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The Impact of Sequencing Human Genome on New Eugenic

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Abstract

This abstract attempts to explore if newlywed couples should have children either by chance or by choice. According to new eugenic, it is not the authority, but parents who decide if their children would be an acceptable member of the human society. Parent should be fully aware that having children by chance presents the greatest risk of pain and suffering from serious illnesses such as Sickle Cell Anemia, Muscular Dystrophy, Color Blindness, Schizophrenia, Bipolar Disorder, Epilepsy, Parkinson Disease, Huntington Chorea, etc. Most of the population of prisons, mental Institutions, and asylums are the result of parents having children by chance. Now, we have sequenced the entire human genome, it is easy to select safe egg and sperm by sequencing and comparing with Reference Sequence to identify any deleterious mutations which are responsible for causing these diseases. Mutations are caused by exposure to radiations, chemical and environmental pollution, viral infections, or genetic inheritance. Current advances in genetic engineering have provided the couple choices to cut, paste, copy, or move around genes from one species to another that is from man to man or to mouse, from mouse to monkey. Given the choices, should the couple be advised to seek experts to perform genetic engineering to remove bad genes and add good genes to enhance good traits. With all the precautions if a severely ill child is born and if sequencing identify the mutated genes, I could show how to design drugs to shut off bad gene.

Keywords: Eugenic, Sequencing Genome, Mutations, Genetic Engineering. Diversity, Genomic diseases, Inbreeding, AZQ

A Note to my readers: The Impact of Sequencing Human Genomes are a series of lectures to be delivered to the scholars of the National Youth League Forum (NYLF) and the International Science Conferences. NYLF scholars are the very best and brightest students selected from all over the USA and the world brought to Washington by Envision, an outstanding organization that provides future leaders of the world. I am reproducing here part of the lecture which was delivered at the International Science Conference that was PCS 6the Annual Global Cancer Conference held on November 15-16, 2019, in Athens, Greece.

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

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

Introduction

Since the dawn of human civilization, we have asked ourselves three important questions: Who are? Where have we all come from? What was it that made us this way? Soon after the formation of our Solar system about four and a half billion years ago, first life giving molecule appeared. A million-lightning strike Earth each day. At some remote corner of the Earth, a lightning struck at a cloud of gases containing, ammonia, carbon dioxide, methane water near a rock containing phosphorous forming the first information molecule nucleotide. The essence of life is information, and the information is located on four nucleotides, and they are Adenine (A), Thiamine (T), Guanine (G) and Cytosine (C). Together they form a string of molecules called the DNA (Deoxyribonucleic Acid). These nucleotides combine and recombine in the presence of enzymes and obeying the laws of Physics and Chemistry organized themselves to become alive which gave rise to the earliest life on Earth. We found no soul, no Holy Spirit, and no ghost in the biological machine. Life evolved and more complex life forms arose following the Darwinian evolution. We are confronted with major ethical issues the moment we realized that Darwin's Theory is not a theory of evolution, but a fact. Following the fossils record, we know with fair certainty how life could have evolved at some remote corner of the Earth about three and a half billion years ago and how it crawled on evolutionary path to fly at will or stay still. In a three-billion-year journey across time, it reached us and help us develop our language, our mind, and our consciousness We are the most intelligent of all living creatures on Earth. We are so intelligent that we ask questions about ourselves who we are and where have we all come from? What was it that made us this way? Now, we can answer the most fundamental question we have asked ourselves since the dawn of human civilization; Who are we? Where have we all have come from and what was it that made us this way. The answers to these questions are based on Darwinian evolution and are embedded in the nucleus of every cell of our body. We are the result of three and a half billion years of Darwinian Evolution.

Our Origin and Expansion

Fossils from the three and a half billion old rock found in Australia showed the impression of earliest fossils on ancient rocks. Fossils found in the younger and younger rocks showed the greater complexity from impression to bony structures until you come to the 250 million old rock from Jurassic Period, when we found the largest bones of Dinosaurs, the might beast that ruled planet Earth for over 150 million years. Sixty-five million years ago, a steroid hit planet Earth and wiped all the Dinosaurs out from the face of Earth. No human bones were found in any of those layers of rocks until we come to the three hand a half million old rock found in Hader Valley in Ethiopia where we found the first human bones belonged to an 18-year-old Chimp/woman called Lucy, mother of us all. Who walked out of Africa about three and a half million years ago? Her children left Africa in search of food, shelter, and water. Within in three and a half million years, their number increased to eight billions, and they covered the entire planet settling in all seven continents and in more than two hundred nations. According to a United Nation population projection survey, we are adding a quarter million children every day and about 100 million each year to this planet. If we continue the present trend, by year 2060, the population of the world is most likely to increase to ten billion. Our planetary resources are limited. We will not be able to feed, clothe and house adequately to all ten billion souls.

Our book of life is written in the nucleus of each cell. Reading the total genetic information that makes us is called the Human Genome. We decided to read our entire genome letter by letter, word by word and sentence by sentence under a project entitled The Human Genome Project. The goal of the human genome project is to determine the total number nucleotides base pairs and the order in which they are arranged that make us human. A string of nucleotides called the Deoxyribose Nucleic Acid (DNA) and identifying how DNA got together to make genes and mapping and sequencing all the genes of the human genome from both a physical and a functional standpoint.

The Sequencing of the Human Genome which is not only reading the entire book of life of human being letter, by letter, word by word and sentence by sentence, chapter by chapter but also the order in which these letters are arranged called sequencing, is the greatest discovery of all times. The sequencing of the Human Genome will answer the most fundamental questions, we have asked ourselves since the dawn of human civilization; what it means to be human; what the nature of our memory is and our conscientiousness and our development from a single cell to a complete human being; the biochemical basis of our senses; the process of our aging; the scientific basis of our similarity and dissimilarity. Similarities that all living creatures from a tiny blade of grass to the mighty Elephants including man, mouse, monkey, mosquitos, and microbes are all made of the same chemical building blocks, the nucleotides, and yet we are so diverse that no two individuals are alike, even identical twins are not exactly identical; they grow up to become two separate individuals.

To understand the basis of all diseases, we must read and understand the total genetic information that makes us humans that is to read the genome of a healthy human being (called the Reference Sequence) and compare with the sick person's genome to identify the spelling errors in the genome responsible for causing the disease. That is how the story of our book of life begins: As we all know that we are the loving union of our parents. Our mother's egg receives our father's sperm, and we are conceived. The fertilized egg carries complete information to make us. More than seventy years ago, the Nobel Laureate, Irvin Schrödinger, was the first person to propose that the hereditary molecule must contain a "code-script" that determined "the entire pattern of the individual's future development and of its functioning in the mature state". This was the first clear suggestion that genes contained some kind of "code". Now, we know that the essence of life is information and genes are the bearers of that information, carrying it in a tiny, complex code inside every cell of our bodies. If we examine for comparison, the fertilized egg of a human with the egg of mouse, and monkey under a microscope, we observed that all fertilized eggs look the same and yet first fertilized egg carries the instructions to make a man, the second carries the information to make a mouse and third carries the information to make a monkey. We are certain that there exists a secret code within those fertilized eggs to make different species; Schrodinger called that secret code, the Script Code, now known as the Genetic Code. To understand the secret code, we must examine the internal structure of the fertilized egg. He proposed that we examine three "C". **The first C** stands for the chromosome, the coloring bodies present inside each cell. The traits to make man, mouse or monkey must be located on the Chromosomes. These traits must be held together tightly by **the second C**, the covalent bonds. As the living cells grow, they must have the ability to copy the instructions accurately that copying is **the third C**. The Genetic Code to make man, mouse or monkey must be written on the chromosomes. Based

on this information Crick and Watson broke the Genetic Code and unlocked the secret of life. If we unlock the secret of life, we will understand how evolution puts the traits together over millennia to separate man, from mouse and mouse from monkey. By unlocking the secret of life, we can understand how the normal cells work and how the normal cells become abnormal leading to all diseases including cancerous.

On further examination, we found that the chromosomes are made of four chemicals and information is located on them and these four molecules are called nucleotides bases. These bases are made of Deoxy Ribonucleic Acid (DNA). DNA is made of a string of nucleotides. It is a storehouse of information and is made of the same four nucleotide bases and they are: Adenine (A), Thymine (T), Guanine (G), and Cytosine (C). According to Crick's Central Dogma, the information flows from the DNA which is transcribed into RNA which is translated in Ribosome into proteins [1]. RNA is converted into an active form and is transcribed into mRNA (or messenger RNA after splicing out noncoding DNA) and by converting Thymine to active form Uracil (U) and from a double stranded DNA to a single stranded RNA and where the sugar Deoxy Ribose is replaced by sugar Ribose. The mRNA is translated by Ribosome into proteins. Gene Expression begins in Ribosome when a 4-letter genetic text is converted to a three-letter Codon which code for a single amino acid. By comparing Gene Profiles of normal genes with mutated genes, one can identify with precision and accuracy the exact location of mutated (altered or damage) nucleotide responsible for causing the disease. Comparing Gene Profiles is an excellent diagnostic method which helps us design drugs to specifically shut off the mutated genes.

Seventy years ago, Schrödinger predicted secret code of life using such a poor resolution microscope that we don't even use in our high school today. Instead, we use electron microscope. We can magnify the same fertilized egg to a million times of its original size, almost the size of a house. What we observe inside the fertilized egg is very analogous to the house. The house has a kitchen; the cell has a nucleus. Suppose your kitchen has a shelf which contains 46 volumes of cookbooks which contain 24,000 recipes which carry instructions to cook food for your breakfast, lunch, and dinner. The nucleus in the fertilized egg contains 46 chromosomes; (23 from our mother and 23 from our father), which carry 24,000 chapters called genes. Genes are units of inheritance which code for all 20 amino acids. Hundreds of amino acids join to form a protein and thousands of proteins interact to make a cell. Millions of cells interact to make an organ and several organs interact to make a man or a mouse or a monkey. The number and the order of the nucleotides determine the composition of a species [2,3].

If the cookbook in your kitchen is written in English language, it uses 26 letters, but the book of life of all living creatures is written in 4 letters and they are A, T, G and C. These are the initials of four chemicals called nucleotide base pairs found the nucleus of all living cells. Nucleotides are made of sugar Ribose (Deoxy Ribose in DNA and Ribose in RNA), a phosphate group and one of the four Nitrogen bases, two Purines and two Pyrimidines and the Thymine is converted to more soluble Uracil in RNA. These molecules are found in the nucleus of all living cells from a tiny blade of Grass to mighty elephant including man, mouse, and monkey. The total genetic information to make any living creature is based on the above four-letter text and out of these four letters, only three letter called Codon which carries the Genetic Code for an amino acid (such as GUU is for amino acid Valine, GCU is for Alanine, GAA is for Glutamine etc.) the building blocks for all proteins. Sixty-four codons code for 20 amino acids and codons for all 20 amino acids have been decoded. All living creatures use the same genetic code. A string of these nucleotides is called the DNA (Deoxy Ribonucleic Acid). Reading the number and the order of nucleotides are called genome sequencing [4, 5].

As I said above, a gene is a piece of DNA. Out of four nucleotides text, three letters code for an amino acid called codon. A gene is made of several hundred codons. On a piece of DNA, a gene is identified by a start and a stop codon. The start codon is AUG which codes for the amino acid Methionine and there are three stop codons, and they are UAG, UGG, and UGA. The extension of DNA synthesis stops once the one of the three stop codons appears. A gene codes for a protein. We found that the smallest gene in bacterial genome and the largest gene is in Duchenne Muscular Dystrophy genome. To code for a protein, between start and stop codon, a gene has accumulated several hundreds to several thousand codons. A single mutation (change or damage) in the coding region of a single codon will alter the gene function. Mutation is caused by either exposure to radiations, chemical or environmental pollution, genetic inheritance, viral infections or DNA deletion, insertion relocation or inversion. Mutation can be good, bad, or neutral. A good mutation can convert a single cell organism to a multicellular creature resulting in evolution. A bad mutation is responsible for coding for a wrong amino acid responsible for causing diseases. A neutral mutation can serve as a gene marker identifying its presence close to a good or a bad gene. By sequencing Human Genome, we have identified a total of 24,000 genes out of which 16,000 are good genes, 6,000 bad genes and 2,000 pseudo or neutral genes. Less than 2% of our genome codes for proteins. The remaining 98% of our genome carry pieces of DNA picked up from bacteria and viruses during evolution which serves as switches, promotors, enhancers etc. The greatest Darwinian transformation is controlled by switches. By switching on and off a gene, the body plan gene called the FOX gene can bring the evolutionary changes in the body. Genes code for protein, it is the switches that turn genes on or off.

As I said above, Gene Expression begins in Ribosome when a 4-letter genetic text is converted to a three-letter Codon. By comparing Gene Profiles of normal genes with mutated genes, one can identify with precision and accuracy the exact location of mutated (altered or damage) nucleotide responsible for causing the diseases. Comparing Gene Profiles is an excellent diagnostic method which helps us design drugs to specifically shut off the mutated genes. Delivering drugs from injection site to the target site is the essential way of treating diseases. We cannot design novel drugs unless we find the abnormal mutations responsible for causing that disease. The reading of the total genetic information that make us human is called the Human Genome. The reading the entire book of our life is authorized by the US Congress under The Human Genome Project.

In 1990, US Congress authorized three billion dollars to our Labs at NIH to decipher the entire Human Genome under the title, "The Human Genome Project." We found that our genome contains six billion four hundred million nucleotides 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 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 in nucleotides

base pairs. Before sequencing (determining the number and the order of the four nucleotides 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 nucleotide base pairs on each Chromosome, but also the number of genes on each chromosome [6].

The following list provide the details composition of each Chromosome including the number of nucleotides and the number of genes on each Chromosome:

We found that the Chromosome-1 is the largest Chromosome carrying 263 million A, T, G and C nucleotides bases and it has only 2,610 genes. The Chromosome-2 contains 255 million nucleotides bases and has only 1,748 genes. The Chromosome-3 contains 214 million nucleotide bases and carries 1,381 genes. The Chromosome-4 contains 203 million nucleotide bases and carries 1,024 genes. The Chromosome-5 contains 194 million nucleotide bases and carries 1,190 genes. The Chromosome-6 contains 183 million nucleotide bases and carries 1,394 genes. The Chromosome-7 contains 171 million nucleotide bases and carries 1,378 genes. The Chromosome-8 contains 155 million nucleotide bases and carries 927 genes. The Chromosome-9 contains 145 million nucleotide bases and carries 1,076 genes. The Chromosome-10 contains 144 million nucleotide bases and carries 983 genes. The Chromosome-11 contains 144 million nucleotide bases and carries 1,692 genes. The Chromosome-12 contains 143 million nucleotide bases and carries 1,268 genes. The Chromosome-13 contains 114 million nucleotide bases and carries 496 genes. The Chromosome-14 contains 109 million nucleotide bases and carries 1,173 genes. The Chromosome-15 contains 106 million nucleotide bases and carries 906 genes. The Chromosome-16 contains 98 million nucleotide bases and carries 1,032 genes. The Chromosome-17 contains 92 million nucleotide bases and carries 1,394 genes. The Chromosome-18 contains 85 million nucleotide bases and carries 400 genes. The Chromosome-19 contains 67 million nucleotide bases and carries 1,592 genes. The Chromosome-20 contains 72 million nucleotide bases and carries 710 genes. The Chromosome-21 contains 50 million nucleotide bases and carries 337 genes. Chromosome-22 contains 56 million nucleotides and carries 701 genes. Finally, the sex chromosome of all females called the (X) contains 164 million nucleotide bases and carries 1,141 genes. The male sperm chromosome contains 59 million nucleotide bases and carries 255 genes.

If you add up all genes in the 23 pairs of Chromosomes, they come up to 26,808 genes and yet we keep on mentioning 24,000 genes needed to keep us function normally because some genes don't code for any proteins. Out of 24,000 genes, we have identified 16,000 good genes, 6,000 bad genes and 2,000 Pseudo genes. As I said above, 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 functional 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, hundreds of tissues interact to give an organ and several organs interact to make a human.

Not all genes act simultaneously to make us function normally. Current studies show that a minimum of 2,000 genes are enough to keep human function normally; the remaining genes are backup support system, and they are used when needed. The non-functional genes are called the Pseudogenes. For example, millions of years ago, humans and dogs shared some of the same ancestral genes; we both carry the same olfactory genes, only in dogs they still function to search for food. Since humans don't use these genes to smell for searching food, these genes are broken and lost their functions, but we still carry them. We call them Pseudogenes. Recently, some Japanese scientists have activated the Pseudo genes, this work may create ethical problem in future as more and more Pseudo genes are activated. Nature has good reasons to shut off those Pseudogenes.

On April 3, 2003, we sequenced the entire Human Genome. We not only read the entire script of our genome, letter by letter, word by word, sentence by sentence, but also, we also read the number of letters and the order in which they are arranged (sequence) called under the title, "The Human Genome Project". We found that less than two percent of the Gene in our Genome codes for proteins and the rest is the non-coding regions which contains switches to turn the genes On or Off, pieces of DNA which act as promoters and enhancers of the genes. Using restriction enzymes (which act as molecular scissors), we can cut, paste, and copy genetic letters in the non-coding region which could serve as markers and which has no effect, but a slight change in the coding region makes a normal cell become abnormal or cancerous. Recent studies showed that mutations can also occur in switches, promotors and enhancers which are present in the non-coding regions are also responsible for some unusual diseases. We need to go back and look at these regions more carefully.

Our Genome provides the genetic road map of all our genes, past, present and future. For example, it can tell us how many good or bad genes we inherit from our parents and how many of those gene we are going to pass on to our children. If a family has too many bad genes, and have a family history of serious illnesses, we can break off the information flow and stop having children or stop donating mutated eggs and sperms.

Our Search for Unknown Diseases has Come to A Closure

There are two most powerful implications of the human Genome Sequencing. One of them is that we have come to closure. What it means is that we have the catalog of all genes in the Human Genome, we can search the entire genome and locate the desired gene. We will not wonder in the wilderness anymore. Everything there is to know about human health and traits are written on these genes in nucleotide sequences. Our Genomes provides the catalog of all genes.

We can scan the whole genome (Reference Sequence) for its response to a given situation. When we look at a normal cell and compare with an abnormal cell, we see the differences. Or when we compare their gene expression looking for a specific proteins, from a specific genes and for a specific nucleotide sequence, we can identify a specific disease.

In the olden days, before sequencing human genome, a physician would order several tests and would say to his patient, I don't know what is wrong with you, I will see if any of these tests show if my guess is right and if it is wrong, he will recommend few more tests to see if he could identify the illness. The guesswork and the trial-and-error days are over. ***Now, after sequencing the human genome, the physician would say I don't know what is wrong with you, but I do know where to find it. It is written in your Genome***. It would be easy for a Physician to scan the patient entire genome and compare against the Reference Sequence to identify the mutations responsible for causing the disease. We will take a small blood sample of the patient, separate his WBC, extract DNA, sequence his Genome and compare with the Reference Sequence letter by

letter, word by word by word and sentence by sentence, we can easily identify the mutations responsible for causing the disease. The sequencing result will provide the best diagnostic method to identify a disease.

Our Genome is not just a diagnostic road map of our genes, it also tells us to clone the good genes and shut off the bad genes. Using the good genes, it also tells us how to make its large-scale protein for worldwide use such as Insulin and Human growth hormone. On the other hand, identifying the bad genes and tell us how to design drugs to shut off bad genes responsible for causing Cancers, Cardiovascular disease, and Alzheimer. We have already demonstrated that using the genetic engineering techniques, we can cut, paste, copy, and sequence a good gene for industrial scale preparation such as Insulin to treat 300 millions of diabetic around the world. Similarly Human Growth Hormone, once available in minute quantities from the pituitary glands of humans' cadaver can now be produced in large amount in the Labs using the same genetic engineering method. Many valuable medicines are being produced including Interleukin-II, for the treatment of the Kidney cancer, Factor-VIII for treating Hemophilia, Hepatitis B vaccine, Eleuthero protein for anemia, Whooping cough vaccine, and for Somatotropin for treating dwarfism.

Once the good and bad genes are identified, we know that the good genes code for good proteins which keep us healthy, and the bad genes produce bad protein that make us sick. Genome sequencing of bad genes start a new era of Genomic Medicine which is based on the genetic make-up of the individuals. The next step would be to design drugs to shut off the mutated genes. Gene Therapy will work if the disease is caused by a single gene mutation. Drug Therapy will work if multiple genes are responsible for causing diseases such as Cancers, Cardiovascular diseases, and Alzheimer.

Chance or Choice

Conception by chance provides random gift at great risk. Sequencing embryo before conception protects children from horrendous diseases such as Tay-sack, dwarfism, Down Syndrome, Trisomy etc., while Choice provides deliberate genetic modifications to achieve perfection. Scientifically, there is no difference between achieving gifts by chance or by choice. We all strive to achieve perfection in our profession. Achieving perfection is not a sin. Force abortion is a sin; segregation is sin; labelling people as feeble minded is a sin; sterilization against the wishes of the person to eliminate feeble mindedness is a sin. Euthanasia is a sin. Will we reject non-perfect humans? When such thoughts allow to go wild in leadership, they produce conditions to justify Holocaust. Nazis used to justify their treatment of Jews, disabled people, and other minority groups to slaughter millions of innocent people. No authority should have such powers.

In new eugenic, it is the parents who pick and choose to save or not save a life, but not the authority. They have the right to examine the sequence of an embryo and decide if they choose to eradicate human suffering by removing a deadly genetic disease running in the family. Not using genetic modification to eliminate illnesses is unethical. It condemns children to unnecessary suffering and denies them the cure. It is the parents who also decide if they would like to alter the existence of new genes or to enhance desired heritable traits (not permitted at this time). Families of children with Down syndrome will also be free to choose not to have prenatal testing or chose to continue a pregnancy after a prenatal diagnosis. Even though screening tests indicate an increased risk for birth defects, including Down syndrome. Parents will also have the option to preselect humans with qualities based on ideal healthy person. We are already living in this world. Tests on dozens of genetic tests have become standard for healthy babies. These tests often predict the end of the pregnancy. In Europe, 90% Down Syndrome babies are terminated. We are preselecting humans based on their medical conditions. We are advancing these modification slowly and respectfully.

Americans are very hesitant; they wonder what happens once we open the door? It cannot be closed forever. Once mutated traits are allowed to be altered, vanity traits cannot be left alone. As we allow the genetic traits to be enhanced, the need will grow, and our ethical problems will also grow. For example, if you control Alzheimer why not enhance metabolism, introduce perfect eyesight, achieve height, produce big muscle, give full hair, and extra ordinarily intelligent etc. Modifying human traits could become a standard in future. During enhancement, what if the new genes accidently effect or interact with other genes resulting in disastrous unintended consequences. We don't know the interplay of all genes to avoid unintended consequences. Checking for accuracy before human trial is most important. Could a country be allowed to produce an army of super soldiers? It would be a mistake to stop genetic research just because of such dangers.

Genetic engineering in plants is not new. Since the beginning of the agriculture age, farmers have been modifying plants and animals for thousands of years. By selective Breeding in plants and animals, we bread plants and animals that are beneficial to us. – the code of life is DNA in all living creatures, a complex molecule that guide growth, development function, and reproduction. DNA is information molecule. Information is included in this molecule includes Clotting factor and Growth hormones in humans, but in plants for example, Tomato was given an extra gene to give longer shelf life. It also carries information to give Super muscle, fast growing Salmon, Featherless chickens, fast growing plants, Fluorescent Zebra fish.

In recent times, a revolutionary technology called CRISPER-CAS-9 enters the stage. It makes Gene editing faster and inexpensive. It could change our methods of manipulating genes forever. CRISPER is faster cheaper and editing short piece of repetitive DNA. CAS-9 it is an enzyme protein which cuts and slice DNA at a specific site. It prepares a guided complimentary DNA which is aligned to mutated DNA. CAS-9 could cleave off the mutated DNA and replace it with the correct DNA. Its outstanding achievement in introducing new traits in plants, animals, and bacteria to prevent diseases like malaria are appropriate and beyond question. A single spelling error in the genetic code in our genome could cause about three thousand genetic diseases. Should we create a modified human by making irreversible changes in the human gene pool? The means to change human embryo already exist. It will alter our entire genome. If germ-line gene therapy is permitted in future, engineered traits will be passed on to our children and could spread for generations; we could modify the gene pool of entire humanity. Using CRISPER, we could replace undesirable traits. By making a perfect race, we create ethical issues. The functions of the new traits in designer babies are completely unknown to us. Will they be far superior in mental and physical capabilities? By giving new traits, we give designer babies unfair advantage. CRISPER could introduce genes which could increase heights, give unusual physical capabilities, and introduce intelligence. What about those babies who have not received this advantage? The designer babies will win because their talents are created

in the Lab. Intelligent babies may not be required to study hard, but your child who has not received such traits may be at disadvantage. Such studies could create new ethical problems. CRISPER-CAS-9 is initially conceived beneficial and efficient in today's world. Its misuse present great danger to science and society. It could be misused trying to purify human race, for example, it could replace genes for brown eyes with blue eyes in the embryo. To prevent its misuse, legislation is required around the world to have concrete limit on its use on humans. How the technology is used, to protect the current and future use on humans.

Traits are expression of genes. By selective breeding, at each generation those traits got more pronounced. After thousands of years, almost all these plants and animals are vastly different from its predestinated stage. If humans have been changing Genes slowly for millennia, why rapidly genetically modified GMO is so different? Selective breeding is successful if you are lucky, genetic modification is precise, accurate and fast. We can choose traits we want. Make grow fruits bigger, immune to pests. Why are people concerned about? We must be fully aware of unintended consequences. The gene flow can introduce new genes in plants and animals which might interact with the natural genes and could create unknown genes of unknown functions.

Americans welcome GMO crops, not Europeans. Some environmentalists in Europe are trying to stop the development of biotechnology use in this age is not achievable. There might be cases where unintentional spread of engineered DNA could occur. There have been cases of GMO plants growing where they were not planted, and traces of modified genes found in foreign crops. The GM plants can't run Wilde in timing. To prevent mixing, many farmers grow crops creating buffer zone to prevent unintentional mixing of plants or at the minimum of GMO crossing with non-GMO food. With repeated testing, we found GM crop is not different from the non-GM crop. Although there was some concern from the very beginning, after 30 years of study the results are in, and we conclude that GM plants are no riskier than the non-GMO plants. Plants that have been engineered to be toxic to pests save to humans and animals. For example, Bt crop carries a gene borrowed from bacterium Bacillus Theragnosis (Bt) that carries an engineered plant gene that produces a protein that destroys the guts and digestive system of a specific insect pest. The plants make its own pesticide. Synthetic pesticides that spray on farms and fields are washed off by rains and flows down to lakes and rivers. These toxins are concentrated in microbial planktons. Planktons are the food of fish. These pesticides are concentrated in fish and guess who eat fish, we do. The toxins end up our systems. On the other hand, the poison in the Bt crops is inside the plant's genome and cannot be removed and washed off by rains. Bt carrying plant genome is harmless to humans, but deadly to insects. Bt crop produces a protein that is tailored to be specifically designed to affect the digestive system of insects; it is completely harmless to us. Another example is coffee which is poison that kills insects, but it is harmless to us; Chocolates is poison to dogs and harmless to us. Today, 90% of all crops we grow in US is herbicide resistant. GMO is alley not an enemy of humanity. GMO crops is helping to save crop with minimum side effect to our environment.

Genetic research in human should be allowed to continue after careful consideration by participating further research by caution, reason, oversight, and transparency. Genetic engineering might be extending natural evolution of intelligence species in the Universe. We might end diseases, extend our life span, and travel to stars. The future is approaching no matter what. It is a reality full of opportunities and challenges.

We could control Aging which is caused by the accumulation of the damage to ourselves over the years. Genetic engineering could slow down aging by borrowing genes from Lobsters which seem to have a very long life. Is it achievable? Next, we will engineer human digestive system to digest high energy food by eliminating many diseases such as obesity. Could we improve our Immune system and become immune to most diseases? It will prepare astronauts for deep space travel. It will also prepare them to cope with different environmental conditions on exo-planets which will be helpful for keeping them alive in hostile environment.

Genetic engineering to eliminate deleterious genes which are responsible for causing serious illnesses are funded by NIH. Hundreds of clinical trials of gene therapies are underway. Germ-line gene therapy experiments to enhance traits to achieve perfection are forbidden by government agencies, but private laboratories could still provide such services. Let me explain this problem. Genome of Somatic cells you keep as long as you live, germ cells that is the genome of egg and sperm you pass on to your children and their children. Patients who are suffering from say sickle cell anemia, a blood disease common in African American populations or Cystic Fibrosis common in European Americans, are carriers of these mutations. In future, we may be able to correct that gene. It is the somatic mutation. When the patients leave this world with corrected gene, the altered gene leaves with them. As I said above, when germ-line alterations are made such as changes in X and Y-Chromosome, you pass on that altered gene in the embryo to your children. The altered gene in the fetus would be passed on to your grandchildren and great grandchildren and their future generations. That gene may pass on to thousands of future generations. Most people would agree that you don't have the right to alter the future of your progeny after you are long gone. No governments and no religions should allow germ-line alterations. However, genetic enhancement to achieve perfection is not funded by NIH at this time, because it is considered unethical. As I said above private research firms are not forbidden. Since I was involved in conducting NIH Study Sections to approve funding, I am in favor of providing some funds to keep control on what private investigators are doing behind closed doors. This kind of work is expensive, and investigators always need funds. Once they receive NIH funds, they are to share the results of their discoveries with us annually and are answerable to study section reviewers' questions if they wish to receive additional funds in future

As the cost of development of second generation Nanopore Sequencers will come down to less than a thousand dollars per genome, as a part of medical record, we must require sequencing the genome of every man, woman, and child on the face of Earth. The ethical problem we confront is to ask if each person wants to see the genetic profile of his genetic make-up. There might be bad news. Your genome may carry deleterious mutations. Some of them may become activated at a later age. It is an individual choice. Personally, I would like to see my genome sequenced because I would prepare myself for future health problems. If there is something bad, I can plan my future; what I should do, what I should not do. I would be able to take care of financial planning for dependence; medical planning for oneself and family etc. are essential. It is an individual choice.

We have deciphered the entire genome twenty years ago, now

we are rapidly approaching our goal to complete the personal genome of all eight billion people that is to inscribe the total genetic information of all people on their personal computer chip (DNA Profile Chip) at a cost of a thousand dollar per genome during the next couple of years. It is only a matter of time. You always carry your DNA chip with you. In case of medical emergency, the hospital staff will compare your genetic profiles and would be able to provide instant medical help.

As I said above, in genetic engineering, we have not only learned to cut, paste, copy, and sequence a gene, but also to move genes from man to man, man to mouse, from mouse to monkey. There are eight billion people live on Earth. It is time to think about sequencing the genomes of all living creatures on Earth. So far, we have identified three million known and thirty million unknown species on Earth. To feed the bourgeoning population of the world, we could borrow useful genes from other species and splice in plants, animals, and bacteria to produce, new food, new fuel, and new medicine to treat every disease known to mankind. Could it create new ethical problems?

New Food

To provide most nutritious food to all of us, we must cut, paste, and copy codons of all essential amino acids in edible plants or seeds. There are more than 4,000 molecular scissors called Restriction Enzymes have been isolated from Bacteria. There are more than 3,500 multi-functional Type II Restriction Enzymes which are commercially available to cut, paste and copy fragments of essential amino acid codons either into double stranded DNA, or into a single stranded RNA of various lengths.

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 flowering plants exist on Earth today. We cultivate just about 150 plants species for Agriculture purposes. To feed over eight 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 nine 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.

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 (after splicing out the non-coding nucleotides). 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. When double stranded DNA is transcribed into a single stranded m-RNA, the nucleotide Thiamin (T) is converted to Uracil (U). 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 Codons 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).

Rice (*Oryza sativa*) is one of the most important crops in the world. Rice, wheat, and maize 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 to prevent blindness in children. Using the same techniques of bioengineering, 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) as internal pesticide 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 nine in a single Rice genome. It depends upon the ease of insertion of a codon using a specific restriction enzyme. We face a new ethical problem; it is known for centuries that when food supply increases so does the population. We add a million new mouths to feed each year. Should we produce more food or control the population?

New Fuel

While millions of people are starving, we are generating ethanol as fuel from Corn to run our cars, is it ethical? Ethanol is also converted to Carbon dioxide contributing to Global Warming. Each year, we collectively release 110 million tons of pollutants in our atmosphere. In addition, during 2017, the Methane emission alone reached 596 million metric tons primarily from agriculture – particularly from red meat and dairy producing animals and to a lesser extent from Rice farming. Although Methane is short-lived in the atmosphere than Carbon dioxide but has a stronger Global Warming Effect. Of all the pollutants in the atmosphere, the major stable pollutant is Carbon dioxide. Carbon dioxide gas is responsible for causing Greenhouse Effect (CO_2 acting as a glass ceiling of a greenhouse trapping Sun's energy heating the internal environment causing global warming). Before the Industrial Revolution, the level of Carbon dioxide in our atmosphere was 175 PPM. After Industrial Revolution, the level of Carbon dioxide has gone up several fold. Today we have measured the level to be 400 ppm Carbon dioxide in our atmosphere and if it continues to increase at the

current level, it is going up to 800 ppm by 2050. The main source of Carbon dioxide is from the decomposition of trees, volcanos and Oil refiners. There are more than a billion cars in the world today. Transportation alone produces 20% of the Carbon dioxide. Excessive Carbon dioxide is not only responsible for Global Warming, but also it destroys Coral Reef, melt polar Ice Caps and erode coast lines causing sea level rise. To mitigate emission of this level, we need to develop a massive technological method to liquify Carbon dioxide and release at the ocean floor.

Marine cyanobacteria called Prochlorococcus thrive on the ocean floor. Their Chloroplast in the Chlorophyll Genome is responsible for converting Carbon dioxide to Oxygen. By conducting Photosynthesis on the ocean floor, these Cyanobacteria convert Carbon dioxide to their food Carbohydrate and produce Oxygen as a by-product. Fifty percent of the photosynthesis is performed by these bacteria at the ocean floor and half of the Oxygen we breathe today comes from them. Billions of Microbes grow layer upon layer forming a thick carpet on the ocean floor near heat producing source like hydrothermal vent.

In the Gulf of California, the Pescadores Basin contains the deepest ocean floor. At a depth of 12,500 feet, it is known to have high-temperature hydrothermal vent in the Pacific Ocean. Dense colonies of cyanobacteria, and tubeworms cling to rocks near the vent in high heat and noxious water. The chimneys on the ocean floor emits dark fluids that are rich in oil-like hydrocarbons and give off diesel-like smelly gases containing Methane, a fuel. Under deep dark ocean floor under tremendous pressure and extremely cold temperature a Cyanobacteria called Methano-coccus converts Carbon dioxide to Methane. In our Lab, we could sequence the Genome of these bacteria brought from the ocean floor and cut, paste, and copy their genes to produce large quantities of Methane in our Labs. Methane could be converted to Propane and Octane, a better fuel. Massive reforestation could remove excessive amount of Carbon dioxide from the atmosphere. Clean energy resources include Solar Panels, Wind Turbine, Geothermal energy, including nuclear energy. The major concern of using nuclear energy is that the Nuclear power plant produces energy by nuclear fission reaction producing a variety of long lasting nuclear radioactive waste products. We don't know how to destroy the radioactive waste, so we stored them in millions of barrels in Nevada as a gift for the future generations.

On the contrary, by conducting nuclear fusion reaction we can generate unlimited amount of clean energy as it is generated by our Sun. Nuclear fusion is a reaction in which two or more atomic nuclei such as isotopes of Hydrogen that is deuterium and tritium are fused under extremely high temperature and pressure to form Helium. The fusion reaction releases subatomic particles as energy. More energy is generated than used. For the first time ever, researchers have carried out a controlled nuclear fusion reaction, producing more energy than the amount pumped into the nuclear fuel to ignite the fusion. The successful experiment was conducted on Dec. 5, 2022, at the National Ignition Facility (NIF) at Lawrence Livermore National Laboratory. They succeeded after more than 60 years of research in which scientists and engineers have worked on designing laboratory equipment that can simulate the extreme temperatures and pressures that drive fusion in the cores of the sun and other stars and inside exploding nuclear weapons. Fusion can occur when two extremely energetic atoms slam together. The process causes the nuclei to coalesce into a single larger nucleus and emits a lot of energy. This process occurs in our Sun and other stars. Creating conditions for fusion on Earth involves generating and sustaining a plasma. Plasmas are gases that are so hot that electrons are freed from atomic nuclei. In the NIF experiment, scientists used a mixture of deuterium and tritium which served as the nuclear fuel. The reaction fused the two heavy isotopes of Hydrogen, forming Helium. To drive the reaction, 192 high-energy lasers fired simultaneously on a centimeter-sized cylinder that held a spherical container the size of a ball bearing. The sphere was filled with the deuterium-tritium fuel and was cooled cryogenically forming a layer of ice on the sphere's inner surface. Directing the laser beams at the cylinder wall generated an intense flux of X-rays that bombarded the sphere. The radiation produced powerful compressive forces that caused the sphere to implode. The implosion heated the gases to millions of degrees for a few billionths of a second, igniting the fuel and triggering fusion. NIF researchers reported that the lasers pumped 2.05 MJ of energy into the target, and the fusion reaction generated 3.15 MJ of energy. Scientists were successful getting more energy out of fusion reactions than the energy required to create them. Unlimited amount of clean energy can be produced free from environmental pollutants such as Carbon or Radioactive waste particles. Years of development are needed before fusion power plants can become a reality. Once fusion power plants start running, the World Bank should provide loan to poor nations to generate all the energy they want. Is it ethical to use Corn as a fuel not as a food?

New Medicine

As I said above, out of 24 thousand genes in our genome, we carry sixteen thousand good genes; six thousand bad genes or mutated genes which are responsible for causing six thousand diseases and two thousand Pseudogenes which are broken and have lost their functions. We also learned that about a minimum of 2,000 genes are essential to maintain a human life and the remaining genes are backup or supporting genes to provide immediate help if needed. Using the Restriction Enzymes, like EcoR1, we could cut out all good and bad genes from the human genome to sequence and clone them. We need to study bad genes as well as good genes to design drugs to shut off defected genes. Diseases are caused by either a single defected gene (called Mendelian genetic defects such as MS, color blindness, hemophilia etc.) or multiple genetic defects (such as Cancers, Cardiovascular diseases, or Alzheimer.).

The Product of Good Gene as Medicine

Before the genetic revolution, Insulin is extracted from pancreas obtained from the slaughtered animals which is used to treat old diseases such as diabetes; a tiny fragment of impurity could set anaphylactic shock and could kill the patients. Now, highly pure human Insulin is produced in Yeast or Bacteria by Genetic Engineering. Today, we treat more than 300 million diabetic patients worldwide without the loss of a single life using the same recombinant technology. Other products of Genomic Medicine such as Growth hormones and Hormone proteins to treat Hemophilia by factor VIII protein are being developed as genomic medicines by recombinant technology. Many valuable medicines are being produced including Interleukin-II, for the treatment of the Kidney cancer, Factor-VIII for treating Hemophilia, Hepatitis B vaccine, Eleuthero protein for anemia, Whooping cough vaccine, and for Somatotropin for treating dwarfism. We have also produced edible vaccines in maize, banana, and potatoes.

Large scale highly pure drug could be prepared using Polymerase Chain Reaction (PCR). The following ingredients are needed to produce large scale drug: First, we need a piece

of double stranded DNA which codes for the active ingredient of the medicine. Second, we need the four nucleotides (A/T and G/C). Third, we need 20-piece long DNA called forward and backward primers. Fourth, the most important enzyme the Taq-polymerase which is heat stable and is needed to complete the reaction. All we need is to heat the solution in water to 94 degree centigrade to break the Hydrogen bonds. As soon as the two single strands separate, the forward and backward primers join each strand, and the Taq-Polymer zip and attach the nucleotide base pairs to produce two double stranded DNA of the drug. Simply heating cooling to 74 degree centigrade and adding the nucleotides, we can produce large quantity of the highly pure drug.

In Gene Therapy, a single bad gene is replaced by a good gene. With single genetic defects, we could cut, paste, and copy good gene in a Vector such as flu virus and infect patients' WBC with the transgenic virus which replace bad gene with the good gene. In a single genetic defect, Gene Therapy works supremely well. For example, in the treatment of SCID (Severe Combined Immune Deficiency Syndrome) which is caused by a single genetic defect. But in multiple genetic defects such as in cancers, Gene Therapy will not work, but Drug Therapy will work. We could design drugs to shut off multiple genes and prevent it from producing bad protein or cancers.

How to Design Drugs to Shut off Bad Gene Variants?

We design drugs to shut off genes responsible for causing cancers because largest amount of funds is available by the National Cancer Institute (NCI), about $5B per year. Cancer is the leading cause of death and has surpassed the death of cardiovascular diseases. Over 636,000 people died of cancer; 1.9 million new cases will be diagnosed this year including 78,000 Prostate Cancer, 40,000 Breast cancer, 16000 Lung and Bronchus Cancer and 15,000 Colon and Rectal Cancer. Once diagnosed by Gene Sequencing, the next step is to design drug to shut off those genes. As I said above, if a gene variant is identified responsible for causing any illness, I would show you how to design drugs to shut off that gene variant. I describe below how I designed drugs to shut off cancer causing genes in animals and then translate the work in humans.

The Rational Drug Design to Treat Cancers

All three old age diseases that is Cancer, Cardiovascular Diseases and Alzheimer carry multiple mutated genes responsible for causing these diseases. In each of the above three diseases, it is the harmful mutated genes that code for wrong protein which causes these diseases. If we design drugs to shut off mutated genes in one disease, using the same rationale, we should be able to shut off bad genes in all three old age diseases. Although Coronary Artery disease is a complex disease, researchers have found about 60 genomic variants that are present more frequently in people with coronary artery disease. Most of these variants are dispersed across the genome and do not cluster at one specific chromosome.

Pro-drugs are designed to seek out the specific malignant gene which replicate faster producing acids. Aziridines and Carbamate moieties are prodrugs, stable in neutral and basic media, but sensitive to acid. Drugs carrying the Aziridines, and Carbamate moieties are broken down in acidic media, releasing true drug, generating Carbonium ions which attack DNA shutting off genes. Only the acid producing genes will be attacked no matter where they are located. It does not matter whether they are clustered or dispersed across the genome.

Shutting off Mutated Genes by Cross-Linking Double Stranded DNA

(By Nitrogen Mustard):

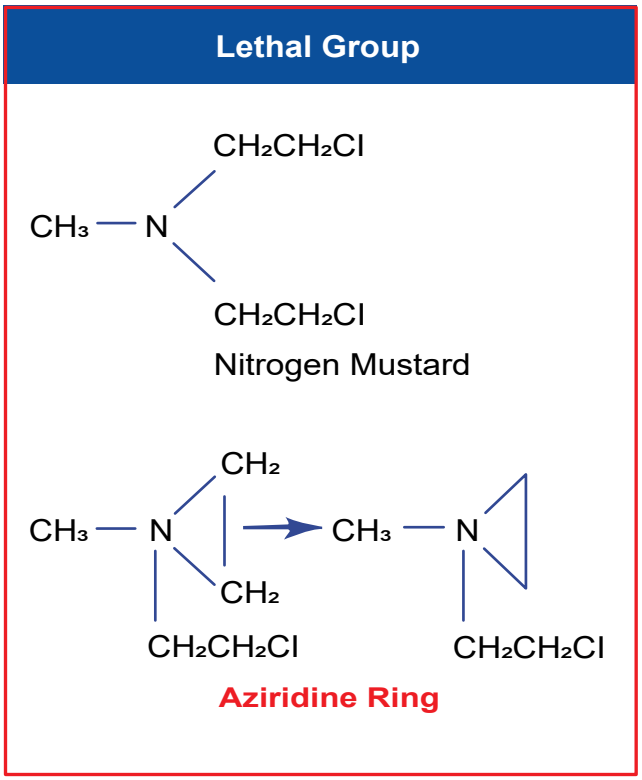
The hero of Drug Therapy to treat cancers is my Professor. WCJ. Ross. As I said above, the supreme intellect for drug design is Ross, an Englishman, who is a Professor of Chemistry at the London University, England. Professor WCJ Ross is also the Head of Chemistry Department at the Royal Cancer Hospital, Chester Beaty Research Institute, 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 data for the toxic effect of Nitrogen Mustard on soldiers 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. He immediately realized that children suffering from Childhood Leukemia have a very high WBC count that is 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 hundreds of derivatives of Nitrogen Mustard. By using an analog of Nitrogen Mustard, called Chlorambucil, he was successful in treating Childhood Leukemia [7,8]. 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 derivatives to modify toxicity of Nitrogen Mustard [9].

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 later. Chlorambucil made Ross one of the leaders of the scientific world. He also made Melphalan and Myrophine for treating Pharyngeal Carcinomas [10,11,12,13].

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, at the Chester Beaty Cancer Research Institute, a post-graduate medical center of the London University. After working for about ten years at the London University, I moved to America when I was honored by the Fogarty International Fellowship Award to work at the National Institutes of Health, NIH, in the Drug Development Laboratory of the National Cancer Institute, NCI, of the USA. NIH has been my home for over a quarter of a century. I am to designed drugs to shut off mutated genes.

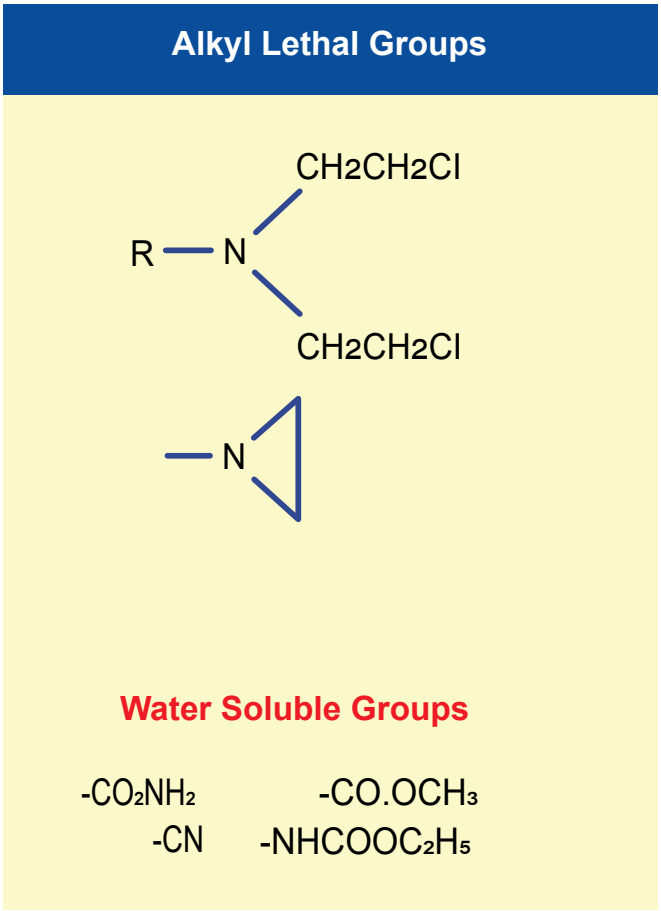
In the following sections, I will describe in detail how I translated animal work which I completed at the London University to humans in America to transport toxic chemicals across BBB to treat mental illnesses particularly making anti-cancer drug like AZQ which was designed to shut off Glioblastoma genes which cause Brain Cancer in humans. Using the same rational all other mental diseases could be treated 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.

As I said above, Professor Ross was designing drugs to attack 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 strands, I am to design drugs to attack only one strand of DNA. This class of pro-drug is called Aziridines.



DNA Binding Aziridine Group

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 generated by the first arm of Nitrogen mustard attacks its own Nitrogen atom forming a stable three-member aziridinium ion. We were unable to isolate the aziridinium ion as growing tumor which produces acid breaks down aziridinium ion. This Carbonium binds to the first strand of DNA. The second arm of the Nitrogen Mustard attack the N-7 guanine of the DNA nucleotide. Within minutes, both strands of DNA are bound by both arms of Nitrogen Mustard. We were able to isolate cross-linking DNA product. This study showed that to attack a single strand of DNA, we must synthesize Aziridine 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 the double stranded 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, the next question was what drug delivery method should be used to deliver Aziridine at the tumor site.



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

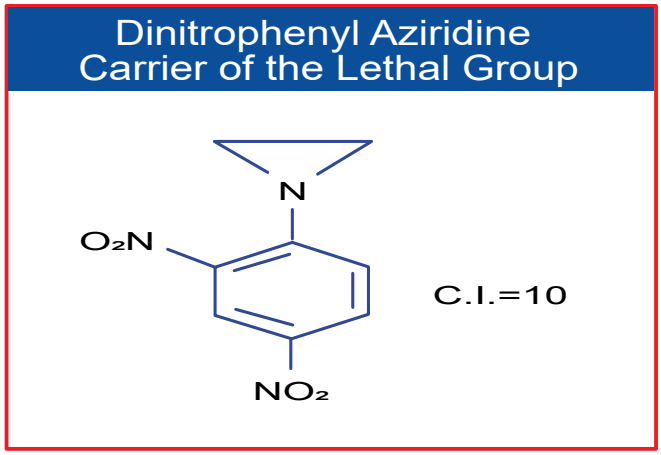
Designing Drugs to Bind to a Single Stranded DNA to Treat Animal Cancers

As a part of my doctoral thesis, I was assigned a different path. Instead of cross-linking DNA by Nitrogen Mustard, 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 Oxidative Phosphorylation of the ATP (Adenosine Triphosphate) which provides energy to perform all our body functions. 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 a tumor called the Walker Carcinoma 256, a solid and most aggressive tumor in Rat. The first molecule I made 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.

Structure Activity Relationship

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 Dinitrophenyl Aziridine to move the drug from the injection site to the tumor site. Because of the lack of an effective drug delivery method, Dinitrophenyl Aziridine stays at the injection site. A very small amount of radioactivity was found on the tumor site.



Dinitrophenyl Benzamide A Novel Drug Delivery Molecule for Aziridine

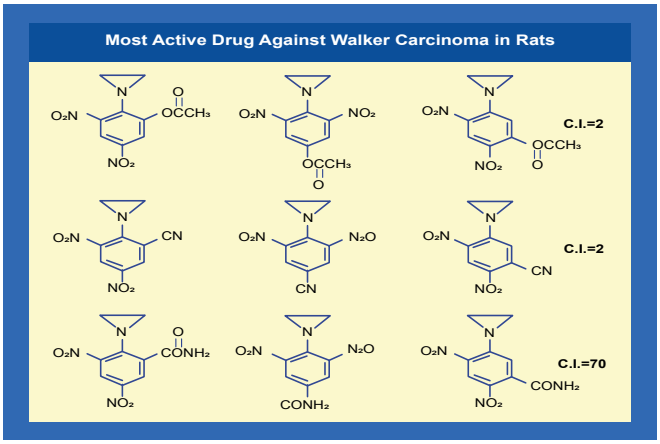
I immediately realized that by making water and fat-soluble analogs of Dinitrophenyl Aziridine, I should be able to move the drug from the injection site to the tumor site. To deliver 2,4-Dinitrophenylaziridine form the injection site to tumor site, I could alter the structure of 2,4-Dinitrophenylaziridine 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 substituent. 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 Walker Carcinoma 256 in Rats.

Derivatization of Dinitro phenyl Benzamide Based on Partition Coefficient

The Most Water-Soluble Substituent

The first three compounds on top line of the above chart carry all three isomer of 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. Within 24 hours of injection, the entire radioactive



compound 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 Substituent

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 activity.

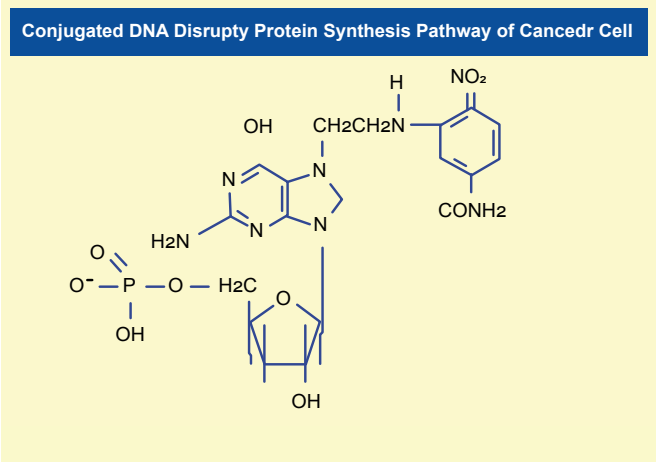
The Moderately Soluble Substituent

The last line of the above chart showed that the first two Amido groups were sterically hindered and did not bind to DNA and 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 [14,15,16].

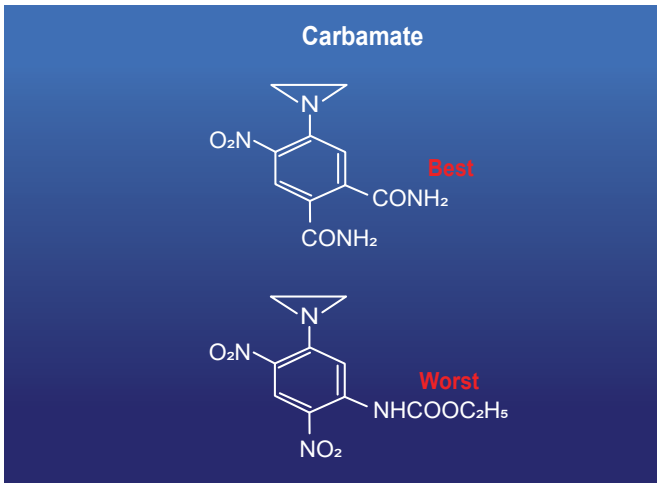
Nitrogen Mustards are highly toxic because they have neither specificity nor selectivity. They attack all dividing cells whether they are normal or abnormal. On the other hand, the analogs of Aziridines and Carbamates serve as prodrug and remain inactive in the basic and neutral media. They become activated 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. 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.

Conjugated DNA Disrupting Protein Synthesis Pathway of Cancer Cell

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 over a hundred 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. To continue my work, I was honored with the Institute of Cancer Research Post-Doctoral Fellowship Award of the Royal Cancer Hospital of London University. To increase the toxicity of CB1954 to Walker Carcinoma, I made additional 20 analogs as a postdoctoral fellow. When I attached one more Carbonium ion generating moiety, the Carbamate moiety to the Aziridine Dinitrobenzene, the compound Aziridine Dinitro benzamide Carbamate was so toxic that its Therapeutic Index could not be measured. We stop the work. Further work in London University was discontinued for safety reason [17,18].

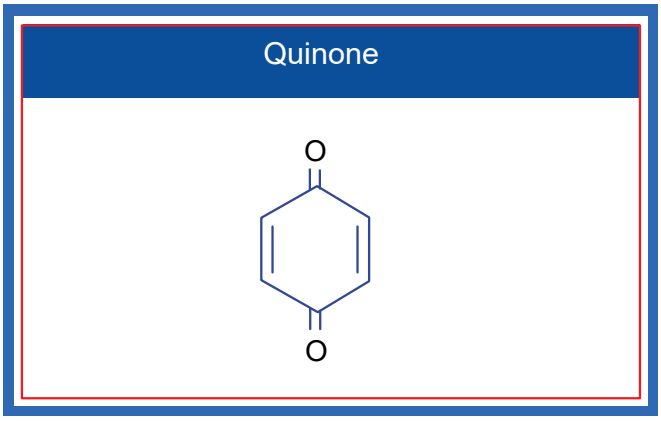


The Best and the Worst Dinitro phenyl Aziridine Analogs

I continued my work on the highly toxic Aziridine/Carbamate combination in America when I was offered the Fogarty International Fellowship Award to continue my work at the National Cancer Institute (NCI) of the National Institutes of Health (NIH). 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

One day, I heard an afternoon lecture at the NIH in which the speaker described that radio labeled Methylated Quinone crosses the Blood Brain Barrier (BBB) in mice. When injected in mice, the X-ray photograph showed that the entire radioactivity was concentrated in the Mice's brain within 24 hours. I immediately realized that Glioblastoma multiforme, the brain tumor in humans, is a solid aggressive tumor like Walker Carcinoma in Rats. I decided to use Quinone moiety as a novel drug delivery molecule to cross BBB delivering Aziridine rings to attack Glioblastomas. By introducing an additional Carbamate moiety, I could increase its toxicity several folds. I planned to use this rationale to translate animal work to human by introducing multiple Aziridine and Carbamate moieties to the Quinone to test against Glioblastomas in humans.



The Structure of A Non-Toxic and Non-Addictive Quinone used for Crossing the Blood Brain Barrier (BBB)

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 adults. Attaching Nitrogen Mustard group 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 remain inactive in the basic and neutral media. They become activated only in the presence of acid producing cancer cells.

DNA Binding Aziridines

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.

I decided to use Quinone moiety as a carrier for Aziridine rings to attack Glioblastomas. By introducing an additional Carbamate moiety, I could increase its toxicity several folds. I planned to use this rational to translate animal work to human by introducing multiple Aziridine and Carbamate moieties to the Quinone to test against Glioblastomas in humans. By attaching two Aziridines and two Carbamate moieties to Quinone, the most useful Diaziridine Dicarbamate Quinone, I named this novel compound AZQ. Over the years, I made 45 analogs of AZQ. They were all considered valuable enough to be patented by the US Government (US Patent 4,233,215). By treating brain cancer with AZQ, we observed that Glioblastoma tumor not only stops growing, but it also starts shrinking. I could take care of at least one form of deadliest old age cancers, Glioblastomas. Literature search showed that AZQ is extensively studied [19].

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 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 on DNA have catastrophic effects on protein synthesis.

With the Quinone ring as a carrier across BBB, I could introduce different combinations of Aziridine rings and Carbamate moieties to Quinine and could create havoc for Glioblastomas. My major concern was how toxic this compound would be to the human brain cells. Fortunately, brain cells do not divide, only cancer cells divide.

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. Besides identifying the site of binding of DNA with C-14 radiolabeled studies, we can also confirm by comparing with the mega sequencing project.

With the completion of 1,000 Human Genome Project, it becomes easier. By simply comparing the patient's genome with the sequencing of 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 treat the disease. By making CB 1054 to treat solid Walker Carcinoma in Rats and by making AZQ to treat human Glioblastoma, we have demonstrated that all bad genes can be shut off using Aziridine or Carbamate as attacking agents to shut off a gene, all we need to do is to identify carriers such as coloring dyes which stains a specific tumor. By attaching Aziridines and Carbamate moiety to the dye, we could attack the tumors.

One of the greatest challenges of nanotechnology is to seek out the very first abnormal cell in the presence of billions of normal cells of our brain and shut off the genes before it spread. I worked on this assignment for about a quarter of a century; conducted over 500 experiments which resulted in 200 novel drugs. They were all tested against experimental animal tumors. Forty-five of them were considered valuable enough to be patented by the US Government (US Patent 4, 146, 622 & 4,233,215). One of them is AZQ which not only stop the growth of Glioblastoma, but also the tumor start shrinking. For the discovery of AZQ, I was honored with, "The 2004 NIH Scientific Achievement Award." One of America's highest Award in Medicine. I was also honored with the India's National Medal of Honor, "Vidya Ratna" a Gold Medal. (see Exhibits 1,2,3,4,5,6,7 & 8)

Based on the Genetic Make-Up, What Other Cancers Should be Explored?

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 patients. On the rational basis, I propose the following approach to develop novel drug 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 takes 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 [19].

As a Fogarty International Postdoctoral Fellow at the NCI, I was given the chance to work on any cancer, I was pleased. Since all other organs including Breast 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 work 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 male Prostate gland. 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

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

2004 NIH Scientific Achievement Award

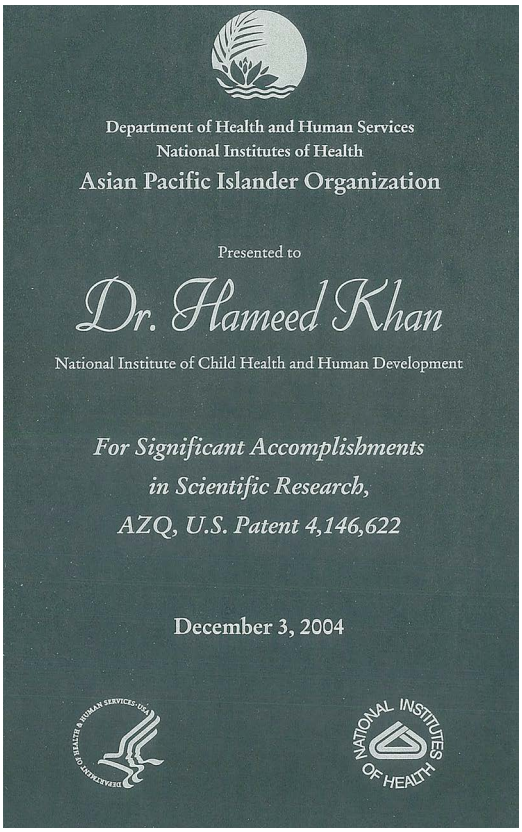


Exhibit # 3

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 # 4

Single Strand DNA Binding Aziridine and Carbamate

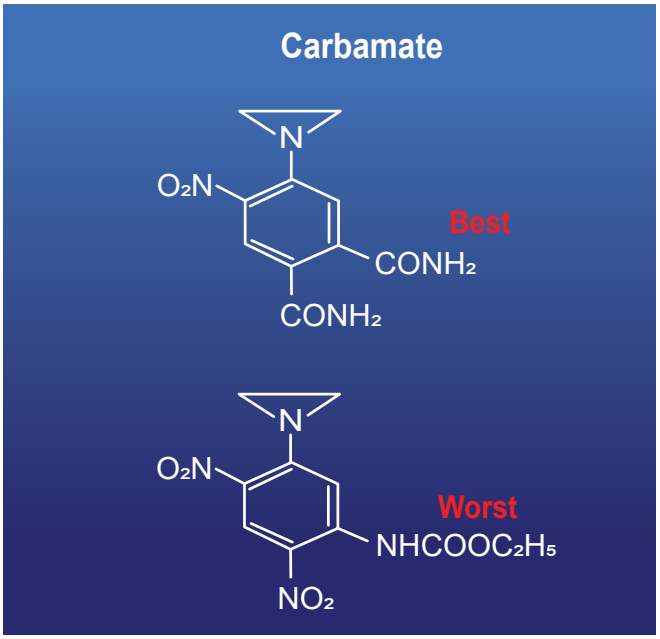
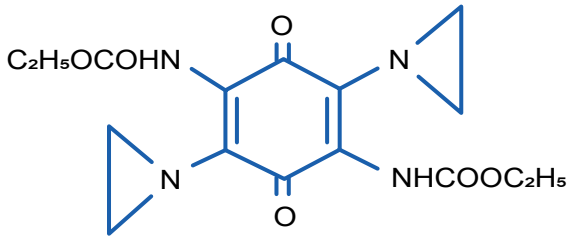


Exhibit # 5

DNA Single Strand Binding Agents

Azirridynl Quinone (AZQ)
Used in treating Brain Tumor



U.S. Patent 4,146,622

Exhibit # 6

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 # 7

2006 NIH Merit Award for Supporting Research

Presented To **Dr. Hameed Khan** by

Dr. Duane Alexander, M.D. Director, NICHD
Dr. Robert Stretch, Director DSR and
Dr.Yvonne Maddox, Deputy Director, NICHD

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

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

Dr. Khan,

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

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

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

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

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

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

Exhibit # 8

2000 NIH Speaker Bureau Award

Presented To **Dr. Hameed Khan** by

Dr. Ruth Kirschstein, Acting Directior of NIH
Dr. Vivian Pinn, Associate Director of NIH
During the NIH/Speaker Bureau's Award Ceremony held on June 12, 2000.

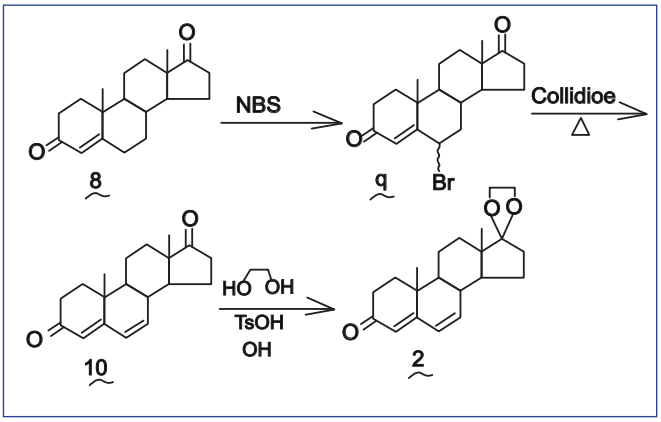
Over the years, Dr. Khan has given over one hundred speeches nationally and internationally. He is a discoverer of AZQ (US Patent 4,146,622), a Novel Drug specifically Designed to Shut Off a Gene that Causes Brain Cancer. The Main Topic of his Speech is, " The Impact of the Human Genome Project on Our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

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 [C. Djerassi et al. J. Amer. Chem. Soc. 72. 4534 (1950)] had demonstrated that we could activate additional positions for substitutions on hormone ring system such as the position 9 and 10 by reacting with Bromo-acetamide which introduce a Bromo ion on position 10 which could be de-brominated by Collidine to introduce a 9,10 double bond which we could be further brominated 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 as a carrier and by attaching multiple Aziridine and Carbamate ions to attack Prostate tumor in Men. Since seventeen positions also available are 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, the future scientists (my students) will conduct these experiments [20-42].



Population Explosion Another Ethical Problem:

The result of all the above discoveries in producing new food, new fuel and new medicine is to keep us healthy and happy. Most people live longer and happier. Our number has multiplied. Four great ages define human development. The first is the Age of Hunting and Gatherings. The second is the Age of Agriculture, the third is the Age of Industrial Revolution and the fourth, not completely here yet is the Age of information and fast communication devices including computers, cell phones, GPS etc.

In the Age of Hunting and gathering, every morning, our ancestors woke up in search for food like deer and cattle in the Serengeti Plains. They said to themselves; they better run faster than the lion or we will be eaten by the lion. The lion wakes up each morning hoping to run faster than humans otherwise it will starve to death. This was the nature's law of selection. Only the stronger survived and the weaker were left behind to die. People in that Age rarely died of old age as soon as they become weaker, they became some creature's food. The population was checked by the laws of nature for thousands of years. We traveled to different continents. In the Age of Hunting and Gathering, people were light, mobile and had small families. Large families were an impediment to moving.

Then came the Agriculture Age, people began to discover agriculture. While men went out for hunting, women started growing food. The early humans realized that they don't have to be on the move at all the time. About ten thousand years ago, we entered the Age of Agriculture.

We became smarter; we learned to grow wheat, corn and rice in the Jericho Valley in the Middle East. The hunter gatherer became the farmers. Our number grew. More hands were needed to cultivate more land. Most religious text says, "be fruitful and multiply." These texts were developed just about the time that people discovered agriculture.

We developed the mentality that more children were better for farming and why not? We had all the resources; there was fertile land; there were brooks, streams, rivers, mountains, everything was available for our species to expand without any problem. Even though we are now entering the information age, our primitive mind set has carried over into the present age - especially in third-world agricultural countries like ours.

In 1850, Industrial Age arrived with the discovery of steam engine. Most routine work on the farms was replaced by machines. With the arrival of the Industrial Age, we spread rapidly across the planet. Our number multiplied from a handful few to almost 8 billion today and we traveled to seven continents and 199 countries and settled down in every corner of Earth. Climate was not a problem; we created artificial comfortable environment in our homes, air conditioning in summer and heating in winter. Now, we could live in the coldest and the hottest place on Earth.

How rapidly did we expand our population? The answer is very rapidly. It took from the beginning of time until 1850 for the world population to reach one Billion - then we expanded even more rapidly; it took only 80 more years for the world population to reach two billion in 1930. It took about 30 years for the world population to reach three billion people in 1960. Then we lost control on growth; it took only 17 years for world population to each four billion in 1977. It took only nine years for world population to reach five billion, and by the middle of this
decade, we have exceeded seven and a half billion. The population is expected to reach 10 billion by year 2060. Let me summarizes below:

Lucy: within 3 million years by = 1850 = Population reached 1 billion

1850 through 1930, within 80 years, the population reached = 2 billion

1930 through 1960, within 30 years, the population reached = 3 billion

1960 through 1977, within 17 years, the population reached = 4 billion

1977 through 1990. Within 13 years, the population reached = 5.77 billion

1996 through 2022, within 26 years, the population reached = 8 billion

If we were to continue with this rate by 2030, the population of the world will reach 9 billion
In terms of net gain (live births minus deaths) the world population increases by 269,000 a day. More than half of everyone who has ever lived on earth is alive today - the dead are in the minority. Is it ethical to ask to limit our number?

More Ethical Issues

Is it ethical to ask if the time has come to limit our population? Should we pay more attention to the quality of the population? If we ignore, Mother Nature is cruel; she takes drastic action and will crash the population explosion. She will unleash natural disasters such as cyclones, tornado, hurricanes, earthquakes, and epidemics of unusual diseases such as Covid-19, AIDS, Ebola, Dengue fever etc. If we continue to increase the population at the current rate, most scientists predict that there will be a massive starvation within the next ten years. By repeated farming on the same piece of land, we are using up Earth's nutrients. We are exhausting Green Revolution. It is time; we ask ourselves a simple ethical question. Do we have an unalienable right to have as many children as we want? The answer seems to be no. We don't have a right to have as many children as we want. Then you might ask, who has a right to decide? The answer is no one person can decide, but we can help educate couple that more children are not going to help you in your old age. Look around your neighborhood, how many children stay around to help their parents in their old age. We all must decide as a society how to educate young couple. There is no doubt that we live in a free countries. But freedom also carries some responsibility. You are free to walk in the street, but you are not allowed to walk on the highways. Police will arrest you. Your freedom is restricted by the society. The society has a right to restrict the number of children a family could afford by increasing taxes to provide adult education in villages. We are the members of the society and we all must decide to limit the number of children per family. Once we decide the number of children then we must decide the quality of life of those children who are likely to live. Some parents who are predispose to genetic defects still would like to have children even if they are determined to be genetically unfit to survive past their teens? For example, some middle-aged couple who have Down syndrome children. Who will pay for their medical bills? Over 6,000 babies are born with Down syndrome in the United States each year. As recently as 1983, a person with Down syndrome lived to be only 25 years old on average. Today, the leading causes of death for persons with Down syndrome is Pneumonia, infectious lung disease, congenital heart defect (CHD) and circulatory disease. At the enormous medical cost, average life expectancy of a person with Down syndrome is nearly 60 years and continuing to climb. A couple with Down Syndrome plans to have children, do they have a right to sequence the genomes of egg and sperms and their fertilized ovum to see if they are bringing a Down baby?

Traits are expression of genes. We thought that traits we inherit from our parents are unpredictable. Advances in genetic engineering has provided us with toolkit not only to cut, paste, copy, and sequence a gene, but also to move the genes from species to species. Good genes could be added to maintain good health or enhance exceptional abilities.

To cure Muscular Dystrophy, scientists at the Penn State University discovered a gene in Rat that triggers muscle growth. By inserting the Rat gene in Mouse, they generated a super strong muscular Mouse called the Mega Mouse. The people who are most interested in this kind of work are Athletes, Coaches and Football players. They intend to generate an army of Bionic athletes. Is it ethical?

Another example is borrowing genes from insects to insert in humans. For example, fruit flies have photographic memory. If a fly finds a food, it goes to different directions and return with family and friend at the same place to share the food. Flies have incredible memory. Could we borrow their memory genes and insert in Alzheimer patient to restore their memory? We have sequenced fly genome and find that while humans have approximately 24,000 genes, fruit flies are not far behind, with approximately 14,000 genes and roughly 60 percent of the fly's genes can also be found in humans in a similar form. You might wonder why fly is so small compare to human and yet it has so many genes because fly defies gravity and can fly but human can't. Once we identify memory genes, we can insert them in genetically modified flu virus to infect Alzheimer patients to study if the genes have been inserted. If sequencing identify that super memory genes, could that be inserted in humans to treat Alzheimer? Can the senior be treated with gene therapy who suffered from age related memory loss? Will the rich parent pay to produce super intelligent children? Is it ethical? While flying an Eagle can focus on its meal a rabbit on the ground at a five-mile distance. Can we sequence Eagle's eye genome to isolate and implant the eyesight gene to improve our newborn's eyesight? Is it ethical?

To summarize, using genetic engineering, is it ethical to produce designer babies with bionic athletic abilities? If we agree to produce designer babies, Rich-parents will provide a list of traits they want in their children such as blue eyes, blond hairs, and high IQ. Next, parents will determine if they want a boy or a girl? Tall or short? green eyes or blue? They wonder which gifts they will share with the rest of the world.

We thought that parents cannot control the genetic makeup of their children. It is not true anymore. Now, we have the control on the future genetic make-up of our kids. Do we dare play God? If we play God, how far should we go? If we go too far what would happen to society? We have wiped out a species from the face of the Earth such as Smallpox. The next biggest killer of human beings is Malaria. Hundreds of millions of people in Africa and Asia are infected and about half a million die each year. Should we eradicate malaria by releasing millions of genetically engineered sterile mosquitoes? Should we eradicate another species from the face of Earth forever. If the use of genetically sterile mosquito is permitted to wipe out Malaria, the manufacturers of plant seeds want to produce sterile seeds so that farmers buy new seeds every year. Is it ethical?

Sex selection presents a more serious problem. In primitive societies, boys are considered more useful than girls. Even in modern times, using sonogram, in China and India most girl fetuses were aborted. In modern times. Serious objection to sex selection. Discrimination abortion has produced 100 girls to 117 boy in China and in India 100 girl to 140 boys. It is easy to have sex selection with disastrous long-term consequences. At each ejaculate, a man produces millions of sperms. Almost half of the sperms carries X-chromosomes to produce female fetus and another half carries Y-Chromosomes to produce male fetus. The X-Chromosomes are heavier than the Y-Chromosomes. The X-Chromosome carries 164 million nucleotide base pairs with 1,144 genes. The Y-Chromosomes carries 59 million nucleotide base pairs, with 231 genes. The cheapest and the easiest way to separate X- and Y-sperms is to dilute the ejaculate with distilled water in a test tube and spin on centrifuge. The spinning separates in two layers. The upper lighter layer contains sperms carrying Y-Chromosome responsible for producing male fetus. Sequencing X- and Y-chromosome will identify any deleterious mutations. After in vitro fertilization, within a week the fertilized egg grows to a 8-celled embryo which can provide a single cell for sequencing. Any deleterious mutations can be identified and discarded. Through artificial insemination, desired sex can be obtained with precision and accuracy; It is 91% effective. The technique was developed to produced super breed cattle. Excessive abortion of female fetuses will produce many crippled boys. If a Y-sperm carrying a genetic defect fertilize an egg free from any defect, the male fetus will be a carrier, but remains healthy. On the other hand, if the egg also carries the same complimentary defected nucleotide on the complimentary strand of DNA, the male fetus has no protection. The genes express resulting male children born with serious genetic defects such as Muscular Dystrophy, color blindness etc. Is sex selection ethical? The following section raises several additional ethical problems.

Old Eugenic: A Failed Experiment

History tells us a disastrous consequence of attempting to produce a Master Race for Nueva Germania. To produce a super race of German which was meant to be an Aryan Utopia in South America, half a century before the Nazis dreamed of propagating a "master race" to rule the world, Elizabeth Nietzsche, the sister of the German Philosopher, Friedrich Nietzsche, went to Paraguay, South America, with a group of White Supremacists to raise a super race of German, to create Nueva Germania in Paraguayan's jungle on the backlands of South America. The colony fell apart within just a few years. It destroyed the lives of thousands of innocent misguided people. Many of the original family members who weren't wiped out by malaria or sand-flea infections fled from Nueva Germania in despair to escape the scorching heat, pouring rain and unyielding land. Of the few who stuck out, those most stubbornly convinced of Nietzsche teachings married among themselves so as not to dilute the racial stock. Inbreeding results in degeneration which is still obvious in the faces of kids in the schools, and in the forest in Paraguay. The members of the inbreeding families are very, very slow learners because of extensive level of inbreeding over generations; They show a "high incidence of mental problems," including drooping eye." Today, about one out of 40 residents of Paraguay, a country of 5.7 million, is of German descent. The inbreeding among themselves results in genetically incompetent race of people who are incapable of living a normal life. They have nothing to show except for the preponderance of blue eyes, blond hair and families named Fischer. The concept of Racial purity dies in the jungle and their Founders saw their Paraguayan settlement as a place that would spawn a race of Aryan supermen dies with them because they didn't consider disease, heat, and the consequences of inbreeding.

Unintentionally, some parents still tend to practice Eugenic. For example, a father says to his son, you are a Catholic and I will not allow you to marry a Jewish girl. If you do, I will disinherit you from my wealth. If you sequence the genome of the members of prisons, mental hospitals and asylums and compare the sequence with their parents' genome, you will be surprised to see how many same mutated genes they inherit from their both parents.

The marriage of our Vice President Kamala Devi (a member of Hindu faith) to Douglas Emhoff Harris (a member of Jewish faith) is a supreme example of American freedom and independence. They are united together regardless of race, religions, or the place of origin. Their marriage is based on mutual love, utmost respect, and utmost friendship. If you would sequence and compare their genomes; their genomes will show no mutation on their complimentary copy of the genes on their chromosome for a specific disease. If they had children, they would show no ill effect. They will be carrier of their common ancestral genes. Their marriage is supremely successful example of freedom and tolerance for more than a billion people of India. Congratulations Madam Vice President.

Some of us are trying to repeat the failed eugenic experiment by conducting unauthorized gene editing experiment of germ cells. As I said above, the sequencing of Human Genome has identified a total of 24,000 genes in our genome out of which 16,000 are good genes, 6,000 mutated genes and 2,000 pseudogenes. Compare to entire genome, human egg and sperm are very small. Human egg is made of 164 million nucleotide base pairs and carries 1,144 genes while human sperm is made of 59 million nucleotide base pairs and carries 231 genes. Using CRISPER, gene editing of egg and sperm is much faster, cheaper, and precise. Although germ-line gene editing is forbidden in western world, in 2018, a Chinese scientist has created two genetically modified sisters by germ-line gene editing. What if the leadership in neighboring North Korea decides to produce an army of Master Race by germ-line gene editing of human embryos? With all the precautions, nobody knows the impact of germ-line gene interaction with 16,000 good genes in our genome. We all know that our genome is

written in four nucleotide bases (A-T and G-C). We also know that it gives 64 combinations. Could you imagine how many different combinations we get by the interaction of 16,000 gene-gene interactions. We must observe the two genetically modified Chinese sisters all their lives. Will they shine like 2020 Nobel Laureate Jennifer Duodena, or will they destroy their creator? Only time will tell us.

American Dream and the Promised Land

America represents the greatest mixing bowl of all nations, including all religions, all caste, creed, and class systems. This massive mixing of all people has produced a new class of outstanding men and women who have earned more Nobel Prizes than any nations on Earth. They alone climbed the tallest mountain, gone to the bottom of the deepest ocean, split the heart of atom, walked on the surface of Moon came home safely, now they are ready to colonize planet Mars and using Mars as a base to launch unmanned spacecrafts in search of a new home for humanity in the nearest solar system. American awakening began with Russian's misadventure.

In 1958, The Russians launched an unmanned spacecraft Sputnik to demonstrate the space superiority. In response to the Russian challenge, President Kennedy addressed the Congress and announced that within a decade, Americans will land men on the Moon and bring them back safely. To accomplish this goal, he opened the American gates to welcome all skilled immigrants to help America to achieve her goal. The call went around the world. America became a nations of immigrants. The Irish came; the Polish came, and the Swedish came. People of the Asian continents were last to arrive at the shores of this country. Two important reasons brought them to America.

First, they see America is a land of opportunity. From the beginning, it opens its gates to all the people regardless of race, religions, or the place of origin. Today, the doors remain, they still come bringing their knowledge, their skills, their hopes, their dreams, their willingness, and determination to work hard and succeed and if they fail, their more ambitious children who are born and raised in the country will climb the ladder of success and get to the Promised Land. This mass immigration has created the greatest ethnic diversity in America nowhere to be found. To welcome a million immigrants each year to this country, has made Americans the most tolerant and patient people in the world. By contributing their knowledge, their hopes and dreams, every new immigrant revitalize America's greatness. Because of their unique contributions, Americans today live in the most prosphoras society mankind has ever created.

The second reason that appeal to the immigrant, is America's love of freedom. They were given the freedom of speech; freedom to read or write any part of the literature; freedom to practice their own religions; freedom to conceive novel scientific or business ideas; freedom to translate theories into practice and concept into results. In this climate new ideas, new capabilities could flourish, and flourish they have. This has resulted in technological achievements in this country unmatched by any other nations in the world. Their achievement has made America the greatest nation of all. The best schools are here; the best colleges are here; and the best medical centers are here. The greatest medical centers of them all is the National Institutes of Health (NIH). For the past hundred years, NIH has become the citadel of research and learning. It is home to some of the greatest minds in the world. More Nobel Laureates walked through the streets of NIH then anywhere on the face of Earth. The discoveries they make here benefit more than eight billion people around the world. NIH has been my home for the past quarter of a century. American achievements are due to love of freedom and independence, and their collective effort to accomplish their goal. The greatest discoveries are the self-discovery described below:

Conclusion

Science means knowledge. We obtained knowledge by conducting experiments which provide reproducible, verifiable, and publishable results. It provides concrete evidence. Eugenic attempts to purify races by removing undesirable traits including the color of our skin to create a superhuman Aryan race. Is there any evidence for this hypothesis? None. On the contrary, by extracting DNA from the Neanderthal fossils, Savant Paabo, 2022 Nobel Laureate, sequenced the entire Neanderthal Genome. He demonstrated that gene transfer had occurred from these now extinct hominins to Homo sapiens following their migration out of Africa around 70,000 years ago. He confirmed our origin from pro humans to homo sapiens and our expansion from Africa to the rest of the world

After spending $3 billion on the Human Genome Project, if you would ask me what is the single most important discovery we made? I would say, reading the entire book of our life itself is one of the greatest discoveries of our time. We are the only species who not only reads his own book of life, but also the book of life hundreds of other species on Earth. It will keep our scientists busy for another century trying to find out what piece of our genome came from what species over three and a half billion years of biological evolution. Of dozens of discoveries we made, one stands out. We made an astonishing discovery. If we could only make its result understand to all the 200 leaders of the World, it will eliminate wars and poverty forever from the face of the Earth. Some outstanding discoveries are made accidently. This is one of them.

When we began our work on sequencing human genome, most of us were focusing on the nuclear DNA of the cell because it is the nucleus that carries all instructions to make us. Some of us start looking outside the nucleus. What we found was that there is a small piece of DNA outside the nucleus which live independently called the Mitochondrial DNA. It is 16,600 nucleotide letters long and carries 37 genes, all of which are essential for normal mitochondrial function Compare to nuclear DNA, which is six billion four hundred million letters long carrying 24,000 genes, Mito-DNA is very short and carries by our mothers only.

When our mother's egg receives our father's sperm, we are conceived. The tail of our father's sperm drops off; our father's Mito-DNA is lost. Just the nuclear DNA joined together to achieve conception because it is the nucleus that carries complete instructions to make us. We inherit only our mother's Mito-DNA. There is no contribution from our father's Mito-DNA. While the nuclear DNA from our both parents combine, recombine, arrange, and rearrange, no changes occur in our Mito-DNA. A single change occurs in our Mito-DNA in10, 000 years called the Random mutation. If you compare the Mito-DNA of my mother from your mother and find 2 random mutations, it means that you and I share the same mother twenty thousand years ago even though we never met. It gives us the idea that if there is a common mother of us all. A search for a common mother of us all began in earnest. The solution was easy, all we must do is to compare the Mito-DNA of all 53 races (population geographically located at difference places) on Earth; the largest random mutations will point out to the oldest race of humans on Earth. When we compare the

random mutations of the Mito-DNA of Asian mothers with the European mothers, we found that the European mothers have three times more random mutations than Asian mothers. It means that the European race is three times more senior than Asian race. The largest random mutations were found in the African populations. It means that if there is a common mother of us all, she must have originated in Africa. With this knowledge, scientists rushed to Africa in search of our common mother. Great Rift Valley is the most logical place. Fossil hunters were already working in the Great Rift Valley for years in search of the oldest fossil.

The Great Rift Valley is 3,700 miles in length. It runs from northern Syria in Southwest Asia to central Mozambique in East Africa. The Great Rift Valley in East Africa has been a rich source of fossils that allow study of human origin and evolution, especially in an area known as Piedmont. Millions of years ago, lava flowed in this valley. Along its long length of The Great Rift Valley hundreds of small lush green forests were formed wherever there were lakes, ponds, and water holes. In such green lush places colonies of Chimpanzee thrived for over 25 million years because they adapted to the local climatic changes. Based on the new diet and environmental conditions, mutations occurred to accommodate the Chimp colonies into the new environment. According to Darwin's survival of the fittest only those Chimps that adapted to the new environmental conditions developed new variations and thrived and the rest perished. Among the hundreds of mutations taking place over millions of years, a single mutation occurred in the brain of a single Chimp which gained her conscientiousness. The fossil we call, "Lucy". She must have been the first Chimp to gain conscientiousness. Lucy must have been the first Chimp to become aware of her surroundings. She is anatomically identical to the present-day humans. Her fossil was found near Hagar Valley in Ethiopia. The environmental condition of the Hagar Valley must have been ideal. There must have been plenty of food, shelter, and fresh water for the member of the Lucy's family. The colony of Lucy thrived. Over millennia, when their number reached a thousand, the food and shelter for the colony member was not enough. In search of food and shelter, about 60,000 years ago, some members of the colony migrated toward West and arrived in Neanderthal Valley in the present-day Germany. The Neanderthal fossil is the first early human fossil found in Europe. Waves of migrants must have arrived in Europe. The most recent fossil found in the caves in France is the fossil of the most modern humans like us called the Cro-Magnons. We are descendent of Cro-Magnons. The advanced Cro-Magnons learn to develop language, tools and protective clothing and walked over the entire surface of the Earth. They conquered all seven continents and 200 countries within 60,000 years. Today, their numbers have increased to 8 billion. We are all brothers and sisters' children of the same mother Lucy. The faster we learn this truth that you and I and all humans on Earth are children of the same mother, a Black woman who was born in Africa three and a half million years ago, the better it is for all of us; then and only then men and women of different races, different religions and different nations will respect each other and treat each other like brothers and sisters and time begins now.

A Note for my students

Accompanying articles are Available on your cell phone: facebook.com/hameed. khan7773

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