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The Impact of Sequencing Human Genome on Darwinian Evolution

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Abstract

This abstract attempt to answer some very important questions about the origin of life on Earth that we have asked ourselves since the dawn of human civilization. Questions like who are we? Where have we all come from? and what was it that made us this way? Religions and Science both seeking to answer the same question about the origin of life. This article describes Darwin's answer with scientific evidence. Now, we can answer with certainty that Evolutionary Biology and the history of fossil records confirm that you and I are the result of three and a half billion years of Darwinian evolution. We originated on Earth by the combination of elements that had already exist on Earth.

Although our Earth is made of 120 different elements, but by the combination of a handful elements first life giving molecule appeared on Earth. A million-lightning strike Earth each day. At some remote corner of the Earth, a single lightning struck at a cloud of gases containing Ammonia, Carbon dioxide, Methane, Water vapor, near a Phosphate rock forming the first information molecules, called the nucleotides: There are four similar nucleotides, and they are Adenine (A), Thiamine (T), Guanine, (G) and Cytosine (C). A string of nucleotides is called DNA (Deoxyribose Nucleic Acid). We are the extension of the same single DNA molecule that was formed nearly four billion years ago. The book of life in all living creatures from the microscopic life form to the present-day humans is written in the same language of DNA using the same four nucleotides. This is the evidence-based information provided by the evolutionary biology. The Human Genome is the collective name for the genetic material that makes us human.

By comparing the genome sequences from the earliest Pre-Cambrian Trilobites to the present-day mighty Sequoia Trees, we can explain the development and complexity of the life based on the Darwinian Evolution. According to Darwinian Evolution of all species of organisms arise and develop through the process of evolution by natural selection from small, inherited variations that increase the individual's ability to compete, survive, and reproduce. After completing the Human Genome Project, we can answer the most important question with great certainty. Why are we here? We are here to explore the Universe. Without intelligent life, Universe was meaningless, purposeless wasteland; there was no purpose for its existence. The Universe was always there, it will always be there. But with intelligent life, Universe becomes purposeful. Our purpose is not only to explore the Universe, but also to protect, preserve and spread human intelligence in every corner of the Universe.

Keywords

Darwinian Evolution**;** Nucleotides; DNA; Genome; Mutations; Genetic Diversity; Genomic diseases; Inbreeding; 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) and the International Science Conferences. 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. I am reproducing here part of the lecture which was delivered at the International Science Conference that was PCS 6the Annual Global Cancer Conference held on November 15-16, 2019, in Athens, Greece.

Special Notes

I am describing below the use of highly toxic lethal chemical weapons (Nitrogen Mustard) which was used during WWI and its more toxic analogs developed as more toxic weapons during WWII. I described the use of Nitrogen Mustard as anti-cancer agents in a semi-autographical way to accept the responsibility of its use. When we publish research papers, we share the glory with colleagues and use the pronoun “We” but only when we share the glory not the misery. In this article by adding the names of my coworkers, the animal handers, I will share only misery. The Safety Committee is interested to know who generated the highly lethal Chemical Waste, How much was it generated and how was it disposed. I accept the responsibility. The article below sounds semi-autobiographical, it is, because I am alone responsible for making these compounds of Nitrogen Mustard, Aziridines and Carbamate. To get a five-gram sample for animal screening, I must start with 80 grams of initial chemicals for a four-step synthesis. To avoid generating too much toxic chemical waste, instead of using one experiment with 80 grams, I conducted 80 experiments with one gram sample, isolating one crystal of the final product at a time. The tiny amount of waste generated at each experiment was burned and buried at a safe place according to safety committee rules.

Ancient References that can be Googled on your cell phone are removed.

Introduction

Darwin's Universe

Only humans in the entire Universe talk about the Universe. How and when did the Universe began? How and when did the subatomic particles interact to become molecules (Physics)? When how did molecules interact to become matter (Chemistry)? How and when did matter organized to become alive (Biology)? When and how did the first living unicellular creature become the multicellular? When and how did microbes become mosquitos and from mosquitos to mouse to monkey to men? When the first primitive man walked out of Africa three and a half million years ago, he saw for the first-time other living creatures who are so different from himself. He observed every creature is so different from one another. Since each is specifically designed, there must be a designer, a supreme being, a God. The mightiest power who resides in the sky above. Only God knows answers to all his questions. His belief was confirmed when he saw God's anger who unleased thunder and lightning which struck at a dry grass land and saw for the first time how brush fire become a forest fire. Only God knows answers to all his questions satisfied him. Questions like who are we? Where have we all come from? What was it that made this way? How the Universe began? Why is Universe expanding at an accelerating speed? How is it likely to end? Are we alone in the entire Universe or are there other creatures who may or may not look like us? He saw the exploding volcanos burning down his village to ashes; he saw the mighty water wave (tsunami) washed down his village. God knows all. His belief was spread in his village like a wildfire. To please God, he offered his most precious possession that is human life. To sacrifice a human being to please God is considered the ultimate gift to God.

The only man who challenged this belief was Darwin. In 1859, Charles Darwin published his book the Origin of Species. Darwin challenged God knows best answer to Man knows better. His answers were based on the evidence. The evolution of life from microbes to men is extremely slow process. Three and a half billion years of biological evolution brought us here from a simpler microbes to complex men. The evidence was everywhere. Entire evolutionary history is trapped in the layers of rocks as a fossil records. If we examine some of the tallest mountains on the face of the Earth, they were at some time were at the bottom of the ocean. If you break a piece of rock at the top of the mountain, you find it is loaded with microscopic shells. Using the radioactive carbon dating, you can determine the exact age of the fossil in billions of years. No human bones were found anywhere in the world except in Africa. The first complete human fossil was found in three and a half million-year-old rock found the Hader Valley in Ethiopia. These were the bones of an eighteen-year-old Black woman, we named her Lucy. We have all descended from her. She was the mother of us all. From the study of the fossil records, we conclude the following:

Evolution is any change across successive generation in the heritable characteristic of biological population. Evolutionary processes give rise to diversity in every level of biological organization including species, individual organism, and molecule such as DNA and protein. Life on Earth originated and then evolved from a Universal Common Ancestor approximately 3.7 billion years ago. Shared sets of biochemical and physical features can be used by shared DNA sequences to infer repeated speciation and

the origin of life. These homologous traits, and sequences are more similar among species that share a more recent common ancestor and can be used to reconstruct evolutionary history using both existing species and fossil record. Existing pattern of biodiversity have been shaped both by speciation and by extinction. Charles Darwin was the first person to formulate a scientific argument for the theory of evolution by means of natural selection which is a process inferred by three facts about population: (1) More offspring are produced than can possibly survive. (2) Traits vary among individuals living to differential rates of survival and reproduction and (3) Traits differences are heritable. Thus, when several population die, they are replaced by the progeny of parents that were better adapted to survive and reproduce in the environment in which natural selection took place. This process develops and maintains characteristics that appear to be appropriate for the functional function they fulfil. The only known mechanism for adaptation is natural selection, although this is not the only mechanism for evolution; other non-adaptive mechanisms include mutation and genetic drift.

Without any genetic or experimental evidence, more than 150 years ago, Darwin correctly predicted that a relationship exists between us and with all living creatures on Earth. When Darwin said that we are all evolved from lowly creatures, he was right. We are not created separately in six days but are part of lowly creatures and are evolved over millions of years through a slow process of evolution and natural selection. Life evolved and nature selected. For example, the microbial life found in the boiling waters near volcanoes, cannot survive in the freezing waters of arctic oceans. Visa versa is also true. Natural selection has generated mutation which helps survive these microbial life forms in the extreme environment. It is hard for the modern-day scientists to believe that fully developed man, mouse, and monkey spontaneously appeared on Earth with all living creatures instantly by the divine order. There is no evidence for this hypothesis. It has taken aeons of sluggish evolution and adaption from simpler to more sophisticated species, according to geological evidence preserved in the layers of rock, according to palaeontologists (who study the history of fossils trapped in the layers of ancient rocks). by a slow process of evolution and natural selection. If we examine the layers of rocks of the Pre-Cambrian Age, about 530 million years old rocks, and compare them to the present-day rocks, we find a gradual change, oldest rocks contain the simplest forms of fossil with simplest bone structure as we examine the younger and younger rocks, we find in the fossils of animals more complex bone structures showing the evidence of evolution and the natural selection of the fossils and their modification of the structure in the existing environment. No human fossils were found in the ancient rocks. Our fossils were discovered in upper most layer of about three million years old rocks.

From the study of geological records, it is certain that neither Adam nor Eve nor any other life form could have burst spontaneously on the planet in a form identical to the ancestors of today. In Darwin's cosmos, there was no sudden manifestation of a Design; instead, there was a steady evolution, which was then followed by natural selection based on the environmental conditions present at the time. Darwin theory proposed that evolution and natural selection is self-regulating, self-organizing and self-evolving and it requires no divine intervention. Some individuals question whether Natural Selection is a part of God's design and plan in order to reconcile science and religion. With the rapid growth of science and technology, the idea becomes more and more critical. Darwin’s evolution and natural selection is

extremely slow process, and it takes eons. Mother Nature put building blocks of life together over millennia. Evolution of our Universe itself is an extremely slow process.

According to the Science of Cosmology, the Universe was a single mass of energy. May be God said, let there be light and there was light. About 13.72 billion years ago, the Universe exploded with a Titanic Force called the Big Bang. Its content spread in every direction. The Universe began to cool, gravitational forces attracted, and the material began to condense forming island of galaxies. The galaxy in which we live is called the Milky Way Galaxy. Further cooling resulted in the formation of Star Systems like our Solar System. The revolving burning material condensed around our Sun forming planets. Planets such as Mercury and Venus are too close to Sun are too hot to support life. Planets too far from Sun such as Mars, Jupiter, Saturn, Neptune, and Uranus are too cold to support life. Planet Earth is in the habitable Zone. It is neither too hot nor too cold. Life is evolved. The early hot Earth was bombarded with comets which brought water to Earth surface forming oceans. Seventy percent of Earth surface is covered with Water. Planet Earth is a Water World. In Summer, Water evaporates and in winter it condensed. Thunders and lightning storms cooled the planets even further. A million-lightnings strike Earth each day. At some remote corner of the Earth, lightning struck at a cloud of gases consisting of Ammonia, Carbon dioxide, Water near a Phosphate rocks forming the first information molecule called nucleotides.

Soon after the Earth was formed about four and a half billion years ago, the surface of the Earth was like visions of hell filled with the oceans of liquid rock, boiling sulfur, and impact craters everywhere. Volcanoes blast off all over the place, and the rain of rocks and asteroids from space never ends. Nitrogen gas released from the volcanic activity filled the atmosphere. Within a billion year, the heavy bombardment slowed down, and the surface begins to cool. The heavy bombardment of comets which brought water to Earth. The hot Earth begam to cool. Every drop of water on Earth was brought by comets. As the climate change over a billion year, there appeared the first sunshine, the first snow melts, and the first rainfall. As soon as the clouds subside, the temperature dropped to zero and the water sets an ice age.

In Darwin's world, there is no life on early Earth. Over 4.6 billion years ago, the Solar System first began to develop. The newly formed Earth was an inhospitable and lifeless planet. One wonders how microscopic life originated on early Earth. As I said above, a million-lightning strikes Earth each day. On a cloud of gases including ammonia, carbon dioxide, methane, and phosphate rock in a far-off region of the planet, a single lightning strike produced the macromolecule RNA. (Ribonucleic Acid) which is made of the same four nucleotide bases. They are Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C). In RNA, Thymine is converted to a more active Uracil (U). Out of four nucleotides, three code for an amino acid called Codon. Several hundred codons join to form a gene which codes for a protein. RNA is a unique molecule which can store information like DNA and catalyze reaction like protein. The very first molecule is what starts the earliest forms of life on Earth. These molecules accumulated over eons giving rise to a more stable molecule, the Deoxyribose Nucleic Acid (DNA), amino acid and proteins the basic building blocks of life. The single cell life forms are established and within a billion years, the surface of Earth was teeming with all kinds of microbial life and one such life form was blue-green algae which conducts photosynthesis that is it absorbs Carbon dioxide and pumped Oxygen in the atmosphere. Proof of the

evolutionary changes came from Wilcock's collection of pre-Cambrian fossils such as Trilobites found in Canada showed the diversity of fossils on early Earth. Early scientists wondered how these complex life forms got on Earth.

Planet Earth was not only cooled but also submerged in Ice age. The climate of the late Precambrian time, the Pro-Triazoic Eon (2.5 billion years ago to 543 million years ago) was typically cold with glaciations spreading over much of the Earth. At this time, the continents were bunched up into a single supercontinent. A supercontinent is a landmass made up of most or all of Earth's land. This term could be used to the landmass that is made up of modern-day Africa and Eurasia. Pangea was the most recent supercontinent to include all of Earth's significant—and possibly most well-known—landmasses. The first single-celled living creatures appeared within a billion year were anaerobic and thrive in the Nitrogen atmosphere. During the Precambrian Period, prokaryotic single-celled creatures constituted the majority of life.

Using modern molecular biology technique and comparing nucleic acid and amino acid sequences across living species, the techniques are enabling the identification of genetic components and patterns stingily conserved by evolution, from those in which times of evolutionary branching of the tree of life can be inferred. Where did they all come from? It is easier for a religious person to understand. He would say God put them here. It was Louis Pasteur who showed that even smallest microorganisms arise from parent microorganisms resembling themselves. We wondered how the first organism appeared on Earth.

RNA World

Millions of nucleotides joined to form a self-replicating complex molecule called RNA (Ribonucleic Acid) the first information molecule for creating life. Our early Earth was filled with Nitrogen gas coming from millions of volcanos on hot Earth. Anaerobic life thrives on Nitrogen filled RNA World. Anaerobic life can store information like DNA and catalyzed reactions like proteins. According to Darwin, life evolved, and nature selected. Millions of nucleotides are created on the early Earth. When 120 to 90 thousand nucleotide base pairs joined together in an organism to form a new organelle called Chloroplast. It has a unique ability to conduct Photosynthesis that is, it can absorb atmospheric Carbon dioxide to convert to its food Carbohydrate and release Oxygen as a by-product. Oxygen gas is very toxic to the anaerobic life-forms. As more and more Oxygen is released, more and more anaerobic life-forms died. With the arrival of Oxygen by plants, RNA world ended, and more complex life-giving molecules were evolved such as DNA (Deoxy Ribonucleic Acid) a more stable molecule which store information, Proteins which carry out body function. Over eons, new molecules appeared such as Carbohydrates to provide energy, and Hormones to support life. These are all scientific facts. Now we know the answers to these questions where they all come from not from Heaven but were formed on Earth.

DNA World

The evolution of the present-day DNA world is due to the evolution of Chloroplast in plant kingdom. Chloroplasts are organelles found in several eukaryotic species and plant cells. Chloroplasts are the most important plastids which is a major double-membrane organelle found in the cells of plants and algae. Important chemical components used by the cell are created and stored in plastids. It is the part of a green

plant cell where photosynthesis takes place. It is a primary site for splicing essential amino acids Codons. The entire nucleotide sequence (the number and the order of the nucleotides) of Chloroplast Genomes has been determined. It is found to contain120-190 thousand nucleotide base pairs. While a typical plant cell might contain about 50 chloroplasts per cell, most land plant chloroplast genomes typically contain around 110-120 unique genes. Some algae have retained a large chloroplast genome with more than 200 genes, while the plastid genomes from non-photosynthetic organisms may retain only a few dozen genes.

Today, we have read (mapped and sequenced the genomes of dozens of living creatures) and identify not only the number of genes on a chromosomes which occupy less than 2% of the chromosome, but also the total number of nucleotide bases and their order in which they are arranged in a species). The four nucleotide bases used to write them all are A-T and G-C. The same four nucleotide bases are used to encode the characteristics we inherit from our parents. All living things have a kinship tie, as evidenced by the language of life. If you sequence and compare the genomes of two people, you find that our book of life is 99.9% the same and if you compare our genome with our closest relation, the Chimp, in the animal world, you find that our genome is 98.9% of the sequence of the genome the same as Chimp. Just 1.1% difference gives us intelligence and conscientiousness and makes us aware of our surroundings. Minutes difference between our genomes makes all the difference, we are free, and they are in the cages. The human chromosome #20 is identical to the mouse chromosome #2 if you compare the sequence of the human genome with the genomes of many other species. Human chromosome #4 and mouse chromosome #5 are aligned. A significant portion of the human chromosome matches the fish, fly, or worm genomes letter for letter when the human genome's sequence is aligned with those of these organisms.

Chloroplast is one of the three types of plastids. As I said above, the chloroplasts take part in the process of photosynthesis, and it is of great biological importance. Animal cells do not have chloroplasts, but they have Mitochondria. All green plant take part in the process of photosynthesis which converts Carbon dioxide into carbohydrates its food in the presence of sunlight energy and the byproduct of the process is Oxygen that all animals breathe. This process happens in chloroplasts. Chloroplasts are distributed uniformly throughout the cytoplasm of the cells, and in some cells, they become concentrated near the nucleus or immediately below the plasma membrane. A typical plant cell might contain about 50 chloroplasts per cell. The extinction of anaerobic life forms in the presence of Oxygen paved the way for a burst of new life, called the Cambrian explosion, during the following Paleozoic Era.

Over eons, planet Earth began to warm and in the presence of Oxygen atmosphere, the appearance of first single cell Pre-Cambrian creatures that attack each other forming a multicellular creature. These earliest forms of life resembled Cyanobacteria. They were blue-green photosynthetic algae that grew well in the highly hot, carbon dioxide-rich environment. For millions of years, the job of blue green algae was to perform photosynthesis that is to absorb Carbon dioxide and release Oxygen.

Essential components of life are RNA, DNA, Proteins, Carbohydrates, Lipids, and Hormones. We always wonder how these non-living chemicals could get together to create living creatures. When did Chemistry became Biology? When did life evolve? Where was it evolved? And how life was evolved? Evolution of

Life on Earth is not a miracle. Life could have been evolved on Earth's surface such as on the oldest rocks found in Australia or it could have been evolved at the bottom of the Hydrogen sulphide gas from the environment reacts with the lava on the ocean floor to generate Black Smokers, which gives energy to creatures like tubeworms and crabs. that thrive on the Ocean floor. Life also could have been evolved underground. Soil sample brought by miners from the Gold mines in South Africa two miles deep underground contained micro worms. Such a life form could be raised in a Petri dish with agar and nutrients mixed in. Unicellular living forms might have existed in the beginning. Could meteors have given life on Earth. Early Earth has no Water. Billions of Comets brought Water on Earth. Would it be possible that some of those Icy comets contained life giving essential components? Life could also have been evolved on the surface of Earth. Formaldehyde polymerization in the environment could result in carbohydrates are yet another vital element for existence. The presence of Acetonitrile, Carbon dioxide, Water in the presence of Ultraviolet light could produce the nucleotides such as Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C) forming a binary code leading to RNA which start replicating itself creating the first living anaerobic creature. We rely on the existence of the first life on Earth from the early fossils found in places like because no one was there to observe its formation and evolution. the layers of ancient rocks.

Complexity emerges as a single replicating living cell first occurs on Earth. To put it another way, all sophisticated life forms have evolved from less complex ones. The remains of ancient life forms are called fossils. The species must have evolved hard components like a shell or bone and must have been stuck in muck that gradually hardened into rock in order to become fossilised. Soft-tissue animals' tissues degrade instead of becoming fossilised. After the Earth created approximately four and a half billion years ago, the first living form appeared on Earth. Over billions of years of evolutionary process give enough time for the chemicals to react together to create Life.

The Geologic Clock

Let me run through the history of life on Earth from its inception to the present. From 3.5 billion years ago to the present, the gradual evolutionary changes can be explained. If we were to examine the fossil record based on the Geologic Time Scale, we can divide this time into three great eras. First, The Paleozoic Era which starts from the very beginning of the Pre-Cambrian Era starting from the 100 million to 400 million years ago. Second, the Mesozoic Era, which lasted between 230 and 70 million years ago. Third, from 63 million years ago to the present, there was the Cenozoic Era.

As more and more chloroplast genomes accumulate, a primitive Blue Green Algae appeared which act as primitive plant life. About 400 million years ago, the first plants appeared on Earth. With the appearance ofplants, Oxygen molecules accumulate in abundance. Plants' chloroplast, which is used for photosynthetic activity, began taking carbon dioxide and releasing oxygen into the environment. The evolution of numerous plants played a key part in converting carbon dioxide to oxygen because forests thrive in an aerobic environment. Of all the plants, Maize is the winner. The maize plants' fields can effectively absorb CO2 and convert it to carbon-based compounds like carbohydrates during photosynthesis, which releases oxygen. As the Sun rays strike the forests on Earth surface, the Chloroplasts in the trees convert the Physical sunlight energy into Chemical energy by photosynthesis.

Photosynthesis powers the majority of the planet. It was plants that introduced Oxygen in Earth's atmosphere.

During the Pre-Cambrian Era, primitive life forms appeared. The creatures with soft tissues in their bodies have no fossils, although some of their impressions can be seen on old rocks. Trilobites and other hard-shelled fossils formed of calcium carbonate were discovered at the conclusion of the Precambrian period. Primitive life forms including algae and orthopods first appeared during the Cambrian Era, some 100 million years ago. Sponge, worm, and mollusc appearances happened considerably later.

Earliest life forms with shell are preserved as fossils. A treasure of fossils was discovered in British Columbia, Canada, called the Burgess Shale, found in the Canadian Rockies of Canada. These are the fossils that the Middle Cambrian Period left behind. In Washington, D.C., the Smithsonian Museum has a portion of this gem on exhibit. These fossils included trilobites, worms, and sea cucumbers. Bony living forms such as Tetracorals, echinoids, and asteroids first appeared on the early Earth during the Ordovician Period, which lasted from 425 to 500 million years ago. The greatest significant alterations to the Earth's atmosphere occurred during the Silurian Period (425 to 405 million years ago). Tall plants appeared for the first time. Up to this time, Earth's atmosphere was full of Nitrogen gas released by the cooling of the hot Nitrate containing volcanic Rocks. Earth's atmosphere also contained the Carbon dioxide contributed by the Volcanic eruption. It was the appearance of Chloroplast that changed the direction of life on Earth. The early plant life known as the Blue Green Algae covered the cooling region of the planet Earth over the next 60 million years at the start of the Devonian period. An huge amount of oxygen was released into the atmosphere over millions of years.

By the end of the Silurian Period, the composition of the Earth's atmosphere was changed from pure Nitrogen gas to 80% Nitrogen and 20% Oxygen gas. The gas Oxygen is extremely reactive, it reacted with the Oceans Iron forming the Iron oxide. Billions of tons of Iron Oxide deposited on the Ocean floor. Oxygen is toxic to the Anerobic life forms. Creatures survive in the presence of Oxygen thrived while Anerobic life forms died. Complex life forms appeared. Darwin's remarkable foresight about the evolution of life on Earth can be confirmed by modern methods using DNA sequencers. By using next generation Nanopore Sequencer, we can read the number and order of nucleotides at each evolutionary stage. We can demonstrate how at each step of evolution some nucleotides are deleted and others are inserted to survive in a changed environment and how new species are evolved. In the Oxygen rich atmosphere, fossils of Fish and Amphibians were found along with the fossils of spiders, millipedes, insects, and corals were discovered.

The Mississippian period, which covers 345 to 310 million years, is known for the appearance of fossils of increasingly complex life forms, including as corals, branchipodids, and foraminifers. The Pennsylvania Period, or the Great Coal Bearing Layers of Rock, emerged between 210 and 280 million years ago. It observed a large, low-lying aquatic that had developed into a coal forest. This period saw the appearance of Clams, shellfish, reptiles, and amphibians.

The Permian Period, which spanned from 280 to 230 million years ago, saw the growth of coal-forest greenery such conifers, tongue-fern, oak, insects, beetles, and dragon flies in the swampy region of the

surface. The Permian Period's plants and animals go extinct as a consequence of climatic changes. The Paleozoic Era ended up coming an end as a result. The Mesozoic Era began about 165 million years ago. It brought the Age of Reptilian. Birds, mammals, insects, and flowering plants including elm, oak, and maples also became popular in this era. Because of the Plate Tectonic movement, new mountains range slowly appeared. The Triassic Period, which covers 230 to 180 million years ago, featured the creation of dinosaurs, a powerful animal that ruled Earth for roughly 150 million years. They were all killed when Planet Earth got hit by a meteorite some 65 million years ago. They left behind their footprints as their fossil around the world. During the Jurassic Period, rainforest spread everywhere the Dinosaurs dominated the land, but the Ocean was dominated by the Plesiosaur, the monstrous carnivorous of the Seas.

The Cretaceous Period which begins about 135 to 70 million years ago, marked the development of sedimentary rock made of Chalk. The moment of the Tectonic Plates formed the mountain range from Andes to Rockies, from Antarctica to Northwestern Asia. Plants thrived during the Cretaceous Period. Trees and shrubs including Magnolia, Oak, Maples, Birch, Holly, and Ivy, which provided food for mammals, birds, reptiles, and insects, were evident in the fossil record. Dinosaurs spread on all seven continents. The globe has been covered in their fossils. As I said above, they all disappeared around 65 million years ago, when a meteorite structed at the Northern Mexico. The Cenozoic Era, called The Age of Mammals, began about 70 million years ago to the present day. The polar regions froze as a result of the climatic a shift, whereas the entire globe warmed. This climate change stayed on to the present day. The Cenozoic Era is dominated by the Flowering Plants, and reptiles are replaced by Mammals. Birds continue to expand everywhere.

Finally, the Quaternary Period in which we now live began with the melting of the 10,000 feet thick ice sheet over much of the Northern hemisphere in which four glaciers advanced which lasted about 11,000 years. The melting of the ice sheet helped to establish an environment that was favourable for the advent of humans. It has just been a few million years since humans first appeared on Earth. In any of the geologic eras from the Precambrian to the Cenozoic, have we discovered human fossils? The answer is no. In 1974, the first human fossil, Lucy, Anthropologist Donald Johansson uncovered an Australopithecus afarensis skeleton in a 3.2 million year old rock in Ethiopia's Hader valley. The Great Rift Valley has housed chimpanzees for the past 25 million years. A more advanced form of the Chimp called Australopithecus appeared in East Africa. He was an advanced forest man called Homo habilis. He was a hunter gatherer of food who built tools. He was a direct ancestor of Man and who lived about 20 million years ago. Next was the ape-man, Pithecanthropus, who lived about 500,000 years ago in Java and China. Neanderthal man lived in Europe. He was also a hunter gatherer and lived about 100,000 years ago. They all died about 30,000 years ago. Cro-Magnon finally evolved modern brain. Cro-Magnons, a term derived from the Cro-Magnon rock shelter found in southwestern France, where the first human fossils were found in 1868.One of the greatest challenges was how to obtain DNA from the fossil to sequence their DNA for comparison with other species to confirm the Darwinian Evolution.

Svante Pääbo the Swedish geneticist and the 2022 Nobel Laureate developed a method to extract and analyzed DNA from fossil and sequence their genomes. In 2010, he succeeded in sequencing the genome

of the Neanderthal, the pro-humans. He discovered a previously unknown hominin, Denisova. He also found that gene transfer had occurred from these now extinct hominins to Homo sapiens following their migration out of Africa around 70,000 years ago. Pääbo's work help us confirm Darwin's Theory of Evolution to Darwin's facts. Darwin's ideas were considered a guesswork that assume a single Finch had probably been blown by storm or otherwise separated to reach one of the 13 islands of Galapagos from the mainland, South America. Over eons, the offspring of the mother Finch have evolved different species of Finch on different islands, their distinctive thick or long beaks being an adaptation to distinct natural habitats or environmental niches. Their different beaks which are suited to different food types such as thick beakto crack open large seeds or long beak to catch worms. From these observations, Darwin predicted that all species of organisms arise and develop through the natural selection of small, inherited variations that increase the individual's ability to compete, survive, and reproduce. He stated that organisms evolve over generations through the inheritance of physical or behavioral traits, There are four important components for the diversity of life on Earth that requires for evolution, and they are variation, inheritance, selection, and time. Darwin's theory provides a powerful framework for understanding nature and is one of the essential theories at the very core of science.

Today, we can confirm over eons of evolutionary process in Finches, by extracting their DNA from their fossil record for comparison and by using second generation Nanopore Sequencer, we can sequence the genomes of all the following 13 finches cheaper, faster and accurate for comparing with the Reference Sequence of the original Finch obtained from South America to identify the mutations responsible for causing the evolution: For example, by comparing with reference sequence, we can show by sequencing the genomes of Green warbler finch (Certhidea olivacea); Grey warbler finch (Certhideafusca); Mangrove finch (Geospiza heliobates); Woodpecker finch (Geospiza pallida); Large tree finch (Geospiza psittacula). Medium tree finch (Geospiza pauper); Small tree finch (Geospiza parvula); Large ground finch (Geospiza magnirostris; Medium ground finch (Geospiza fortis); Medium ground finch (Geospiza fortis); Small ground finch (Geospiza fuliginosa; Large cactus finch (Geospiza conirostris); Common cactus finch (Geospiza scandens); Sharp-beaked ground finch (Geospiza difficilis), what kind of mutation in finches was responsible for binging changes to survive in the altered environment? Was it deletion of DNA base pairs, insertion, translocation, inversion, or nucleotide base pair changes? This comparative genome sequence study will confirm that Darwinian evolution is not a theory, but it is also a fact.

Science means knowledge and knowledge can be obtained by conducting doable, reproducible, and verifiable experiments. Can Darwinian Evolution be demonstrated in the Lab? Can we produce in the Lab basic building blocks of life such as amino acids, proteins, DNA etc. The answer is yes.

In 1953 Stanley Miller, the student of the Nobel Laureate, Harold Urey, at the Chicago University conducted an experiment in the Lab to create life's essential components the amino acids. He created primitive Earth like conditions in the Lab. He took two flasks connected with a condenser. One flask contained water vapors and the other filled with gases found on the primitive Earth such as Methane, Carbon dioxide and Ammonia. To mimic thunder and lightning, a source of energy, on Earth, he sparked electric current in the flask. The high energy electric spark, split the stable molecules of Nitrogen, Oxygen, and Carbon, producing extremely reactive radicals which reacted with one another recombing to produce

a more stable new molecule. Within a week, the clear solution in the flask became pink and dark. The analysis of the colored material showed the formation of Amino Acids, the essential building blocks of life which perform all body functions. In similar experiments, Francis Crick and Lesli Orgel, attempted to synthesize Nucleotides the replicating molecules which carry information to make life. Using Formaldehyde, the other essential components of life such as sugars and hormones were synthesized.

Our journey began in the RNA world. RNA can copy itself. Self-replicating RNA molecules proliferated before the evolution of more stable DNA and proteins. The earliest life forms were anaerobic 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. A class of bacteria called the Cyanobacteria evolved to become blue green algae, which turned it into an internal solar power plant. They developed the Photosynthetic apparatus. Land plants evolved from ocean plants. 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. Thousands of nucleotides join to form a string of letter called the DNA (Deoxyribose Nucleic Acid).

Heritable traits are known to passed on from one generation to the next via DNA, through a molecule, that encodes genetic information. DNA is a long polymer composed of four types of nucleotide bases. The sequence of bases along a particular DNA molecule specifies the genetic information. In a manner like a sequence of letters spelling out in a sentence. Before a cell divides, the DNA is copied so that each of the resulting two cells will inherit the same DNA sequence. Portions of a DNA molecule that specify a single functional unit are called a gene which is made of a string of nucleotides. A gene is a unit of inheritance. It codes for a protein. A gene has a single start codon (AUG which codes for an amino acid, methionine) and three stop codons (UAG, UGG, UGA). Different genes have different sequence of bases consisting of several three-letter codons. Within cell the long strand of DNA form condense structure called chromosome. The specific location of a DNA sequence within a chromosome is known as locus. If the DNA sequence at a locus varies between individual that is different forms of sequence are called allele. DNA sequences can change through mutation producing new allele. If a mutation occurs within a gene, the new allele may affect a trait that the gene controls altering the phenotype of the organism. However, while the simple correspondence between an allele and a trait work in more cases most traits are more complex and are controlled by multiple interacting genes. Evolution in organism occurs through changes in heritable traits which are characteristics of an organism and in human, for example, eye color is an inherited characteristics an individual might inherit brown eye traits from one of their parents. Inherited traits are controlled by genes and the complete set of genes within an organism’s genome is called its genotype. The complete set of observational traits that makes up structure and behavior of an organism is called its phenotype. These traits come from the interaction of genotype and the environment.

The thread-like structures known as chromosomes are found in the nucleus of cells in plants as well as animals. Deoxyribonucleic acid (DNA), a protein-coated long chain of four nucleotides, making up each chromosome's double strand. As I mentioned before, DNA is the information molecule that is handed from parents to children; these precise instructions are what give each kind of living thing its individuality. As living things develop, their complexity rises along with their chromosomal count. Modern sequencing supports Darwin's theory of how life evolved. It takes a very long time for life on Earth to evolve. About a billion years after the formation of Earth that is about three and a half billion years ago, life appeared; thousands of nucleotides organized themselves to become alive; Chemistry became Biology. The bacterium Phage Phi-X 174 contains around 5,000 nucleotide bases, making it one of the smallest known organisms. Since it just has one chromosome, it has the majority of bacteria. In order to survive in the altered environment, complexity and chromosomal number increased as evolution progressed in both plants and animals.

For instance, whereas bacteria only have one chromosome, Jack Jumper Ants have two. The deer Muntiacusrnunrjak has only 3 chromosomes; Spider mite, and Cricotopus, have 4 chromosomes; Olkopleura duiuca, Yellow fever mosquito, Indian munjac have 6 chromosomes; muntiacus muntjak has 7 chromosome; Fruit fly has 8 chromosomes; Marchantia polymorpha has 9 chromosomes. Swamp wallaby and Thale cresss has 10 chromosomes and Swamp Wallaby have 11 chromosome; Nematode has 12 chromosomes; the Australian daisy also has 12 chromosomes; the spider mouse, Aloe Vera, and cucumber all have 14 chromosomes; garlic has 16; itch mites have 17; radish, carrot, cabbage, and passion fruit all have 18; maize and cannabis both have 20; Virginia possum and Bean both have 22 chromosomes.; Snail, Melon, Rice, Sweet Chestnut have 24 chromosomes; Giraffe, American mink, and Pistachio all have 30 chromosomes; Edible frog has 26; Axolotl has 28; Beg Bug has 29; There are 31 chromosomes in the Japanese oak silk moth, 32 in the yeast, European honey bee, American badger, and alfalfa, and 34 in the red fox, sunflower, and porcupine. 36 chromosomes are found in the yellow mongoose, Tibetan sand fox, starfish, red panda, meerkat, and earthworm; 38 chromosomes are shared by the tiger, sea otter, sable, raccoon, pig, lion, and European mink; 40 chromosomes are shared by the mouse, mango, hyena, ferret, beaver, and peanut. Rat, Wheat, Oats, and Wolverines all have 42 chromosomes. Dolphin, Sable antelope, European rabbit, Eurasian badger, Moon jellyfish, Dolphin, Arabian coffee have 44 Chromosomes; and Human have 46 chromosomes. Humans are arrived. Humans are superior to all other creatures.

With 46 Chromosomes Humans Are arrived

There is something fundamentally different from humans to the organic world. We are not the special creation. Some species have special gift for example, elephants have trunks, birds have feathers, they can fly and defy gravity. Cheetah can run faster, turtles have a protective shell to cover themselves, the presence of co-location device in bats, help them fly at night. Migrating birds have special sonar gift in navigation during long distance night flight. These are a few examples characteristics that we do not have. That make other species superior to humans in these regards. What we have is a large brain that make us special. With 46 chromosomes, Homo Sapiens as a species stabilize about 200,000 years ago. With increase in the brain size. Brain has been expanding ever since compare to our body size. Brain is a hungry organ, It consumes about 20 to 30 percent of Oxygen, circulating through our blood. According to Darwin, the advantage of large brain has increased its plasticity and ability to advance our culture during the last

5,000 years. With the development of our brain, we progressed rapidly, the Age of Agriculture arrived about 30,000 years ago; our ability to trade about 100,000 years ago, reading and writing about 5,000 years ago, math and science about 500 years ago, These developments brought huge changes the way in which we live. Our cultural phenotype is spectacularly different today even a 1,000 years ago. Those changes affect the way in which we behave and the way we interact with each other. These achievements cannot be explained by simple genetic changes, nor can we explain our cultural and cognitive phenotype. That is distinctive. Our cognitive function and cognitive ability have increased as our brain's capacity which has expand in the last few hundred years, The distinctive features that is our biological make-up modify our brain through our experience; every time we learn something new something change in our brain. We canabsorb those change to the extraordinary ability, through language we transmit new knowledge and new skill to others that is to change their brain as well; we call it educations; it is different from any other species. It is determined by our genetic make-up we share the plasticity of our brain through language; we move ideas and experience to others. The genes that allow us to form new memories and to learn things to share with others is not found in any other species, we have genetic pattern expression that makes neurons capable of change giving us consciousness.

Forty-six chromosomes give us the optimum achievement of consciousness. The sequencing of Human Genome in later pages will show that the 46 chromosomes are made of six billion four hundred million nucleotides half we receive from our mother and another half from our father consisting of 24,000 genes whose interactions give humans their consciousness. All those species who achieved above and below 46 chromosomes lose consciousness. The facts mentioned above make it very clear that humans are not the pinnacle of evolution, but rather are superior to all other living things. There are creatures who have more chromosomes than us. Our capacity for oral and written communication, as well as our attainment of consciousness, make us superior, and we pass on our knowledge to succeeding generations. Our achieving the 46 chromosomes over millions of years give us the ability not only to read our own book of life, but also the book of life of all other living creatures. The reading the number and the order of the nucleotides in our book of life that is sequencing our genome, give us the ability to confirm the development of the complexity of life accurately explained by the Darwinian Evolution. Humans are not only the most creative, but also the most destructive. The following section explains the destructive nature of Humans.

Paleontology is the study of the history of the fossils record trapped in the layers of rock. The study of the fossil record show that the ancestors of the native Americans Indians cross the Bering Strait about 13,000 years ago. They left Russia and arrived in the new world now known as America. The DNA sequencing of their fossil record suggest that a single population of modern humans migrated from Southern Siberia toward the land mass known as the Bering Land Bridge as early as 30,000 years ago and crossed over to the Americas by 16,500 years agoThe new immigrants who came to New World, they were converted to a New Religion. Their new theology refers to as the old testament which justifies human domination of nature which says man was created in His image, God said, Let them have dominion over the Fish of the sea; over the foul of the air; and over cattle and all the species on Earth. After using the philosophy of the dominion, they justify conquering the natural world and destroying their environment at home. European societies used their new scientific and industrial capabilities to brutally colonize and ruthlessly exploit the rest of the world, The new world was full of novel species of Darwinian evolution. Before the arrival of the

humans in the New World, a menagerie of animals roamed the plane among the most exotic were the Wooly Mammoth, Mastodons, Giant Wolf, Large number of fossils confirmed that the species discovered in the New World were all slaughtered by humans. When animals kill animals, they kill to eat. Not humans. Similar findings confirm, when humans arrived in Hawaii, New Zealand, Australia, Easter Islands, these places were full of new species, they were all wiped out by humans. Forty million bison were killed by the new European settlers who came to America in search of Gold. Humans kill humans for name, fame, or fortune. Modern cities like Hiroshima and Nagasaki with thousands of people were turned to ashes in minutes. Twenty million people died in the WWI and forty millions killed each other during WWII.

Humans are also the most creative. Among all the species, we have the most advanced brain. No other species can answer the most fundamental questions we have asked ourselves since the dawn of human civilization. What does it mean to be humans? What is the nature of our memory and our consciousness andour development from single cell to a complete human being; the biochemical basis of our senses; the process of our aging; and the scientific basis of our similarities and dissimilarities. Similarity that all living creatures froma tiny blade of grass to mighty elephant, inclining man, mouse and monkeys all are made of the same building blocks and yet we are so diverse that no two individuals are alike. Even identical twin is not exactly identical, they grow up to become to separate individuals. Genome sequencing confirmedour three and a half billion years of Darwinian evolution. As evolution continues, complexity increases from simple to more complex species accumulating more chromosomes and more genes to survive in the altered environment. Although other species gain more chromosomes, but they lost consciousness. The following species have more chromosomes than humans: for example Water buffalo, Tobacco, Potato, Orangutan, hare, Gorilla, Deer mouse, and Chimpanzee have 48 chromosomes; Zebrafish, Water Buffalo, Striped skunk, Pineapple have 50 chromosomes; Spectacled Bear, Platypus, and Cotton have 52 chromosomes; Sheep, Hyrax, Racoon dog and Capuchin monkey have 54 Chromosomes; Strawberry, Gaur, and Elephant have 56 chromosomes; Woolly mammoths have 58 chromosomes, but Bengal foxes, Yaks, Goats, Cows/Bulls, American Bison, and Scarlet Macaws all have 60 chromosomes. Mules have 63 chromosomes, while guinea pigs, horses, spotted skunks, and fennec foxes have 64; grey foxes, red deer, elks, and roadside hawks have 68.; White-tailed deer have 70 chromosomes; Black nightshade and Bat-eared fox have 72 chromosomes; Asiatic black bear, and American black bear have 74 chromosomes; maned wolf, have 76 chromosomes; Grey wolf, Golden Jackal Dog, Dingo have 78 Chromones; Turkey, Sugarcane, and Pigeon have 80 chromosomes; Great white shark have 82 chromosomes; Hedgehog genus have 88 chromosomes; Moon Worts, hedgehog Genus and Grape fern have 90 chromosomes; Pitter's crab-eating rat. Prawn and Aquatic rat have 92 chromosomes; Kamaraj (fern) have 94 chromosomes; Carp has 100 chromosomes; Red vizcacha rat have 102 chromosomes; Walking catfish has 104 chromosomes; American paddlefish have 120 chromosomes; Northern lamprey has 174 chromosomes; Rattlesnake fern has 184 chromosomes; Red king crab has 208 chromosomes; Field horsetail has 216 chromosomes; A. butterfly has 268 chromosomes; black mulberry has 308 chromosomes; Atlas blue has 448 chromosomes; adders-tongue has 1260 chromosomes' here is a Fern called Ophioglossum, which has the highest number of chromosome count of any known living organism, with 1,260 chromosomes. This fern has roughly 630 pairs of chromosomes or 1,260 chromosomes per cell.

Why Humans are so unique?

The fact that we share our thoughts, experiences, hopes, and dreams with other people is what makes humanity so special, isn't it? Exchanging ideas is a unique human feature; not found in any other animals. The more we exchange ideas, the more we innovate them to change to improve. When we innovate, we want the new product to be superior to the one that came before. According to contemporary thought, if a device can be improved through alteration, we should do so in order to eliminate the need for the outdated version. Our greatest achievement is our cooperative thinking. We are the only species that communicate with each other by language. We have developed elaborate form of thought sharing. For the past 150 to 200 thousand years, each of us have specialized in one profession and then we exchange them for goods, services, knowledge, and skill with each other. To exchange, we require language. Now that the human genome has been sequenced, the complete book of life has been read. We have determined that the evolution of the FOXP2 genes, which produce the proteins that regulate our speaking characteristics, is what gives us the ability to talk. Our voice box and vocal cord are made of these proteins. Recombinant technology has previously been created to introduce 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 DNA sample extracted from the Neanderthal fossil obtained near the Rock of Gibraltar has provided enough genetic material, to read its entire genome or its complete book of life. We could determine which genes, besides FOXP2 genes, are present in us by comparing the Neanderthal genome with the contemporary Human genome, giving us the capacity to speak verbally like modern humans.

What makes humans so unique is that we live in the cooperative society in which we exchange goods and services with each other. That is, we trade with each other our skill and knowledge for goods and services. For example, you go to any restaurant and order a meal. The best dish is served in an hour. Do you know how many people work on making your food? Farmers plant the seeds and vegetables, someone refines the food, supplies it to the restaurant, the cook combines the components, and in an hour, the cuisine is ready. 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 the world 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. In short, what makes humans so unique is that only humans live in the cooperative society in which we exchange goods and services with each other. That is, we trade with each other.

The Origin of Human Conscientiousness

Chimps were living in the Afar Valley in Ethiopia in the heart of dark Africa for over six million years. A

female chimpanzee named Lucy had a few brain changes that caused her to develop conscientiousness, making her the first pro-human. She was anatomically identical to contemporary humans and could stand on two feet. There was enough of fresh water, food, and shelter. 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 Europe. Their fossil was found in the Neanderthal Valley in Germany. Early African waves landed in various regions of Europe. The Cro-Magnon, more recent hominins that resemble modern humans, arrived in France. Their fossil, which was discovered in French caverns, was radioactively dated, and it revealed that they painted the cave walls about 100,000 years ago. Early humans that travelled east during the Ice Age traversed the icy ocean and arrived in Australia approximately simultaneously. Australian fossils have a radioactive age of roughly 85,000 years. Modern people expanded across all seven continents of Earth in less than 100,000 years. We number eight billion people worldwide and reside in more than 200 countries. Our population is growing so quickly that we are adding roughly 90 million people each year. 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 exoplanet another Earth like planet in the nearest Solar Systems.

We must examine ourselves if we want to comprehend the intricacy and originality of the human mind. What characterises humans? The Human Genome is the collective genetic material that makes up an individual human. Information, which we discovered to be the core of life, is stored on the four genetic letters known as nucleotide bases. As stated above, they are (A), (T), (G) and (C). These are the first four genetic letters that can be found in the DNA of every living thing, including humans, mice, monkeys, and microorganisms. All living things' existence is recorded in these four letters. Deoxyribonucleic acid (DNA) is a collection of nucleotides. DNA contains the genetic material that each of us is made of. We cracked the genetic code and discovered the life's mystery. According to Central Dogma of Crick and Watson, [1] the information on DNA is transcribed onto RNA which is translated in Ribosome to protein. In the nucleus, the double helical DNA replicates (makes its own copies), and as it exits the nucleus as mRNA in the cytoplasm, it transcribes into single stranded RNA. (RNA is converted to mRNA by splicing out non-coding sequences) which is translated in the Ribosomes into proteins. Out of four nucleotide genetic text, three nucleotide code for an amino acid called Codon. Hundreds of codons form a gene which code for a protein. Information from both healthy and unhealthy genes goes from the nucleus into the cell, determining whether an organism is healthy or ill. While harmful proteins from mutant genes result in bad proteins that make us ill, good proteins from good genes keep us healthy. Information is being shared continuously and without interruption. To understand the normal function of a human being, we must read his entire book of life that is his genome.

Cerebral Cortex and Hippocampusare the Library of Human Language & Consciousness

What does it mean to be humans? How do the genes-genes or protein-proteins interact to give us the conscientiousness? How can we tweak genes to create novel treatments that increase human lifespan? In order to prolong human life, new treatments are based on either delivering harmful proteins or

sequencing the causative genetic variants. Human genome sequencing enables us to better understand how humans differ from all other Earth organisms. We stand out from all other animals on Earth because our brain, which weighs three pounds, is housed inside our skulls. All of our other organs can be transplanted except the brain. Neurons are the 86 billion cells that make up our brain. Each neuron has 10,000–100,000 connections, or synapses, that connect it to other neurons. Their permutation and combination result in more synapses overall than the total number of synapses. Millions of synapses join to form neuronal circuits that is where our memory is stored. Millions of neuronal circuits interact to generate our thoughts our ideas and our visions. The complexity of our brain is the result of three and a half billion years of Darwinian Evolution. Is it the limit of our complexity? Not yet. Each nucleus in each of the 86 billion neurons carries a complete genome made up of six billion four hundred million nucleotides, half from each parent. All genes do not function at the same time. A methyl group (called epigenetic) blocks the function of all other genes by methylating a nucleotide. Only a specific gene function at a time. If we wish, we could remove the methyl group by using demethylating agents, azacytidine.

The next generation of scientists (my students) will have the opportunity to sequence not only the site of human consciousness, but also the genomes of all above species and their genes. They could add new genes to our GenBank to be used not only to control our consciousness, but also to develop new food, new fuel, and new medicine to treat every disease for the burgeoning population of the world.

The Impact of Sequencing Human Genome on Darwinian Evolution

As I said above, the entire book of life of all living creatures on Earth is written in four genetic letters called nucleotides. These nucleotides are found in the nucleus of all living cells including humans, plants, and animals DNA (Deoxyribose Nucleic Acid) is the name given to the thousands of AT/GC base pairs that make up each gene and are linked together in a straight line to carry out instructions. Crick, Watson, and Morris Wilkins received the Nobel Prize for discovering the double helix nature of the DNA structure which is transcribed into a single stranded of RNA (in mRNA the less water soluble methyl group, Thiamine, T, is converted to more water soluble Uracil, U, by replacing Methyl group with a Hydroxyl group) which leaves the nucleus and moves into Cytoplasm where it is translated in Ribosomes into Amino Acids leading to proteins). When thousands to millions of AT/GC base pairs contain information to make a single protein, we call that portion of AT/GC base pairs a gene (Nobel Prize was awarded to Khorana & Nauenberg for making a functional gene). If we count all the AT/GC base pairs in a single cell of our body, we will find that there are 3.2 billion pairs of bases present in the nucleus of every cell. The entire AT/GC sequence of 3.2 billion base-pair is called the Human Genome or the book of our life which carries total genetic information to make us. The reading of the total genetic information that make us human is called the Human Genome.

Under the name "The Human Genome Project," the US Congress granted three billion dollars to NIH (my institute) in 1990 for the purpose of deciphering the whole human genome. We discovered that the genome contains six billion four hundred million nucleotides bases half comes from our father and another half comes from our mother Genes that code for proteins make up less than 2% of our genome. Switches, promoters, terminators, and other components make up the remaining 98% of our genome. The largest collection of the Human Book of Life on Earth is comprised of the 46 chromosomes that are

found in each cell of our body. Genes are carried by chromosomes and are written in nucleotides. Before sequencing (determining the number and the order of the four nucleotides arranged on a Chromosomes), it is essential to know how many genes are present on each Chromosome in our Genome. The Human Genome Project has identified not only the number of nucleotides on each Chromosome, but also the number of genes on each chromosome.

A single cell is so small that are invisible to the naked eye. To magnify the internal structure of the object, we must use a strong microscope. Under an electron microscope, we can enlarge that one cell up to nearly a million times of its original size. Under the electron microscope, a single cell looks as big as our house. There is a good metaphor with our house. For example, our house has a kitchen, the cell has a nucleus. Imagine for a moment, that our kitchen has 23 volumes of cookbooks which contain 24,000 recipes to make different dishes for our breakfast, lunch, and dinner. There are 24,000 genes in the nucleus' 23 pairs of chromosomes, which contain instructions for making proteins. Proteins combine to form cells, cells combine to form tissues, tissues combine to form an organ, and several organs combine to form a person, a mouse, or a monkey. We have sixteen thousand good genes, six thousand mutant (bad) genes that cause six thousand diseases, and two thousand pseudo-genes that have lost their functions during the course of evolution in every cell of our body.

The Human Genome: The greatest Catalog of Human Genes on Planet Earth

We deciphered all 46 chromosomes, 23 from each parent. The largest collection of the Human Book of Life on Earth is comprised of the 46 chromosomes that are found in each cell of our body. The following genes have been found to be located on each chromosome by the Human Genome Project: We discovered that chromosome 1 is the biggest chromosome, with just 2,610 genes and 263 million A, T, G, and C nucleotide bases. There are only 1,748 genes on chromosome 2, which comprises 255 million nucleotide bases. 1,381 genes and 214 million nucleotide bases are found on chromosome 3. There are 1,024 genes and 203 million nucleotide bases on chromosome 4. 1,190 genes are located on the 194 million nucleotide bases that make up chromosome 5. There are 1,394 genes and 183 million nucleotide bases on chromosome 6. A gene on chromosome 7 is 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 carries 701 genes. Finally, the sex chromosome of all females called the chromosome-X contains 164 million nucleotide bases and

carries 1,141 genes. The male sperm called chromosome-Y contains 59 million nucleotide bases and carries 255 genes.

The 23 pairs of chromosomes have 26,808 genes altogether, although we frequently refer to the 24,000 genes that are necessary to maintain our normal function. 6,000 defective or mutated genes, 16,000 healthy genes, and 2,000 pseudogenes exist. Not all 24,000 genes that make up the human genome code for proteins. Less than 19,000 genes are thought to encode proteins. Each gene codes for several proteins as a result of alternative splicing. Less than 50,000 proteins are produced by all the genes in our body, which combine in many ways to form a single cell. Numerous tissues and millions of cells work together to form an organ and multiple organsm[2-6]. Our next step is to isolate proteins from the good genes and design drugs to shut off bad genes. We can isolate and manipulate a single gene from human genome. We can insert a single gene in the fertilized egg of an experimental animal in such a way that the new gene is turned on in the host cell producing a new protein. Using the restriction enzyme, (like EcoR1 which acts like molecular scissors), we cut down the chromosomes to pieces at specific sites. We separate and isolate a genes by gel electrophoresis. We prepare a restriction site map. Each gene is confirmed by comparing with the Reference Sequence. A Molecular Vehicle, Vector (such as disabled Viruses, Bacteria, or Plasmids), is created that will carry the gene into the nucleus of the cell where it permanently integrates into the genome of the host cell creating a trans-gene. As the cell begins to grow and divide, it makes copies of the trans-gene. For example, Insulin isolated from a gene located in Pancreaswas harvested in large scale in bacteria. It is now used to treat 300 million diabetics around the world. Similar method could be used to make proteins from all 16,000 good genes of our genome.

Not all genes work together at once to enable us to function normally. According to recent research, humans only need 2,000 genes to function normally; the additional genes serve as a backup support system that are activated when necessary. The remaining genes are called the pseudogenes. 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 pseudogenes, this work may create ethical problem in future as more and more pseudogenes are activated. Nature shuts off those pseudogenes for good cause. The genetic road map of all of our genes, past, present, and future, is provided by our genome. For example, it can tell us how many good or bad genes we inherit from our parents and how many of those gene we are going to pass on to our children. If a family has too many bad genes, and have a family history of serious illnesses, they can break off the information flow either by stop having children or stop donating mutated eggs and sperms.

Reference Sequence

We can scan the whole genome (Reference Sequence) for its response to a given situation. We can see differences among a normal cell and an unhealthy cell by looking at both side by side. Or when we compare their gene expression looking for a specific proteins, from a specific genes and for a specific nucleotide sequence, we can identify a specific mutation responsible for the disease. When a patient visited a doctor in the past, before the human genome was sequenced, for an unidentified illness, the

doctor would run multiple tests and declare to his patient, I do not know what is wrong with you, but I will see if any of these tests show if my guess is right and if he is wrong, He will suggest a few additional tests to see if he can pinpoint the illness. The days of assuming and experimenting are passed. Now, after sequencing the human genome, the physician would say to his patient, I do not know what is wrong with you, but I know where to find it. It is written in your Genome.He would order the sequence of patient's genome. It It would be simple for a doctor to scan a patient's entire genome and compare it to the Reference Sequence to find the mutations that are the disease's cause. He will refer the patient to a biotechnology Lab. A small blood sample will be taken from the patient by the lab technician who will then separate his WBC, extract DNA, sequence his genome, and compare it to the Reference Sequence letter by letter, word by word by word, and sentence by sentence. The physician will receive the results and can quickly determine the mutations that are causing the disease. The result will provide the best diagnostic method to identify a disease.

The Advantages of Sequencing Human Genome

The knowledge gained by sequencing human genome has summarized the past 150 years of genetic science. We have taken away the power from Mother Nature to alter billions of years of our evolutionary past. We now have all the tools we need to alter the genetic make-up of our species. Genetic Revolution has taught us that Darwinian evolution can be hastened by the rules of genetic engineering. By using the genetic tool kits, we can cut, past, copy and sequence a gene in days not in eons. The development of new tools like CRISPER-Cas 9 is making it possible to edit the genes of all species including our own with far greater precision, accuracy, speed, flexibility, and affordability than ever before. Now, we control our own destiny. We ignore the scientific facts at our own peril.

One of the advantages of sequencing the personal genome is that after seeing our own sequence most of us will conceive our offspring in the Lab rather than in our bed. What they see in their personal genome is the three and a half billion years of random mutations whose ancestors have continuously out competed their competitor in a never-ending cage match of survival. From this point onward, no one will take an unnecessary risk. Our offspring will not carry random mutations. It will be self-designed. Our choice won't be random from this point forward. It will operate independently. The current version of our Homo Sapiens species will never be evolutionary endpoint, but always be a stop along the way in our continuous evolutionary journey. During the last few hundred years, we moved from Agricultural Age to Industrial Age and then from Atomic Age to the present Information Age. Now we are entering the Space Age trying to find out how to survive on exo-planets.

The best advice for those couples who have a family history of long-term illnesses to compare their personal sequence with the Reference Sequence. In the entire human genome, we find five thousand mutations responsible for causing five thousand diseases. Each of us carry a single copy of at least five to six deleterious mutations; we are carrier, but if we marry someone who is also carrying the other copy, we are most likely to have a sick child. In the lab, before conception, we could sequence and discard a defected embryo to prevent the high cost of raising a sick child. The defected embryo can always be replaced by an embryo free from all mutations. Some parents may consider the possibility of not just selecting the best embryo for invitro fertilization but also to introduce superior traits to genetically

altering the future of their children Although invitro fertilization is encouraged to prevent the introduction of mutated genes in the gene pool, but introduction of gene enhancing traits are not permitted at this time. The following studies are forbidden: For example, a combination of genes which impart long life, high athletic or singing ability, or to make them smarter and superior to the other children, or to the introduction of new genes which make them resistant to many infectious diseases, or to introduce genetic traits associated with genius, or animal like extra-sensory perception, or to synthesize new traits, not yet known in humans, but made from the same nucleotide sequence which give rise to great diversity of life.

Prolonging human life: (Such studies are not funded at this time). We need to sequence the Genomes of Centenarian who live beyond hundred years. By comparing with the Reference Sequence, we should be able to identify the rare allele which prolong their lifespan. Once identified the allele, we need to conduct genetic engineering that is to cut, paste, copy, and splice the allele into the Genome of volunteers to study its function. The Human Genome Project showed that our Aging is a combustion process. The tail end of each chromosome carries a set of a six-letter code called Telomer. Aging is related to the loss of Telomeres, the six-letter code (TTAGGG) that shorten the length our DNA also shorten our lifespan. During replication, each Chromosome loses about 30 Telomeres each year. If we slow down the loss of Telomeres by using the enzyme Telomerase Reverse Transcriptase (TRT), we could slow down the aging process. We have already demonstrated in the worm C. Elegance that by using TRT gene, we have increased its lifespan by several folds. Now, we could translate this work first in mice then in human embryo; we could try by making a Vector, a virus, carrying TRT gene when infected the embryo and harvested to eight-cell and sequence to confirm the presence of the trans gene. The TRT gene would have been inserted in the entire genome of every cell of the growing embryo. By sequencing a single cell to confirm that the TRT transgene is spliced, we could implant TRT gene carrying embryo in the mice womb. If this transgenic experiment in mice is reproducible and verifiable, we could try in human embryo. Suppose this experiment conducted in humans is successful and suppose the sequence show that at each replication only 15 Telomeres are lost instead of 30 Telomeres. Since the longevity treatment with the TRT transgenic virus is safe, inexpensive and would be easily available to human. Should we provide the treatment to every man, woman, and child on the face of the Earth or make it available to long distance space travelers only?

To control early symptoms of a disease, frequent genome sequencing will help us identify a single gene mutation that will begin to grasp more complex genetic patterns that could lead to polygenic or multigenic conditions such as coronary heart diseases, cancers, and Alzheimer. Early detection will help us control their expansion. Some genes are activated at the later part of our life causing serious illnesses. If there is a family history of such diseases, frequent sequencing becomes more important for early detection. With development of the genetic toolkit, we can perform genetic engineering. We can separate good and bad genes. We can cut a good gene (using restriction enzyme such as EcoR1), paste a gene (using enzyme DNA ligase) and copy a gene or move the gene from species to species. As I said above, we can harvest good genes to produce large scale protein such as Insulins to treat diabetics or design drugs to shut of bad genes to treat diseases cancers.

Human body carries two genomes besides Human Genome, there is also a microbial genome captured millions of years ago called the Mitochondrial genome. Mitochondria live in human cytoplasm in a symbiotic relationship. It provides energy to host cells by breaking down phosphate bond of ATP (Adenosine Triphosphate) to ADP (Adenosine Diphosphate) to AMP (Adenosine Monophosphate). In the presence of enzyme Phosphokinase and Phosphate ions, AMP is converted back to ATP. For providing energy, in return, Mitochondria get free food, shelter and protection from the host. During conception, when mother's egg is fertilized by father's sperm, the tail of the sperm is dropped off and father's Mitochondria are lost. We inherit only mother's Mitochondria. Any mutations in the Mitochondrial genome, could cause sever diseases in the infants. During in vitro fertilization, if mutation is discovered in Mitochondria, it can either be discarded or could use a healthy Mitochondria carrying embryo to prevent the transmission of the disease.

Forbidden Areas

Our genetic toolkits contain all the essential tools to clone any species including humans. Human Cloning is forbidden by all the governments of world. Copying humans deprive genetic diversity. Other forbidden areas include manipulating Oncogenes, Toxic genes isolated from snake venom or rare bacteria. Darwinian Evolution can be hastened by the methods of genetic engineering by cutting, pasting, copying, and sequencing a gene or by moving genes from species to species with precision and accuracy. Although such studies are not permitted at this time, but with time, the restriction could be relaxed. Future studies will show that Proteins obtained from the toxic genes could be used to develop antibodies for treating various diseases.

Genomic Medicine

Once we sequenced the genome, we thought that we can compare the entire genome of a healthy person with the genome of a sick person and easily identify mutated nucleotides responsible for causing diseases. We called GWAS: Genome Wide Association Studies. It is not as simple as we thought. We found that while some people having the mutated nucleotide come down with the disease, others with the same mutation do not show any signs and symptoms. We have no idea if other genes are protecting them. In some cases, we found the presence of a single copy of the mutated gene responsible for causing the disease called dominant gene while in other cases both copies of the mutated genes, called the recessive genes, do not cause any disease. The only way to solve this problem is to have as many genomes sequenced as possible and compare them using computers to identify the mutated nucleotides responsible for causing the disease with precision and accuracy. To pinpoint a specific gene responsible for causing a disease, we need to compare the genome of a healthy person with the genomes of hundreds and thousands of genomes of sick persons. The cost of sequencing is high, but the next generation of sequencers (Nanopore sequencer) could bring the cost of sequencing down to $100 per genome, it would be less expensive to sequence the egg and sperm to identify specific inheritable diseases in the family. To develop the next generation of DNA sequencers, my institute, NIH, provided enormous funds to Dr. Leroy Hood and his group. They accomplished miracle. The next generation of DNA sequencers uses Nanopore technology that electrically pushes DNA fragments through tiny pores of proteins to read their content with the fastest speed. The faster we read the genome; the cheaper sequencing becomes. Presently, we

could sequence the entire genome in one day at a cost of $700. Further improvement could bring the cost down to $100 per genome.

Many nations are providing large sum of money to sequence as many genomes of their population as possible. For example, United Kingdom launched a 1000-Genome Project. My own institute, NIH, in America launched a ten-years project at a cost of one and a half billion dollars to sequence a million genomes. The Chinese government is launching the most ambitious project; they committed $9 billion to sequence millions of genomes. Eventually, we will have to sequence the genome of every man, woman and child on Earth and use this data as a part of the medical record. Now, we have digitized the entire Human Genome that is we converted the analog language of biology that is from A-T to G-C nucleotides bases to digital language of computer that is Zero and One. Once the genome is digitized, it could be uploaded on the internet and could be moved around the world with the speed of light. Once the genomes move to the distant part of the world with the speed of light, the recipient countries will have convertors to convert back from the digital language of computers to analog language of biology. The great advantage of this conversions is that if a new deadly virus appears in one part of the world, its genome would be sequenced and sent to distant labs with the speed of light. For example, the recently identified Black Fungus in India could be sequenced and send it to Labs around the world. Identifying lethal genes on its chromosome, we could prepare its vaccine which would be readily prepared on large scale and within days it could be made available to everyone around the world.

Replication is a rapid process. It also occurs in germ cells. Mistakes also occur in genetic cells like eggs and sperms during replication. In his lifetime, a man produces enough sperms to populate the entire world. Most sperms are damaged and broken and unacceptable for breeding purposes. A sperm carries a single string of 59 million AT-GC nucleotides base pairs which carry 355 genes. On the other hand, a woman produces a single mature egg each month. The egg carries 164 million AT-GC nucleotides and 1,144 genes. Of course, T (Thiamine: the more fat-soluble methyl group in DNA is replaced by a water-soluble Hydroxyl group in RNA) in DNA, T is replaced by U (Uracil) in RNA. Because a Woman produces one matured egg per month, she has a right to make her own reproductive decision. The choice to reproduce or not to reproduce; with whom to reproduce; and how many times to reproduce. In a pregnant mother so many genes are turned on to provide growth hormones and nourishment to the fetus. Once the baby is born, those genes are not turned off immediately. Her body faces havoc produced by hormones. Soon after the baby is born, she is euphoric due to the production of a high level of Oxytocin, a kind of opioid. Once Oxytocin is depleted, she undergoes severe depression. She sees herself fat, ugly, sick and no good. This is the worst time of her life. Some women suffer quietly, others behave violently.

We can detect all mutant genes in a genome by looking over and comparing the sequences of thousands of defective and normal egg and sperm genomes. One copy of 12 faulty genes is carried by each of us. If we marry someone who has the other mutant copy of the same gene and they are closely connected to us, the foetus will be affected because we are carriers of one copy of the faulty gene. They are most likely to have children who inherit both recessive copies of the same gene: related couples in which both parents are carriers of the same mutant gene. Such a couple is most likely to produce a child who develops terrible hereditary problems, and they are most likely to abort the pregnancy. Although it is a painful decision, it

is better than watching their children suffer and die of a terrible disease. If the fetus carries both bad copies, it will be severely sick. Let me explain with an example how this work will help parents to decide to have a baby even before conception or during pregnancy. A newlywed couple might use test tubes or their bedroom to conceive a child. Invitro fertilisation is advised if there is a family history of a disease. Before conception, the couple provides a sample of eggs and sperms for genetic testing. Detection kits for several hundred genes are already being developed. The test result may show that the sperm is carrying a genetic defect on Y-chromosome that will make the baby a color blind or give him MS (muscular dystrophy). Doctors will inform the parents whether the child will be incurably blind, or carry a gene for defected heart, kidney, or liver. During the ancient times when Eugenic was at its peak, the authority makes the decision about the fate of the fetus. These days, Parents make the decision whether to bring this child into this world. How many parents will love to have a blind or permanently sick child in their families? Not many. We must run the census among our people to get the results. It seems reasonable to assume that most parents will not be able to care for that fetus. We may not be able to correct that defects tomorrow, but day after tomorrow may be or in some distant future. We will be able to fix that flaw at a significant cost. Is there any justification for those impoverished parents to keep that foetus alive and allow it to develop to term at great medical expense? I have no doubt that some wealthy parents will do everything to have children. Such wealthy families' children won't be a burden on society or our healthcare system. Since completing the Human Genome Project, out of six thousand mutated genes, we have already developed over 1,500 tests to identify mutated genes, we can provide invitro fertilization (IVF) of fertilized egg free from all genetic defects. Couples will be able to choose the very healthy eggs and sperm, fertilise them in a test tube, and implant them in the mothers instead of having children in the bedroom. By doing this, we can ensure that the children we choose to have are of the highest calibre. Invitro fertilisation could be used to maintain the population's quality. A total of 25,000 Mendelian disorders (single gene abnormalities) have been found, and a total of 10,000 diseases have been linked to particular genes. Developing novel drugs to treat those diseases is expensive and time consuming.

Different over-populated countries are practicing different methods to stabilize the world population. Let us see if we want to adapt any of those methods. I doubt it if you would accept them, but I will explain to you anyway. On one extreme, we have China where government controls population (now they permit three children per couple) and on the other extreme is India where nobody does anything to stabilize the over population. You can have as many children in India as you want whether you could afford them or not. Most of the people live in thousands of cities across the nation. How many villagers understand the difference between "Family Planning" and "Population Control?" China practices population control. Now, they have relaxed the rule. For almost a decade and a half, the Chinese government has mandated the insertion of Intra-Uterine Devices (IUD) for all those mothers who have one child. Mothers are forced to undergo sterilization after two children. The third child is aborted without the consent of mothers. (now they permit a third child). China has the largest population in the world. India is number two and most likely to be number one soon. China does not have a democratic system of government. A handful of strong men rules the country. They have adapted an undemocratic system to control over population. In Western countries China's policy on newborn is considered Eugenic and repugnant and for that reason most Western countries refused to send their delegates to attend a conference on population control in China over the years.

In South America, Mexico follows Chinese policy. Mexican women will receive an IUD without their consent or knowledge after the third child. In Peru, a mother gets a fifty-pound free food if she agrees to Tubal Ligation which could be removed later if a mother decides to have children. The government is also putting heat on doctors. If they want to practice medicine in Peru, each doctor must provide Tubal Ligation to six women per month or loose privilege to practice medicine. If sequencing confirms an abnormal fetus, RU486, is one of the cheapest and safest agent to terminate a pregnancy. Once the diagnostic tests confirm the location of mutated genes for either monogenic or poly genic diseases such as cancers, cardiac diseases, or Alzheimer; we could design drugs to shut off those genes. The greatest challenge is either to replace a mutated gene by gene therapy or to shut off genes by drug therapy. On April 3, 2003, several teams simultaneously sequenced the entire human genome, confirming that only 2% of it encodes for proteins. The remaining 92% of the genome is made up of non-coding regions that contain switches to turn genes on and off as well as DNA fragments that act as promoters and enhancers of genes. Using restriction enzymes, we can cut, paste, and copy genetic letters in the non-coding region which could serve as markers, but a slight change in the coding region of the genome called mutations could make a normal cell abnormal or cancerous.

Our search for unknown diseases has come to a closure

The two biggest consequences of the human genome sequencing are as follows. One of them is that we've reached a conclusion. It means that since we have a list of every gene found in the human genome, we can search the entire genome for the specific gene we're looking for. We won't longer be lost in the wilderness. These genes' nucleotide sequences contain all the information known to exist concerning the health and characteristics of humans. Our Genomes provides the catalog of all genes. The second implication is that we can scan the entire genome against the suspect region of the genome to identify the mutation responsible for causing the disease. Using the recently completed 1000-genome project, we can scan the suspect region a thousand time to identify the disease-causing nucleotide with precision and accuracy. Once the nucleotide is identified, it will point to the codon which codes for the wrong amino acid. The mutated codon will point to the gene which codes for wrong protein responsible for causing the disease. The next step is to shut off that gene either by gene therapy or drug therapy.

Gene Therapy

The first step is to cut the human genome with specific enzymes (prepare a El Salvador Luria, Max Delbruck, and Hamilton Smith were the first to use restriction enzymes (molecular scissors such as EcoR1) at the precise places. If the single gene (a piece of human DNA) is not safeguarded, an antibody will annihilate it. If not protected by recombinant technology (creating a hybrid), that is by recombining with the DNA of viruses, plasmids, or chloroplasts (for plants), naked genes are pieces of DNA with a start codon AUG and end at one of the three stop codons UAG, UGA, or UGG as Vectors. If not protected it will be destroyed by enzymes. Once the human DNA fragment is stabilised in the vectors by recombinant technology, one can store the fragments or genes there. We can then purify this fragment (genes) and make millions of copies (clones) of it by transferring it into host cells like bacteria, mammalian cells, or yeast cells. which autonomously replicates to produce library of genes. Each Library contains millions of copies of similar proteins are produced by same genes. Prior to the genetic revolution, insulin was collected from the pancreas of dead animals and used to treat chronic illnesses like diabetes; a minute

impurity might cause anaphylactic shock and kill the patients. Now, large scale highly pure human Insulin produced by Genetic Engineering firm named Genentech is used to treat 300 million diabetic patients worldwide without the loss of a single life. Other genomic medications are also being developed using recombinant technology, such as growth hormones and hormone proteins to treat haemophilia with factor VIII protein. Drugs are being developed in an effort to target cancer cells at their DNA, RNA, and protein levels. Herceptin is a new kind of medication that effectively combats protein. Double stranded RNA was created by Craig Milo to turn off genes and stop them from being translated into proteins. One of the greatest challenges in designing drugs is to attack the DNA to shut off a gene. It was successfully carried out by Ross using highly toxic Nitrogen Mustard.

Drug Therapy

Gene Therapy cannot be applied to treat diseases with multiple genetic defects such as cancers or heart diseases. Drug therapy may be employed to create new remedies.

Historical Background for Using Nitrogen Mustard for Treating Cancer

German Army officer Fitz Haber focused on creating chemicals as weapons of war. Making deadly nerve gases and nitrogen mustards was his responsibility. He received a Nobel Prize prior to World War I for using direct atmospheric nitrogen capture to create nitrate fertilisers. by burning the element Magnesium in the air forming its Nitride. Upon hydrolysis, Nitride is converted to its Nitrate. Using this method, we could make unlimited amount fertilizer. Nitrate is also used for making explosive. Haber was accused of committing a crime against humanity shortly after World War I for discharging thousands of cylinders of chlorine gas on the Western front, killing soldiers in the trenches. When Germany lost the war and Allied forces were looking for Haber. When they reached his residence, his son shot himself and his wife committed suicide. Haber went in hiding in Swiss Alps. After the War, German Government got his release as a part of the peace negotiations. Haber returned home to hero's welcome. Although he promised never to work on the chemical weapons again, secretly he continued to develop more lethal analogs of highly toxic chemicals like Nitrogen Mustards. It was Haber who first made the notorious Bis-dichloro-ethyl Methyl Amine. Because it smells like Mustard seeds, it is called as Nitrogen Mustard. During the next 20 years, before the beginning of the WWII, hundreds of more toxic analogs of Nitrogen Mustard were developed. The bad news is that they are highly toxic, and the good news is that they shut off genes.

Ross' Rationale for Using War Chemicals to Treat Cancers

Professor WCJ Ross of London University was the first person who used Nitrogen Mustard, a chemical weapon, to attack DNA for Cancer Treatment. Nitrogen mustard is able to turn off a gene by cross-linking the two strands of DNA that we receive from each of our parents, according to a radiolabeled study. It was the same Cross-linking agents such as Nitrogen mustard made by Haber. Solders exposed to Nitrogen Mustard showed a sharp decline of White Blood Cells (WBC) from 5000 cell/CC to 500/CC. WBC counts in children with childhood leukaemia are extremely high (above 90,000/CC). The majority of WBCs are immature, defective, and incapable of protecting the body against microbial diseases. Ross reasoned that since cancer cells divide more quickly than healthy cells, he could use nitrogen mustard to cross-link DNA and stop cell division. Once he showed that he could shut off a gene by cross-linking DNA, he was able to develop a dye that could precisely colour that tissue, which allowed him to shut off any faulty gene,

including the genes of all 220 tissues found in a human. To attack the cancer genes in any of those 220 tissues, he could link the Nitrogen Mustard group to the dye.

Ross was the first person to use war chemicals successfully to treat cancer. Although such drugs are highly toxic, more cancer cell will be destroyed than the normal cells. Over decades, As cross-linking agents, Ross created several hundred derivatives of nitrogen mustard. Some nitrogen mustards are effective in treating malignancies, such as chlorambucil, which was used to treat paediatric leukaemia and reduced the WBC count to 5,000/CC. and Melphalan and Myrophine for treating Pharyngeal Carcinomas. Nitrogen Mustard's extreme toxicity prevented the development of additional medications to treat other forms of oral or lung cancer [7-12].

When we sequenced our entire genome, we read our book of life, letter by letter word by word, sentence by sentence, chapter by chapter all forty-six volumes (chromosomes) 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 a comparative sequence. We spent $3 billion and 13 years sequencing the whole human genome using the Nano Capillary Sequencing technique. With the development of next-generation sequencers like Nanopore technology, the complete genome can now be sequenced more quickly and inexpensively. To determine the quantity and position of all mutations or damaged genes brought on by smoking, we can sequence the genome of a single cell from the lung or oral tumour of a smoker using a biopsy sample, and compare the results with the Reference sequence. Our 1000-genome project, which will provide thousands of copies of the same gene sequence for comparison, was also just finished. We also learned how to translate biology's analogue language into computer language. Now, we can write a program and design a computer to read and compare and send the data to any countryin the world at the speed of light. When comparing With the Reference Sequence and the smoker's gene sequence, it will precisely and accurately detect all the mutations. Once the mutations responsible for causing any cancer including Lung, or Oral Carcinoma are identified, we can design drugs to shut off those genes.

Nitrogen Mustard was mercilessly used as a weapon during the WWI by both German and Italian Armies against Allied forces. Most soldiers who were exposed to nitrogen mustard died from freezing. A White Blood Cell (WBC) study of their blood revealed a dramatic decrease. Professor Ross and his team at London University in England questioned if a minimal amount of nitrogen mustard could be used to treat leukaemia in cancer patients because patients with the blood cancer known as leukaemia showed a rapid increase in WBC. It was discovered to be accurate. Ross created hundreds more Nitrogen Mustard compounds throughout the course of the next 30 years to treat various malignancies. His most successful drugs are Chlorambucil, Melphalan and Myrophine [13]. The following 10 years, while I was his graduate student, I produced for Professor Ross dozens of analogues of nitrogen mustards. The Phenylenediamine Mustard was the deadliest of them all. We use these compounds to check the sensitivity of the Experimental Tumors in the Tumor Bank. If tumours in the tumour bank develop resistance, we must swap them out for new, more susceptible tumours to test different drugs.

Synthesis of Nitrogen Mustard as Anti-Cancer Drugs

As I said above, I had made several dozens of analogs of Nitrogen Mustards for Professor Ross. I'll explain how to create nitrogen mustard using Haber's simplest technique. Methylamine and ethylene oxide were combined by Haber to create 2-bis dihydroxy ethyl methyl amine. It was chlorinated by heating with Phosphorus Penta Chloride in the Phosphoric Acid. Congratulations, you have Nitrogen Mustard if you smelled a faint mustard seed aroma. You should cool the solution and dilute it with ice cold water before extracting the oil float in the aqueous solution using chloroform. The solution is dried, and Hydrogen chloride gas is passed through the solution to make its solid Hydrogen-Chloride salt. Nitrogen Mustard Hydrogen Chloride salt is separated. No matter how much precautions you take, after the completion of the experiment, if you would take an alcohol swab of working bench or walls, doors, knobs and run a mass spectra of the alcohol extract, you find a spectral line corresponding to Nitrogen Mustard. If you are exposed to Nitrogen Mustard and cross the threshold level, your WBC drops sharply and the energy providing Mitochondria die and you are most likely to freeze to death even during summer. Someone in the Defense department may make it, now-a-day. Safety committee will not approve this study in the University Research Lab. Your idea will be rejected by the safety committee and your institutional review board; who will pay for such a pricey study? The Chemotherapeutic Index (CI), a measure of toxicity based on the drug sensitivity of cancer cells compared to normal cells, was developed. The higher the ratio the more toxic the chemicals are to cancer cells. When tested against Walker Carcinoma 256 in Rats, most Nitrogen Mustards analogs cross-link both strands of DNA and give a CI of ten.

Aziridine Analogs as Anti-Cancer Pro-Drugs

According to a radiolabel study done to better understand the mechanism of action of nitrogen mustard, DNA cross-linking takes place in two stages. The first step is involved in the formation of a three-member aziridine intermediate which remains stable and inactive in the neutral media (acts as a pro-drug). The second arm of the Nitrogen Mustard generates a highly reactive carbonium ion by enzyme which attacks the first arm of the double stranded DNA. The second arm is attacked, as the cancer cells grow; they se Glucose as a source of energy. Glucose is broken down the Lactic Acid. In the presence of acid, the Aziridine ring become activated by generating the carbonium ion which attacks the second arm of the DNA resulting in the cross-linking. This study result showed that cross-linking both strands of DNA is not necessary to shut off a gene, only binding to a single strand of DNA by aziridine could also shut off a gene with half the toxicity. To attack a single strand of DNA, aziridine analog are separately synthesized. For my doctoral thesis, I was given a new route to follow. Instead of cross-linking DNA strands, I am to design drugs to attack only one strand of DNA. The following chart describes the formation of Aziridine ring intermediate (Figure 1).

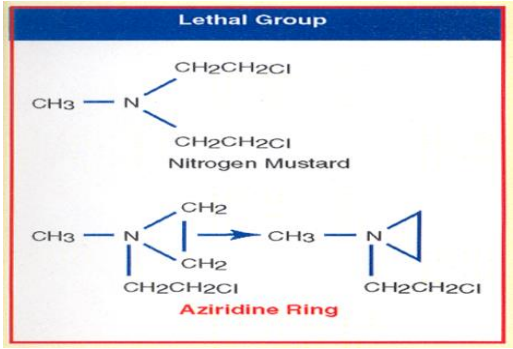


Figure 1: DNA Binding Aziridine Group.

This study showed that to attack a single strand of DNA, we must synthesize Aziridine in the Lab by using ethyl amino methyl sulphonate in sodium hydroxide. The distillate was pure aziridine. Two benefits over nitrogen mustard will result from the synthesis of aziridine analogues: First, Aziridine attaches to one strand of DNA instead of cross-linking, lowering the toxicity of the double stranded DNA. stranded Nitrogen Mustard by half. Second, it gives selectivity, the Aziridine ring serves as a prodrug. Its ring opens only in the acidic medium. Once the active component Once it was established that Aziridine attacked DNA, the issue of how to get the medicine to the tumour site arose (Figure 2).

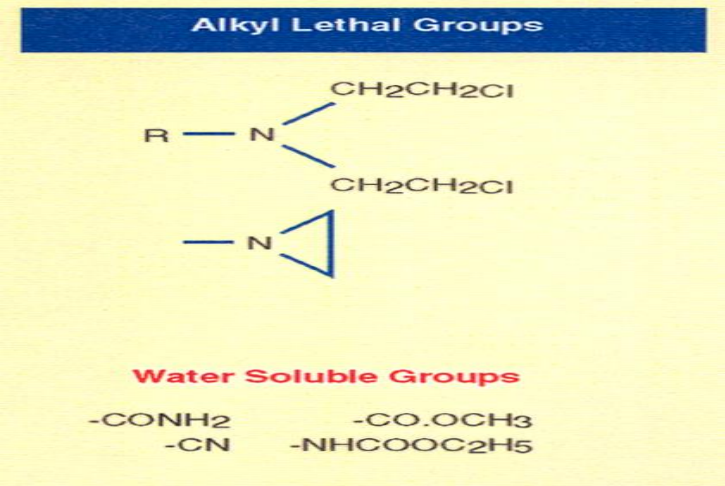


Figure 2: The above structures are Nitrogen Mustard (2-bischloroethyl methyl amine) and Aziridine. DNA Binding Lethal Groups.

Designing Drugs to Bind to a Single Stranded DNA to Treat Animal Cancers

I was given a new course to follow for my doctoral thesis. I will create medications that target just one strand of DNA by creating analogues of aziridine rather than using nitrogen mustard to cross-link both strands of DNA. In order to turn off a gene by binding to a single strand of DNA, we chose to use the Aziridine moiety (as an intermediate of Nitrogen Mustard). To deliver Aziridine to the target site which is the N-7 Guanine of DNA, we decided to use Dinitrophenyl (DNP) moiety as a drug delivery agent. DNP is a dye which colors the tissues of the experimental animal tumor such as Walker Carcinoma 256 in Rats. It is generally known that analogues of DNP, such as dinitrophenol, interfere with ATP's oxidative

phosphorylation, which gives our bodies the energy they need to function. The high energy phosphate link in ATP is broken down to ADP (adenosine diphosphate), which is then broken down to AMP (adenosine monophosphate) to power our physiological functions. Mono Phosphate), the enzyme Phosphokinase put the inorganic phosphate group back on the AMP giving back the ATP. This cyclic process of Oxidative Phosphorylation is prevented by Dinitrophenol. As a part of my doctoral thesis, I decided to use Dinitrophenol as drug delivery method for the active ingredient aziridine. The analog of DNP such as Aziridine Dinitrophenol could also serves as a dye which stains Walker Carcinoma 256, a solid and most aggressive tumor in Rat. The first compound I made by attaching the C-14 radiolabeled Aziridine to the DNP dye. Utilising dinitrochlorobenzene and C-14 radiolabeled aziridine in the presence of triethyl amine, which neutralises the hydrochloric acid produced during the reaction, dinitrophenyl aziridine was created. When the compound Dinitrophenyl Aziridine was tested against the implanted experimental animal tumor, the Walker Carcinoma 256 in Rats, it showed a TI (Therapeutic Index) of ten. The TI of ten was like most of the analogs of Nitrogen Mustard. Since this Aziridine analog was not superior to Nitrogen Mustard, it was dismissed as unimportant.

On further reexamination of the X-ray photographs of Dinitrophenyl Aziridine, it appeared that most of the radioactivity was concentrated at the injection site. Very little radioactivity was observed at the tumor site. It was obvious that we need to make derivatives of Dinitrophenyl Aziridine to move the drug from the injection site to the tumor site. Dinitrophenyl Aziridine does not dissolve in fat or water, making it ineffective as a medication delivery mechanism; nonetheless, a very small amount of radioactivity was discovered at the tumour site (Figure 3).

Figure 3: Dinitrophenyl Aziridine carrier of the Lethal Group.

Structure Activity Relationship

I immediately realized that by altering structure, I could enhance biological activity by making water and fat-soluble analogs of Dinitrophenyl Aziridine. By attaching water soluble groups, I should be able to move the drug from the injection site to the tumor site. To deliver 2,4-Dinitrophenylaziridine form the injection site to tumor site, I could alter the structure of 2,4-Dinitrophenylaziridine by introducing the most water-soluble group such as ethyl ester to the least water-soluble group such as Cyano- group or to introduce an intermediate fat/water soluble such as Amido group. An additional substituent in the Dinitrophenyl Aziridine could give three isomers, Ortho, Meta, and Para substituent. Here confirmational chemistry

plays an important role in drug delivery method. Ortho substituent always give inactive drug. Model building showed that because of the steric hinderance, Aziridine could not bind to DNA shutting off the genes. On the other hand, Meta and Para substituents offer no steric hindrance and drug could be delivered to DNA. When injected in Rat, because of the high solubility, most of the drugs was pass down through urine and extracted the drug from Rat urine by chloroform, The following chart showed that I synthesized all nine C-14 radiolabeled analogs of 2,4-Dinitrophenyl aziridines and tested them against implanted Walker Carcinoma 256 in Rats (Figure 4).

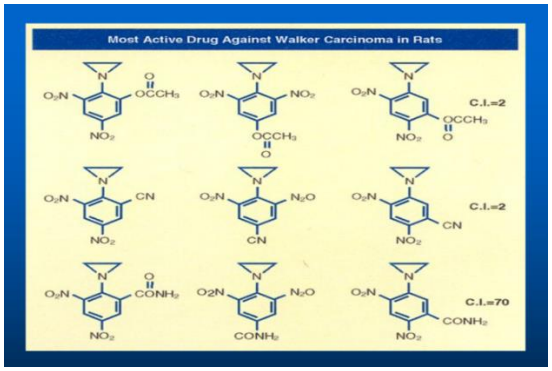


Figure 4: Derivatization of Dinitro phenyl Benzamide based on Partition Coefficient.

The most water-soluble substituent

The first three compounds on top line of the above chart carry all three isomer of the most water-soluble Ethyl Ester group attached to 2,4-Dinitropehny aziridine. The compound invivo is hydrolyzed Ethyl Ester to produce most water-soluble carboxylic group. Since it is the most water-soluble substituent, within 24 hours of injection in Rats, the entire radioactive compound was passed down from in the Rat urine and it can be extracted by Chloroform. It exhibited no biological action because the Ortho position was not available for DNA binding, while the third molecule, in which the Ortho position was free to attach to DNA, had some anti-tumor activity in rats.

The least water-soluble substituent

On the other hand, the majority of the compound remained at the injection site when the least water-soluble Cyano-group was linked to all three isomers of the chemical 2,4-Dinitrophenyl aziridine, as indicated in the second line of the above chart. Only the last Cyano-derivative attached to DNA showed some anti-tumor activity.

The moderately soluble Amido-substituent

The last line of the above chart showed that the first two Amido groups were sterically hindered and did not bind to DNA and shown little biological activity, yet the final substance offers the ideal drug delivery system. The entire drug was delivered from the injection site to the tumor site. The drug 1-Aziridine, 2,4-dinitro, 5-benzamide (CB1954) showed the highest anti-tumor activity. It has a CI of 70 and is the most toxic substance ever found against Walker Carcinoma 256 in rats, being seventy times more harmful to cancer cells [14-16]. As I said above, Nitrogen Mustards are highly toxic because they have neither specificity nor selectivity. They attack all dividing cells whether they are normal or abnormal. However,

the analogues of aziridines and carbamates operate as prodrugs and are inert in neutral and basic environments. They become activated only in the presence of acid produced by growing cancer cells. In an acidic environment, aziridine specifically targets the N-7 Guanine in DNA. Walker Tumour and the dye Dinitro benzamide have a strong affinity. The Aziridine Dinitro benzamide (CB1954) has the highest toxicity to Walker Tumor cells ever recorded. As the tumor grows, it uses Glucose as a source of energy. Glucose is broken down to Lactic Acid. The Aziridine ring is activated by the acid. The ring opens to generate a carbonium ion which attacks the most negatively charged N-7 Guanine of DNA (as shown below) shutting off the Walker Carcinoma gene in Rat. The conjugate structure below demonstrates how CB1954 attaches to a single strand of DNA to turn off the gene (Figure 5).

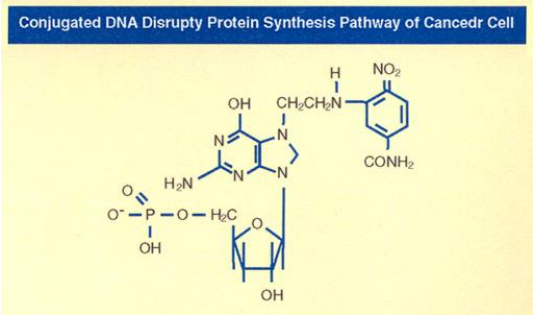


Figure 5: Conjugated DNA Disrupting Protein Synthesis Pathway of Cancer Cell.

For the discovery of CB1954, The University of London received a post-doctoral fellowship award from the Institute of Cancer Research (ICR) in recognition of the discovery of CB1954, which will be used to create additional CB1954 analogues. Over the years, I created more than a hundred more Dinitro phenyl aziridines analogues in an effort to enhance drug delivery methods. In my role as a postdoctoral researcher, I created an additional 20 analogues to raise the toxicity of CB1954 to Walker Carcinoma. When I attached one more Carbonium ion generating moiety, the Carbamate moiety to the Aziridine Dinitrobenzene, the compound Aziridine Dinitro benzamide Carbamate was so toxic that its Therapeutic Index could not be measured. We stop the work. Further work in London University was discontinued for safety reason (Figure 6).

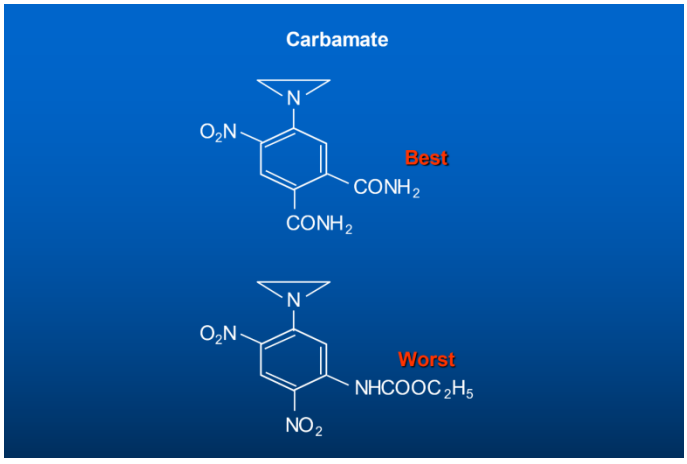


Figure 6: The Best and the Worst Dinitro phenyl Aziridine Analogs.

Although Aziridine Carbamate is extremely toxic, it is also very useful in testing the sensitivity of tumors in Tumor Bank. Over the years, some tumors in the tumor bank could become resistant. If a tumor culture survives in a petri dish by adding a solution of Aziridine Dinitrobenzene Carbamate, it means that this tumor has become resistant over the years and must be replaced by new sensitive tumor cells.

As a part of the inter-government agreement between UK and USA, all novel drugs developed in England were sent to the National Cancer Institute (NCI) in America for further screening. To translate animal work to human, I was invited to continue my work on the highly toxic Aziridine/Carbamate combination in America when I was offered the Fogarty International Fellowship Award to continue my work at the National Cancer Institute (NCI) of the National Institutes of Health (NIH), USA. I borrowed the strategy from London University for producing additional Aziridine/Carbamates, which involves hitting one strand of DNA with both Aziridine and Carbamate without employing the same dye, dinitro benzamide. My greatest challenge at NCI is to translate the animal work to humans.

We selectively poison bad DNA when creating medications for treatments. All poisons are a class of chemicals that attacks all DNA good and bad alike. At a safe dose, chemicals that cause cancer can also treat the disease. Science teaches us to target problematic DNA sets while avoiding hurting healthy DNA sets. 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 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.

Glioblastoma (GBM) is a primary type of brain cancer which originates in the brain, rather than traveling to the brain from other parts of the body, such as the lungs or breasts. GBM is also called glioblastoma multiforme which is the most common type of primary brain cancer in adult humans. Attaching Nitrogen Mustard group to a carrier dye will produce highly toxic compound which will have neither specificity nor selectivity. Such a compound will attack all dividing cells whether they are normal or abnormal. On the other hand, the analogs of Aziridines and Carbamates serves as prodrugs that is they remain inactive in the basic and neutral media. They become activated only in the presence of acid produced by cancer cells.

Designing drugs to treat Glioblastoma, the human brain cancers

One day, I heard an afternoon lecture at the NIH in which the speaker described that radio labeled Methylated Quinone crosses the Blood Brain Barrier (BBB) in mice. When injected in mice, the X-ray photograph showed that the entire radioactivity was concentrated in the Mice's brain within 24 hours. I immediately realized 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 novel drug delivery molecule

to cross BBB (Blood Brain Barrier) delivering Aziridine rings to attack Glioblastomas. By introducing an additional Carbamate moiety, I could increase its toxicity several folds. I planned to use this rationale to translate animal work to human by introducing multiple Aziridine and Carbamate moieties to the Quinone molecule to test against Glioblastomas in humans (Figure 7).

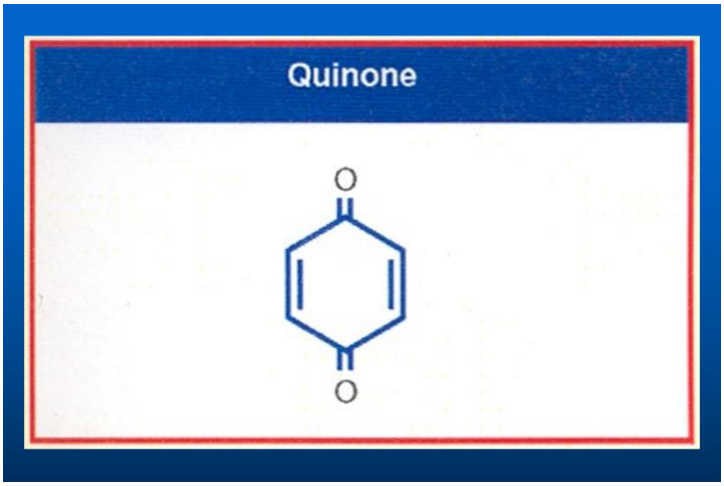


Figure 7: The Structure of a non-toxic and non-addictive Quinone used for crossing the Blood Brain Barrier (BBB).

With the Quinone ring, I could introduce two Aziridine rings and two Carbamate moieties and could create havoc for Glioblastoma. Within three years, I made 45 analogs of Quinone. One of the Quinone carries two aziridines and two carbamate moieties which was highly toxic to Glioblastoma. The tumor stops growing and started shrinking. I named the Di-aziridine Dicarbamate Quinone, AZQ. My major concern was how toxic this compound would be to the normal brain cells. Fortunately, brain cells do not divide, only cancer cells divide. AZQ acts as a Prodrug. A Prodrug is compound carrying a chemical by masking group that renders it inactive and nontoxic. Once the prodrug reaches a treatment site in the body, removing the mask frees the active drug to go only where it is needed, which helps avoid systemic side effects. Aziridine and Carbamate show selectivity. As I said above, to grow rapidly, cancer cells use Glucose as a source of energy. Glucose is broken down to produce Lactic acid. It is the acid which activates the prodrug aziridine and carbamate moieties generating Carbonium ions attacking Glioblastoma which stop growing and start shrinking.

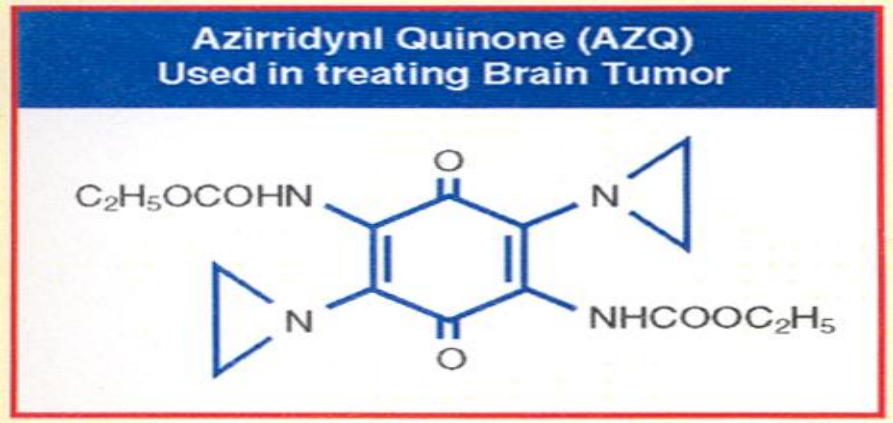
My drug AZQ is successful in treating experimental brain tumor because I rationally designed to attacks dividing DNA. Radio labeled studies showed that AZQ bind to the cancer cells DNA and destroy brain tumor and normal brain cells are not affected at all. AZQ is a new generation of drugs. Not so long ago, brain cancers mean death. Now, we have changed it from certain death tocertain 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 a random trial 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 [17,18].

DNA Binding Aziridines

I decided to use Quinone moiety as a carrier for Aziridine rings to attack Glioblastomas. By introducing an additional Carbamate moiety, I could increase its toxicity several folds. I planned to use this rational to translate animal work to human by introducing multiple Aziridine and Carbamate moieties to the Quinone to test against Glioblastomas in humans. Over the years, I made dozens of analogs of Aziridine Quinone. By attaching two Aziridines and two Carbamate moieties to Quinone, I synthesized the most useful compound, Diaziridine Dicarbamate Quinone, I named this novel compound AZQ. Over three-year period, I made 45 analogs of AZQ. They were all considered valuable enough to be patented by the US Government (US Patent 4,233,215). By treating brain cancer with AZQ, we observed that Glioblastoma tumor not only stops growing, but it also starts shrinking. I could take care of at least one form of deadliest old age cancers, Glioblastomas. Literature search showed that AZQ is extensively studied as a pure drug and in combination with other anti-cancer drugs (Figure 8).



U.S. Patent 4,146,622

Figure 8: Single Strand DNA Binding Aziridine and Carbamate.

As I said above, Glioblastomas, the brain cancers, is a solid and aggressive tumor and is caused by mutations on several sites in chromosomal DNA. Deleterious genetic mutations are the result of damaging to DNA nucleotides by exposure to radiations, chemical and environmental pollution, viral infections, or genetic inheritance. The other factors responsible for causing DNA mutations are due to the fast rate of replication of DNA. For example, the bacteria E-coli grows so rapidly that within 24 hours, a single cell on a petri dish containing nutrients forms an entire colony of millions when incubated on the Agar Gel. Mistakes occur in DNA during rapidly replication such as Insertion of a piece of DNA, Deletion, Inversion, Trans location, Multiple Copying, Homologous Recombination etc. When an additional piece of nucleotide is attached to a DNA string, it is called Insertion, or a piece of DNA is removed from the DNA

string; it is called Deletion or structural Inversion of DNA is also responsible for mutations. Since the gene in a DNA codes for Proteins, Insertion and Deletion on DNA have catastrophic effects on protein synthesis. With the Quinone ring as a carrier across BBB, I could introduce different combinations of Aziridine rings and Carbamate moieties to Quinine and could create havoc for Glioblastomas. My major concern was how toxic this compound would be to the human brain cells. Fortunately, brain cells do not divide, only cancer cells divide.

Attempting to find the site of mutations on Glioblastomas represent the greatest challenge. In Glioblastomas, three major changes occur on Chromosomes (C-7, C-9 & C-10) and two minor changes occur on Chromosomes (C-1 & C-19). These mutations are responsible for causing brain cancers in humans. Let us examine the effect on each chromosome. In a normal human cell, Chromosome-7 which is made of 171 million nucleotide base pairs, and it carries 1,378 genes. When Insertion occurs on Chromosome-7. Ninety-seven percent of Glioblastoma patients are affected by this mutation. On the other hand, a different mutation occurs on Chromosome-9 which is made of 145 million nucleotide base pairs, and it carries 1,076 genes. A major Deletion of a piece of DNA occurs on Chromosome-9 which results in eighty- three percent patients who are affected by this mutation. A minor Deletion of DNA also occurs on Chromosome-10 which is made of 144 million base pairs, and it carries 923 genes. Although it is a minor deletion of a piece of DNA and yet it contributes to ninety-one percent patients with Glioblastoma. To a lesser extent, small mutation occurs on Chromosome-1 (the largest Chromosome in our Genome). It is made of 263 million nucleotide base pairs and carries 2,610 genes) and Chromosome-19 (it is made of 67 million base pairs and carries 1,592 genes) is also implicated in some forms of Glioblastomas.

All known Glioblastomas causing genes are located on five different chromosomes and carries a total of 9,579 genes. It appears impossible to design drugs to treat Glioblastomas since we do not know which nucleotide on which gene and on which chromosome is responsible for causing the disease. It becomes possible by using C-14 radiolabeled Aziridines, we can confirm the binding site of a nucleotide on a specific gene and on a specific chromosome. By comparing with the mega sequencing genome project, we can further confirm the sites of mutations. With the completion of 1,000 Human Genome Project, it becomes easier. By simply comparing the patient's genome with the sequencing of 1000-genomes, letter by letter, word by word and sentence by sentence, we could identify the differences called the variants with precision and accuracy, the exact variants, or mutations responsible for causing the disease. Once the diagnosis is confirmed, the next step is how to treat the disease. As I explained above, by making CB 1954 to treat solid Walker Carcinoma in Rats, I established the structure activity relationship, and by making AZQ to treat human Glioblastoma, we have demonstrated that all bad genes can be shut off using Aziridine or Carbamate or both as attacking agents to shut off a gene. If you plan to develop drugs to treat other cancers, all we need to do is to identify carriers such as coloring dyes which stains a specific tumor. By attaching Aziridines and Carbamate moiety to carriers to the dyes, we could attack other tumors.

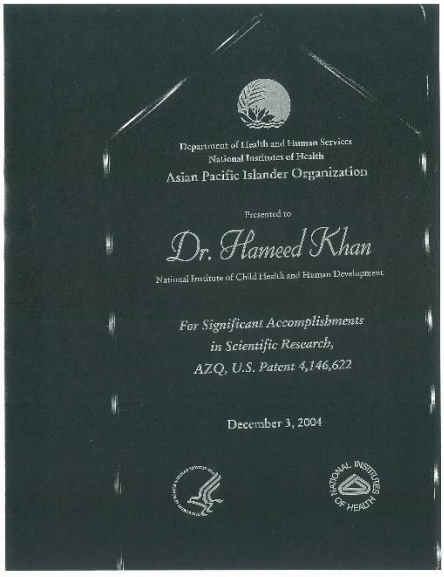
One of the greatest challenges of nanotechnology is to seek out the very first abnormal cell in the presence of billions of normal cells of our brain and shut off the genes before it spread. I worked on this assignment for about a quarter of a century; conducted over 500 experiments which resulted in 200 novel drugs. They

were all tested against experimental animal tumors. Forty-five of them were considered valuable enough to be patented by the US Government (US Patent 4, 146, 622 & 4,233,215). One of them is AZQ which not only stops the growth of Glioblastoma, but also the tumor starts shrinking. For the discovery of AZQ, I was honored with, "The 2004 NIH Scientific Achievement Award." One of America's highest Award in Medicine. I was also honored with the India's National Medal of Honor, "Vidya Ratna" a Gold Medal. (see Exhibits 1,2,3,4)

Exhibit # 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.

Dr. Khan is the Discoverer of AZQ (US Patent 4,146,622 & 4,233,215), 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.



NIH Scientific Achievement Award

Exhibit # 2

His Excellency, Dr. A.P.J. Abdul Kalam, The President of India Greeting Dr. A. Hameed Khan as shown in below image.

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

The Royals of Travancore

Dr. Hameed Khan of NIH was invited to give the "Maharaja Thrumal Memorial Award Lecture" "On the Impact of Genetic Revolution on our lives during 21st Century and Beyond" at the University of Trevandrum. After the lecture, His Royal Highness Sree Padmanabha Dasa Marthanda Varma (the brother-in-law) of Her Royal Highness Maharani Travancore (on his left) invited Dr. Hameed Khan and Mrs. Vijayalakshmi Khan for the Tea at the Pattom Palace at Thiruvanthapuram on May 12, 1999. Standing on Dr. Khan's right is the Son-in-law of Her Royal Highness, the Maharani.

Exhibit # 4

Gold Medal for Dr. Khan

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 Bran Cancer. While Genome Center was supporting sequencing and mapping of the Genomes, my Institute NICHD was supporting research on Gene Markers associated with diseases. Over a quarter of the century of work, I was able to accomplish all the goals of NIH that is to conduct research, support research and report research. I describe below all three missions of NIH.

NIH Mission # 1

In the Lab, using Quinone ring to transport across BBB, I introduced different combinations of highly toxic Aziridine rings and Carbamate moieties and created havoc for Glioblastomas. My major concern was how toxic this compounds would beto the normal brain cells. Fortunately, brain cells do not divide and do not grow only cancer cells divide and grow. AS I said above, Radiolabeled studies showed that AZQ has the ability to cross organ after organ, cross the Blood Brain Barrier, cross the nuclear membrane and attack the nuclearDNA shutting off the cancerous gene. X-ray studies showed that the radioactivity is concentrated in the tumor region. Glioblastoma stop growing and start shrinking for this discovery, I was honored with the above scientific achievement award.

NIH Mission # 2

NIH Speaker Bureau informed me that when you teach the students, you touch the future. It is the responsibility of the scientists to train a new generation of scientists. I was told that of all teaching organizations, one organization, Envision, stands out. Envision is an outstanding organization that trains and provides future leaders of the world. Envision performs a Herculean task by selecting thousands of best and brightest students from around the country and from all over the world and bring them to Washington DC to train them to become the future leaders of the world.

From: NYLF/Med Washington
[MedWashingtonCA@envisionemi.com]
Sent: Monday, July 09, 2007 7:29 PM
To: Khan, Hameed (NIH/NICHD) [E]
Subject: NYLF - Feedback
Dr. Khan,

You were the most popular speaker at our seminars! Congratulations! The students absolutely loved you, and your average score was a 5 out of 5. Here are some of their comments:

□ I loved his discussion, he was so knowledgeable about his field and I found it very interesting.□

□ It was so interesting and really well presented. Definitely bring him back!□

□ This speaker provided great insight into the behind the scenes work on the Human Genome Project.□

Thank you so much! I look forward to seeing you next forum!

Zaree Gliddon
Conference Assistant
National Youth Leadership Forum on Medicine
Washington, D.C.
Phone/Fax 703-584-9238
MedWashington@nylf.org

Over the years, Dr. Khan has given over one hundred speeches nationally and internationally. He is a discoverer of AZQ (US Patent 4,146,622), a Novel Drug specifically designed to silence a Gene that Causes Brain Cancer. The Main Topic of his Speech is, "The Impact of the Human Genome Project on Our Lives During The 21st Century and Beyond." His Aim is to encourage Young Scientists and Investigators to use the same rationale as was developed for AZQ to design drugs to silence all other Oncogenes that cause cancers. He is a Fellow of the American Institute of Chemistry and was elected to the American Science Advisory Board.

NIH Mission # 3

Of all the challenges of NIH Missions, supporting research presents the greatest challenge. I was accidentally involved in supporting research. I was invited to speak at an International Conference in Europe. I was shocked when I saw the program. Someone is presenting a paper for treating Breast Cancer with my drug AZQ. My rationale for designing AZQ was that Quinone cross the Blood Brain Barrier and take the Aziridine in the vicinity of Glioblastoma. As the tumor grows, it uses Glucose as a source of energy. The Glucose is broken down to produce Pyruvic Acid. The acid activates the Aziridine which is broken down to generate a Carbonium which attack Glioblastoma stopping the tumor growth. I was curious to know the rationale for using AZQ to treat Breast Cancer. The speaker informed the audience that AZQ has no effect against Breast tumor. At the end of the presentation, I asked the speaker for the rationale for using AZQ. The shocking answer was that AZQ is extensively- studied on different cancers so this group tried to study the Breast Cancer because funds were available. Upon my return to NIH, I told my colleagues what a waste of precious resources.

One of my colleagues was promoted to become the Director of the Division of Scientific Review. He asked me to join him in controlling the Research Funds and help the new investigators by reviewing their Research Proposals. NIH annual budget is $50 billion. About twelve percent of the budget is spent in house (called the Intramural Program). The remaining eighty-eight percent money is given out as extramural Program nationally and internationally as Research grants, Research contracts and Research co-operative Agreements. He gave me a couple of research proposal to review. As I read the research proposal, I immediately pulled out strengths, the weakness in the proposal I checked the Principal Investigator (PI) qualifications, experience, his publications, his support staff, research environment availability of instruments, the budget. I like to help the PI and accepted the challenge and joined his group. I was given incredible freedom to set up committees to invite the best and the brightest scientists from any part of the country to serve as the reviewers to serve as the expert on panels. NIH treat these experts with utmost

courtesy, utmost respect and accommodate them in the best hotels, paid all their expenses with honorarium. Reviewing Research Proposals in the beginning was a passion for me, then it became obsession.

During the following twenty years, I had set up more than 250 Expert Panels Committees called the Study Sections, reviewing thousands of research proposals, inviting hundreds of scientists. Anyone interested in finding these committees can either find in the Federal Registered Notices appear in Google or the entire list of all committees in my above Facebook website. The Director of NICHD honored me with the NIH Supporting Research Award.

2006 NIH Merit Award for Supporting Research Presented to Dr. Hameed Khan By Dr. Duane Alexander, MD Director, NICHD Dr. Robert Stretch, Director DSR and Dr. Yvonne Maddox, Deputy Director, NICHD. In recognition of his superior commitment, dedication and accomplishment in the planning and executing of over 250 Peer Review Meetings for both Grants and Contracts. Dr. Khan was honored during the Director's Award Ceremony held on October 11, 2006.

Mission of NIH consists of the following three goals:
To
Conduct Research, Report Research and Support Research

2004 NIH Scientific Achievement Award presented to Dr. Hameed Khan By Dr. Elias Zerhouni, Director of NIH

2000 NIH/Speaker Bureau's Award presented to Dr. Hameed Khan during Ceremony held on June 12, 2000, in Wilson Hall, at the National Institutes of Health (NIH), Bethesda, MD, USA.

In recognition of his superior commitment, dedication and accomplishment in the planning and executing of over 250 Peer Review Meetings for both Grants and Contracts. Dr. Khan was honored during the Director's Award Ceremony held on October 11, 2006.

Dr. Khan Achieved all Three Goals

Today, Dr. Hameed Khan servers as a
Senior Scientist
National Center of Medical Rehabilitation Research (NCMRR)
National Institutes of Health (NIH)
11965 Old Columbia Pike
Silver Spring, Maryland 20904, USA
E-mail = Hameedkhan111@comcast.Net

What Should we explore next?

The next generation of scientists, my students,will face the great challenge to design novel drugs to treat breast cancer the largest killer of women. In the early history for developing drugs for treatments of cancers, we poison bad DNA selectively. All poisons are a class of chemicals that attacks DNA molecules good and bad alike. At a safe dose, chemicals that cause cancer can also treat the disease. Science teaches us to target problematic DNA sets while avoiding hurting healthy DNA sets. Living things are injured by poisons. They are known as carcinogens or cancer-causing substances because they alter human DNA activity and alter normal cells when they are exposed to them.

In the absence of any rational drug, 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. After all the current treatments, the remaining cancer cells return within three years as metastatic cells and kill breast cancer patients. A decade from now, these methods could be considered as brutal and savage, but today that is all we have. Based on rational design, we hope to develop new treatment for Breast Cancer. Hopes means never ever to give up. To design drug rationally to treat Breast Cancer, and to shut off a gene of a specific cancer by using Aziridine or Carbamate, we need a carrier for these groups. For example, to treat Breast and Prostate cancers in humans, may I suggest that we try using hormones which could serve as carriers for Aziridine and Carbamate moiety. Could I use the same rationale for treating Breast tumor as I used for making AZQ for treating Brain cancer? Although the BRCA1 gene on Chromosome-17, which contains 1,394 genes and 92 million nucleotide base pairs, was discovered years ago, we still don't understand why breast cancer treatments have been so challenging. By the time a patient's diagnosis of breast cancer is confirmed, the BRCA1 gene has amassed more than 3,000 mutations. Genotyping of the blood would also show that composition of many cells carrying mutated cell for creating secondary depositsAdditionally, it is thought that by the time breast cancer is diagnosed, metastatic cancer cells have travelled from the liver to the lung and are headed towards the brain. Since all other organs including breast could be removed and replaced by breast implant except brain, I thought that protecting brain is utmost important treatment. I may concentrate on the Breast once AZQ (US Patent 4,233,215) is created to safeguard the brain. and Prostate Cancers.

Radiolabeled studies showed that male hormone Testosterone has great affinity for female Breast, Ovary, and Fallopian tube cells. On the other hand, the male prostate gland has a strong affinity for the female hormone oestrogen. By using male and female hormones as carriers, I could attach multiple Aziridine rings and Carbamate ions to both Hormones to attack the Breast and the Prostate cancer. Over 200,000 nucleotide base pairs of the BRCA1 gene have been trapped in a breast tumour between the start and stop codon. There are roughly 3,000 mutations in the BRCA1 gene. These mutations are caused by radiations, chemical or environmental pollutants, viral infection, or genetic inheritance. I could bind several radio-labeled aziridine and carbamate ions to the male hormone testosterone in order to assault the altered nucleotides among the three thousand cells in the BRCA1 gene. BRCA1 mutations. By using MRI [19], I could show how many radio-labeled nucleotides were bound to which mutations. Out of seventeen positions on Testosterone, only three positions that is 1,3 and 17 are available for substitution on Testosterone ring system (Figure 9).

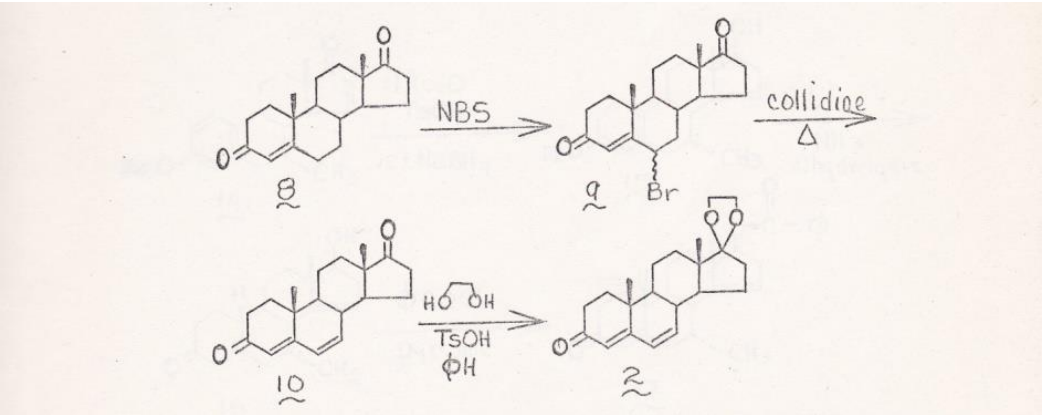


Figure 9

Carl Djerassi (C. Djerassi et al. J. Amer. Chem. Soc. 72. 4534 (1950) had demonstrated that we could activate additional positions for substitutions on hormone ring system such as the position 9 and 10 by reacting with Bromo-acetamide which introduce a Bromo ion on position 10 which could be de-brominated by Collidine to introduce a 9,10 double bond which we could further brominate to produce 9,10 dibromo compoundAziridines or carbamate ions may be added to replace these bromo ions. To achieve the most effect, we might raise or reduce the number of Aziridine and Carbamate ions by further brominating positions like 15 and 16 to add more Aziridine and Carbamate. moieties.

Similarly, we could use the female hormone Estrogen and by attaching multiple Aziridine and Carbamate ions to attack Prostate tumor in Men. Since only three of the seventeen locations on the oestrogen ring are open, we could use Djerassi's approach to change the amount of azoridine and carbamate ions to produce the best results, just as we did with testosterone. By exploiting a patient's genetic makeup to create medications to treat breast and prostate cancers, the aforementioned techniques are unique approaches to the treatment of metastatic tumours. The next generation scientists, my students, [20-44] will have the opportunity to translate this dream into reality.

Genome Sequencing Confirms Darwinian Evolution

Had Darwin live today, he would have been truly proud of our accomplishments to prove his theory. Within 150 years of his theory of evolution by natural selection, we proved this theory (guesswork) to be a scientific fact. We proved by sequencing the of hundreds of species from the simplest to the most complex including humans. On April 3, 2003, Dr. Francis Collins, the Director of my Institutes, The National Institutes of Health (NIH) announced that we have re-read the book in which God created life.

After spending $3 billion on the Human Genome Project, if you would ask me what the single most important discovery iswe made. My answer would be that sequencing the entire book of our life itself is one of the greatest achievements of our time. We are the only species who had not only read his own book of life, but also, we read the book of life hundreds of other species on Earth. Sequencing confirms the evolution of life from the simplest to the more complex life forms. Comparative sequencing of many species will keep our scientists busy for another century trying to find out what piece of human genome

came from what species over three and a half billion years of biological evolution. Of dozens of discoveries, we made since the completion of the Human Genome, one stands out. We made an astonishing discovery about our own origin. Now, we can answer the questions, we, both science and religions, have been asking ourselves since the dawn of human civilization. Who are we? Where have we all come from? What was it that made us this way? Now, we can answer these questions with certainty that we are the result of three and a half billion years of Darwinian Evolution. We are the extension of the same single DNA molecule that was form on Earth about four billion years ago. Darwin's extraordinary prediction was confirmed by sequencing genomes or reading the book of lives of over a thousand species evolved on Earth. Of all the experiments in Biology, the Sequencing of Human Genome was the greatest accomplishment of all times. Sequencing human genome identifies the number and the order of nucleotides which are arranged in our book of life. We found that less than two percent of our genome contains regulatory region, a piece of DNA, which controls the function of genes. More than 300 regulatory regions have been identified. More than ninety eight percent of our Genome contains non-coding region used to be called Junk DNA which makes up to sixty percent of our entire Genome. The non-coding regions contains repetitive piece of DNA which is tightly packed and mostly remain silent. The sequencing of this region showed that the non-coding region is the part of Viruses and Bacteria picked up by our Genome during the millions of years of our evolutionary process. During Bacterial or Viral infection, the non-coding DNA could unfold transcribing into RNA resulting into hazardous protein which could create havoc for our health. Once the mutated genes are identified, we can design drugs to shut off those genes.

Over thousands of years, we traveled a long distance from the Stone Age to Information Age. The ancient idea that reading and writing the book of life or sequencing human genome is in the domain of God that belongs to God alone is simply unacceptable. God loves scientists, He revealed the secrets of life to us not revealed to anyone before us. The Sequencing of Human Genome has enlightened us in ways; we have never been enlightened before. Now we know the answers to questions like who are we? Where have we all come from? What was it that made us this way. It was Darwin's theory of evolution and natural selection that gave our ancestors human intelligence and human conscientiousness. They had little knowledge and understanding of survival when they came out of Africa about three million years ago, and within seven thousand generations, they walked around the world and settled down on all seven continents. They not only, circumnavigated the world; they climbed the tallest mountain and gone the bottom of the deepest ocean; they split the heart of atom and walked on the surface of the Moon and came home safely. We are ready to take Darwinian evolution across the Universe. Our next step in the search for life in the cosmos is our dream to create settlements on the surface of Mars and send unmanned spacecrafts in search of habitable planets in distant star systems.

Darwin's evolutionary ideas taught us that the future can be greater than the past. Fifty-five years ago, we touched greatness when we walked on the surface of the Moon and came home safely and that was a turning point in history. There was a time when we soar to the Moon now, we must dream again to soar to the Mars. If we do not destroy ourselves by going to Nuclear War, as threatens by one superpower, within a million year, we will have human settlements on distant star systems and we could spread human intelligence in every corner of the Universe. This the message for the future generation of humans. For

the present generation, the most important lesson is that we are the extension of the same DNA molecule that was formed three and a half billion years ago. Life must have started in some little worm pond as suggested by Darwin. Through the same DNA molecule, all living creatures relate to each other including humans. Recent mitochondrial DNA sequencing pointed to our origin to a single chimp/woman who was born in Hader Valley in Ethiopia about three million years ago called Lucy. Over the years, the dark, uninformed, and ignorant minds have divided us based on race, religions, or the place of origin. The enlightened mind must unite us all as a single people. Science presents the undeniable truth that you and I are brothers and sisters, children of the same mother Lucy, a Black woman who was born in Africa about three and a half million years ago. Today, our number has increased to eight billion. We are adding a hundred million new mouths to feed each year. Are we the last generation to survive on Earth?

America is one of the most democratic countries in the world. Also, being the richest country in the world, America provides the best information to her people to decide when and if parents would like to have children. Only 3 to 4 percent work force is unemployed in America, the lowest in the world. Both parents go to work. They hire babysitters to take care of their children. None of the parents has time to take care of their children. Some parents delay having babies until their carriers are well-established. When women have children at later age, they tend to accumulate genetic defects. They want to make sure before conception if it would be a healthy baby. Nowadays, the young couples are saving their fertilized eggs in frozen state in Cryo-Preservation Banks at an early age to be used when they become well-established. If parents ignore to check the sequence of egg and sperm, they must make that awful decision when to abort a defected fetus. Parents in the Western world are wondering if we should have an acceptability test for all newborn children. To see if their children are born healthy and that they are acceptable members of human society. Most people in the West believe that we have a moral obligation to take care of all those children who are already here whether they are healthy or not. They have right to be taken care of. But we are talking about children who are not here yet. What rights do they have?

The completion of the Human Genome Project helps us follow the selective genetic breeding by invitro fertilization by discarding defected eggs and sperms. Some conservative members of our society will not accept the new discoveries. The question they must ask is should we add physically handicapped or mentally retarded children to our future gene pool? Or should we develop a series of medical tests on the fetus to eliminate unacceptable members to our society? How could we accomplish this goal? There are various biomarker tests (very expensive), we could conduct on the unborn fetus, such as examining the functioning of brain, nervous system, lungs damage, incurable blindness, kidney defect and malfunction of liver. Shouldn't we check before birth if the heart and blood pressure is functioning properly? All those children who fail these tests, will place severe burden on our medical and financial resources. Should we allow the nature to take its course and let them die or should we bring them into this world by providing medical intervention and prolong their life, even though they will not live a quality life? Do you know that some handicapped children in America are suing their parents for bringing them into this world where they become burden on society? Simple economy works here. The cost of medical treatment is unaffordable. May be some handicapped children will have to sue their parents in our country that will teach their parents a lesson

Conclusion

Darwin's Evolution by Natural Selection taches us that individual who are fit to survive in the existing environment will thrive and whose who are not fit will die. Modern science could bring those unfit children to this world at a very high cost financially and emotionally. We have moral responsibility to take of all those children who are already here. They have a right to be taken care of. What about those children who are not here? Do they have the same rights? Genetic sequencing of egg and sperm by Nanopore Sequencer will identify the genetic defects in an embryo, cheaper, faster with high precision and accuracy. In future, conception by invivo fertilization will be the order of the day.The important point I want to convey to my students and readers is thatWe need new ethical principles based on modern science. This is the main thrust of my arguments. The old ethical principles also came from people's head, but they were based on the information available to our elders hundreds of years ago. Most ethical principles we used today were developed by Socrates about 2,500 years ago and everything that is written in philosophy since then is a footnote to his work. Although we have made a little progress in philosophy, we have made tremendous progress in Darwinian Evolution and in understanding genomic science. We are developing genomic medicine to keep people alive past one hundred years. Based on the genetic make-up, we are developing novel drugs to treat old age diseases such as Alzheimer, Cardiovascular diseases, and Cancers.What should we do, for example, to Mongolian babies (Down Syndrome who carries an additional chromosome-21) who do not survive past thirty years? Should we set up committees to draw guidelines for medical professionals so that they will make a rational judgment to determine if child A will receive the precious treatment and will live and child B will not receive the treatment and therefore will die. One person cannot provide answers to these ethical questions. What I want to do is to raise these questions in your mind. My aim will be fulfilled if I have made you think along these lines.

The ideas expressed in this article are mine and do not represent NIH Policy.

References

1. Watson JD, Crick FHC. (1953) A structure for deoxyribose nucleic acid. Nature. 171(4356):737-38.
2. Lander ES, Linton LM. (2001) The Impact of Sequencing Human Genome on Genomic Food. Nature. 9(1):6-19.
3. Lander ES, Linton LM. Initial sequencing and analysis of the human genome. Nature. 409(6822):860-21.
4. International Human Genome Sequencing Consortium. Finishing the euchromatic sequence of the human genome. Nature. 431(7011): 931-45.
5. Lindblad-Toh K, Wade CM, Mikkelsen TS, Karlsson EK, Jaffe DB, et al. (2005) Genome sequence, comparative analysis, and haplotype. Nature. 438(7069):803-19.
6. Shendure J, Balasubramanian S, Church GM, Gilbert W, Rogers J, et al. (2017) DNA sequencing at 40: past, present and future. Nature. 550(7676): 345-53.
7. https://www.rxlist.com/
8. Ross WC. (1953) The Chemistry of Cytotoxic Alkylating Agents. Adv Cancer Res. 1:397-49.
9. Ross WCJ., "Biological Alkylating Agents" Butterworth, London, 1962
10. Ross WCJ. Journal of Chemical Society, 183, 1949
11. Ross WCJ. J. Chem. Soc., 2257 (1950)

12. Ross WCJ. Mitchley, B.C.V., Ann. Rep. Brit. Empire Cancer Campn, 42, 70 (1964)
13. Facon T, Marry JY, Hulin C, Benboubker L, Attal M, et al. (2007) Melphalan and prednisone plus thalidomide versus. Lancet. 370(9594): 1209-18.
14. Cob LM, Connors TA, Elson LA, Khan AH, Mitchley BC, et al. 2,4-Dinitro-5-Ethyleneiminobenzamide (CB 1954): A Potent and Selective Inhibitor of the Growth of the Walker Carcinoma 256. Biochem Pharmacol. 18(6):1519-27.
15. Khan AH, Ross WC. Tumour-Growth Inhibitory Nitrophenylaziridines and related compounds: Structure-Activity Relationships. Chem Biol Interact. 1(1):27-47.
16. Khan AH, Ross WC. (1971) Tumour-Growth Inhibitory Nitrophenylaziridines and related compounds: Structure-Activity Relationships PART II. Chem Biol Interact. 4(1):11-22.
17. Khan AH, Driscoll JS. (1976) Potential Central Nervous System Antitumor Agents: Aziridinylbenzoquinones. PART I. J Med Chem. 19(2):313-17.
18. Chou F, Khan AH, Driscoll JS. (1976) Potential Central Nervous System Antitumor Agents: Aziridinylbenzoquinones. PART II. J Med Chem. 19(11):1302-8.
19. Khan AH. (2021) The Impact of Diagnostic MRI on the Early Detection of Lethal Genes in Human Genome and to Develop Genomic Medicine to Treat Brain Cancers. J Med Clin Res Rev. 5(6):1-9.
20. intechopen.com/chapters/63395
21. https://link.springer.com/book/10.1007/978-3-319-48054-1
22. Berhardt LV. (2021) The Impact of Sequencing Human Genome on Genomic Medicine and the Discovery of AZQ (US Patent 4,146,622) Specifically Designed to shut off genes that cause Brain Cancer. Adv Med Biol. 180:1-63.
23. https://www.intechopen.com/chapters/73119
24. https://www.sciencepublishinggroup.com/journal/paperinfo?journalid=116&doi=10.11648/j.ijgg.20210901.12
25. Khan HA. (2021) The Impact of Sequencing Genomes on The Human Longevity Project. J Med Clin Res Rev. 5(7):1-12.
26. Hameed AK. (2021) The Impact of Diagnostic MRI on the Early Detection of Lethal Genes in Human Genome and to Develop Genomic Medicine to Treat Brain Cancers. J Med - Clin Res Rev. 5(6): 1-9.
27. Khan AH. (2021) The Impact of Sequencing Genomeson The Human Longevity Project. J Med Clin Res Rev. 5(7):1-12
28. Khan HA. (2021) The Impact of Sequencing Human Genomeon Genomic Food & Medicine. *Int J Genet Genom*.9(1): 6-19.
29. Khan HA. ADVANCES IN MEDICINEANDBIOLOGY, VOLUME180. The Impact of Sequencing Human Genome on Genomic Medicine and the Discovery of AZQ(USPatent4,146,622) Specifically Designed to Shut off Genes That Cause Brain Cancer. Hameed Khan
30. https://www.intechopen.com/books/9831
31. Khan AH. (2021) Genomic Medicine: Using Genetic Make-up of the Human Genome, Genomic Medicine: Using Genetic Make-up of the Human Genome, AZQ was Designed to Treat Glioblastoma, the Brain Tumor, Crimson Publishers AZQ was Designed to Treat Glioblastoma, the Brain Tumor. Nov Appro in Can Study. 6(2): 592-93.
32. Khan AH. (2021) The Impact of Sequencing Human Genome on Cancer Chemotherapy J Can Res Rev Rep. 3(2):1-10.
33. Khan AH. (2021) The Impact of Sequencing Genomes on the Under¬standing of the Origin of Life on Earth. Bi¬omed J Sci Tech Res 40(2).
34. Khan AH. (2022). The Impact of Sequencing Human Genome on the Genetically Engineered Life. J. Cancer Research and Cellular Therapeutics. 6(1).

35. Khan HA. (2022) Sequencing the Human Genome to Study the correlation between Genes and Violence, Horizon publishers
36. Khan HA. (2022) Sequencing the Human Genome to Study the correlation between Genes and Violence, Horizon publishers
37. Khan AH. (2022) Assessment of Human Genome Sequencing on the New-World Order. Res Asp Biol Sci. 4:84-33.
38. Khan AH. (2022) The Impact of Sequencing Human Genome on Novel Drug Delivery Method to Treat Cancers, *Int J Gene Genom.* 10(3):64-78.
39. Khan AH. (2022) The Impact of Sequencing Human Genome on the 2nd Genesis on Earth. J Cur Tre Agri Envi Sust 5(1): 1-21
40. Khan AH. (2023) The Impact of Sequencing Human Genome on Idiopathic Diseases. Biomed Sci. 5(2):1-17.