our atmosphere. Today, our atmosphere is filled with eighty percent Nitrogen and about twenty percent Oxygen and 800-ppm Carbon dioxide. Mutations provides fuel for evolution. Four and a half billion years of biological evolution brought us here. Today, there are at least three million known, ten times as many unknown living species exist on Earth, and yet we share the same 20 amino acid and 4 nucleotides with all living creatures on Earth. There were no humans on Earth three and a half million years ago.

The Origin of Human Conscientiousness

Chimps were living in the Afar Valley in Ethiopia in the heart of Africa for over six million years. A few mutations occurred in the brain of a female Chimp we named her Lucy who gained conscientiousness making her the first human. She walked on her two feet and was anatomically identical to modern humans. There was plenty of food, shelter, and fresh water available in the Afar Valley, the offspring of Lucy thrived. When their population exploded and their number reached to about a thousand, the food and water supply was running out. They left Afar Valley in groups in search of food, water, and shelter. Those groups of early human who went west arrived in the present-day Europe. Their fossil were found in the Neanderthal Valley in Germany. Waves of early African arrived in different parts of Europe. The more modern humans who look like the present-day humans arrived in France about 100,000 years ago. Radioactive dating of their fossil found in the caves in France showed that they left paintings on the walls of the caves about 100,000 years ago. Those early humans who went east crossed the frozen ocean during ice age and went to Australia within almost the same time. The radioactive dating of fossil found in Australia is about 85,000 years old. Within 100,000 years, the modern humans spread on all seven continents of Earth. Today, we are about eight billion and divided in over 200 nations. Our number is increasing so rapidly, we are adding about 90 million individuals each year to this planet. We are running out of essential resources. Like our ancestor Lucy and her children who left Afar Valley in search of food, water, and shelter, we are wondering if we could search for another Earth like planet in the nearest Solar Systems.

I wrote in my several previous lectures [1-18] about the impending problems facing humanity such as the environmental, social, and ethical problems and try to make some prediction as how to avoid them. I informed you that the future of the world was bleak; the population explosion was unstoppable as we are adding 90 million people each year to our planet; global famine was inevitable as it has not rain in southern part of Africa for many years; cancer epidemic caused by chemicals pollution in our environment would shortened our life and the death rate in America from cancer alone is over half a million each year; the acid rain from the air pollution was falling on the forests destroying millions of trees on the Appalachian trails and one third of Black Forest in Germany has charred, burnt and destroyed; the desert was advancing by a mile or two each year as we clear cut trees and destroying forest in Amazon where 28 thousand acres of land is cleared each year for building the Trans-Amazon High Way which is almost complete; the oil was running out as we consume over 100 million barrel of oil each day. The number of nuclear club countries is increasing. As of January 2021, the following eight nuclear club countries have accumulated 13,080 nuclear warheads: Russia - 6,255 nuclear warheads, United States of America - 5,550 nuclear warheads, China - 350 nuclear warheads, France - 290 nuclear warheads, United Kingdom - 225 nuclear warheads, Pakistan - 165 nuclear warheads, India - 156 nuclear warheads and Israel - 90 nuclear warheads. We have accumulated over 13,080 nuclear warheads. Only a fraction of the explosions of these warheads will create the nuclear winter, which will finish us all. Fortunately, none of those terrible things happened. On the contrary, we are more prosperous today than at any time in human

history. To name a few, the per capita income has triple, even in developing countries. The life span is up by thirty percent; even child mortality is down by two third even in developing countries. The per capital food production is up by a third even in India. The massive wind farming worldwide and solar panels in Europe and in America is reducing oil consumption. Today, thousands of nuclear warheads are being dismantle although smaller and more efficient are replacing them. All these developments are happening when the population has double to about eight billion; how did we achieve this. How did we become the only species that become more prosperous as we become more populace?

To understand the creativity and complexity of human mind, we must study ourselves. What makes us humans? The total genetic information that makes us humans is called the Human Genome. We found that the essence of life is information, and the information is located on the four genetic letters called nucleotide bases and they are Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C). These are the initials of four genetic letters found in the nucleus of living creatures including man, mouse, monkey, and microbes. The book of life of all living creatures are written in these four letters. A string of nucleotides is called the Deoxy ribonucleic acid (DNA). The information to make all of us is written on DNA. We broke the genetic code and unlocked the secret of life. According to Central Dogma of Crick and Watson, [19] the information on DNA is transcribed on RNA which is translated in Ribosome to protein. The double helical DNA replicates (makes its own copies) in the nucleus and it transcribes into the single stranded RNA as it leaves nucleus as mRNA in the cytoplasm (RNA is converted to mRNA by splicing out non-coding sequence) which is translated in the Ribosomes into proteins. Information flows from both good genes and bad genes from nucleus into the cell keeping the organism healthy or sick. Good proteins from good genes keep us healthy and bad proteins from mutated genes produce bad proteins that make us sick. The flow of information is continuous and uninterrupted. To understand the normal function of a human being, we must read his book of life that is his genome.

In 1990, the US Congress authorized us, NIH, three billion dollars to decipher the entire Human Genome, to decode, and to map the location and function of all 24,000 genes present in the nucleus of every cell of human being. Out of 24,000 genes, we identified sixteen thousand good genes that make good proteins that keep us healthy. There are at least six thousand defected genes known to occur in humans which are responsible for causing all diseases and we also carry two thousand Pseudogenes which has lost their functions because they are no longer in use.

We deciphered all 46 chromosomes, 23 from each parent. The 46 chromosomes present in each cell of our body are the greatest library of the Human Book of Life on planet Earth. The Chromosomes carry genes, which are written in nucleotides. Before sequencing (determining the number and the order of the four nucleotides on each chromosome), it is essential to know how many genes are present on each chromosome in our Genome. The Human Genome Project has identified the following genes on each chromosome: We found that the chromosome-1 is the largest chromosome carrying 263 million A, T, G and C nucleotides bases and it has only 2,610 genes. The chromosome-2 contains 255 million nucleotides bases and has only 1,748 genes. The chromosome-3 contains 214 million nucleotide bases and carries 1,381 genes. The chromosome-4 contains 203 million nucleotide bases and carries 1,024 genes. The chromosome-5 contains 194 million nucleotide bases and carries 1,190 genes. The chromosome-6 contains 183 million nucleotide bases and carries 1,394 genes. The chromosome-7 contains 171 million nucleotide bases and carries 1,378 genes. The chromosome-8 contains 155 million nucleotide bases and carries 927 genes. The chromosome-9 contains 145 million nucleotide bases and carries 1,076 genes. The chromosome-10 contains 144 million nucleotide bases and carries 983 genes. The chromosome-11 contains 144 million nucleotide bases and carries 1,692 genes. The chromosome-12 contains 143 million nucleotide bases and carries 1,268 genes. The chromosome-13 contains 114 million nucleotide bases and carries 496 genes. The chromosome-14 contains 109 million nucleotide bases and carries 1,173 genes. The chromosome-15 contains 106 million nucleotide bases and carries 906 genes. The chromosome-16 contains 98 million nucleotide bases and carries 1,032 genes. The chromosome-17 contains 92 million nucleotide bases and carries 1,394 genes. The chromosome-18 contains 85 million nucleotide bases and carries 400 genes. The chromosome-19 contains 67 million nucleotide bases and carries 1,592 genes. The chromosome-20 contains 72 million nucleotide bases and carries 710 genes. The chromosome-21 contains 50 million nucleotide bases and carries 337 genes. The Chromosome-22 contains 56 million nucleotide bases and carry 701 genes. Finally, the sex chromosome of all females called the X-chromosome contains 164 million nucleotide bases and carries 1,141 genes. The male sperm called the Y-chromosome contains 59 million nucleotide bases and carries 255 genes.

If you add up all genes in the 23 pairs of chromosomes, they come up to 26,808 genes and yet we keep on mentioning 24,000 genes needed to keep us function normally. We have identified 16,000 good genes, which keep us healthy and 6,000 bad genes responsible for causing diseases. The remaining 2,000 genes are called the pseudo genes, which lost their function. For example, millions of years ago, humans and dogs shared some of the same ancestral genes; we both carry the same olfactory genes needed to search for food in dogs. Since humans do not use these genes to smell for searching food, these genes are broken and lost their functions in humans, but we still carry them. We call them Pseudogenes. Recently, some Japanese scientists have activated

the pseudo genes, this work may create ethical problem in future as more and more pseudo genes are activated. Genes code for proteins. The proteins control the function of all genes. We have identified specific proteins, which perform specific function. For example, there is specific gene, which carries instructions to switch on or switch off a gene. Are there specific genes, which carry instructions to create human consciousness? Is there a master gene, which controls the function of all 24,000 genes in human genome? Is cerebral cortex being the site of human consciousness? Once identified the genes whose proteins create human consciousness, using genetic toolkit we should be able to cut, paste, copy, and sequence its genome. Although gene codes for a protein, not all 24,000 genes code for proteins. It is estimated that less than 19,000 genes code for protein. Because of the alternative splicing, each gene codes for more than one protein. All the genes in our body make less than 50,000 protein, which interact in millions of different ways to give a single cell. Millions of cells interact to give a tissue and hundreds of tissues interact to give an organ and several organs interact to make a human [20-24].

Not all genes act simultaneously to make us function normally. Current studies show that a minimum of 2,000 genes are enough to keep human function normally; the remaining genes are backup support system, and they are used when needed. The old cells begin to die, and they are constantly being replaced by healthy cells. Why do the normal cells become abnormal or become cancerous. Damage to functional gene called Mutations are responsible for causing normal cells to become abnormal. Mutation is caused by exposure to Radiations, Chemical/Environmental Pollution, Viral Infections or Genetic Inheritance. Mutations also occurred during DNA replication, such as insertion, deletion, relocation, multiple copying, inversion etc. Anyone those factors will disrupts the two percent of the coding region of our genome will alter its function by slightly altering its code; an altered codon will code for a wrong amino acid and wrong amino acid will give a wrong protein and it will make normal cell become abnormal. When the functions of Codons are disrupted intentionally or unintentionally, we alter the Codon's function. For example, intentionally we alter a codon by smoking and unintentionally by exposure to environmental pollution such as chemicals or radiations. Altered Codons have wrong information to make wrong amino acids. Wrong amino acids make wrong proteins and wrong proteins make wrong cells and wrong cells grow much faster than the normal cells and become abnormal or cancerous and they form a lump, we call these lumps, tumors.

Our ability to read the book of our own life makes us unique and separates us from the rest of the living world. We not only predict the future course of our health, but also, we could alter its outcome. Looking at the genomes of the families who are suffering from long illnesses, we predict the future course of these diseases by diagnostic methods that we have already developed for many of these diseases. Alteration in the somatic cell lines to prevent diseases is permitted, but germ-line gene therapy is prohibited. Alteration in the eggs and sperms could last for generations. Germ line gene therapy raises several ethical moral questions. It would be easy to eliminate diseases permanently and knock out badly mutated genes, which have affected families for generations. Unfortunately, knocking out the mutated genes from eggs and sperms before fertilization would conceive a child free from diseases like Mental retardation, such as Anger, Aggression, Depression, Schizophrenia, Bipolar Disorder, Parkinson, Epilepsy, Autism, Down syndrome, Alzheimer, but also as stated above, the alteration made now would carry in future generations. Should we alter genetic makeup of children who would not even be born for the next several decades? In 2003, we completed the Human Genome Project. We learned that our brain is made of 86 billion cells called Neurons. Like all cells, each neuron carries 24,000 genes. Not all genes in all cells function simultaneously. While small number of genes function in our kidney, lung, and liver, almost one-third genes function in our neurons giving us awareness of our unique thoughts, memories, feelings, sensations, and environments. Essentially, our consciousness is our awareness of ourselves and the world around us. Genes code for proteins. Is protein-proteins interaction that give our consciousness? This awareness is subjective and unique to us. Consciousness enables us to integrate information from all five different senses and we seem to be more self-aware than most other animals.

We sequenced (read the entire script of our genome, letter by letter, word by word) the entire Human Genome that the number of letters and the order in which they are arranged (sequence) called the Human Genome Project. We found that less than two percent of the Gene in our Genome codes for proteins and the rest is the non-coding regions, which contains switches to turn the genes ON or OFF, pieces of DNA which act as promoters and enhancers of the genes. Using restriction enzymes (which act as molecular scissors), we can cut, paste, and copy genetic letters in the non-coding region which could serve as markers and which has no effect, but a slight change in the coding region makes a normal cell become abnormal or cancerous. Recent studies showed that mutations in switches, promotors and enhancers which are present in the non-coding regions are also responsible for some unusual diseases. We need to go back and look at these regions more carefully. Everything we want to know about humans is locked in our genome. It is the greatest library of our genes. Since we sequence the human genome about 20 years ago, we learn to manipulate our genome in three different ways:

First, **good genes** from our genome, we could make large-scale good protein like Insulin and growth hormones to treat deficiencies to keep us healthy.

Second, **bad genes,** we could shut off those genes either

by Gene Therapy/CRISPER or Drug Therapy. SCID for Gene Therapy and Chlorambucil or AZQ for Drug Therapy.

Third, introducing **super genes** to create super quality humans (enhancing extraordinary qualities) can be done, but are not permitted at this time).

For example. Children born with Down syndrome have made an extraordinary contribution to the science of genetic. We are all born with 46 Chromosomes, and they are born with 47 Chromosome. Their extra chromosome is Chromosome-21. They proved for the first time, that humans could survive with an additional chromosome. Chromosome-21 is neither a simple nor a small chromosome. It is made of 50 million Nucleotide base pairs and carries 337 genes. By comparing the Chromosome-21 of the Down syndrome babies with the Reference sequence, we could identify the gene variants responsible for their low IQ and sensitive to some diseases. (Down syndrome causes a distinct facial appearance, intellectual disability, developmental delays, and may be associated with thyroid or heart disease.). We could replace those bad genes with good gene. We could splice the super IQ genes in Chromosome-21, could we make them super achievers. For example, Albert Einstein is recognized as the man of the century because of his accomplishments. Einstein's brain is stored in a museum. Could us barrow a single neuron from his brain and sequence its genome. As I said above, our genome is the catalog of all our genes. The greatest book of our genes on Planet Earth. We could compare Einstein genome with the Reference Sequence and identify gene variants responsible for his high IQ.

Although this experiment will not be permitted in any Labs, let us conduct a thought experiment. From the previous lectures, my students know that in Genetic Engineering, we cut, paste, and copy a gene. By using Restriction enzymes, we can cut all genes at a specific site and prepare a Restriction site map. We can purify a specific variant by Gel Electrophoresis. By using recombinant technology, we could cut and paste this gene in Plasmid genome. The transgene plasmid protects pure gene variant from enzyme destruction. Millions of colons are made of transgene plasmid by harvesting in Yeast cells or viruses. Pure genes are released from transgene plasmid by restriction enzymes. Millions of copies of the pure gene variant can be saved in cell-lines or viruses. Purified Einstein's high IQ variants in Viruses could be used to infect the chromosome-21 of down babies. After infecting, we could sequence Down syndrome baby's genome to ensure that we have successfully cut, paste, and copy a gene to produce down babies with very high IQ. No agency will provide funds to conduct such studies. FDA requires safety and efficacy studies as described in CFR. Although Insulin extracted from animal pancreas was in used for years, before approving genetically manufactured Insulin, FDA still required limited safety and efficacy studies. The point I am trying to make is that humans have extraordinary ability to solve insoluble problems. Among all the living creatures on Earth, only humans can bring their brain together, enables their ideas to combine and recombine to meet and cross-fertilize, and accomplished miracles. We thrived because of this extraordinary quality of the modern human's mind to work collectively. This was not true with some ancient civilizations. Those civilizations who refused to change such as in Neanderthal are perished.

Our collective minds accomplish miracle, for example if you go to any local museum, and you find a handheld stone axe made by our ancestors, the pre-human. Home erectus, made this stone axe about 30,000 years ago for their personal use and compare it with today's modern cell phone. They both are the same size. They both designed to fit in the human hand. Homo erectus made the stone axe over 30 thousand generations ago. This axe was made for their personal use. There was no progress and no innovations because they never shared this axe making skill with anyone. On the other hand, your cell phone is undergoing intense innovation by dozens of skill workers. So many innovations are constantly inserted in your cell phone, it become obsolete almost every other year. When you buy a new cell phone, your old cell phone has become useless. The stone tool is made by one substance silicone dioxide; but your cell phone is made by a variety of substances, such as silicone, metal, plastic. It is not only the combination of different substances but also it is the combination of many ideas; the idea of making electronic circuits which control the flow of electrons and the idea of using laser; the ideas of transistor; the ideas of silicone; all these substances and dozens of novel ideas combine in this technology resulting in the cell phone. This cumulative knowledge is the great secret to understanding human uniqueness, a quality no other species possess. We draw upon each other's specialization. The stone axe made by Homo erectus was made by one person and he knows how to make another one if he needs it. On the other hand, hundreds of thousands of people make the cell phone. No one person knows exactly how to make the cell phone. The factory that assembles different parts to make the cell phone has no idea how to make any part. The people who make parts have no idea where and how to get the basic materials. We all rely on each other's expertise.

Similarly, our body is the accumulation of 220 different tissues; our brain cells; our liver cells and kidney cells performing different function and when functioning together keep us fit and healthy. To study life, we study a single living cell that is bacteria. Bacteria grows and reproduce in two ways; either by budding out making one cell into two; genetically identical copy, or by cross-fertilizing with other bacteria reproducing two different cells by exchanging genetic information. Bacteria that have been making identical copies are confined to its own linage; its own genome and remain bacteria for three and a half billion years; Bacteria that cross fertilize are not confined to its own linage; they inherit

mutations from each other giving the variety of life forms we see around us today. When two species cross-fertilize, they exchange their genetic material, and they inherit the genetic innovation of the entire species? To survive the early harsh environment, species evolve, and evolution selects only those species, which acquired and accumulate useful mutation to thrive. We are the result of the three and a half billion years of biological evolution. What made human so unique is that we exchange our ideas, our hopes, and dreams with other human beings? Exchanging ideas is a unique human feature; not found in any other animals. The more we exchange, the more we innovate to change to improve. When we innovate, we hope that the new device would be better than the previous one. The current thinking is that if you can change a device to improve it, we must change it and make the old device redundant.

You go to any restaurant and order a meal. Within an hour, the best food is served. Do you have any idea how many people prepare your food? The farmers grow the seeds, vegetable, some person refines the food, supply to the restaurant, the cook combines various ingredients, and within an hour, the most nutritious food is served. Preparing food for you is a collective effort. We work for each other. We rely upon the specialization of each other. We work for each other across the colony, across the nations and across the continents. When nations export goods and services to each other, we export our specialization. Our cars are made in Germany and TV sets are made in Japan. The change must be going on since the appearance of the first living creature on Earth. Trade is ten time as old as farming. Exchange between groups is going on for hundreds of years. Jasper and shell have been moving around for hundreds of years. People started exchanging objects between groups for a very long time that led to specialization. Long distance travel of tools is a sign of exchange not migration. What happen when you cut people off from the exchange? When they lose their ability to exchange, they lose their specialization, they not only slow down technological progress but also you throw them into reverse. An example is Tasmania; when sea level rose, and Tasmania became an island about ten thousand years ago; it was cut off from the mainland Australia; Tasmania was isolated; they had only four thousand people and the population was not large enough to maintain the specialized skill to develop technology they had. There was no trading contact with the mainland Australia. There was no progress in Tasmania; the population regressed. Tasmania is the least populated state of Australia. Today, more than half a million people live mostly in its capital Hobart. Aboriginal descent varies according to the criteria used to determine this identity, ranging from 6,000 to over 23,000.

Compared to all other animals, the greatest intellectual achievement of humans is that we work collectively. The finest example is landing men on the moon and returning safely. Sharing the collective specialization of countless people make us possible to assemble a five-million-piece rocket, called Apollo, which landed men on the moon and brought them back safely. No single person knows how to assemble a rocket. It is a collective effort of thousands of specialists. We are a society of specialists who work for each other. Our collective brains have accomplished miracles. Today, we are dreaming of colonizing Mars. We have sent rovers to find a suitable place to develop settlements on the surface of Mars. As of May 2021, there have been **six** successful robotically operated Mars's rovers; the first five, managed by the American NASA Jet Propulsion Laboratory, were (by date of Mars landing Sojourner (1997–1997), Opportunity (2004–2018), Spirit (2004–2010), Curiosity (2012), and Perseverance (2021). Using Mars as a base, we plan to launch unmanned spacecraft in search of exoplanets finding a next home for humanity in a distant star system. What we have done in human society through exchange and specialization is that we have created ability to do things, we cannot even understand. In technology, we created things beyond our understanding beyond the capacity of individual human mind to an extra ordinary degree. How are we communicating and how we are cooperating with each other. We have created something with our collective brain. It is the interchange of ideas meeting and mating that is causing technological progress incrementally, bit by bit, our ability to combine and recombine our ideas and our expertise technology will advance and therefore improve our living standard and that is how we advanced. Everybody has something to contribute; it is our collective brain that will accomplish our unthinkable dreams. We are surely accelerating the rate of innovation. This is our unique ability not found in any other living species.

Our ability to speak through language and gestures is also of enormous advantage over other species. We speak in digital language, which has infinite variety. Altruism is unique quality to humans. For example, in a primitive society, we tell our neighbors that there is an apple orchid on the other side of the hill. It benefits our neighbor at our expense. No other species does it. We specialize in a single skill, and we exchange that skill with the skills of others. We live in a cooperative society in which we exchange each other's talent. For example, you have a skill to fly the plane. I have a skill to make drugs to treat an illness. I sell my drugs and pay you to fly me in your plane. Sharing of each other talents and skills is unique to humans. Continuing evolution of culture causes our brain to evolve. Our brain is continuously evolving. When we gain a new knowledge, some changes occur in our brain. We retain this information for future use. New neuronal circuits are formed where our new memory is stored. This means that we are continuously evolving and constantly improving. This evolution of brain is unique to humans. The unit of inheritance is called a Gene and the unit of knowledge, thought, culture, or an idea is called a Meme. Gene travels slowly vertically from parents to children, but Meme travels faster horizontally from person to

person. The ideas move so rapidly and multiply so exponentially, they must be renewed frequently otherwise Knowledge gains three years ago is already outdated. Another unique feature of human beings is that we accumulate our knowledge outside our brain in books and in computers. We also have incredible ability to extract new important ideas from a book or extract useful information from a massive amount of database generated by computers.

As science advance, technology advance as well. Human uniqueness also advances. The size of our brain becomes larger. Our brain is only a three-pound flesh that we can hold in the palm of our hand and yet it consumes about ten percent of our blood supply even though no parts in our brain are moving. As the brain size increases, our understanding of the world begins to increase. We begin to understand life at molecular level. We begin to read the book of life at the molecular level, the total genetic information that makes us is called our Genome. We not only read our book of life, but we develop the ability to read the book of life of other living creature as well. We learnt that forty percent of our genes we share with a tiny worm called C. elegance; almost seventy five percent of the genes we share with mouse and almost ninety-eight-point nine percent of the genes we share with our closest relative Chimps. Only one point one percent of the difference between our genomes makes us superior to chimps. It makes us superior to all other creatures on Earth. It gives us our thoughts, our ideas, our consciousness, and our vision. Just a few switches turned on in few genes in our brain that gave us the consciousness and make us humans. About twenty years ago, we completed the Human Genome Project. We read our entire book of life, letter by letter, word by word and sentence by sentence consisting of 24 thousand chapters (called genes) and 46 huge volumes of encyclopedia (called chromosomes). This is the greatest library of genetic information of a human being on planet Earth and it is the result of three and a half billion years of biological evolution. Thousands of scientists around the world worked for thirteen years to complete the Human Genome Project which costs the US government over three billion dollars. We are the first living creature to read our own book of life and store the information on a CD Rohm to monitor any changes, which might cause diseases.

We begin to decipher the book of life of other living creatures. We have read the Genomes of several hundred plants and animals. They provide proteins of high commercial value. For example, we were curious to know how spider produces silk to make its web. We read the book of life of spider, identify, and isolated the gene that produces the silk. We also read the genome of sheep. We cut and paste the spider silk making genes into the milk producing genes of the sheep and isolated the spider silk from the sheep's milk. The spider silk is very useful during surgery. After surgery, the surgeon used to sew the wound with the cotton thread. In the olden days, after the wound is healed, the surgeon used to remove the thread from the wound, which is extremely painful process. Now, the surgeons do not have to remove the thread because the spider silk protein is dissolved during the healing of the wound. What is so unique about humans is that we take care of each other's need from the cradle to the grave without the knowledge and without our permission. With the geneticists, help farmers developed high quality and most nutritive GM (genetically modified) food for another group. We took the Rice genome apart and put it back together with an additional Vitamin A genes isolated from carrots to produce transgenic Rice, which prevents blindness in children. We successfully inserted Ferro-lectin genes in Corn and Wheat Genomes to produce transgenic Corn and Wheat to prevent iron deficiency in our diet.

A small group of scientists isolated a gene that produces insulin to treat diabetes. Today, we supply insulin to over 300 million diabetics around the world. There are 24 thousand genes in our genome. We must cut and paste these genes to use their proteins as Genomic Medicine. Based on the genetic make-up of individual, we are developing genomic medicine not only to treat human diseases, but also to treat diseases in plants and animals. We have recently identified gene that cause Aging and learn to prolong life, which will be robust, strong, and energetic. We do not have feathers to fly, but we build airplanes to fly others around the world. With fairly certainty, we could answer questions like who we are, where we have all come from and what was it that made us this way. What is the fate of life on Earth? Now, we know our origin in Africa and our wondering around the world as hunters and gatherers in search of food and shelter. Three and a half million years later, we occupy all seven continents on planet Earth. Today, our numbers have multiplied to about eight billion. Our collective brain if remain creative will take us to other star systems. If we remain creative and war free for a million years, we will be travelling among star systems. We could spread human intelligence in many of those recently discovered 5,000 exoplanets in our Milky Way Galaxy.

The following three greatest lessons we learned by reading, our genome, our book of life:

First, by reading our own book of life, we have captured the function of all good and bad genes within our genome. The interaction of our genes is responsible for our good health or bad health. All good and bad genes are within our genome. We have a closure of our book of life. There is nothing outside our genome. All six thousands genetic diseases are the result of mutations in our genes caused by either radiations, or chemical environmental pollutions, or viral infections or genetic inheritance.

Second, we have developed the ability to scan our entire genome in hours and compare with the genome of sick people and immediately recognized what variations in A-T and G-C base pairs, which are responsible for causing that mutation that made that person sick. We have also developed the high throughput DNA

sequencers which sequence thousands of genes simultaneously to scan the entire genome within hours to check if any DNA variations (mutation) responsible for a specific disease. Frequent scanning of the entire genome of several patients will help us pinpoint a mutation and help us develop accurate diagnostic methods, its prevention, and its treatment.

Third, now we can answer the question, why no two people look alike. Why are we so different from each other? By comparing genomes of two individuals, we found that no two genomes are identical, and no two people look alike (except in the identical twin). If you compare the genome of two different people, within a thousand to thirteen hundred base pairs, you find one A-T or G-C base pair is located at a different place called SNP (Single Nucleotide Polymorphism). In a three billion two hundred million base pair human being, there are at least three million mutations or SNPs that make us different from each other. Because of three million variations in each of us, no two people look alike. In other word, we are all-different from each other and are differently gifted. Once you recognize your gift, you are to master the gift. Once you master the gift, you are to share the gift with the rest of the humanity; this way you serve humankind and serve God. Moreover, this is one of the purposes of life. There is also a higher purpose of life, which is to preserve our species from extinction at all costs. If human life is extinguished from Planet Earth, intelligent life will never evolve on Earth again since not enough energy left in the Sun.

Without energy, we cannot survive. Our only source of energy is our Sun. Our Sun has been burning for the last four and a half billion years. It burns seven hundred million tons of Hydrogen every second. During the last four and a half billion years, it has used up about half of its energy. It is a middle age dying Star. As it burns more and more Hydrogen, it will cool and expand. As it expands, it will sallow Planets Mercury and Venus. On further cooling, its outer rim approaches Earth, its intense heat will evaporate our oceans, burn our Oxygen, and char every living creatures on Earth. Once Earth becomes part of the Sun, it will collapse on itself and explode as a Super Nova. Although our Solar System collapse in a flash of light, if life exist on other galaxies, the observers on other Star System will see a little spark of light on the third arm of our Milky Way Galaxy. What happens if we do nothing? Sir Winston Churchill, the hero of the World War II, once said half a century ago, "if we fail, we all will fail. If we die, we all will die together."

Humans are unique and they have this extraordinary ability not only to preserve themselves, but also to save humanity from extinction. Dr. Daniel Golden who was an administrator of NASA during April 1992 through 2001 under whose leadership, we landed men on the Moon and brought them back safely had said that he had a dream, a dream to land men on the Red Planet Mars before this century is over. Not only to land men on Mars, but also to colonize Mars and use Mars as a base to launch unmanned spacecraft is in search of Earth like planets. Within less than ten years after his speech, astronomers have discovered over 500 Earth like planets within ten light year distance. To fulfill his dream, he challenged NASA and NIH to confront three challenges: NASA's first challenge is to build city size space craft using the hardest and the lightest material such as a new generation of superconductor; NASA's second challenge is to increase the speed of the space craft to about half the speed of light and third challenge is to control the fusion reaction, which is taking place on the surface of Sun, to provide unlimited supply of energy for deep space travel. To scientists at NIH, he also presented three challenges: he said that he could not send astronauts on a one-way journey in search of a second Earth who are suffering from pain or suffering from illnesses or who lives less than one hundred years. NIH three challenges include: First, to identify genes, which causes pain and suffering; second, to identify genes that causes diseases and third, to identify genes that cause aging. Within ten years after completing the Human Genome Project, we have identified half dozen genes that causes pain and suffering; we have identified about six thousand genes that cause diseases and we have identified Aging genes for which Carol Greider and Elizabeth Blackburn shared the 2011 Nobel Prize. Mice usually die in two years; we have a new generation of mice who defy aging and who are three years old, and they have not even reached middle age.

The speed with which we are progressing, it appears that we would turn Daniel Goldin's dream into reality before this century is over. If we survive on Earth for a million years, with the current rate of progress, we could send human intelligent life in every corner of the Universe. Only human can dream such gigantic dream and only humans can convert them into reality. That is what makes us human, and that unique quality makes us different from all other species on Earth.

Sequencing Cerebral Cortex may provide the site of Humans Consciousness

What does it mean to be humans. How do the genes-genes or protein-proteins interact to give us the conscientiousness? How do we manipulate genes to develop new therapies to extend human life? New therapies are based on genome sequencing variants responsible or introducing toxic proteins, which will disrupt the normal biological function to reduce human life span. The sequencing of human genomes helps us understand how human are superior to all other creatures on Earth. We have no wings to fly, no shell to protect ourselves and cannot run like Cheetah, but we distinguish from all other creatures on Earth because we carry a three-pound flesh in our skull called the brain. We can transplant every other organs in our body except brain. It is a made of 86 billion cells called neurons. Each neuron is liked to other

neuron by 10,000 to 100,000 connections called synapses. The total number of synapses their combination and their permutation exceed the number of visible stars at night sky. Is it the limit of our complexity? Not yet. All 86 billion neurons carry nucleus, and each nucleus carries complete genome consisting of six billion four hundred million nucleotide half from each parents.

Our genome is our book of life. It is the greatest catalog of human genes. It is made of 46 volumes called Chromosomes consisting of 24,000 chapters called genes. Genes carry instruction to make proteins. Which perform all the body functions. The entire book of life is written in four letter called nucleotides and they are [Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C)] and they are AT and GC base pairs which are the initials of four chemicals found in all living creatures. Out of four nucleotides, three nucleotides code for an amino acid called the Codon. Four letter text and three letter codons give 64 combination which codes for all 20 amino acids. A gene carries several hundred codons to make a protein. A gene has a start codon (AUG codes for amino acid Methionine) and carries three stop codons: UAG, UGG & UGA). Appearance of anyone of those stop codon, stops the extension of DNA. Hundreds of amino acids joined to give a protein, thousands of proteins interact to give a cell, and millions of cells interact to make an organ like our brain. Several organs interact to make a man, or a mouse or a monkey.

Interaction of thousands of proteins give humans our conscientiousness. It is the function of our conscientiousness that makes us humans. Although we share 98.9 % genes with Chimps, 75% genes with rhesus Monkeys and 62% of our genomes with mice, they lack their conscientiousness and none of them is aware of their surroundings or remembers of their past, present or their future. This 1.1 % of genomic difference between Chimps and us give us conscientiousness. It is the gift of consciousness that makes us humans. Now, we know the answers to the most fundamental questions we had asked ourselves since the dawn of human civilization what it means to be human. It is our conscientiousness that explains the nature of memory and our consciousness and our development from single cell to a complete human being. The biochemical basis of our senses the process of our aging. The scientific basis of our similarity and dissimilarity. Dissimilarity that all living creatures from a tiny blade of grass to mighty elephant including man mouse monkey, mosquito and microbes are all made of the same building blocks, the four nucleotides AT and GC and yet we are so diverse that no two individuals ae alike even identical twins are not identical they grow up to become to separate individuals. A gene codes for a protein, not all 24,000 genes code for proteins. It is estimated that less than 19,000 genes code for protein. Because of the alternative splicing, each gene codes for more than one protein. All the genes in our body make less than 50,000 protein, which interact in millions of different ways to give a single cell. Millions of cells interact to give a tissue and hundreds of tissues interact to give an organ and several organs interact to make a human. Not all genes act simultaneously to make us function normally. Current studies show that a minimum of 2,000 genes are enough to keep human function normally; the remaining genes are backup support system, and they are used when needed. As I said above, the old cells begin to die, and they are constantly being replaced by healthy cells. Why do the normal cells become abnormal or become cancerous? Damage to functional gene called Mutations are responsible for causing normal cells to become abnormal. Mutation is caused by exposure to Radiations, Chemical/Environmental Pollution, Viral Infections or Genetic Inheritance. Mutations also occurred during DNA replication, such as insertion, deletion, relocation, multiple copying, inversion etc.

Anyone those factors will disrupts the two percent of the coding region of our genome that will alter its function by slightly altering its code; an altered codon will code for a wrong amino acid and wrong amino acid will give a wrong protein and it will make normal cell become abnormal. When the functions of Codons are disrupted intentionally or unintentionally, we alter the Codon's function. For example, intentionally we alter a codon by smoking and unintentionally by exposure to environmental pollution such as chemicals or radiations. Altered Codons have wrong information to make wrong amino acids. Wrong amino acids make wrong proteins and wrong proteins make wrong cells and wrong cells grow much faster than the normal cells and become abnormal or cancerous and they form a lump, we call these lumps, tumors. Since we sequence the human genome about 20 years ago, we learn to manipulate our genome in three different ways: First, (1) using good genes from our genome, we could make large scale good protein like Insulin and growth hormones to treat deficiencies to keep us healthy. Second, (2) using bad genes, we could shut off those genes either by Gene Therapy/CRISPER or Drug Therapy. SCID for Gene Therapy and Chlorambucil or AZQ for Drug Therapy. Third, (3) introducing super genes to create super quality humans (enhancing extraordinary qualities) can be done, but are not permitted at this time). Let me discuss the last one (3) first, Gene enhancing studies in humans are not permitted. Conducting research is an expensive business. Funds are not available to incorporate genes to enhance your IQ or athletic ability or prolonging your age including Germ-line gene therapy are not permitted at this time because genetic changes made in fetus will last several generations. Can we make decisions about the future of the children who will not be born during next decades? The answer is no, but do we have the capability to insert useful gene to human genome.

The answer is yes; here is the example:

Children born with Down syndrome have made an extraordinary contribution to the science of genetic. We are all born with 46 Chromosomes, and they are born with 47 Chromosome. Their extra chromosome is Chromosome-21. They proved

for the first time, that humans could survive with an additional chromosome. Chromosome-21 is not an ordinary chromosome. It is made of 50 million Nucleotide base pairs and carries 337 genes. They proved that we could survive with an additional chromosome. We could synthesize 21-chromosome with exceptional quality genes.

By comparing the Chromosome-21 of the Down syndrome babies with the Reference sequence, we could identify the gene variants responsible for their low IQ and their sensitivity to some diseases. By inserting high IQ genes in Chromosome-21, could we make them super achievers? For example, Albert Einstein is recognized as the man of the century because of his accomplishments. Einstein's brain is stored in a museum. Could us barrow a single neuron and sequence his entire genome. As I said above, our genome is the catalog of all our genes. The greatest book of our genes on Planet Earth. We could compare Einstein genome with the Reference Sequence and identify gene variants responsible for his high IQ. Although this experiment will not be permitted in any Labs, let us conduct a thought experiment. From the previous lectures [1-18], my students know that in Genetic Engineering, we cut, paste, and copy a gene. By using Restriction enzymes, we can cut all genes at a specific site and prepare a Restriction site map. We can purify a specific variant by Gel Electrophoresis. By using recombinant technology, we could cut and paste this gene in Plasmid genome or viral genome. The transgene plasmid protects pure gene variant from enzyme destruction. Millions of colons are made of transgene plasmid either by PCR or by harvesting in Yeast cells. Pure genes are released from transgene plasmid by restriction enzymes. Millions of copies of the pure gene variant can be saved in cell-lines or in viruses. Purified Einstein's high IQ variants in Viruses could be used to infect the chromosome-21 of down babies. After infecting, we could sequence Down syndrome baby's genome to ensure that we have successfully cut, paste, and copy a gene to produce down babies with very high IQ. On the other hand, we also can synthesize the entire Chromosome-21 inserting the best genes available to future astronauts who will travel in deep space in search of a suitable home for humanity. To approve such studies in humans, US Food & Drug Administration (FDA) requires safety and efficacy studies, as described in the Code for Federal Regulations (CFR). FDA safety guidelines require several safety and efficacy tests before approving a drug for use in humans. The first test is the Ames's test, which is a method of testing mutagenicity of a drug, by harvesting a colony of bacteria on Agar Gel plate and incubating for 24 hours. Each cell divides millions of times giving a circular colony on the Agar plate. Each bacteria make a circular colony. Among all the colonies, if a single colony is irregular in shape, it predicts mutation, which could become cancerous if grown in mice. This drug is rejected. On the other hand, if no irregular colony was found, the drug passes the Ames' test. The next test is 90-rat toxicity test. Different doses of the drug are given to a set of mice to determine the safe level of the drug. Next is the Teratology Test, different levels of drug are tested on pregnant mice to see if the newborn mice is free from any abnormality. Next, is allergen test to see if the drug is allergic to mice? Next is the 2-year chronic study in Rats to see if the drug produces how many carcinogenic tumors in Rats. If a drug passes these tests, we are allowed to conduct clinical trials to study the safety and efficacy of the drug in humans. In the first clinical trial, 30 patients are tested which is followed by a second clinical trials in which different levels of the drug is tested in 300 patients. If the drug continues to be safe, it will go for the third clinical trials in which 3,000 patients are tested. When a drug is passed all these tests, it is approved for use for a year. Each year, the drug manufacturer submits Adverse Reaction Report. If the drug shows any adverse effect, its approval is withdrawn. For several years, FDA continues to receive Safety Reports. For more information, check CFR.

Good Genes

Out of 24,000 genes, our genome carries 16,000 good genes which are responsible for producing good proteins. Products of good genes are produced on large scale for human consumption. For example, large scale Insulin was synthesized by the techniques of biotechnology. By sequencing, the human pancreatic cells, scientists at Genentech, cut, paste, and copy the human Insulin gene. By inserting the Insulin gene in Bacteria, they produce large scale Insulin. Large scale Insulin is also produced by PCR method to provide Insulin to 300 million diabetics around the world. Similar methods are used to produce large scale Somatostatin and Human Growth Hormone.

Bad Genes

Our genome also carries 6,000 bad or mutated genes responsible for causing six thousand different diseases. Several methods are developed to treat these diseases. Diseases are developed either by a single genetic defects or multiple genetic defects. Diseases developed by single genetic defects are called Mendelian diseases are being treated by Gene Therapy while multiple genetic defects are treated by drug therapy.

Gene Therapy

Scientist at the NIH provided the most successful example of Gene Therapy. Children born with SCAD (Severe combined immune syndrome), have no resistance against infection such as cold and flu virus and are kept in isolation. They generally die within a year. These children are born with a defect in their Adenosine deaminase gene, which is responsible to break down the excess adenosine and to clear up from the system. The presence of the excessive amount of adenosine destroys the B2 and T3 cells, which are responsible for building up immunity against the foreign infection. As a result, the level of adenosine rises, and excessive

amount of Adenosine is responsible for destroying the immunity in these children. French Anderson et al in our laboratories at NIH conducted Ex-vivo genetic engineering of the White Blood Cells (WBC). The WBC obtained from the affected children were infected with Flu virus carrying the Adenosine Deaminase gene. They harvested the WBC carrying deaminase gene and injected back into those children. The deaminase gene become functional and started producing the enzyme deaminase, which started breaking down adenosine molecule and started clearing up excessive amount of Adenosine from their blood. The children are cured and function normally. This is the most successful example of Gene Therapy. Nearly five thousand children who were born without the deaminase gene who could have been dead within few years are living a normal life. Despite of its success, to date, almost 2,600 gene therapy clinical trials have been completed, are ongoing or have been approved worldwide. As of February 2020, there are nine-gene therapy products approved in the U.S. Gene Therapy will work only with the single genetic defect treatment, with multiple genetic defects, gene therapy will not work, drug therapy will work.

Drug Therapy

The essence of life is information, and the information is located on the four-nucleotide bases A-T and G-C. As stated above, according to Central Dogma of Crick and Watson, the information on DNA is transcribed on RNA, which is translated in Ribosome to protein. Attempts are being made to design drugs to attack cancer cells on all three level that is DNA, RNA and Protein. Herceptin, a novel class of drug, has been successful in attacking protein. Craig Milo has designed double stranded RNA to shut off gene and prevents its translation into protein. Drug designed to attack DNA to shut off a gene was carried out by Ross. Gene Therapy cannot be applied to multiple genetic defects such as cancers or heart diseases. Drug Therapy could be used to develop novel treatments. Professor WCJ Ross of London University was the first person who designed drugs to attack DNA for Cancer Treatment. He designed drugs to cross-link both strands of DNA that we inherit one strand from each parent. Cross-linking agents such as Nitrogen mustard are extremely toxic and were used as chemical weapon during the First World War (WWI). Hundreds of more toxic analogs of Nitrogen Mustard were synthesized during the Second World War (WWII). Solders exposed to Nitrogen Mustard showed a sharp decline of White Blood Cells (WBC) from 5000 cell/CC to 500/CC. Children suffering from Childhood Leukemia have a very WBC count over 90,000/CC. Most of the WBCs are premature, defected, and unable to defend the body from microbial infections. Ross rationale was that cancer cells divide faster than the normal cell, by using Nitrogen Mustard he could cross-linking DNA and prevent cell division. Once he demonstrated that he could shut off a gene by cross-linking DNA; he could shut off any mutated gene of all 220 tissues present in a human by finding a dye that could specifically color that tissue. He could attach the Nitrogen Mustard group to the dye and attack the cancer genes in any one those tissues.

Ross was the first person to use Nitrogen Mustard successfully to treat cancer. Although such drugs are highly toxic, and they are more toxic to cancer cells and more cancer cells will be destroyed than the normal cells. Over decades, Ross made several hundred derivatives of Nitrogen Mustard as cross-linking agents. Some of the Nitrogen Mustards such as Chlorambucil [25,26] are used for treating childhood leukemia (which brought down the WBC level to 5,000/CC) and Melphalan and Myrophine are used for treating Pharyngeal Carcinomas [27-33]. Because of the high toxicity of Nitrogen Mustard, new derivatives could not be developed to treat other types of Oral Cancers. As I showed above, we sequenced our genome, our book of life, letter by letter word by word, sentence by sentence, chapter by chapter all forty-six volumes written in six billion four hundred million genetic letters (nucleotide) of a healthy human being under the Human Genome Project. We can use our healthy Genome as a Reference Sequence for comparison. It took 13 years to sequence the entire human genome. Now, we developed next generation sequencers like Nano pore technology, which will sequence the entire genome cheaper and faster. Using biopsy sample, we can take a single cell from the Lung or Oral tumor of smoker, sequence its genome, and compare with the Reference sequence to identify the number and location of all mutations or damage genes caused by smoking. To obtain precision and accuracy, recently, we also completed the 1000-genome project, which will provide thousand copies of the same gene sequence for comparison. We also learned to convert Analog language of Biology into the Digital language of computer. Now, we can write a program and design a computer to read and transport our genome to anywhere in the world at the speed of light.

Comparing with Reference Sequence is very helpful in identifying a mutated gene. For example, when comparing with the smoker's gene sequence, it will identify all the mutations with precision and accuracy. Once the mutations responsible for causing Lung or Oral Carcinoma are identified, we can design drugs to shut off those genes. Using the same rationale, but binding to a single strand of DNA, it has taken me about ten years to make Aziridine dinitro benzamide (CB1954), a novel class of drug to shut off a mutated gene responsible for causing Walker Carcinoma 256, a solid aggressive experimental tumor in Rat [32] and about a quarter of a century to make Aziridine dicarbamate Quinone (AZQ) to shut off Glioblastoma gene in human responsible for causing brain tumor. The following example explains how easy it is to get Lung or Oral cancer by simply smoking a dozen genetically modified high Nicotine content Cigarette and how expensive, time-consuming, and exhaustive it is to find a possible cure. The Drug must be safe and effective. After a year use, if the

FDA receives an Adverse Effect Report, the Drug is withdrawn. All the effort is wasted. Detail information is provided below: At the London University, I was a graduate student of Professor Ross then his doctoral, Post-doctoral Fellow and then his Special Assistant. For almost ten years, I had worked with Professor Ross making derivatives of Nitrogen Mustard as anticancer agents. While Professor Ross was designing drugs to attack both strands of DNA, which are extremely toxic, as a part of my doctoral thesis, I was assigned to design drugs to attack only a single strand of DNA. I was successful in designing a novel class of drugs, which attack only one strand of DNA. This class of drugs is called Aziridines [33,34]. Over the years, I had made over 100 Aziridine dinitro-benzamide (CB1954) analogs, which attack the DNA of Walker Carcinoma 256 in Rat, a solid aggressive tumor.

Toxicity is measured as the ratio of toxicity to normal cell when compared to the abnormal cell called Therapeutic Index (TI). Higher TI means, the drug is more toxic to cancer cells. The TI of most Cross-linking Nitrogen Mustard are ten; it means that they are ten times more toxic to cancer cells. The Therapeutic Index of one of my Aziridine compounds (Aziridine dinitro benzamide) CB1954 is (T/I = 70) which showed that CB1954 is seventy time more toxic to cancer cells compared to normal cells, highest toxicity to cancer cells ever recorded. The Walker Tumor not only stopped growing but also it shrank to normal size. I used a simple rationale, the Aziridine attacks a single strand of DNA in acidic medium, and particularly the N-7 Guanine nucleotide is attacked. The dye Dinitro-benzamide has great affinity for Walker Tumor. The Aziridine dinitro benzamide (CB1954) stain the tumor. CB1954 acts as a Prodrug that is it remains inactive at neutral or basic pH but activated in acidic solution. As the tumor grows, it uses Glucose as a source of energy. Glucose is broken down to Lactic acid. It is the acid, which activate the Aziridine ring. The ring opens to generate a Carbonium ion, which attacks the single strand of most negatively, charged N-7 Guanine shutting off the Walker Carcinoma gene. To continue my work, I was honored with the Institute of Cancer Research post-doctoral fellowship award of the Royal Cancer Hospital of London University. To increase the toxicity of CB1954 to Walker Carcinoma, I made additional 20 analogs. When I attached one more Carbonium generating moiety, Carbamate to the Aziridine Dinitrobenzene, the compound Aziridine Dinitrobenzene Carbamate was so toxic that its Therapeutic Index could not be measured. Because of the safety reason, further work at the London University was stopped.

I developed the same rationale to continue my work in America when I was offered the Fogarty International Award to continue my work at the National Cancer Institute (NCI) of the National Institutes of Health (NIH) in Bethesda, Maryland, USA. I brought the idea from London University of attacking one strand of DNA using Aziridine, but I do not want to use the same dye Dinitro benzamide. One day, I heard a lecture at NIH in which the speaker stated that methylated radio labeled Quinone crosses the Blood Brain Barrier. When injected radiolabeled Quinone intravenously in mice, within 24 hours, the X-ray photograph showed that the entire radioactivity was concentrated in the mice Brain. I knew that Glioblastoma multiforme, the brain tumor in humans, is a solid aggressive tumor like Walker Carcinoma in Rats. I decided to use Quinone moiety as a carrier for Aziridine rings to attack Glioblastoma. I recalled my last part of the work at the London University, by introducing just one Aziridine and one Carbamate moiety to Dinitro Benzine ring, I had produced such a toxic compound against Walker tumors that its toxicity could not be measured. With the Quinone ring, I could introduce two Aziridine rings and two Carbamate moieties and could create havoc for Glioblastoma. Over the years, I synthesized several dozen analogs of Aziridine Quinone. One of them is highly toxic to Glioblastoma, which carries two aziridine and two carbamate moieties.

I named the Di-aziridine Dicarbamate Quinone, AZQ US Patent 4,233,215). My major concern was how toxic this compound would be to the brain cells. Fortunately, brain cells do not divide, only cancer cells divide. AZQ acts as a Prodrug. A Prodrug is a compound, which carry a chemical masking group that renders it inactive and nontoxic. Once the prodrug reaches a target site in the body, removing the mask frees the active drug to go only where it is needed, which helps avoid systemic side effects. To grow, cancer cells use Glucose as a source of energy. As I stated above, Glucose is broken down to produce Lactic acid. It is the acid, which activates the aziridine and carbamate moieties generating Carbonium ions attacking Glioblastoma, which stop growing and the tumor start shrinking. My drug AZQ is successful in treating experimental brain tumor because I rationally designed to attacks dividing DNA. Radio labeled studies showed that AZQ bind to the cancer cells DNA and destroy brain tumor and normal brain cells are not affected at all. AZQ is a new generation of drugs. Not so long ago, these cancers mean death. Now, we have changed it from certain death to certain survival. The immunologists in our laboratories are developing new treatment technique by making radio labeled antigens to attack remaining cancer cells without harming normal cells. We have cured many forms of cancer. We have eliminated childhood leukemia, Hodgkin disease; testicular cancer and now AZQ type compounds, which are being developed rationally. While most anti-cancer drugs such as Adriamycin, Mitomycin C, Bleomycin etc., in the market are selected after random trials of thousands of chemicals by NCI, AZQ is rationally designed for attacking the DNA of cancer cells in the brain without harming the normal cells. We are testing combinations of these drugs to treat a variety of experimental cancers in animals [35-37].

In developing drugs for treatments, we poison bad DNA selectively. All poisons are a class of chemicals that attacks all DNA good and bad alike. Chemicals that cause cancer, at a safe

level, can also cure cancer. Science teaches us to selectively attack bad sets of DNAs without harming the good sets of DNAs. Poisons are injurious to living creatures. There is a small class of chemical, when exposed to humans, disrupt the function of DNAs, and make normal cells abnormal and they are called cancer causing chemicals or carcinogens. I must confess, we still use surgery to cut off a cancerous breast; we still burn cancer cells by radiations; and we still poison cancer cells by chemicals. The largest killer of women is breast cancer. After all the treatment, the remaining cancer cells return as metastatic cancer cells and kill breast cancer patients in three years. A decade from now, these methods could be considered as brutal and savage, but today that is all we have. We hope to develop new treatment for Breast Cancer. Hopes means never ever to give up. As I said above, I rationally design drugs to treat Brain cancer. I am the discoverer of AZQ (US Patent No. 4,146,622 & 4,233,215). I shared a 17-year royalty with two of my colleagues. The discovery of AZQ has been a quarter century long effort starting from the Royal Cancer Hospital, University of London, England and ending in the National Cancer Institute, Washington, America. Some may think that we are very lucky. The fact is that luck has nothing to do with it. It is a shear hard work. I had already made over one hundred derivatives of Aziridine drugs which tested against experimental animal tumors and published with Professor Ross before I came to America and joined NCI (National Cancer Institute). Let me share with you how we sweated for making AZQ. To introduce one successful drug for treating one kind of cancer, over the last 25-year period, I conducted over 500 experiments, out of which 200 drugs were tested in thousands of animals and only 45 drugs were considered valuable enough to be patented by US government and only one drug, AZQ, has recently completed a Phase-III clinical trial which showed that patients receiving AZQ live 20 to 24 months longer than the untreated patients. This period gives physicians enough time to develop alternative treatment to eliminate the remaining resistant cancer cells by Immunotherapy. For the discovery of AZQ, I was honored with the "2004 NIH Scientific Achievement Award", one of America's highest awards in medicine.

Exhibit-1:

Figure 1: 2004 NIH Scientific Achievement Award Presented to Dr. Hameed Khan By Dr. Elias Zerhouni, The Director of NIH. During the NIH/APAO Award Ceremony held on December 3, 2004.

Exhibit-2:

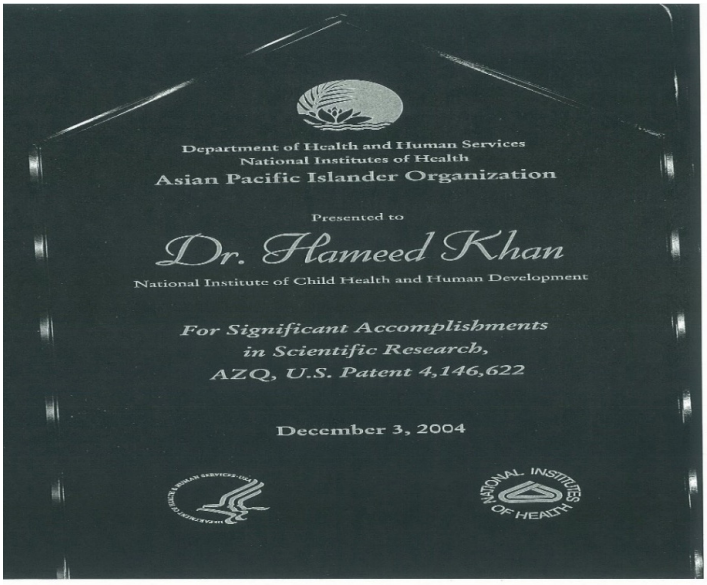
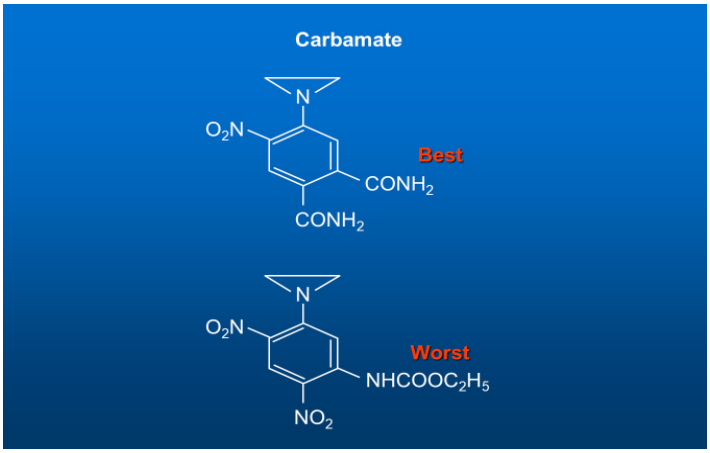


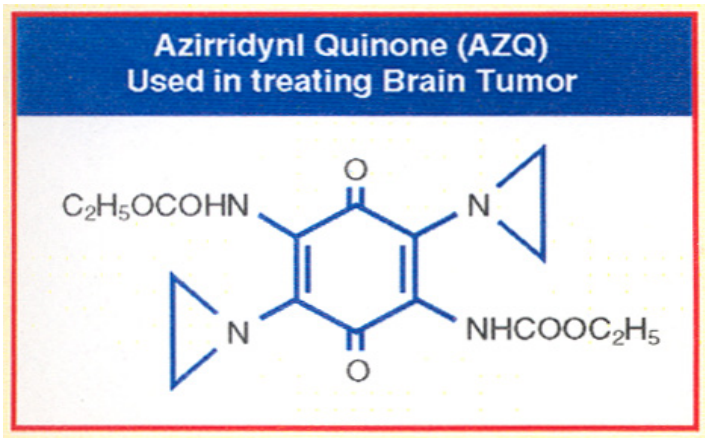
Figure 2: Dr. Khan is the Discoverer of AZQ (US Patent 4,146,622), a Novel Experimental Drug Specifically Designed to shut off a Gene that causes Brain Cancer for which he receives a 17-year Royalty for his invention (License Number L-0I9-0I/0). To this date, more than 300 research papers have been published on AZQ. The award ceremony was broadcast live worldwide by the Voice of America (VOA). Dr. Khan is the first Indian to receive one of America's highest awards in Medicine.

Figure 3: His Excellency, Dr. A.P.J. Abdul Kalam, The President of India. Greeting to Dr. A. Hameed Khan. Discoverer of anti-cancer AZQ, after receiving 2004, Vaidya Ratna, The Gold Medal, One of India's Highest Awards in Medicine. At The Rashtrapathi Bhavan (Presidential Palace), in Delhi, India, during a Reception held on April 2, 2004.

Exhibit-3:



Single Strand DNA Binding Aziridine and Carbamate



U.S. Patent 4,146,622

Exhibit-4:

Figure 4: Dr. A. Hameed Khan, a Scientist at the National Institutes of Health (NIH) USA, an American Scientist of Indian Origin was awarded on April 2, 2004. Vaidya Ratna; The gold Medal, one of India's Highest Awards in Medicine for his Discovery of AZQ (US Patent 4,146,622) which is now undergoing Clinical Trials for Treating Brain Cancer.

Conclusion

What makes us humans? My students the next generation of scientists, will answer this question, my advice is that they must search in our genome. Our genome carries the complete catalog of all our genes. The greatest challenge for the next generation of scientists is to understand the collective function of genes. Genes code for proteins. Is it the protein-proteins interactions that give our consciousness? Each gene is responsible for carrying out a single specific function. In our genome, a gene produces a unique protein, which is programmed to perform one function either to switch on or to switch off a gene. A gene has no conscientiousness; it does not have any control over our mind or operate any higher controlling center. Is Cerebral Cortex or Hippocampus the seat of our consciousness? Could we sequence a single neuron from the cerebral cortex to identify its gene whose protein produces human consciousness? Proteins are three-dimensional working machine. As soon as the liner DNA codons produce liner protein, it begins to fold to become functional. It folds in several different ways, the protein with the right confirmation is retained and the wrong folds is degraded. Random folding and misfolding of the proteins would aggregate and clog the neuron's function causing diseases such as Alzheimer and Mad Cow disease.

Recently completed thousand-genome project may answer all the questions what makes us rational thinkers? What does it mean to be human? What is the nature of our memory, our consciousness, and our development from single cell to a complete human being? What is the biochemical basis of our senses, the process of our aging? And what is the scientific basis of our similarity and dissimilarity. Similarity that all living creatures from a tiny blade of grass to the mighty elephant including man mouse monkey, mosquito and microbes are all made of the same chemical building blocks, the four nucleotides AT and GC and yet we are so diverse that no two individuals are alike even identical twins are not identical they grow up to become to separate individuals. As I said above, our genome carries the complete catalog of all our genes. To answer these questions, we must search that variant in our genome. Since all human organs could be replaced by implantations except Brain, we must narrow our search in our Brain as the site of our consciousness. Of all the living species on Earth, Chimps are closest to humans. We share 98.9% of our genome with Chimps. We must further narrow our search and carefully examine within 1.1% of our genome for the seat of our consciousness which gives humans exceptional ability to land men on Moon and bring them back safely to Earth.

Genes code for proteins. The proteins control the function of all genes. We have identified specific proteins, which perform specific function. For example, there is specific gene, which carries instructions to switch on or switch off a gene. By designing AZQ (US Patent 4,233,215), I have demonstrated that I could punch hole in the Iron curtain called the Blood Brain Barrier (BBB), the fatty layer that protect the human brain from exposure to all toxic chemicals and transport Quinone moiety across the BBB. If we identify genes for human consciousness either in the cerebral cortex or in hippocampus, we could design drugs to alter our consciousness. Is consciousness evolved because of gene-gene interactions or protein-protein interaction? What makes us rational thinkers and what make us creative to work together. We borrow each other's ideas, skill and thought and merge them to create a novel product that no single individual has accomplished. For example, I made AZQ (US Patent 4,233,215) for treating Glioblastoma, the human brain cancer. I did not make all its ingredients. Someone made Quinone; someone made Aziridine and still others made Carbamate. I have no idea who made them, but I combined their products and made AZQ. Someone tested against Glioblastoma and found that the tumor instead of expanding, starts shrinking. This ability to combine different ideas to make a new product is granted by evolution to humans only. Some of the greatest gifts of evolution given only to humans are Altruism and Free Will. Now, we find that the answers to all our questions are locked in our genome, and the interactions of genes or proteins make us human. We are so different from all other creatures on Earth that we plan to protect our species even after the death of our solar system. We also have the ability not only to help each other, but also to harm each other, on a mass scale. We have built so many weapons of mass destruction, we could kill every man, woman, and child on this planet twenty times. We could wipe out all life forms from Earth. We learned that good and evil pass through the heart of every human on Earth. It is our responsibility to encourage each other to do well and stay away from evil. If we could survive for a million year without destroying each other by going to nuclear war, we have the extraordinary ability not only to colonize Mars, but also using Mars as a base to launch unmanned spacecraft's in search of exoplanets, the next habitable home for humanity in a distant star system. of all the living creatures on Earth, only humans have the extraordinary ability to protect, preserve, and spread human intelligence in every corner of the Universe.

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