Journal of Current Trends in Agriculture, Environment and Sustainability

Katalyst Publishing Group

Open Access

Review Article

The Impact of Sequencing Human Genome on the Evolution of Life on Earth

Dr. A. Hameed Khan, Ph.D. (London)

Senior Scientist, Department of Genetics & Robotics, NCMRR (National Center for Medical Rehabilitation Research), National Institutes of Health (NIH), Bethesda, Maryland, USA

***Corresponding Author:**

Hameed Khan, Senior Scientist, Department of Genetics & Robotics, NCMRR (National Center for Medical Rehabilitation Research), National Institutes of Health (NIH), Bethesda, Maryland, USA.

E-mail: Hameedkhan111@comcast.net

Received Date: 08 Sep, 2022
Accepted Date: 12 Sep, 2022
Published Date: 19 Sep, 2022

Abstract

This abstract attempts to explain why there is a stunning diversity of life on Earth. Charles Darwin answered this question; it is the evolution. Darwin explains how species adapt and change over eons. It is the best and the most rational idea anyone ever had. The Tree of Life on Earth connects all living species with one another. Life journey began when a single self-replicating molecule RNA (Ribonucleic Acid) which was formed at some remote corner of the primitive Earth. About three and a half billion years ago, thunders and lightning's struck at a cloud of gases consisting of Ammonia, Methane, Carbon dioxide and water near Phosphate rocks forming the first self-replicating RNA (Ribonucleic Acid) molecule. RNA was converted to a more stable DNA (Deoxyribonucleic Acid) which stored and copied that information creating a variety of life forms from a tiny blade of grass to mighty elephant including man, mouse, monkey, and microbes on Earth. Now extraordinary science of genome sequencing is answering that extraordinary question. By sequencing and comparing the genomes of a variety of life forms, we confirm that Darwin Theory of Evolution is doable, reproducible, and verifiable. The transformation of simpler life to more complex life form is the result of the accumulation of variations over eons. It explains how the species transformation works. The Genome Sequencing is uncovering the hidden mechanism inside creatures' body, explaining astonishing transformation which explains how birds can evolve from dinosaurs and how a fish was once our ancestor. We both share the same body plan genes called the HOX genes which control other genes by throwing genetic switches to turn them on or off by making either fins in fish or fingers in human. The role of genetics switches is to help us solve the biggest Darwinian puzzle of all time; it reveals the great mystery of transformation. And above all, it tells us what makes us humans.

Keywords: Evolution, Biodiversity, Mutations, Genome Sequencing, Drug Design, AZQ

I. 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.

II. Special Notes: I am describing below the use of highly toxic lethal chemical weapons (Nitrogen Mustard) which was used during WWI and developed more toxic weapons during WWII. I describe 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 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, 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.

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

Introduction

Since the dawn of human civilization, we have asked ourselves some very important questions like Who are we? Where have we all come from? What was it that made us this way? How this Universe began? How is it likely to end? Why is the Universe expanding at an accelerating speed? How is it likely to end? Are we alone in the entire Universe or are there living creatures who may or may not look like us? According to the science of Cosmology, 13.72 billion years ago, the Universe was a single mass of energy. (May be God said let there be light and there was light) The Universe exploded with a Titanic force. Over billions of years, the cosmic dust cooled, the gravitational forces attracted material to form the islands of star systems called Galaxies. Each galaxy carries 400 hundred billions stars. Our Sun is the only one star in our Solar System. The Solar System consists of 8/9 Planets, 140 Moons and billions of comets and asteroids revolving around our Sun forming the Solar System. There are about 100 billion Solar Systems in our Milky Way Galaxy alone. There are over 400 Billion Galaxies in the visible part of the Universe. We have no idea how many more galaxies exist in the invisible part of the Universe. Universe is a vast place.

Our Earth is third planet from the Sun. Early Earth was very hot. During this era, the surface of the Earth was like popular visions about Hades: Oceans of liquid rock, boiling sulfur, and impact craters everywhere. Comets brought all the Water to cool the Earth surface. The cooling Earth produced steam and smoke that blocked the sunlight freezing the water creating the ice age which lasted for about a billion year. About three and a half billion years ago, thunder and lightning struck at some remote corner of the primitive Earth at a cloud of gases consisting of Ammonia, Methane, Carbon dioxide and water near Phosphate rocks forming the first self-replicating organic molecule called RNA (Ribonucleic Acid) molecule. The RNA world was anaerobic; only RNA based life survived.

Pre-Cambrian Era

Precambrian era began at the very beginning of the early Earth formation four and a half billion years ago. As the Icy comets cooled Earth's surface, during the early Precambrian era, a unicellular Anaerobic life appeared around a billion years after the formation of Earth. Precambrian, period extending from about 4.6 billion years ago (the point at which Earth began to form) to the beginning of the Cambrian Period about 540 million years ago. The earliest life forms we know of were microscopic organisms (microbes) that left signals of their presence in about 3.7-billion-year-old rocks. The impression found on fossils consisted of a type of carbon molecule that is produced by living things. Billions of years later a more stable self-replicating DNA (Deoxyribonucleic Acid) was formed which created the first Cyanobacteria called the Blue Green Algae. The Algae carry Chloroplast genomes whose *primary* function was to perform photosynthesis that is to absorb the Carbon dioxide in the presence of water and sunlight and convert Carbon dioxide to Carbohydrate, its food, and pump Oxygen in the atmosphere as a by-product. In the presence of Oxygen replicating life thrive on early Earth. Given the importance of oxygen for animals, researchers suspected that a gradual increase in the Oxygen to near-modern levels in the ocean could have spurred the pre-Cambrian explosion of life in water.

About 540 million years ago, the first DNA based single cellular living creature appeared. As atmosphere beginning to warm, the Ice Age ended when ice melted, and the single cellular life form begin to conjugate with other single cellular life transforming to a multicellular organism starting the evolution of life on early Earth. The cross fertilization of DNA of the unicellular life brought Cambrian era when, a variety of new life appeared. As soon as Blue Green Algae appeared, it started pumping Oxygen in the atmosphere, the explosion of multicellular life appeared. When the DNA of unicellular life form combine and recombine, with DNA of another unicellular life forms, it generates a variety of multicellular new life forms including Tributes to Trees. The Cambrian explosion unleashed the unparalleled emergence of organisms between 540 million and approximately 530 million years ago marked the beginning of the Cambrian Period. The event was characterized by the appearance of many of the major phyla (between 20 and 35) that make up modern animal life.

Cambrian Explosion

The Cambrian explosion was inevitable as the Blue Green Algae carpeted the solid surface of the planet Earth. As Chloroplasts of the Blue Green Algae performed photosynthesis and started absorbing Carbon dioxide in the presence of sunlight to convert to its food Carbohydrate and pumping Oxygen as the by-product in the atmosphere bringing to the present level. It was Oxygen which converted anaerobic life forms to aerobic life. The emergence of multicellular organisms between 540 million and approximately 530 million years ago marked the beginning of Cambrian Period. It was comparable to the Biological Big Bang when practically all major animal phyla started appearing in the fossil record. The Cambrian Explosion saw an emergence of incredible diversity of life, including many major animal groups alive today. Among them were the chordates, to which vertebrates (animals with backbones) such as humans belong.

The Cambrian Period marks an important point in the history of life on Earth; it is the time when most of the major groups of animals first appeared in the fossil record. This event is sometimes called the "Cambrian Explosion," because a vast variety of life forms appeared in relatively short time. Before early Cambrian diversification, most organisms were relatively simple, composed of individual cells, or small multicellular organisms, occasionally organized into colonies. As the rate of diversification subsequently accelerated, the variety of life became much more complex, and began to resemble that of today. Among them were the chordates, to which vertebrates (animals with backbones) such as humans being.

The most important question is what evolutionary processes followed from the Cambrian era to the appearance of modern humans on Earth? How modern human walked out of Africa about three and a half million years ago in search of food, water, and shelter. After covering all seven continents, they settled down at places, starting the Agricultural Age. During the last 100,000 years, they started Industrial Age, followed by Atomic Age to the present Information Age. In the computer age, we have captured space/time. Within seven second, from your cell phone, you can talk to anyone around the world. We have sequenced the Human Genome and converted the analog language of Biology to the digital language of computer. Now, using Internet, we can send the Human Sequence with the speed of light to any part of Universe. About 50 years ago, we landed men on the Moon and brought them back safely. Today, our spacecrafts have landed rovers on the surface of Mars searching for water and suitable place for landing. Before this decade is over, we plan to colonize Mars. How is it possible?

It was Charles Darwin who provided the most rational answer. Darwin was one of the greatest biologists ever lived. In 1859, in his book, the Origin of Species, he stated that Life evolves, and Nature selects. What he meant was that the designs and complexity of living creatures on Earth was due to slow evolutionary processes from the simplest to the more complex species is not by the act of any Divine Intervention, but by the slow process of Natural Selection responding to the surrounding environment. Species which evolve traits over billions of years to respond to the changing environment survive and the rest of the species that resist evolution die. Their fossils remained trapped in the layers of rocks as the proof of their existence. The ancient fossil records also show that within a half a billion years of the formation of Earth, the first life form appeared during the Pre-Cambrian era which lasted for about 25 million years, there were hundreds of new species evolved from Pre-Cambrian era to the Cambrian Explosion. Most of the pre-Cambrian life forms were unicellular soft tissues creatures which decomposed over the years and their fossils impressions on the rocks were preserved.

Only creatures evolved hard shells near the beginning of the Cambrian Explosion were fossilized in the earliest sedimentary rocks. From the pre-Cambrian era, the only creatures that left their fossils behind are the Trilobites, the multicellular crab like creatures which crawled at the bottom of the ancient riverbeds. Darwin critiques argue that the earliest life should be unicellular creatures not multicellular Trilobites. They forgot that unicellular soft tissue creatures don't fossilized and there were millions of soft tissue creatures during the Pre-Cambrian Era. As we approach near the Cambrian Explosion during the 25 million years, the multicellular hard-shell creatures appeared. The only hard-shell creatures from the Pre-Cambrian era like Trilobites left their fossils behind.

Darwin had the greatest foresight. By comparing the fossils, he brought from Galapagos, he saw the evidence of evolution. Paleontology is the study of the history of life on Earth trapped as fossils in the layers of rocks. Fossils are the remains of plants, animals, fungi, bacteria, and single-celled living organisms that have left remnant of bones as fossils embedded in rock material or impressions of microbial organisms preserved in rock. We study of layers of rocks to trace the evidence and ecology of plants and animals from the distant past to the present day. Most fossils are found in the sedimentary rocks and clay deposited on the layers of rocks. Over eons, one layer deposited on the top of other. Trapped in these layers are millions of years old fossil at various stages of evolution. As the rivers dried up, the sedimentary rocks become hard. To Paleontologists, the sedimentary rocks unfold like pages of a gigantic reference book. The earliest fossil of simple structures is found in the lowest or the oldest layers. As he examined younger and younger rocks, he finds complexity of structures. No human bones were ever found in any of these ancient rocks. During the pre-Cambrian era, about 450 million years ago when the climate changed, the Cambrian explosions occurred when the frozen Earth began to warm. The single cell living creature instead of growing by asexual reproduction began to grow by sexual reproduction. The interaction of two separate chromosomes resulted in variations in gene pool which led to divergence of life forms and evolution from the simplest to the more complex life forms began. We called this era the Cambrian Explosion of life. The progeny of the recombinant genes produced complexity. Only those recombinant daughter cells which carry genes that produced functional proteins in the existing new environment survived and the rest died. If your religious beliefs require proof, it is fossilized and preserved. The proof of the Cambrian Explosion is trapped in the fossil record which lasted for about 25 million years. Extracting fossils from the ancient, eroded rocks is a real challenge. The erosion of sedimentary rocks over the years is due to rain falls, windstorms, running waters, and the movement of the rocks. Once DNA extraction is purified from the fossils, its genome could be sequenced, and its date could be estimated by Radioactive Dating method. From these observations, we are certain that it has taken three and a half billion years of evolution of a single cell to become a hundred trillion cell human being.

Evolution

Nothing in biology makes sense except in the light of evolution. Our elders say that God has created Heaven and Earth. And God has created every species on Earth. And, what God had created is perfect and cannot be changed. Darwin disagreed. He wondered why would the Great Creator bother with making slightly different finches on each of the 13 different islands of Galapagos and even though they all look alike? Looking at the variety of life on Earth on land as well as in sea, the prevailing religious view just did not make sense to him. The tree of life on Earth is of stunning diversity. More than 11,000 species of birds that have been identified including 35,000 different kinds of beetles, 28,000 types of fish. Why such an amazing variety of animals exist? Why there is so many types of fish? So many species of beetles. More than 2 million living species are identified and counting. And we are just one of them. How does such an extraordinary perfusion of life come about on Earth?

Seventy percent of our planet is covered with water which harbors a variety of sea creatures. Out of vast oceans, thirty percent of Earth is landmass, less than five percent is arable land. This piece of land is home to 2 million known and about 15 million unknown species of Life. In addition, Earth is home to 20,000 species of worms, about 30,000 formally named species of microbes that are in pure culture and for which the physiology has been investigated. According to a new estimate, there are about one trillion species of microbes on Earth, and 99.999 percent of them have yet to be discovered. In addition, there are about eight billion people live on Earth. There is such an immense diversity among us that no two people look alike even identical twin are not exactly identical, they grow up to become two separate individuals. God could not have created so much variety of Life in seven days. Nothing in Biology make sense except in the light of evolution. Today, we celebrate the Man who ultimately answered that question, Charles Darwin.

His quest began, when Darwin visited Galapagos which is located 600 miles from the shores of Ecuador, he found that there is piece of land which is made of 13 islands home to Finches. Finches on each island has a distinct separate beck. He observed that no two islands have Finches with the same becks. If one island has Finches with Thick flat beak suitable for cracking nuts, the other island has Finches with long thin beaks to suck honey from flowers or to eat worms. Finches with Thick short beak is found only on nut producing island. Thin beak finches have no ability to crack the nuts and will not survive. On the other hand, island where there is no nut, Thick beaks finches cannot survive. Based on these observation, Darwin came with the Theory of evolution. Finches that are evolved to survive in their existing environment will live and the rest will die.

What Darwin did not know?

The essence of life is information, and the information is located on four building blocks of life called the nucleotides and they are (A)adenine, (T) Thiamine, (G) Guanine, and (C) Cytosine.

These building blocks always come in pairs. Nucleotide A is always linked to nucleotide T as they are A-T and nucleotide G- is always linked to C as in G-C and are called the nucleotide base-pairs. A string of nucleotide base-pairs is called DNA (Deoxyribose nucleic Acid). If (A) comes from father, (T) comes from mother. Out of four nucleotide, three nucleotides code for an amino acid called codons. Several codons interact to code for a protein called a gene. On a string of nucleotides, a genes have a start codon AUG (which codes for amino acid Methionine) and has three stop codons (UAG, UGA, UGG). Several genes are located on a single of chromosome. The smallest bacteria carry a single chromosome, and a well evolved human being carries 46 chromosomes. The total book of life of all living creatures from a tiny blade of grass to the mighty elephant is written with these nucleotides. The total genetic information that makes a living creature is called its genome. The complete genome is passed on from parents to the children. We all carry the same DNA which was formed on the early Earth about three and a half billion years ago.

What Darwin also did not know was how the species are evolved? And what is the mechanism of evolution. Today sequencing of their genomes answered that question. Finches on all 13 islands carry the same gene that code for the same cartilage protein that forms becks. What controls the size and shape of the becks are the switches that are found in the ninety-eight percent of the non-coding part of the genome. Pieces of DNA on the non-coding genome act as switches. What is true for Finches is true for humans. Humans are evolved from Fish. We both share the same body plan genes called the HOX genes. It is the same HOX genes that control other genes by throwing switches to turn other genes on to make fins in fish and fingers in human by merely switches on and switches off the same HOX genes at different times and with different intensity. The role of switches is to help us solve the biggest Darwinian puzzle of all time; it reveals the great mystery of transformation. Genes code for protein and make our bodies, it is the switches that control the gene function. It controls when to turn on and when to turn off a gene. The body plan gene, the HOX genes that throw switch to tell the Codon what amino acid to code for when to code for and how differently to make proteins to form animal bodies. How does the evolution solve the great transformation was the great Darwinian puzzle? This knowledge helps us design drugs to shut off a bad gene responsible for causing diseases.

Darwin's critiques will be proved wrong. We have recently learned a technique to extract DNA from the fossils. Using the new technique, a group of German scientists extracted DNA from our ancient ancestors Neanderthal and completely sequenced (decoded) the Neanderthal Genome. Neanderthal died over 30,000 years ago. We could use the same technique to extract the DNA of creature of Pre-Cambrian Era. Any fossil or their impression left on the pre-Cebrian rocks could be extracted and sequenced to prove the slow evolution of life from the simplest to the complex forms. Soon after the formation of planet Earth four and a half billion years ago, Mother nature has taken over a billion years to create the first living creature in the anaerobic RNA World. To convert the anaerobic to aerobic world, Mother nature has taken more than a billion years. In the entire history of over three billion years of the evolution of life on Earth, humans walked out of Africa only three and a half million years ago. By the time we appear at the scene, the Sun has used up more than half of its energy. Mother nature is too slow to respond to our need. Our population has increased to eight billion and we are adding 90 million new mouths to feed each year. To feed eight billion people on Earth, we cannot allow Mother nature to control the evolution. We must cease power from her. We must control the power of evolution. Darwin accurately understood that life evolved from simpler to more complex forms, but how does it work. To understand the mechanism of evolution, we have to look inside the cell. It was Irvin Schrodinger who predicted in his book, What is Life? he presented the concept of a secret code, he called it the "Script Code". Today, we call it the Genetic Code. Where do we find the Script Code? It is located inside the nucleus of each cell. The coloring body inside the nucleus we call the Chromosome. The book of life of all living creature are written on their chromosomes. Step by step, we reveal the process of evolution. We broke the genetic code and unlocked the secret of life. The genetic toolkit developed during the genetic engineering revolution helped us sequence the genomes of ancient fossils creatures for comparison. Now, we can sequence the genomes of all life forms, from simplest genome of microbes to more complex genomes of mouse to monkey to men and compare to see how the simplest to complex organism are evolved by aggregation of building block nucleotides over eons.

Life is a series of coordinated chemical reactions of basic building blocks called the nucleotide bases. How the four nucleotides, the building blocks of life, first synthesized on Earth by the interaction of Carbon, Nitrogen, Oxygen to form nucleotide and how they organized themselves to become alive. If we sequence the genomes of living creatures from the simplest to the most complex life form and compare their genomes, you see how the same four nucleotide aggregate differently in different species over ions in response to the surrounding environment. We deduced from the sequence of fossils genomes how cell transformation occurred and how the simplest unicellular life became multicellular life like us.

The following seven processes are responsible for evolution: They are: Selection, Mutation, Gene Flow, Genetic Drift, Bias variations, Movable elements, and non-random mating. Allele frequency in population will remain constant generations after generations if certain processes did not occur that would lead to the loss of existing genes (deletion) or the acquisition (insertion) of new genes or a piece of DNA. The replacement of a single or multiple base pairs is called the gene mutation. However, there are a lots of changes of the genotype such as gene arrangement as occur in chromosomal inversion. These are referred to as the Chromosomal mutations. Mutations may also be caused by the insertion of the transposable elements in the chromosome or any mutations that induces that changes the phenotype either favored or discriminated against the Natural Selection

Our Journey Began with A Single Cell

You and I are the loving union of our parents. Our mother's egg receives our father's sperm, and we are conceived. The fertilized egg attaches itself to our mother's womb. It draws its nourishment; it grows, multiply, replicate and differentiate and in nine months, we are born as a complete human being. By the time, we are matured that same single cell has replicated over a hundred trillion times. The nucleus of all cells carries the same instructions to make us. If you observe under microscope the embryo of the man, mouse and monkey all look the same, but they carry instructions to make separate species. When a mouse embryo implanted in mouse always gives birth to a mouse, monkey gives birth to a monkey and a human gives birth to a human.

Our logical approach to understand the mechanism of evolution began at the beginning of the last century. There are certain characteristics that we inherit from our parents for example

color of eyes, color of our hairs, facial features. Based on these observations, the Nobel laurate Physicist, Irwin Schrödinger wrote a book in 1944 called, "What is Life". In this book Schrodinger observed that the features we inherit from our parents are written in a chemical language, he called the Script Code. This code carries instructions to make a man, mouse, or monkey. Always to produce their kinds. It was Schrodinger who coined the phrase the Script Code (he called it a periodic crystal. It is a solid, crystal and carries information). According to Schrodinger the code (now we call it a genetic code) carries information to make their own species. He predicted that the information must be coded on (1) Chromosome, (2) the Coded information must be tightly held together by a covalent bond and (3) the code must be copied exactly from Chromosome to Chromosome to produce the same species from parent to offspring.

It has taken us more than 70 years to confirm Schrödinger's observations. It was Schrodinger who laid down the foundation for creating the New-World Order (we did not come from Heaven but were created on Earth) by providing the concept of Genetic Code. Over the decades, an army of young intellectuals decoded the Genetic Code to find the code of Life. The Genetic Revolution set in motion step by step described below:

The following are the sequence of events of our evolutionary process. According to Charles Darwin, we exist through evolution. He has a unique life story. He carried Bible in one hand and Charles Lyell's book on Geology on the history of Earth in another hand. He observed that the evolutionary development in the becks of Finches is based on the availability of food in different locations. As I said above, it is the same HOX genes that control other genes by throwing switches to turn other genes to make fins in fish or fingers in human by merely switches on and switches off the same HOX gene at different times. HOX genes are the aristocratic gene of the genetic community. They are at the very top of the chain of commands. They control the entire network of switches and genes that makes the body. They are essential for the developing embryo they control the shape and the form of the developing creatures.

In 1859, Charles Darwin published his book, "The Origin of Species by Means of Natural Selection, or the Preservation of Favored Races in the Struggle for Life". It is the foundation of Evolutionary Biology. Based on the appearance of the species, he classified them.

As the Darwinian evolution progressed from the unicellular to multicellular life forms, it developed a variety of genetic tools made up of all the same biological building blocks that have given rise to creates the great diversity of life. With the knowledge we gained during the 150 years of genetic science, we have collected enough devices in our genetic toolkit to alter billions of years of our evolutionary past. Over the years, we have developed all the tools we need to change the genetic make-up of our species.

In 1866, seven years later, Gregor Mendel conducted his Garden Pea Experiment and drew the rules of inheritance. Mendel observed that when Green Pea plant is crossed with Yellow Pea plant. The first generation of the plant carries all green and yellow color peas disappear. When it is crossed in the same generation. The Yellow color peas returns. One in four is Yellow. The Yellow traits return in its entirety. Today, we call these traits or genes as dominant and recessive. In this case, the Green color peas is dominant, and Yellow color peas is recessive. The important fact we observe is that Genes travel from generations to generations in its entirety, never blend and never mix.

In 1869, a Swiss scientist named Friedrich Miescher isolated DNA for the first time. Miescher was studying white blood cells in Pus. From the Pus, he isolated an acidic material rich in phosphorus and he called it Nuclein because it was extracted from the Nucleus of the Pus cells. Later it was found to be the Deoxyribonucleic Acid (DNA). The traits are written on DNA.

In 1881, the German scientist, Albrecht Kossel, identified Nuclein as a nucleic acid and provided its present chemical name, Deoxyribonucleic acid (DNA). He isolated the five nucleotide bases that are the building blocks of DNA and RNA. They are adenine, cytosine, guanine, thymine, and uracil (in RNA). Mandel's work was essentially ignored for over 30 years. At the beginning of the twentieth century, however, Mendel and his laws of genetics were "rediscovered" by Hugo Marie de Vries, Karl Franz, Joseph Correns, and his colleagues. They firmly attached Mendel's name to the basic laws of genetics. William Bateson, who came close to rediscovering Mendel's laws through his own experiments, became one of the leading advocates of Mendelian genetics.

In 1903, Walter Sutton, also rediscovered Gregor Mendel's work. He observed that genes are located on chromosomes. He presented Chromosome theory of heredity. He provided the first conclusive evidence that Chromosomes carry the units of inheritance, the gene.

In 1909, English physician Sir Archibald Garrod associated diseases with genetic defects and explained that the Black Urine is the result of an inborn error of genetic metabolism. He initiated the analysis of inborn errors of metabolism in humans in terms of biochemical genetics. Alkaptonuria, inherited as a recessive gene, is characterized by excretion from the Urine of large amounts of the substance called Alkapton, or homogentisic acid, which renders the urine black.

In 1910, Thomas Hunt Morgan performed an experiment at Columbia University, in New York that helped identify the role of Chromosomes play in heredity. That year, Morgan was breeding Drosophila, or fruit flies. After observing thousands of fruit fly offspring with red eyes, he obtained one that had white eyes. He identified that mutant due to genetic defect.

In 1927, it was Hermann Joseph Muller who conducted three experiments during 1926 and 1927 that demonstrated that exposure to X-rays, a form of high-energy ionizing radiations, can cause genetic mutations, changes to an organism's genome, particularly in egg and sperm cells.

In 1944. It was Avery, MacLeod, and McCarthy working in the Rockefeller Institute, New York, isolated a long stretch of molecule from the nucleus of a cell and called it a Nuclein which later turned out to be DNA which is the site of heredity characteristics and gene resides in DNA.

In 1950, it was Irwin Chargaff of Columbia University who published his finding that DNA is made of four chemical building blocks: Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C) and they exist in one-to-one ratio.

In 1953, Morris Wilkins and Rosalind Franklin working in King's College, London University, determined the crystallographic Structure of DNA by X-ray diffraction. Using their diffraction pattern data, Francis Crick and James Watson at the Cambridge

University, England, determined the double helix structure of DNA which provides a copying mechanism of replication essential for Life to reproduce. It explained how the information is stored and copied in the double helix of DNA, a property only living creatures possess.

In 1959, Arthur Kornberg isolated from E. coli an enzyme called DNA polymerase which can joins individual nucleotides to form long liner polymer building blocks. It can join the two single strands of DNA to synthesize a double strand of DNA critical to replication. Martin Gallagher at NIH discovered enzyme Ligase which connects the two sticky ends of DNA together.

In 1960, Hamilton Smith discovered, the molecular scissors, restriction enzymes which can cut the long string of DNA at a specific site allowing us to make a restriction site map of the DNA.
Sydney Brenner discovered cDNA (DNA without intron – after splicing out non-coding DNA) using DNA reverse transcriptase mRNA by removing non-coding nucleotide from RNA and discovered the START and STOP codons on the m-RNA. There is one start codon and three stop codons. The start codon is AUG condes for amino acid Methionine and there are three stop codons, and they are UAG, UGG, UGA. Once any one of the stop codon appears, DNA synthesis stops.

In 1961, Marshall Nierenberg ultimately deciphered the Genetic Code and unlocked the secrets of Life that Crick/Watson had predicted. Marshall Nierenberg in our Lab at NIH demonstrated that long string of RNA carries the information, and it reads three letter code at a time called Codon. For example, three letter UUU codes for amino acid Phenyl alanine. He demonstrated that information flows from DNA to RNA in a series of codons which is translated in the Ribosome to Protein. Ribosomes serves as a de-coding machine.

Khorana, Gilbert, and Ochoa were honored with a Nobel Prize for discovering the three letter codes for all twenty amino acids.

Using the above information, the first and the most successful Gene Therapy experiment was conducted by French Anderson and Mike Blaise for SCAD (Severe Combined Immune Deficiency Syndrome). Gene Therapy will give SCAD children a normal life.

In 1961 Jacob and Monod discovered gene regulation. The idea that control of enzyme levels in all cells occurs through regulation of transcription. They demonstrated how genes are switched on in E. coli by removing all Glucose and replacing it with Galactose. E. coli switched on Galactosidase genes to break down Galactose to produce Glucose and Fructose.

In 1969, Jon Beckwith of Harvard University isolated the first gene from the Bacterial Chromosome. Today, we know a gene is a unit of inheritance. It is a strip of DNA which has one start codon AUG (codes for Methionine) and one of the three-stop codons, UGG, UAG, UGA. Between the start and stop codons, a gene has captured several hundred codons to code for a protein.

In 1970, Howard Tieman and David Baltimore demonstrated the existence of Reverse Transcriptase in RNA viruses, an enzyme that synthesizes DNA from RNA. It is the DNA which replicates then it is transcribed into RNA which is translated in the Ribosome into protein.

In 1972, Stanley Cohen: shuttle Hybrid plasmids into E. coli by using Calcium chloride. Genetic Revolution began with three elements, cut, paste, and copy a gene by using restriction enzyme like EcoR1. Using Paul Berg's techniques,
Using Genetic Engineering, Boyer and Cohen were able to cut, paste, copy, and shuttle plasmid carrying human Insulin gene from human to E. coli to copy human to scale up human Insulin where E. coli could serve as factories to make large scale human insulin for diabetics. These days, we use PCR to introduce Insulin genes instead of plasmids.

In 1972, Paul Berg: moved strip of mammalian DNA from eukaryote Genome to procaryote Genome. He successfully spliced Frog's genes into E. coli genome. Using plasmid or SV-40 viruses as Vectors.

Herbert Boyer: made Hybrid DNA by using restriction enzymes to cut DNA and paste using ligase enzymes to cut and paste antibiotics Kanamycin and Tetracycline resistant genes into Plasmid.

In 1973, Stanley Cohen and Eric Boyer demonstrated how to cut, paste, and copy a gene in different species and made it possible to shuttle a gene among different species. They started the science of Biotechnology. They produced large scale Insulin to treat the 300 million diabetics around the world.

In 1976, Gilbert and. Khorana's group, culminating a nine-year effort, constructed the gene primer by assembling the four basic molecular units of the genetic code into the sequence which identify the number of the nucleotides and the order in which they are arranged.

In 1977, Philip Sharp: Genes exist in pieces on mRNA. Fred Sangar: Di-deoxy DNA stop DNA extension. He made Di-deoxyribose derivatives for all four nucleotides. He could determine DNA at all four bases. This way, he could produce short and long pieces of DNA for sequencing.
In 1978, Hamilton Smith was awarded the Nobel Prize for discovering type II Restriction enzymes. A specific molecular scissors to cut and paste DNA. He isolated molecular scissors, the Restriction Enzyme which cut DNA at a specific site and splice them from one species to another. It was Paul Berg who spliced Frog gene into E coli. He demonstrated that genes could be transferred from one species into another in its entirety.

In 1983, Kary Mullis started the Polymerase Chain Reaction (PCR). Using PCR, we could make millions of copies of a single gene within hours. He could scale up any gene by simply heating and cooling a piece of double stranded DNA, by adding a piece of forward primer and backward primer with nucleotides with polymerase enzyme.

In 1986, it was LeRoy Hood who computerized reading sequencing rapidly and launched the sequencing of the entire Human Genome.
Science of Genetic was progressing smoothly. All the elements were ready to start the Genetic Revolution by starting the Human Genome Project, the greatest biological experiment ever conceived by human mind, to read the entire human book of life. To start a mega science Project, all it needed was a great visionary leader. The man who conceived the idea of sequencing the entire Human Genome single handedly was Robert Sinsheimer, Chancellor of UC Santa Cruz. With above information in hands, we are ready to sequence the entire Human Genome.

For Craig Venter it was easier to find EST (Express Sequence

Tag) in a stretch of DNA to identify Genes. The process of sequencing by EST without the entire text of DNA is called the short-gun sequencing Using Short-gun sequencing, he came up with a quicker and faster method for whole genome shotgun sequencing. While Venter and his group only sequenced the EST, which constitute less than 2% of the entire Human Genome, We at NIH were sequencing the entire genome.

In May 1985, molecular biologist and UC Santa Cruz Chancellor Robert Sinsheimer shared with a group of eminent biologists a radical proposal to launch a massive project to determine the complete DNA sequence of the Human Genome.

Francis Collins of NIH and his International group of scientists from six countries (This effort is led by US followed by, Germany, France, England, China and Japan) and 20 biomedical centers sequenced the entire Human Genome consisting of six billion four hundred million nucleotides base-pairs including the 24,000 genes. While Craig Venter and Hamilton Smith used short-gun approach to read the EST sequence of Human Genome, Francis Collin and his International group read the Human Genome nucleotide by nucleotide that is letter by letter, word by word and sentence by sentence the entire human genome consisting of six billion four hundred million nucleotides with precision and accuracy.

Using four nucleotides, could we decipher the entire Human Genome of three billion four hundred million letters, the entire Book of Life. Among the participants who proposed to sequence the entire human genome was Nobel Laureate Ronald Gilbert who suggested that to read, analyze and map accurately every nucleotide of the entire Human Genome will be extremely expensive. If we spend one dollar per base pair, it will cost us about three billion dollars.

Only US Congress could provide such a fund. Congressional Hearings were held, and they concluded that it would be a worthwhile project for the scientific community. Since NIH (National Institutes of Health), the largest biomedical center in the world, has the manpower and expertise to complete the work on human genome in a reasonable time frame, the US Congress will approve the funding, if NIH accepts this responsibility. NIH happily accepted the responsibility and work began. To read the entire Human Genome is a colossal undertaking, it requires billions of additional dollars and years of effort of thousands of scientists from around the world. To read the Human Genome not only requires the funding from multi-national governments, but also requires the effort of thousands of scientists from six industrialized nations and 20 biomedical centers.

In 1990, US Congress authorized three billion dollars to decipher the entire human genome. This effort was led by US followed by Germany, France, England, China, and Japan. We at NIH know that this was the greatest biological experiment ever conceived by Human mind. It will answer the most fundamental questions, we asked ourselves since the dawn of human civilization. What does it mean to be human? What is the nature of our memory and conscientiousness? And our development from a single cell to a complete human being? The biochemical basis of our senses and the process of our aging? The scientific basis of our similarity and dissimilarity? Similarities that all living creatures from a tiny blade of grass to the mighty Elephants including Man, Mouse. Monkey, Microbe, and all plants from the plant kingdom are all made of the same chemical building blocks. And yet we are so diverse that no two individuals are alike. Even identical twins are not identical, they grow up to become two separate individuals.

The Impact of Sequencing Human Genome on the Evolution of Life:

After sequencing and comparing the genomes of many species, we confirm that Evolution is a plain fact and is overwhelmingly established in many species. We find that evolution is not a simple change in a single nucleotide or a single gene or a single chromosome, it is a total recombination of nucleotides which produces the alteration of the entire genome and is it the Natural Selection that produces all the adaptions. DNA is information molecule; it provides the blueprint of information for making the proteins for building the species and the information flows in one direction from DNA to proteins. The material to make the protein of the phenotype is available in the sea of chemicals present in the Cytoplasm. The molecular discovery of the greatest importance is that Evolution alters not only the genetic code, but also the molecular cellular mechanism of development for all species from a tiny blade of grass to mighty elephant including man, mouse, monkey or microbes and the process is the same in all species.

As I said above, our entire book of all life, our genome, is written in four genetic letters called nucleotides in a three-letter code called codon, and they are A (adenine), T (thymine), G (guanine) and C (cytosine). These four chemicals are called nucleotide. The essence of life is information which is carried on these four nucleotides. These nucleotides are found in the nucleus of all living cells including humans, plants, and animals. Instruction in a single gene is written in thousands of AT/GC base pairs that are linked together in a straight line. A string of nucleotides is called DNA (Deoxyribose Nucleic Acid),
Nobel prize was awarded to Crick, Watson & Morris Wilkins for discovering the double helical nature of the DNA structure which is transcribed into a single stranded of RNA (in RNA the less water-soluble methyl group Thiamine, T, is converted to more water-soluble Uracil, U, by replacing the 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) [1]. 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).

As I said above, a gene is a string of DNA which codes for a protein. The starting Codon for a gene is AUG which codes for the amino acid Methionine. It is the first amino acid to dock in the ribosome during the synthesis of proteins. After several hundred Codons for different amino acids, comes the stop codon. There are three stop Codons, and they are UGG, UGA, UAG. After the appearance of a single stop Codon, no more nucleotides are added to the chain, and DNA synthesis stops. 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 Project.

We found that from our genome of six billion four hundred million nucleotide base-pairs, half comes from our father and another half comes from our mother. Less than two percent of our Genome contains genes which code for proteins. The other 98 percent of our genome contains switches, promoters, terminators, enhancers etc. The 46 Chromosomes present in each cell of our body are the greatest library of the Human Book of Life on planet Earth. The Chromosomes carry

genes which are written on 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 we cannot even see with our naked eyes. We must use a powerful microscope to enlarge its internal structure. Under an electron microscope, we can enlarge that one cell up to nearly a million times of its original size. The image of electron microscope of 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. The nucleus in our cell has 23 pairs of chromosomes which contain 24,000 genes which carry instructions to make proteins. Proteins interact to make cells; cells interact to make tissues; tissues interact to make an organ and several organs interact to make a man, a mouse, or a monkey.

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

As I said above, our genome is very long and is made of six billion four hundred million nucleotide base-pairs spread over 23 pairs of chromosomes. To read a genome, scientists first chop up all that long stretch of DNA into smaller pieces consisting of hundreds to thousands of letters long segments. Sequencing machines then read the individual letters in each piece, and scientists try to assemble the pieces in the right order. Most cells contain two genomes: one from the father and one from the mother. When researchers try to assemble all the pieces, sequences from each parent can mix, obscuring the actual variation within each individual genome. About eight percent of our genome carries big chunk of highly repetitive sequences previously dismissed as junk DNA. Some regions of the genome repeat the same letters over and over. Repetitive regions include the centromeres, the parts that hold the two strands of chromosomes together and that play crucial roles in cell division. It also includes Ribosomal DNA, which provides instructions for the cell's protein factories. Still other repetitive parts include new genes that may help species adapt to the surrounding environment.

On April 3, 2003, several groups simultaneously sequenced the entire Human Genome and confirmed that less than two percent of the Genome codes for proteins the rest is the non-coding regions which contains switches to turn the genes on or off, pieces of DNA which act as promoters and enhancers of the genes. Using restriction enzymes like EcoR1 (which acts as molecular scissors), we can cut, paste, and copy genetic letters in the non-coding region which could serve as markers, and which has no effect on cells' function, but a slight change called mutations in the coding region makes a normal cell to become abnormal or cancerous.

Human Genome contains a catalog of traits written on genes in nucleotide sequence. Our Genome also provides a catalog of all 24,000 genes; it also provides the number and location of each gene on the chromosome. Out of all the genes, the catalog provides 16,000 good genes, 6,000 bad genes and 2,000 pseudogenes (pseudogenes have lost their functions). The Human Genome Project has identified the following genes on each chromosome:

We found that the chromosome-1 is the largest chromosome carrying 263 million A, T, G and C nucleotide bases and it has only 2,610 genes. The chromosome-2 contains 255 million nucleotides bases and has only 1,748 genes. The chromosome-3 contains 214 million nucleotide bases and carries 1,381 genes. The chromosome-4 contains 203 million nucleotide bases and carries 1,024 genes. The chromosome-5 contains 194 million nucleotide bases and carries 1,190 genes. The chromosome-6 contains 183 million nucleotide bases and carries 1,394 genes. The chromosome-7 contains 171 million nucleotide bases and carries 1,378 genes. The chromosome-8 contains 155 million nucleotide bases and carries 927 genes. The chromosome-9 contains 145 million nucleotide bases and carries 1,076 genes. The chromosome-10 contains 144 million nucleotide bases and carries 983 genes. The chromosome-11 contains 144 million nucleotide bases and carries 1,692 genes. The chromosome-12 contains 143 million nucleotide bases and carries 1,268 genes. The chromosome-13 contains 114 million nucleotide bases and carries 496 genes. The chromosome-14 contains 109 million nucleotide bases and carries 1,173 genes. The chromosome-15 contains 106 million nucleotide bases and carries 906 genes. The chromosome- 16 contains 98 million nucleotide bases and carries 1,032 genes. The chromosome-17 contains 92 million nucleotide bases and carries 1,394 genes. The chromosome-18 contains 85 million nucleotide bases and carries 400 genes. The chromosome-19 contains 67 million nucleotide bases and carries 1,592 genes. The chromosome-20 contains 72 million nucleotide bases and carries 710 genes. The chromosome-21 contains 50 million nucleotide bases and carries 337 genes. The chromosome-22 contains 56 million nucleotide bases and 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.

If you add up all genes in the 23 pairs of chromosomes, they come up to 26,808 genes and yet we keep on mentioning 24,000 genes needed to keep us function normally. A gene codes for a protein, not all 24,000 genes code for proteins. It is estimated that less than 19,000 genes code for protein. Because of the alternative splicing, each gene codes for more than one protein. All the genes in our body make less than 50,000 protein which interact in millions of different ways to give a single cell. Millions of cells interact to give a tissue and hundreds of tissues interact to give an organ and several organs interact to make a human [2-6].

Biological scientists like to count the accumulation of DNA changes called mutations. Mutations can be good (which is responsible for transforming a single cell to a complete human being over millions of years). Mutations can also be bad (when mutations are bad, they are responsible for causing six thousand diseases) and mutations can also be neutral like in pseudogenes (lost their functions)

In looking across the whole genome of a species, changes are thought to accumulate at a slow and steady rate over millions of years. The greater the number of accumulated differences in DNA between human and another species, the farther back in time you must go to find a common ancestor from which their evolutionary paths diverged. Humans and chimpanzees shared a common ancestor approximately 5-7 million years ago (Mya). The difference between the two genomes is not approximately 1% as we thought, but approximately 4%--comprising approximately 35 million single nucleotide differences and approximately 90 Mb of insertions and deletions. Humans share about 99% of our DNA with chimpanzees, making them

our closest living relatives. Compared with nucleotide-for-nucleotide, we are by about 1.23 percent different. Comparing with the entire genome, this difference amounts to about 40 million nucleotide differences in our DNA, half of which likely resulted from mutations in the human ancestral line and half in the chimp line since the two species diverged about six million years ago.

Today, our number has increased to eight billion. To feed the increasing population of the world, we must accelerate the evolutionary process by training an army of new generation of scientists to cut, paste, copy genes. The new generation of scientists will perform genetic engineering. They will be responsible for not only to clean up our environmental pollution, but also to produce new food, new fuel and new medicine to treat every diseases known to mankind.

To Clean up our Environmental Pollution: We must genetically modify all green vegetates from tiny blade of grass to the mighty Sequoia. The green grass Chlorophyll carries the Chloroplast Genome which conduct Photosynthesis that is in the presence of Carbon dioxide, water and sunlight, it removes Carbon dioxide from the atmosphere and converts it to its food Carbohydrate and release Oxygen as the by-product. Every cell of the green grasses, plants, trees will be genetically modified to insert multiple Chloroplast genome in each cell of vegetables. If you wish to control climate change, every man woman and child will be required to plant genetically modified plants distributed by their governments.

To Provide New Food: We open the Seed Bank to the world. The army of genetic engineers will sequence every seed and insert essential amino acid genes in every edible plant to create most nutritious food. The eight essential amino acid codons are available.

Genes that carry essential amino acids are expressed in a two-step process and they are Transcription and Translation. First, the essential amino acids Codons are spliced or inserted into a double stranded of plant DNA which is later transcribed into a single stranded m-RNA. As I said above, it is the m-RNA which is translated in the Ribosomes into all 20 amino acids. The Cells decode m-RNA in groups of three nucleotides called Codons which carry instructions to produce the amino acids. As I said above, when double stranded DNA is transcribed into a single stranded m-RNA, the nucleotide Thiamin is converted to Uracil. The Methyl group of Thiamine is replaced by a more water- soluble Hydroxyl group forming the Uracil. The nucleotide T for Thiamin is replaced by U for the Uracil. The m-RNA is translated into amino acids in Ribosomes. The gene expression has a Start Codon (AUG) which codes for amino acid Methionine and there are three Stop Codon which are UGG, UAG and UGA. Once the Stop Codon appears at the tail end of the DNA, amino acids synthesis stops. The Codons for each essential amino acid and their alternative codons are described below:

Valine (GTT, GTC, GTA, GTG), Leucine (CTT, CTC, CTA, CTG; TTA, TTG), Isoleucine (ATT, ATC, ATA), Phenylalanine (TTT, TTC), Tryptophan (TGG), Lysine (AAA, AAG), arginine (CGT, CGC, CGA, CGG; AGA, AGG), Histidine (CAT, CAC), Methionine (ATG), Threonine (ACT, ACC, ACA, ACG).

Fortunately, there are more than one codon which codes for the same amino acid. If one codon does not transfer easily from animal to plant, we could use the other codons. About a quarter million of flowering plants exist on Earth today. We cultivate just about 150 plants species for Agriculture purposes. To feed over seven billion people of the World, we cultivate a mere nine species of these plants on large scale. They are Corn, Rice, Wheat, Barley, Sorghum/Millet, Potatoes, Tomatoes, Sugar Cane and Soybean. The other vegetables, fruits and nuts are cultivated in smaller amounts. The Genomes of most of these edible plants have been sequenced. Luckily, there are only eight essential amino acids. It would be most useful to splice these codons in their genomes to produce the most nutritious food. The world's population will get all essential amino acids without eating meat or large quantities of vegetables. Besides fruits and vegetables, there are three major plants eaten by most people of the world and they need our immediate attention, and they are Rice, Wheat and Corn.

Rice *(Oryza sativa)* is one of the most important crops in the world. Rice, Wheat, and Corn, together account for about half of the world's food production, and Rice itself is the principal food of half of the world's population. Using Genetic Engineering method, we must splice the essential amino acids codons in the Rice genome first. Rice contains 12 Chromosomes which carry 37,544 genes which are distributed over 400 to 430 Mb nucleotides long DNA. Rice is consumed in most poor countries and more than two billion people around the world eat Rice. It is a good source of carbohydrate, proteins, fiber, lipid and fats, minerals (potassium, phosphorous, magnesium, calcium, sodium, copper and iodine) and vitamins (thiamine, riboflavin, niacin, vitamin B6 and folic acid). Unfortunately, Rice is devoid of essential amino acids in sufficient quantities. Biotech Rice with provitamin A (Golden Rice) has been developed and is being used to transfer Beta Carotene. Using the same Bio-tech methods, we can produce new food and new medicine in plant kingdom. For example, the transgenic Rice carries genes to produce Iron, Vitamin A and E and amino acid Lysine. We have also successfully spliced Bt genes (Bacillus thuringiensis) in the Rice Genome to introduce Bacterial resistant Rice against infectious worms.

Our next challenge is once we sequence the Rice genome, how many genes of essential amino acids, we could splice in a single Rice genome, one amino acid at a time or all eight in a single Rice genome. It depends upon the ease of insertion of a codon using a specific restriction enzyme. Restriction Enzymes serve as molecular scissors, they cut DNA of various sizes from a double stranded DNA to Single Stranded DNA at different lengths. There are more than 300 different Restriction enzymes are available.

Provide New Fuel

To run the engine of the modern society, we need electricity. To generate electricity, our power plants are fired by fossil fuels such as Coal, Petroleum, Natural gas, and Wood. By burning fossil fuel in our cars or in our power plants, we generate Carbon dioxide and oxides of Nitrogen which act as glass ceiling of a Greenhouse, and which traps sun's energy and retains heat raising internal temperature. Compared to Nitrogen gas (about 80 percent in our atmosphere) and Oxygen gas (about 20 percent) in our atmosphere, the amount of Carbon dioxide (about 0.04 percent) is negligible. Unfortunately, it is not the level of Carbon dioxide that concerns us; it is its function which acts as a glass ceiling of a greenhouse. The enormous amount of Carbon dioxide release by burning fossil fuels in cars, power plants and industrial complexes generate Carbon dioxide which spread as a thin sheet covering the entire planet which does not allow the heat to escape but trap the heat like a Greenhouse. As a result of the trapping of this heat energy, it heats up the internal atmosphere raising temperature worldwide melting polar snow

resulting in sea rise. It is this trapped heat which concerns us. In a Greenhouse, we can open the windows and let this heat out. Unfortunately, we don't have such window in our planet.

Worldwide rise in temperature, could also release the trapped Methane from the permafrost and polar ice sheet frozen over millennia. Methane is another greenhouse gas which is trapped in the ice sheet since the dawn of our planetary origin. The rise in temperature decreases the ice sheet of the polar cap releasing Methane on one hand and causing the rise in sea level on the other hand. Our challenge in the next century is not only to slow down the release of Greenhouse gases but also to stop the increase level of Carbon dioxide, and to reverse the trends achieving the pre-industrial or more acceptable level. To replace the Greenhouse gases, we must develop alternative source of energy such as Wind turbine, geothermal energy, nuclear fusion, and solar panels.

Until we perfect and develop for worldwide scale of the above sources of energy, we could use biotechnology methods to generate large scale Methane as a source of natural gas. In 1996, an organism called Methanococcus Jannachil, was discovered at the bottom of the ocean floor thriving near the hydrothermal vent at extremely high temperature and pressure. It is a single cell organism belongs to the third branch of life called Archaea. It has extraordinary ability to convert Carbon dioxide (a pollutant) to Methane (a fuel). Its genome has been sequenced and almost sixty percent of its genes are unknown to science. Next generation of scientists will have to identify and isolate those specific genes responsible for converting Carbon dioxide to Methane. That gene has a start codon AUG (codes for Methionine) and will end in one of the three stop codons (UAG, UGG, or UGA). Once identified, the gene can be spliced in Chloroplast genome and harvested on industrial scale in Yeast for worldwide use.

To Provide New Medicine: We must design drugs to shut off the six thousand mutated genes responsible for causing six thousand diseases. As I said above, out of 24,000 genes, 16,000 are good genes which produce good proteins that keep us healthy. There are 6,000 mutated genes which code for wrong proteins that make us sick and there are 2,000 pseudogenes which are unused and have lost their function over eons. Once the good and bad genes are identified, the good genes codes for good proteins which keep us healthy, and the bad genes produce bad protein that make us sick. Using good genes, we make good protein on large scale such as Insulin to treat 300 million diabetic around the world. On the other hand, we could identify bad gene and design drugs to shut off bad genes to prevent diseases. This starts a new era of Genomic Medicine based on differences of the genetic make-up of everyone. To produce proteins from good genes on large scale, thousands of scientists are working in about three thousand biotechnology firms producing good proteins. Single genetic defect can be treated with the Gene Therapy by replacing the bad genes with the good genes.

Gene Therapy

In Gene Therapy, a single mutated gene could be replaced by a normal gene. The most successful example of Gene Therapy is the treatment of (Bubble Baby Syndrome) SCAD (Severe Combined Immuno-Deficiency Syndrome). French Anderson and Mike Blasé the fathers of Gene Therapy in our Labs at NIH, cut, paste, copy, and harvested normal SCAD gene in vitro (in the WBC obtained from the same patient after harvesting), and returned the harvested gene to the same patient. After receiving the harvested normal cell, the patient is cured of SCAD and more than five thousand patients live a normal life.

More than three thousand single nucleotide mutated genetic diseases have been identified so far. Diseases like Cancer, Cardiac and Diabetic illnesses are due to the multi-nucleotide genetic mutations. These diseases cannot be treated by Gene Therapy, but Drug Therapy will work.

A good gene code for a good protein which keeps us healthy. Using the genetic engineering technique, we can isolate a single gene from large chromosome (for example, Insulin gene from pancreas). Using Restriction Enzyme, (molecular scissor), we can cut a large chromosome into several fragments. These fragments are separated by electrophoresis. (preparing a Restriction Site Map). By sequencing each fragment, a gene is identified by the start codon AUG (which codes for amino acid Methionine), after several dozen codons, the gene ends in one of the three stop codons (UAG, UGG & UGA). To prevent the free gene from enzymatic destruction, a gene is protected by making its recombinant with Plasmid. The recombinant Plasmid is spliced in either bacteria or yeast and harvest in bioreactors to produce in large scale. Pure protein is isolated from the transgene plasmid by reacting with restriction enzyme.

Drug Therapy

Most diseases are due to multiple genetic defects. They cannot be treated with Gene Therapy, but Drug Therapy will work. Treating multiple genetically defected diseases with novel drugs is a laborious and expensive process. It requires a series of safety and efficacy and drug delivery tests before it goes for clinical trials in humans.

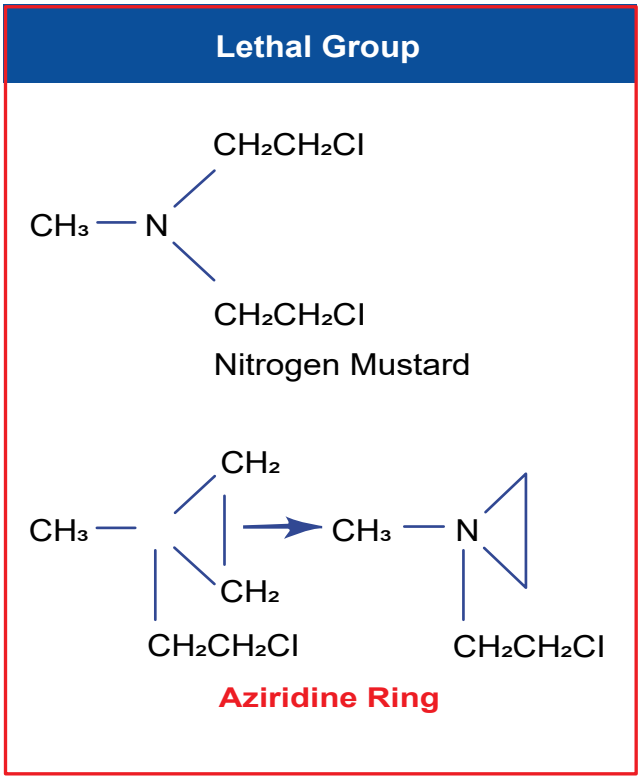
Drug Design to Treat Cancers

It is easy for the master genes to turn on and turn off other genes with great ease but trying to turn off a disease-causing gene in the Lab is the greatest challenge. The sequence of base-pairs is often so conservative that one can determine when a certain mammalian gene can also be a part of the genome of the fruit fly, drosophila, or the nematode, C. elegance. Indeed, it seems possible to trace some genes all the way from animals or plants to bacteria. This fact is particularly important in the study of diseased human genes. For instance, one can treat a mouse with an inserted human diseased gene with all sorts of drugs to tests their curative capacity. For example, the sequencing of Human Genome has identified six thousand mutated genes responsible for six thousand different diseases. By using genetic engineering, we could cut, paste, and copy each and identify each mutated gene which is responsible for causing what specific disease. A comparison of the same of genes in the different kinds of organisms usually makes an important contribution to understanding of the gene function. Since the genomes of mouse, rats and monkey are written in the same four nucleotide A-T and G-C, scripts, we can splice the diseased human gene in the mouse genomes. As the disease progress, we could design drugs to treat those diseases. Switching off the bad genes in humans is essential for preventing diseases. Switching off a bad gene to treat diseases in human is expensive and time consuming for modern science. How can we design drugs to switch off a bad gene to treat diseases? I explain below how we successfully design drugs to treat cancers first in animals and then in humans.

The supreme intellect for Drug Design to shut off a gene is Ross, an Englishman, who is a Professor of Chemistry at the London University. Professor WCJ Ross is also the Head of Chemistry Department at the Royal Cancer Hospital, a post-graduate medical center of the London University. Ross was the first person who designed drugs for treating Cancers. He designed drugs to cross-link both strands of DNA that we

inherit one strand from each parent. Cross-linking agents such as Nitrogen mustard are extremely toxic and were used as chemical weapon during the First World War (WWI). More toxic derivatives were developed during the Second World War (WWII). Using the Data for the toxic effect of Nitrogen Mustard used during the First World War, Ross observed that Soldiers exposed to Nitrogen Mustard showed a sharp decline of White Blood Cells (WBC) that is from 5,000 cell/CC to 500 cells/CC. Children suffering from Childhood Leukemia have a very high WBC count over 90,000 cells/CC. In sick children, most of the WBCs are premature, defected, and unable to defend the body from microbial infections. Ross rationale was that cancer cells divide faster than the normal cell, by using Nitrogen Mustard to cross linking both strands of DNA, one can control and stop the abnormal WBC cell division in Leukemia patients. It was indeed found to be true. Professor Ross was the first person to synthesize many derivatives of Nitrogen Mustard. By using an analog of Nitrogen Mustard, called Chlorambucil he was successful in treating Childhood Leukemia [7-9]. In America, two Physicians named Goodman and Gilman from the Yale University were the first to use Nitrogen Mustard to treat cancer in humans. Nitrogen Mustards and its analogs are highly toxic. Ross was a Chemist, over the years, he synthesized several hundred derivatives of Nitrogen Mustard molecules to modify toxicity of Nitrogen Mustard [10-12].

Although analogs of Nitrogen Mustard are highly toxic, they are more toxic to cancer cells and more cancer cells are destroyed than the normal cells. Toxicity is measured as the Chemotherapeutic Index (CI) which is a ratio between toxicity to Cancer cells versus the toxicity to Normal cells. Higher CI means that the drugs are more toxic to cancer cell. Most cross-linking Nitrogen Mustard have a CI of 10 that is they are ten times more toxic to cancer cells. Some of the Nitrogen Mustard analogs Ross made over the years are useful for treating cancers such as Chlorambucil for treating childhood leukemia (which brought down the WBC level down to 5,000/CC). Children with Childhood Leukemia treated with Professor Ross Chlorambucil showed no sign of Leukemia even after 20 to 25 years after the treatments. Chlorambucil made Ross one of the leaders of the scientific world. He also made Melphalan and Myrophine for treating Pharyngeal Carcinomas [13].



As I said above, Professor Ross was designing drugs to shut off genes attacking both strands of DNA simultaneously by cross-linking double stranded DNA using Nitrogen Mustard analogs, which are extremely toxic. As a part of my doctoral thesis, I was assigned a different path. Instead of cross-linking DNA, I am to design drugs to attack only one strand of DNA. This class of drugs is called Aziridines.

Nitrogen Mustard neither have selectivity nor specificity. They attacked all dividing cells including normal cells. During the study of the mechanism of action of radiolabeled Nitrogen Mustard on DNA, it was discovered that the two arms of Nitrogen Mustard do not bind to the double stranded DNA simultaneously. It binds to one strand of DNA at a time. The carbonium ion of the other arm of Nitrogen mustard attacks its own Nitrogen atom forming a stable three-member aziridinium ion. (see above chart). We were unable to isolate the aziridinium ion as growing tumor which produces acid which break down aziridinium ion to produce a second carbonium ion which attacks the second strand of DNA. We were able to isolate cross-linking DNA product. This study showed that to attack a single strand of DNA, we must synthesize Aziridine compounds in the Lab. Synthesis of Aziridine analogs will give two advantages over Nitrogen Mustard: first, instead of cross-linking, Aziridine binds to one strand of DNA, reducing its toxicity of double strand Nitrogen Mustard by half. Second, it gives selectivity, the Aziridine ring opens only in the acidic medium. Once the active ingredient Aziridine was determined to attack DNA in the acidic medium produced by cancer cells, the next question was what drug delivery method should be used to deliver Aziridine at the tumor site.

Designing drugs to bind to a Single Stranded DNA to Treat Animal Cancers:

As a part of my doctoral thesis, I am to design drugs to attack only one strand of DNA by making Aziridine analogues. We decided to use Aziridine moiety that would be an excellent active component to shut off a gene by binding to a single strand of DNA. To deliver Aziridine to the target site DNA, we decided to use Dinitrophenyl moiety as a delivery agent because its analog Dinitrophenol disrupt the energy providing Oxidative Phosphorylation of the ATP (Adenosine Triphosphate). To provide energy to our body function, the high energy phosphate bond in ATP is broken down to ADP (Adenosine

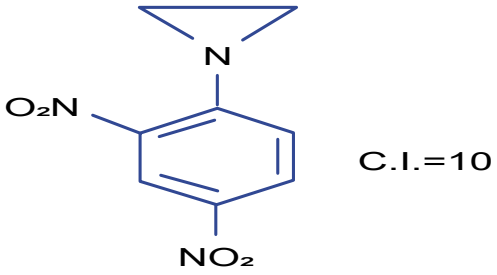
Diphosphate) which is further broken down to AMP (Adenosine Mono Phosphate), the enzyme Phosphokinase put the inorganic phosphate group back on the AMP giving back the ATP. This cyclic process of Oxidative Phosphorylation is prevented by Dinitrophenol. I decided to use Dinitrophenol as drug delivery method for the active ingredient Aziridine. Dinitrophenol also serves as a dye which stains an experimental animal tumor called the Walker Carcinoma 256, a solid and most aggressive tumor in Rat.

The first molecule I synthesized by attaching the C-14 radiolabeled Aziridine to the dinitrophenol dye. The Dinitrophenyl Aziridine was synthesized using Dinitrochlorobenzene with C-14 radiolabeled Aziridine in the presence of Triethyl amine which removes the Hydrochloric Acid produced during the reaction. 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 was like most of the analogs of Nitrogen Mustard. Since this Aziridine analog was not superior to Nitrogen Mustard, it was dismissed as unimportant compound.

Reexamination of the X-ray photographs showed 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. Because of the lack of water soluble groups, most of Dinitrophenyl Aziridine stays at the injection site. A very small amount of radioactivity was found on the tumor site.

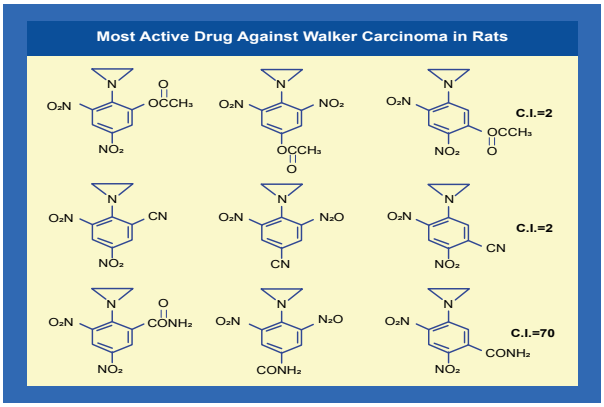
Dinitrophenyl Aziridine Carrier of the Lethal Group



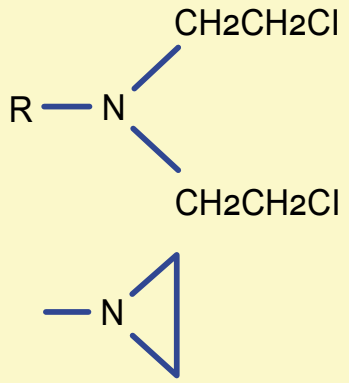
Structure Activity Relationship

I immediately realized that by making water and fat-soluble analogs of Dinitrophenyl Aziridine, 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 least water-soluble group such as Cyano- group or to introduce an intermediate fat/water double Amido group.

An additional substituent in the Dinitrophenyl Aziridine could give three isomers, Ortho, Meta, and Para substituents. Here confirmational chemistry plays an important role in drug delivery. 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. The following chart showed that I synthesized all nine C-14 radiolabeled analogs of 2,4-Dinitrophenyl aziridines and tested them against implanted



Alkyl Lethal Groups



Water Soluble Groups

$-CO_2NH_2$ $-CO.OCH_3$

$-CN$ $-NHCOOC_2H_5$

The above structures are Nitrogen Mustard (2-bischloroethyl methyl amine) and Aziridine.

Walker Carcinoma 256 in Rats.

The Most Water-Soluble Substituents

The first three compounds on top line of the above chart carry all three isomer of most water-soluble Ethyl Ester group attached to 2,4-Dinitropehny aziridine. The compound in vivo is hydrolyzed ester to produce most water-soluble carboxylic group. The compound was so soluble that within 24 hours of injection, the entire radioactive compound was extracted through urine. Most of the drug was extracted from the Rat's urine washed down from the cages. Since the Ortho position was not available for DNA binding, it showed no biological activity, but the third compound in which Ortho position was free to bind to DNA showed some activity.

The Least Water-Soluble Substituents

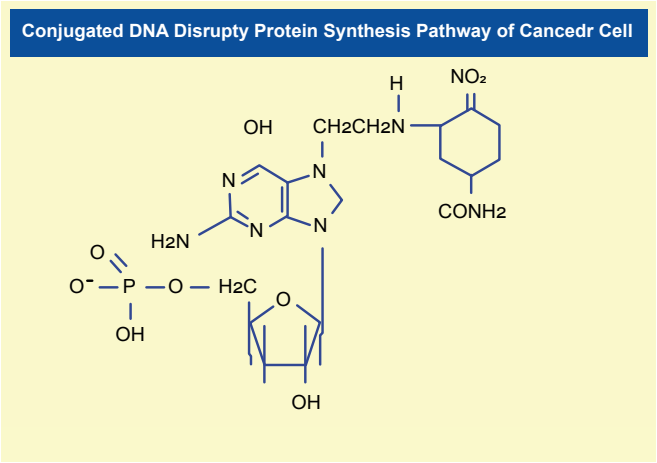
On the other hand, when the least water-soluble Cyano-group was attached to all three isomers of the 2,4-Dinitrophenyl aziridine compound as shown in the second line of the above chart, most of the compound stayed at the injection site. Only the last Cyano-derivative attached to DNA showed some anti-tumor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

The Moderately Soluble Substituents

The last line of the above chart showed that the first two Amido groups were sterically hindered and did not bind to DNA and showed no biological activity, but the last compound presents the perfect drug delivery method. 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 biological activity. It has a CI of seventy; it is seventy times more toxic to cancer cells, highest toxicity ever recorded

against Walker Carcinoma 256 in Rats [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. On the other hand, the analogs of Aziridines and Carbamates serve as prodrug and remain inactive in the basic and neutral media. They become activated only in the presence of acid producing cancer cells. Aziridine attacks DNA in acidic medium, particularly the N-7 Guanine. The dye Dinitro benzamide has great affinity for Walker Tumor. The Aziridine Dinitro benzamide (CB1954) stain the tumor. It is a prodrug and remain inactive. As the tumor grows, it uses Glucose as a source of energy. Glucose is broken down to Lactic Acid. It is the acid which activates the Aziridine ring. 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



following conjugate structure show how CB1954 binds to a single stranded of DNA shutting off the gene.

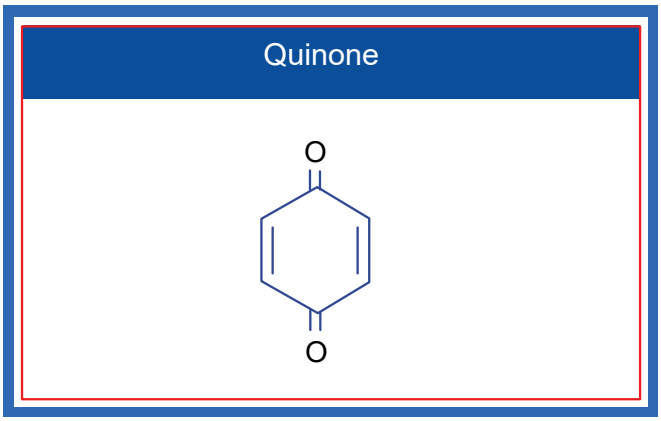
For the discovery of CB1954, The University of London, honored with the Institute of Cancer Research (ICR) post-doctoral award to synthesize more analogs of CB1954. To improve drug delivery method, over the years, I made 20 additional analogs of Dinitro phenyl aziridine, one of them is aziridine dinitrophenyl Carbamate which 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.

As I said above, at the London University, I was trained as an Organic Chemist in the Laboratory of Professor WCJ Ross of the Royal Cancer Hospital, a post-graduate medical center of the London University. I graduated from London University. After completing my doctorate and post-doctorate, I worked for about ten years at the London University, I moved to America when I was honored by the Fogarty International Fellowship Award by the National Institutes of Health, NIH, and the National Cancer Institute, NCI, of the USA. NIH has been my home for over a quarter of a century, I designed drugs to shut off mutated genes. I continued my work on the highly toxic Aziridine/Carbamate combination in America. I brought the idea from London University of attacking one strand of DNA using not only Aziridine, but also Carbamate without using the same dye Dinitro benzamide. My greatest challenge at NCI is to translate the animal work which I did in London University to humans.

Designing Drugs to Treat Glioblastoma the Human Brain Cancers

In the following sections, I will describe in detail how anti-cancer drug like AZQ was designed to shut off Glioblastoma genes which cause Brain Cancer in humans. Using the same rational, we will consider how each of the other two old age diseases namely cardiovascular disease and Alzheimer could be treated by shutting off their genes to save human life: The order of the treatment of these diseases is arranged based on the level of funding provided by NIH specifically by the NCI (National Cancer Institute).

Now, I will describe in detail how I translated animal work to humans to transport toxic chemicals across the Blood Brain Barrier (BBB) to treat brain tumor (Glioblastoma) particularly synthesizing anti-cancer drug like AZQ which was designed to shut off Glioblastoma genes which cause Brain Cancer in humans. Using the same rational, we will consider how the other mental disorders could be treated by shutting off their genes to save human life: The order of these diseases is arranged based



on the level of funding provided by NIH specifically by the NCI (National Cancer Institute).

DNA Binding Aziridines

I continued my work on the highly toxic Aziridine/Carbamate combination in America at the National Cancer Institute (NCI) of the National Institutes of Health (NIH), at Bethesda, Maryland. I brought the idea from London University of attacking one strand of DNA using not only Aziridine, but also Carbamate without using the same dye Dinitro benzamide.

At NCI, I work on human Brain. The most complex organ in the Universe. I design drugs to treat Brain Cancer. Our Brain is a three-pound flesh that you can hold in the palm of your hand. It can contemplate the vast distances among billions of Galaxies across Universe. It can contemplate the concept of Infinity. It convinces us to believe in existence or non-existence of God. It questions our Ethics; our Morality, our Altruism and our Free-will. It is only a three-pound flesh and yet it can contemplate itself contemplating the meaning of life, asking questions. Questions like; Who are we? Where have we all come from? What was it that made us this way? How this Universe began? Why is it expanding at an accelerating speed? How is it likely to end? Are we alone in the entire Universe or there are other creatures who live in deep dark space of this vast Universe who may or may not look like us?

Our Brain is a three-pound flesh. It is made of 86 billion neurons. Each neuron is linked to other neuron by 10,000 to 100,000 connections called Synapses. Total number of Synapses, their combination and their permutations exceed the number of visible stars at night sky. Millions of Synapses join to form

Neuronal Circuit. That is where our memory is stored. Our memory connects our past present to our future. Through our five senses, we receive a billion bits of data each day. When we sleep, our Brain process the information. A small fraction of the information is retained in Hippo campus and Cerebral Cortex of our Brain, which is the library of our language and our Consciousness. The rest of the information is discarded. The retained information is restored, retrieved, cut, and paste and process faster than any computer. All the information is stored in Neuronal circuits and Cerebral Cortex of our Brain. Neuronal Circuits connects every neuron with every other neuron forming a Wiring Diagram linking the entire Brain. Millions of Neuronal Circuits interact to generate our thoughts and our ideas and our visions. The complexity of our Brain is the result of three and a half billion years of Biological Evolution. It is a perfect organ in the Universe. It is a seat of our consciousness.

One day something terrible happens to our Brain. A single molecule of a single nucleus of a single neuron is damaged by radiation, chemical/environmental pollution or Viral infection, or genetic inheritance, the whole Brain collapse like a house of card, it becomes non-functional. A single normal cell becomes abnormal leading to cancer forming a tumor called Glioblastoma, one of the deadliest forms of Brain cancer. Brain Cancer is very different from Liver or Lung cancer. For example, if a Liver cell is similar damaged by radiations or chemical/environmental pollutants. The damaged Liver cell will mutate, divide, multiply, replicate, differentiate, metastasize, invade, and spread, shutting genes after genes and organ after organ killing the patient. It takes years, but not Brain tumor. Glioblastoma is a solid and aggressive tumor. It grows so rapidly within months it becomes so large. Its sheer size will crush the synapses, crush the neuronal circuits, and crush the wiring diagram and most patients will internally bleed to death within fourteen months.

One day, I heard an afternoon lecture at the NIH in which the speaker stated 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 the BBB delivering Aziridine rings to attack Glioblastomas. By introducing an additional Carbamate moiety, I could increase its toxicity several folds.

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 humans. Attaching Nitrogen Mustard group (IRB: safety committee will not permit its use) to Quinone 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 prodrug) remain inactive in the basic and neutral media. They become activated only in the presence of acid produced by cancer cells.

I planned to use this rationale 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 synthesized 45 analogs of Quinone in different combination of Aziridine and Carbamate. One of them is AZQ. By attaching two Aziridines and two Carbamate moieties to Quinone, the most useful Diaziridine Dicarbamate Quinone, I named this novel compound AZQ. All the 45 analogs of AZQ were 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 [17,18].

As I said above, Glioblastomas, the brain cancers, is a solid and aggressive tumor and is caused by mutations on several chromosomal DNA. Deleterious mutations of DNA are the result of damaging 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 synthesis during rapidly replication such as Insertion of a piece of DNA, Deletion, Inversion, 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 of DNA have adverse effects on protein synthesis. Children who inherit these mutations suffer from catastrophic illnesses during their short lives.

With the Quinone ring as a carrier to 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 these compounds would be to the human brain cells. Fortunately, brain cells do not divide, only cancer cells divide.

Glioblastomas represent such an example. 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. 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 don't know which nucleotide on which gene and on which Chromosome is responsible for causing the disease. With the completion of 1,000 Human Genome Project, it becomes easier. By simply comparing the patient's Chromosomes with

the one thousand genomes, letter by letter, word by word and sentence by sentence, we could identify the difference 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 design drugs to treat the disease.

As I said above, with the Quinone ring, I could introduce different combinations of Aziridine rings and Carbamate moieties 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.

Our Rational Drug Design to shut off deleterious genes responsible for causing diseases began in the University of London, England, and completed in the Laboratory of the National Cancer Institute (NCI), of the National Institutes of Health (NIH), in Bethesda, Maryland, USA. Over this period, I conducted over 500 experiments which resulted in 200 novel drugs. They were all tested against the experimental animal tumors. As I said above, forty-five of them were considered valuable enough to be patented by the US Government (US Patent 4,146,622). One of them is AZQ. Radiolabeled studies showed that AZQ can cross organ after organ, cross the Blood Brain Barrier, cross the nuclear membrane and attack the nuclear DNA shutting off the gene. X-ray studies showed that the radioactivity is concentrated in the tumor region. Glioblastoma stops growing and starts shrinking. For the discovery of AZQ, I was honored with the "2004 NIH Scientific Achievement Award" one of America's highest awards in medicine and I

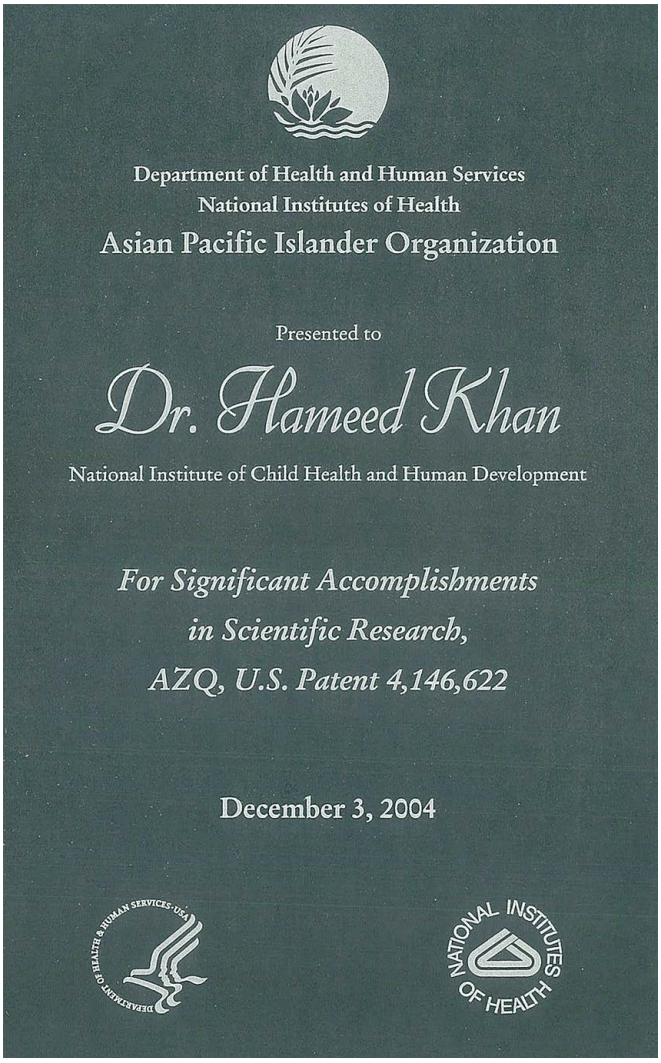


Exhibit # 1

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), 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-019-01/0). 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.

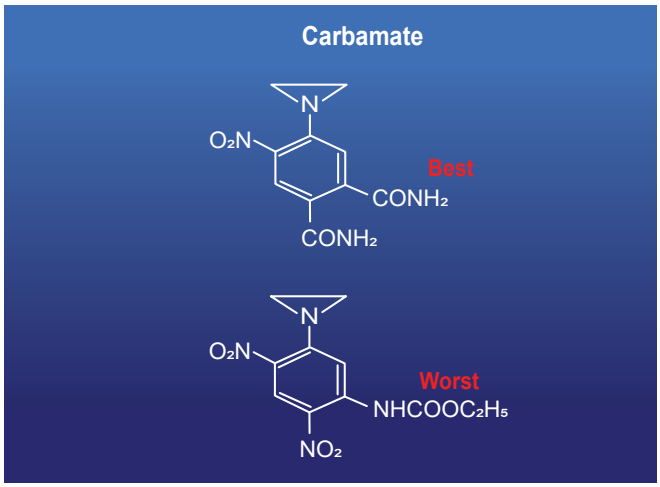
Exhibit # 2

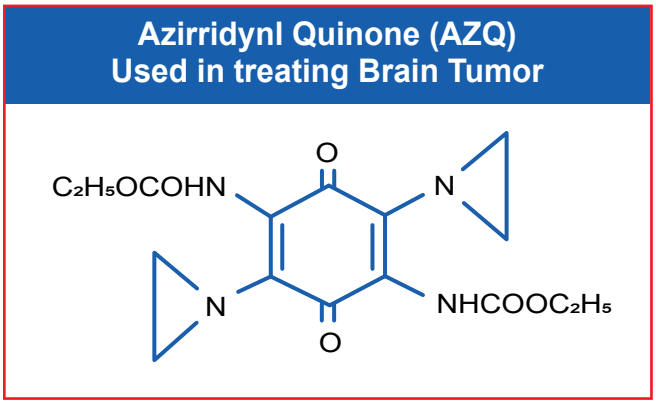
His Excellency, **Dr. A.P.J. Abdul Kalam,** The President of India Greeting Dr. A. Hameed Khan

Discoverer of anti-cancer AZQ, after receiving 2004, Vaidya Ratna, The Gold Medal, One of India's Highest Awards in Medicine At The Rashtrapathi Bhavan (Presidential Palace), in Delhi, India, During a Reception held on April 2, 2004.

Exhibit # 3

Single Strand DNA Binding Aziridine and Carbamate





U.S. Patent 4,146,622

Exhibit # 4

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.

Exhibit # 5

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 Higness 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.

was also honored with the India's National Medal of Honor, "Vidya Ratna" a Gold Medal (seeExhibits 1,2,3,4,5).

The discovery of AZQ opens path to design drugs to attack and shut off genes of other mental illnesses which include, Anxiety disorders, Aggression, Mood disorders, Psychotic disorders, Eating disorders, Personality disorders, Post-traumatic stress disorder (PTSD), Impulse control and addiction disorders, Factitious disorders, schizophrenia, Epilepsy, including

psychosomatic illnesses if genes are identified.

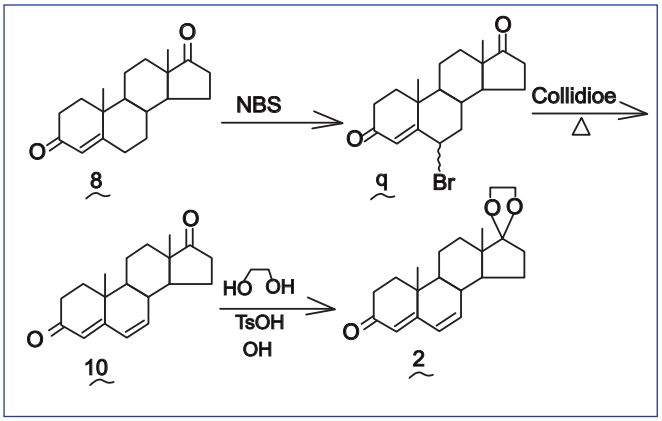
What Other Cancers Should be Explored Next?

A.Designing Drugs for Known Carrier for Aziridine:
Of all cancers, the largest killer of women is the Breast Cancer. Despite the use of highly advanced treatment methods such as Chemotherapy, Radiation therapy and Surgery, within three years, the tumor returns as metastatic cancer and kill the patient. On the rational basis, I propose to the next generation of scientists (my students) the following approach to develop novel drug design to treat Breast Cancer.

Although mutations on BRCA1 gene responsible for causing Breast Cancer located on Chromosome-17 has been identified years ago, so few drugs were designed on rational grounds. Now, we have sequenced Chromosome-17. We found that it is made of 92 million nucleotide bases pairs carrying 1,394 genes. By comparing with the Reference Sequence, we can easily identify which nucleotide on which gene of the Chromosome-17 is responsible for causing Breast Cancer. As I said above, Genomic medicine is a predictive medicine. By MRI (Magnetic Resonance Imaging which take three-dimensional images) and gene sequencing, we should be able to predict if the abnormal changes in the cellular DNA will lead to Breast Cancer. Without this knowledge, it has been so difficult to design drugs on rational basis to treat Breast Cancer. By the time the Breast Cancer diagnosis is confirmed in a patient, the BRCA1 gene has accumulated more than three thousand mutations. Genotyping of the blood sample would also show the existence of many cells carrying mutated cells responsible for creating secondary deposits. It is also found in some cases when not detected earlier, by the time Breast Cancer is confirmed, metastatic cancer cells have already been spread from Liver Lung on their way to Brain.

As a Fogarty International Postdoctoral Fellow at the NCI, I was given the chance to work on any cancer. Since all other organs including Breast, lung and Liver could be removed and replaced by organ transplant except Brain, I thought that protecting Brain is utmost important to save life. For years, I worked on the development of AZQ. Once the AZQ was developed to protect the Brain Cancer, I could focus on the Breast and Prostate Cancers. Recent, Radiolabeled studies in mice showed that male hormone Testosterone has great affinity for female organs like Breast, Ovary, and Fallopian tube cells. On the other hand, Estrogen, the female hormone, has great affinity for Prostate glands in men. By attaching multiple Aziridine rings and Carbamate ions to both Hormones, I could design novel drugs to attack both the Breast and the Prostate cancers. Now, I found that I could increase its toxicity several folds to abnormal cells by attaching more than four Aziridine and Carbamate moieties to both Male and Female Hormones.

In a Breast tumor, within the start and stop codon, BRCA1 gene has captured over two hundred thousand nucleotide bases. The BRCA1 gene carries about three thousand mutations. These mutations are caused by exposure to radiations, chemical or environmental pollutants, viral infection, or genetic inheritance. To attack the mutated nucleotides among the three thousand mutations in BRCA1 gene, we could use male hormone, Testosterone, and bind multiple radio labeled Aziridine and Carbamate ions to attack BRCA1 mutations. By using three dimensional MRI, we could show how many radio-labeled nucleotides were bound to which mutations. Out of seventeen positions available for substitutions on Testosterone ring system. There are only three positions that is 1,3 and 17 are available for substitution on Testosterone ring system.



Carl Djerassi [23] 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 compound. These bromo ion could be replaced by additional Aziridines or Carbamate ions. We could increase or decrease the number of Aziridine and Carbamate ions to get maximum benefit by further brominating position 15 and 16 to introduce additional 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 there are seventeen positions also available on Estrogen ring as well; again, we could increase or decrease the number of Aziridine and Carbamate ions to get the maximum benefit by using Djerassi' method as we did with Testosterone. The above methods are novel approach to designing drugs to treat Breast and Prostate cancers using genetic make-up of a patient to treat metastatic cancers.

B.Designing Drugs for unknown mutations:

Challenge to treat Huntington (HTT) Disease:
Sequencing the entire genome of a healthy person and comparing with the genome of a sick patient will help us identify which nucleotide in which gene is damaged and is responsible for coding for a bad protein for causing the disease. What if the sequencing does not identify any specific mutation? There is no mutated nucleotide, no damaged genes and yet the patient suffers from a neurological degenerative disorder called Huntington Disease. During evolutionary development, a normal gene became defected by accumulating more than thirty CAG codons. The CAG codon is made of three nucleotides consisting of nucleotides cytosine-adenine-guanine. The CAG codon codes for the amino acid Glutamine. Large number of CAG repeats produce a string of glutamines known as polyglutamine Chain which damage the nerve cells resulting in neurological disorder. Although Huntington is known for over a hundred year, there is no cure to this date. Patients with Huntington Disease suffer from difficulty in concentrating, memory lapses, depression, mood swings, irritability, or aggressive behavior. If there are fewer than 26 CAG repeat, a person remains normal. Early signs of Huntington appear as the number of CAG repeat exceed 35. Huntington gene is dominant. If only one parent carries the gene, the child has fifty percent chance of inheriting the disease. If both parents carry the recessive gene, the child has a seventy-five percent chance of inheriting the Huntington Disease. How to treat Huntington Disease?

Challenge to Treat Acute Lymphocytic Leukemia:
Again, sequencing the human genome of a sick patient and comparing with the Reference sequencing does not identify any specific mutation responsible for causing the disease neither in the nucleotide sequence nor in the gene sequence. How would you design a drug to treat a disease like chronic myelogenous leukemia caused by the translocation of a part of DNA? There is no damage to nucleotides, or genes or chromosomes; simply a piece DNA has moved from one chromosome to another. The Philadelphia chromosome presents such a problem in which chromosome-9 and chromosome-22 break up and exchange portions of DNA. This creates an abnormally small chromosome-22 and a new combination of instructions for your cells that can lead to the development of chronic myelogenous leukemia. Bone marrow cells that contain the Philadelphia chromosome are often found in chronic myelogenous leukemia and sometimes found in acute lymphocytic leukemia. The mutation is a translocation. This abnormal chromosome contains a fusion gene, consisting of the ABL gene and the BCR gene, producing the BCR-ABL oncogene.

I have good news for the next generation of scientists (my students). Professor Ross and I are bench scientists have worked in the same Lab for almost ten years. We have demonstrated above that Nitrogen Mustards, Aziridine and Carbamate covalently bind to DNA shutting off a gene. The Carbonium ions generated by the above molecule bind to N-7 site of Guanine shutting off the gene. Fortunately, the CAG codon of the Huntington Disease carries Guanine. It is a perfect project for postdoctoral students. First, find a dye which stains the Huntington gene. Next, attach Aziridine to the dye. Professor Ross used highly toxic Nitrogen Mustard to cross-link double stranded DNA to shut off a gene. (If you use Nitrogen Mustard, the safety committee (called the IRB - Institutional Review Board) will question you how much toxic waste you generated and how safely you disposed it.) My advice, use Aziridine which is a non-toxic prodrug, and it binds to a single strand of DNA of the Guanine and shuts off the gene. Your greatest challenge is to distinguish the guanine molecule between the normal CAG and the abnormal CAG.

Let me share the secrets with you. By making C-14 radiolabeled AZQ (US Patent 4,233,215), I have demonstrated in mouse model which nucleotide in the Glioblastoma (the brain tumor) was bound to Aziridine Carbonium ion. If radiolabeled Aziridine bind to any Guanine, by taking a MRI, you could identify which CAG codon is responsible for causing Huntington Disease. Similar method could be used to identify mutation in chronic myelogenous leukemia. Once identified, you can develop treatment from mouse to men by making analogs of Aziridine by attaching to different dyes. To make one AZQ to treat Glioblastoma, I had made 45 analogs of Quinone. All 45 analogs were considered so valuable that they were all patented by the US Government.

(FDA toxicity testing guideline is described in the CFR – New methods include advances in new technologies, such as micro physiological systems—2D or 3D cellular systems that mimic human organs—combined with in vitro cellular tests and in silico computational models).

Evolution of the Intellectual Development (Mental Big Bang):
Evolution of human brain unleashed the human creativity. Our ability to communicate orally played a vital role in the evolution of our brain. Humans are genetically best equipped to thrive, succeed in environment dominated by developing language. Improvement in the ability to use language expand our vocabulary. The greatest advantage of using language is the development of cross fertilization of ideas. Language facilitates the communication of complex ideas and helps us develop acute social skills, solicits information for exchange technical knowhow and helped our ancestors exchange what is the best way to make a spear to hunt in old days or in modern days help us write a new program for our cell phone; or help us during negotiations, There are several kinds of communications methods including gossips. Language forces modern culture to improve and modify. Today, it tells us who we are and who we belong. Language helps us develop cultural evolution. We prefer to talk about the meme (unit of ideas) instead of gene (unit of inheritance). Meme could also be units of ideas, skills, stories, songs anything that we pass mentally from person to person. Genes we copy them in our biological system pass through during reproduction. Memes are copies of our mental thoughts consisting of ideas, habits, skills, copies of behavior that we pass on from person to person. Gene shapes all biological evolution; it is in competition with Memes which shapes our mind and our culture. Memes carry forces that drive our social evolution. Specially some of our mind's big bang (mental development) some fifty thousand years ago. We see ideas, trends, prejudices, breakthroughs behavior, much like genes, self-replicating and accumulating from mind-to-mind society to society, generation to generation. Memes are the building blocks of ideas a new kind of evolution. If you need a culture which replicates itself something like the same way as DNA molecules replicate themselves then we have the possibility of completely new kind of Darwinism. Changes in the human lifestyle of the last 50,000 years have had very little to do with any biological change in our brain. The reason we look so different today from the way caveman lived is not because we have better brain because we have been accumulating all of the thousands of discoveries that our ancestors have made and we have the benefit of huge history of the invention so that we communicate non-genetically through language through documents through customs. Memes are not merely treasure of knowledge or ideas. They are not static, but they are dynamic; their cross-fertilization generates new ideas and new knowledge. They can be titanic they can modify the world, revolutionize life even suppress the forces of biological evolution.

Since the dawn of human civilization, we have asked ourselves simple questions like Who are we? Where have we all come from? And what was it that made us this way? How this Universe began? Why is it expanding at an accelerating speed? How is it likely to end? Are we alone in the entire Universe or there are other creatures who live in deep dark space of this vast Universe who may or may not look like us? Now, we can answer some of these questions: The Sequencing of Human Genome has enabled us to answer these questions on the origin and Evolution of Life on Earth. We are the result of three and a half billion years of biological evolution which brought us here. Among all creatures on Earth what makes us so unique? It is the development of our brain, our conscientiousness, our awareness of our surrounding and our ability to communicate with each other. We also learned when we sequenced our genome that ninety-eight of our genome contains non-coding region which carries pieces of the genomes of earliest creatures on Earth. The two percent of our genome codes for proteins. Thousands of Proteins interact to make cells and millions of cells interact to make tissues. There are only 220 different tissues which interact to make an organ and several organs interact to make a human. What lies within that two percent of our genome that make us superior to all other creatures on Earth? The two percent of our genome is the information center which contains about 80 million nucleotide base pairs, the information molecules, which give us the ability to think, read, write and edit our own

book of life and books of life of all other creatures on Earth. It gives us consciousness, an extraordinary ability to make us capable of self-analysis, mental time travel, imagination, abstract reasoning, cultural establishment, familiarity with our own mortality, our free will, and our ultraism. These higher-level quality separate us from the rest of the animal kingdom and form the basis of our global culture as a species and make us superior to all other living creatures on Earth. It is not a gift from Heaven but from the three and a half billion years of biological evolution.

Are we the endpoint of Darwinian Evolution?

The answer is No. Evolution is a continuous process. Humans have evolved to become conscious; became aware of their surroundings. They remember their past, present and plan course of their actions. Is it the endpoint of evolution? Religions say Yes and Science say No. If you look at the human evolution of mind during the last three and a half million years, the first human/chimp woman "Lucy" mother of us all walked out of Africa from the Hader Valley in Ethiopia, with her children in search of food, water, and shelter. Within three and a half million years, her children walked around the world. They settled in all seven continents. They not only climbed the tallest mountain; they have also gone to the bottom of the deepest ocean; they split the heart of atom; they broke the genetic code, unlocked the secrets of life. walked on the surface of moon and came home safely. Our number has increased to eight billions. And we add 90 million new faces each year. By the end of this decade, we plan to colonize Mars. Martian humans will have to evolve if they want to survive on Mars. Although we have taken three and a half million years to colonies the entire Earth, Within a million years, human settlement will cover on the entire surface of Mars. The Martian humans will have to terraforms Martian climate. Our micro robots will have gone in every directions in the Universe in search of exoplanets.

The Martian farmers will grow their food in Bioreactors. Millions of bioreactors will cover the surface of Mars. They will grow their food 24 hours a day and seven day a week. All mental work will be done by humans and all physical work will be done by robots. Robots will not control us we will control them. We are their creators. We will have complete control to switch off whenever we want. Our mental evolution has no limit. Our mental evolution will continue to advance in response to the climate of the exoplanet. Within three and a half million years, we came from Hader valley in Ethiopia to the surface of Mars. Within the next three and a half million years, we will have many settlements on the exoplanets in the Milky Way Galaxy.

Among all the creatures on Earth, we alone can read our own book of life. We are ready to manipulate life not only to clean up our environmental pollution, but also to produce new food, new fuel, and new medicine to treat every disease known to mankind. In future, most of us will conceive our offspring in the Lab instead of in our bed. Our future generation will not inherit mutations at random, they will be self-designed. Our embryo selection will not be natural but self-directed. More parents will want children conceived outside the mother.

Many couples will come to see conception through sex as a dangerous and unnecessary risk. Governments and insurance companies will want prospective parents to use in vitro fertilization and embryo selection to avoid having to pay for the lifetime of care avoidable and expensive genetic diseases. The children of the future generations will receive selected mutations that will make them smarter, stronger, resistant to many diseases, long-lived and will carry novel traits associated with genius. They will carry genes of super keen sensory perception then the naturally conceived children. To survive on a long-distance travel in search of exoplanets, they will carry genes of super quality humans not yet known in the human world but will be made by using the same biological building blocks, the four nucleotides, that has given rise to great diversity of life on Earth.

Knowledge gained during the 150 years of genetic science has given us an extraordinary ability to alter billions of years of evolutionary past in hours. We now have all the tools in our genetic toolkit we need to alter the genetic makeup of any living species. Using these tools, we want to eliminate genetic diseases, alter, and enhance other capabilities to survive on distant exoplanets. The residents of exoplanets will prepare themselves to survive in hotter or colder climate, or at lower or higher gravity planets with little Oxygen. By mastering the use of these tools over time, they will be genetically manipulating themselves which will come to be seen as perhaps the greatest innovation in the history of our species. The key to unlocking the secretes of our genome and including insertion of novel traits will provide almost unimaginable potential and, in many ways, an entirely new future. We will determine in many ways who we are and what we value and how we move forward.

Let me summarize what I have said so far. Darwinian Evolution is not a theory, it is a fact. By sequencing and comparing the genomes of many species, we observe that the complexity increases from a unicellular to multicellular species over millions of years. Mother nature is too slow to bring changes. We seized the power from Mother nature and accelerate the evolutionary processes. We developed the techniques of genetic engineering. We learned to extract from bacteria Restriction enzymes like EcoR1 which serve as molecular scissors. We developed methods to cut, paste, copy, sequence and move around genes from species to species to generate complexity in species in days rather than in centuries.

To meet the demands of the bourgeoning population of world, I repeat, we need to practice the quality control of the population. This is especially important for couples who have a family history of mental illnesses. We can sequence the genome of egg and sperm. After in vitro fertilization, we incubate the embryo for 3-4 days until it becomes 8-cell embryo. After siphoning off a single cell for sequencing, the cell is implanted if no bad mutations are identified. The genes the couple exchange during conception will not be random; it will be self-designed. Their fertilized egg selection will not be natural, it will be self-directed. The offspring will be free from all genetic defects.

Although Germ-line gene therapy is not permitted at this time, the same techniques developed for quality control of the population could be used to enhance genetic traits. Most parents will like their offspring to carry genetic traits to make them stronger, smarter, than the other children; we could introduce traits to make them resistant to many diseases, long-lived and will carry new genetic traits not even discovered such as high I.Q., athletic ability, and super keen sensory perception. In future, whenever the moratorium on germ-line gene therapy is lifted for space travelers, parents may consider genetically altering their future children. Because of the availability of the genetic toolkit, to prepare an army of space travelers, preliminary germ-line gene therapy work must be conducted on Earth.

Gene editing technology, CRISPER-case9, is making it possible to edit the genes of all species including our own embryos not only with far greater precision with speed, but also accuracy, and flexibility than ever before. CRISPER-case9 and tools like it have given us unlimited power to alter the genetic make-up of embryo. It will ultimately be scientifically possible to give

embryos new traits and capability by inserting DNA from other humans, animals and someday from synthetic sources. We have gained enough knowledge not only to cut, paste, copy, and sequence a gene, but also to move the genes from species to species, to convert the analog language of biology to the digital language of computer, to up-load its entire sequence of the genome on the internet and to send its entire sequence with the speed of light to any part of the Universe. We walked on the surface of moon and came home safely. Within a decade we plan to colonize planet Mars. Using Mars as a base, we will launch unmanned spacecrafts in search of habitable planets in distant galaxies to protect preserved and spread human intelligence in every corner of the Universe. Our travel in deep space is not the evolutionary endpoint, but always a stop along the way in our continuous evolutionary journey The new generations of scientists, my students, will open an era of explorations and discoveries unsurpassed in the history of mankind [19-42].

What is the Fate of Humanity on Earth?

Our Sun has been burning for the past four and a half billion years. It is a middle age dying star. It burns 700 million tons of Hydrogen every second. It has used up more than half of its energy. Humanity is trapped in the middle age dying Solar System. We have a choice either to stay on Earth and die or to get out of this Solar System and survive. If you are religious person, you will leave your fate in the hands of God. If you believe in Science, you will plan to escape Earth before it dies. Your prime responsibility is to protect, preserve and spread human intelligence in every corner of the Universe.

Humanity has come on a crossroad; one path leads to total inhalation and destruction of all life forms on Earth and the other path leads to escape from Earth before the Earth with all life forms turn to ashes and become the part of the big cosmos. We came from stardust and end up as stardust. We have a choice either to learn the facts about evolution of life on Earth or parish with it. On the above pages, I attempted to explain how Darwinian evolution began and now I will explain how it is likely to end on Earth if we sit on our hands and pray to be sent to Heaven. Prayers may be a good thing; it may help you make up your mind, but it will not protect you.

If you don't believe in the Darwinian evolution on the religious ground and decided to stay on Earth, you will pay a very high price. No one prays harder and longer than the Buddhists Monks. Have you ever seen a Buddhist monk going to work? They live on hands-out. They go to pray rather than go to work. Some in America are also following their example asking for charity for their churches.

Those of us who believe in Darwinian Evolution, must start making plans to escape and survive. The Universe is a very big place. Our Sun is mostly made of 74% of Hydrogen, 25% of Helium and one percent the other elements. Under intense temperature and pressure, Hydrogen atoms fused to form Helium and releases subatomic particle like Photons as Sunlight which travels 93 million miles (which forms one AU: Astronautical Unit) to reach Earth as sunlight in eight minutes. As it continues to burn, the Helium is converted to Carbon. As more and more Hydrogen is used up, the Sun begins to cool and begins to expand. As it expands, the outer rim of the Sun begins to evaporate, melt, and engulfs the nearest two planets Mercury and Venus within the Sun. On further cooling, the Sun will expand its outer rim even further approaching Earth. As its expansion reaches Earth, the intense temperature will boil off oceans, incinerate all life forms including us. As it exhausts its energy, the Sun will expand no further; it will collapse on itself and explode as Super Nova. The explosion forms all 120 elements from Iron to Gold including all essential element to make us. We are made of Star Dust. The Titanic explosion will destroy the gravitational forces holding all planets and moons together resulting in multiple explosions destroying the entire Solar System.

Mother Nature has not been very kind to us. To develop technologically for deep space travel, she should have created us at least a billion years ago. We could have populated many Solar Systems in the Milky Way Galaxy. The great tragedy is that we came out of Africa recently when the Sun has used up half of its energy. Despite this delay, we still have enough energy in the Sun to get out of this Solar System only if we don't destroy ourselves by either going to Nuclear War or inviting Environmental collapse, or Meteorite impact followed by global forest fire or Tectonic plate shift resulting in colossal Tsunami drowning life under oceans. We made more scientific discoveries during the last twenty-five years than the entire history of humanity on Earth. We have enough technology to take humanity out this Solar System. We have planned to take the following baby steps for deep space travel:

In 2024, we plan to send men on Mars. It is the first step in the right direction. It will technologically prepare us to survive on Mars under extremely cold condition on a tree-less water-less planet without Oxygen. Mars' atmosphere however is 95% carbon dioxide, 3% nitrogen, 1.6% argon, and it has traces of oxygen, carbon monoxide, water, methane, and other gases, along with a lot of dust. Dust hanging in the air colors Martian skies tan in photos taken from the Earth's surface. Relative to Earth, the air on Mars is extremely thin.

Terraforming is heating planet Mars to alter its atmosphere. Artificially creating an atmosphere suitable for human habitation may be possible, but it would be very expensive and challenging. Terraforming an entire planet will probably take a very long time — centuries or more." But scientists have proposed other, more feasible ways we could make Mars habitable.

For those inhabitants of planet Earth who chose to stay to see the end of life on Earth, they could do us a favor; they could stay behind to broadcast live what they witness on Earth. They could show the deep space travelers, the final sunset on Earth; the end of life on Earth; how the inhabitants will feel the intense heat, witness the worldwide burning of Oxygen, the boiling off the oceans, the massive forest fire. They could broadcast live the end of the Earth to the space travelers who might be light years away from Earth on the way to the next star system, the Alpha Century in search of habitable planets for humans. As our Sun used up most of its energy, it will expand no further. Humans may not survive, but their drones could continue to broadcast us how our Sun will explode as Super Nova and how it will collapse on itself by exploding with Titanic force. The gravity of the planets and millions of meteorites and comets orbiting around Sun will collapse and all other planets and their moons will fall on each other causing further explosions destroying the entire Solar System. The inhabitants of distant galaxy such as Andromeda Galaxy, about 2.48 million light-years from Milky Way, will see the destruction of our Solar System as a tiny flash of light on the third arm of the Milky Way Galaxy.

Conclusions

We have a long journey ahead of us. To confirm the existence of intelligent life in the nearby exoplanets, Frank Drake of SETI (Search of Extra-terrestrial Intelligence Institute) is waiting to receive a single reproducible radio-signals for the past 70 years

and have not received any reproducible signal so far. It may be that there is no technologically advanced society within the 70 light year distance to respond to his radio-signals. Moreover, we have been sending Radio and TV signals for the past 100 years in every direction. We have not received any reply. It tells us that there is no technologically developed intelligent life on any Star System within a hundred Light Years. It also tells us how rare and precious life in the Cosmos is and that we must prepare for a long journey beyond 100 Light Year. We must learn to travel for centuries in our city size spacecrafts. We must learn to grow food, produce Oxygen, and recycle water for the endless journey. Comets are water world. We must learn to capture comets and attach them to our space crafts as a continuous source of water, Hydrogen and Oxygen for a long journey. With the speed we are progressing in making scientific discoveries, Darwinian evolution predicts that we are not the evolutionary endpoint but are in the continuous evolutionary journey to create super humans. If we don't destroy ourselves by going to Nuclear wars or Environmental collapse, within decades, we colonize Mars, within centuries we colonize Milky Way galaxy and within millennia colonize the entire Universe; we are in the process of enlarging our physical and mental capacity. I tell my students, to succeed and survive on an endless journey in space, we need outstanding men and women. Who among you will be the vanguard of research and technology to protect, preserve and spread human intelligence in every corner of the Universe? We bequeath the future of humanity in your hands; we know that you will do your best to take humanity out of this Solar System to a safer place in the Cosmos before the Sun dies. You alone will be responsible for spreading human intelligence in every corner of the Universe.

Opinions Expressed in this Article are Mine and do not Represent NIH policy.

References

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

1. Watson JD, Crick FHC (1953) A structure for deoxyribose nucleic acid. Nature 171: 737-738.
2. Lander ES, Linton LM (2001) The Impact of Sequencing Human Genome on Genomic Food. Nature 409: 934-941.
3. Lander ES, Linton LM (2001) Initial sequencing and analysis of the human genome – PubMed. Nature 409: 660-921.
4. Sequencing of Human Genome, Scholarly articles for Nature (2004). Nature 431: 931-945.
5. K Lindblad-Toh (2005) Genome sequence, comparative analysis, and haplotype. Nature, 438: 803-810.
6. J Shendure (2017) DNA sequencing at 40: past, present and future – PubMed. Nature, 550: 345-353.
7. Ross WCJ (2015) Chlorambucil Drug Information: Description, User Reviews, Drug Side Effects, Interactions – Prescribing Information at RxList. Journal of the American Chemical Society 136: 5860-63.
8. Ross WCJ (1953) The Chemistry of Cytotoxic Alkylating Agents. In Advances in Cancer Research by Greenstein JP, and Haddow A, Academic Press, Inc., New York 397-449.
9. Ross WCJ (1962) Biological Alkylating Agents. Butterworth London.
10. Ross WCJ (1949) Journal of Chemical Society 183.
11. Ross WCJ (1950) J Chem Soc 2257.
12. Ross WCJ, Mitchley BCV (1964) Ann Rep Brit Empire Cancer Campn 42: 70.
13. Ross WCJ (2007) Melphalan and prednisone plus thalidomide versus. Lancet 370: 1209-18.
14. Cobb LM, Connors TA, Elson LA, Khan AH, Mitchley BCV, et al. (1969) 2,4-Dinitro-5-Ethyleneiminobenzamide (CB 1954): A Potent and Selective Inhibitor of the Growth of the Walker Carcinoma 256. Biochemical Pharmacology 18: 1519-1527.
15. Khan AH and Ross WCJ (1969/70) Tumour-Growth Inhibitory Nitrophenylaziridines and related compounds: Structure-Activity Relationships. Chem-Biol Interactions 1: 27-47.
16. Khan AH and Ross WCJ (1971/72) Tumour-Growth Inhibitory Nitrophenylaziridines and related compounds: Structure-Activity Relationships. Chem-Biol Interactions 4: 11-22.
17. Hameed Khan A and John Driscoll (1976) Potential Central Nervous System Antitumor Agents: Aziridinylbenzoquinones. Journal of Medicinal Chemistry 19: 313-317.
18. Ed Chou, Hameed Khan A and John Driscoll (1976) Potential Central Nervous System Antitumor Agents: Aziridinylbenzoquinones. Journal of Medicinal Chemistry 19: 1302.
19. 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. 2021; 5: 1-9.
20. 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: 1-9.
21. 2020 – A chapter was Published in the Book entitled, Prevention, Detection and Management of Oral Cancer: Chapter entitled, "The Impact of Sequencing Human Genome on Drug Design to Treat Oral Cancer: Published in the IntechOpen.
22. 2018 – A chapter was Published in the book entitled, "Development of Oral Cancer – Risk Factors and Prevention Strategies": Published by Springer & Edited by Ala-Eddin Al Moustaf.
23. The Impact of Diagnostic MRI on the Early Detection of Lethal Genes in Human Genome and to Develop Genomic Medicine to Treat Brain Cancers. (2021) J Med - Clin Res & Rev 5: 1-9.
24. Leon V. Berhardt e-Book (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. 180: 1-63.
25. The Rational Drug Design to Treat Cancers Abdul Hameed Khan. The Rational Drug Design to Treat Cancers: Drug Design - Novel Advances in the Omics Field and

Applications: Edited by Arli Aditya Parikesit. A book published in London, Page 117 (2021).

26. The Impact of Sequencing Human Genome on Genomic Food & Medicine. (2021) International Journal of Genetics and Genomics 9: 6-19.

27. The Impact of Sequencing Genomes on The Human Longevity Project. J Med - Clin Res & Rev 2021 5: 1-12.

28. 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: 1-9.

29. Khan H (2021) The Impact of Sequencing Genomes on The Human Longevity Project. J Med - Clin Res & Rev 5: 1-12.

30. Hameed Khan (2021) The Impact of Sequencing Human Genome on Genomic Food & Medicine. International Journal of Genetics and Genomics 9: 6-19.

31. Hameed Khan. The Impact of Sequencing Human Genome on Genomic Medicine and the Discovery of AZQ (US Patent 4,1446,622) Specifically Designed to Shut off Genes that Cause Brain Cancer. Advances in Medicine And Biology 180.

32. Drug Design - Novel Advances in the Omics Field and Applications. The Rational Drug Design to Treat Cancers. 95-115.

33. Abbreviated Key Title: EAS J Biotechnol Genet ISSN: 2663-189X (Print) & ISSN: 2663-7286 (Online) Published By East African Scholars Publisher, Kenya.

34. 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). NACS.000634. 2021.

35. The Impact of Sequencing Human Genome on Cancer Chemotherapy (2021) Journal of Cancer Research Reviews & Reports.

36. Journal of Cancer Research Reviews & Reports- The Impact of Sequencing Human Genome on Cancer Chemotherapy.

37. A Hameed Khan (2021) The Impact of Sequencing Genomes on the Under¬standing of the Origin of Life on Earth. Bi¬omed J Sci & Tech Res 40.

38. Hameed Khan A (2022) The Impact of Sequencing Human Genome on the Genetically Engineered Life. J Cancer Research and Cellular Therapeutics 6.

39. Hameed Khan A (2022) Sequencing the Human Genome to Study the correlation between Genes and Violence. Horizon publishers.

40. Hameed Khan A (2022) The Impact of Sequencing Human Genome on the 2nd Genesis on Earth. Journal of Current Trends in Agriculture, Environment and Sustainability, Katalyst publisher.

41. Hameed Khan A (2022) Assessment of Human Genome Sequencing on the New-World Order, Research Aspects in Biological Science 4.

42. Hameed Khan A (2022) The Impact of Sequencing Human Genome on Novel Drug Delivery Method to Treat Cancers. International Journal of Genetics and Genomics 10: 64-78.