EAS Journal of Biotechnology and Genetics
Abbreviated Key Title: EAS J Biotechnol Genet
ISSN: 2663-189X (Print) & ISSN: 2663-7286 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-3 | Issue-3 | May-Jun-2021 | DOI: 10.36349/easjbg.2021.v03i03.002

Review Article

The Impact of Genomic Science on Society & the Discovery of AZQ (US Patents 4,146,622 and 4,233,215) rationally Design to attack Glioblastoma, The Brain Tumor

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Article History
Received: 11.05.2021
Accepted: 24.06.2021
Published: 28.06.2021

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: This abstract describes the Genomic Impact of science on society. How progress in Genomic has provided us enormous benefits for designing drugs like AZQ to treat brain cancer and at the same time raised some serious ethical problems. Instead of finding new treatment of cancers by the old trial-and-error methods, we are developing rational drug design to treat cancers based on the genetic make-up of a specific disease. Sequencing Human Genome has identified 24,000 genes that provides total information to make us. In our genome, we carry 16,000 good genes that code for good proteins that keep us healthy. There are 6,000 bad or mutated genes responsible for causing six thousand different diseases. There are 2,000 Pseudogenes that have lost their functions because they are no longer in use. The 6,000 mutated genes are damaged by radiations, chemical or environmental pollution, viral infection or genetic inheritance. The mutated genes code for wrong proteins which make them responsible for causing diseases. For example, when we sequence a bad gene and compare with the Reference Sequence, we could easily identify the location of the mutated gene on a specific chromosome. The rational drug design requires that we synthesize drugs based on the genetic make-up of the sequence. AZQ (US Patents 4,146,622 and 4,233,215) was rationally design to attack Glioblastoma, the Brain Tumor. This abstract present not only the discovery of AZQ, but also presents some possible solutions to serious ethical problems.

Keywords: AZQ, Dinitro Benzamide, DNA, RNA, Genome Sequencing, Epigenetics.

HISTORICAL BACKGROUND

We climbed the tallest mountain, gone to the bottom of the deepest ocean; we split the heart of the atom; we walked on the surface of the Moon and came home safely. We not only sent the Perseverance rover on the surface of Mars to find a suitable place to start human colonization of Mars, but we also sent spacecraft Cassini to study the rings of the Planet Saturn, and the spacecraft Galileo to study the atmosphere of Jupiter, the largest planet on our Solar System. Even with the help of Hubble Space Telescope, we saw the very edge of the Universe at the dawn of time. In short, we have chartered our course from the inner most heart of the atom to the farthest reaches of the Universe. We triumphed in every human endeavor except life. Now, we have unlocked the secret of life. On April 13, 2003, Dr. Francis Collins, the Director of our institute, NIH, (National Institutes of Health), announced that we read the book in which God created life. We read the book of life of a human being, letter by letter, word by word sentence by sentence, chapter by chapter all six billion and four hundred million letters called nucleotide. In a few sentences, he described the Human Genome Project. The greatest biological experiment ever conceived by human mind. Never in the history of mankind have we spent $3 billion on a single experiment; never in the history of Science, thousand of scientists from six industrialized nations participated in a single experiment and never in the history of Science the President of the United States and the Prime Minister of England gone on the television addressed the citizens of World describing Ethical and Moral problems concerning the completion of the Human Genome Project.

The sequencing of Human Genome will answer some of the most important questions we have asked ourselves since the dawn of Human civilization. What does it mean to be human; what is the nature of our memory and our conscientiousness' our development from a single cell to a complete Human being; the biochemical basis of our sense; the process of

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our aging. The scientific basis of our similarity and dissimilarity. Dissimilarity that all living creatures from tiny blade of grass to mighty Elephant including Man, Mouse, Monkey or Microbes are all made of the same building blocks 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.

In 1990, United State Congress authorized three billion dollars to my institute NIH to decipher the entire human genome within 15 years that is get total genetic information that makes us human called the Human Genome Project. Thousands of scientists from six industrialized nations and 20 biomedical centers joined our effort. This effort was led by US followed by Germany, France, England, China and Japan and within 13 years the entire human genome was deciphered and published in the Scientific Journal Nature and linked to the website. If you have access to a computer key-board, you have access to all that information.

In this lecture, I will cover three areas: First, the impact of the development of Genomic Science on Society particularly the Impact of Sequencing Human Genome identifying good and bad genes responsible for keeping us in good health; Second the Impact of developing Biotechnology and Genetic Engineering for cutting, pasting and copying good genes like the gene that produces Insulin to treat diabetics around the world and for developing novel drugs like my own work on designing AZQ (US Patent 4,233,215) for shutting off bad genes like the gene that causes Glioblastoma, the brain cancer. Third, since we are using highly toxic drugs for treating cancers, we need new ethical principles based on modern science. The old ethical principles also came from people's head, but they were based on the outdated information available to our elders at that time. Let me first outline the impact of science on society. The rational science we pioneered, has given us enormous benefits everything from Antibots to Electricity; increase life expectancy health and leisure provided by modern medicine and industrial technology has given more people more time never before to educate themselves about our creativity and to ponder our existence. And yet into this better world, we generated equally enormous problems. In this article, I will outline not only the problems, but also will try to find some possible solutions:

The Impact of Population Explosion: Are we the last generation on Earth?

Today, more than seven and a half billion people live on Planet Earth. We are adding 90 million new mouth to feed every year. About one billion three hundred million, almost 20 percent of all humanity, live in India alone. It has placed the greatest burden on the country's resources. Our people work so hard and yet, they cannot raise their standard of living. The progress we have made since the independence, more than seventy years ago, is enormous. It is eaten up by new mouths. At the time of India's independence, the population of our country was less than half what it is now. Should we continue to add new mouths knowing well that we cannot feed or provide shelter to all our people? Let me share some facts with you:

According to a United Nation population projection survey, we are adding a quarter million children every day to this planet. Can we provide housing, employments, transportation, food, fuel and medicine to all? If we fail, we will see a new generation of protesters in the streets like we see protesters for months destroying properties in the streets of Paris. There are more than half a dozen cities with population exceeding 20 million. Will the world come to end as soon as we are gone? These are not mere academic questions that are exactly what is happening now. The answers seem to be that the world will not come to an end, even if China allows to add an additional child to the family, but we are likely to face unimaginable consequences of catastrophic proportion. We are breeding mindlessly as if we are the last generation to live on Earth.

If we continue the present trend, by year 2050, 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. 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, Coronavirus virus, 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. For example, farmers in India depend on Monsoon Rains, what if it fails to come due to climate change. 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 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 country. 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 rich and to provide free 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.

The Impact of Sequencing Human Genome on the Quality Control of the Population

Quantity control of the population is really challenging, it is the quality control of the population that would be expensive, but easier. Some parents who are predispose to genetic defects (such as Epilepsy, Alzheimer, Schizophrenia, Bipolar disorder, Psychotic disorder, Autism etc.) 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 and they are financially well off and will pay for their medical bills. Rich families could afford, but the rich families don't produce too many children anyway.

The old Eugenics moment was an evil practice of an authority aiming to introduce improve genetic quality by terminating pregnancies in children with genetic defects in a couple against their wishes. On the other hand, the Neo Eugenics provides the couple with the complete sequence of the entire genome so that they could examine for the presence of both copies of the same bad genes and make the decision. So many horror stories are attached to Eugenics even Neo Eugenics should not be used. Instead, I suggest, we use the phrase Quality Control (QC) babies. After examining the nucleotide sequence of egg and sperm or the nucleotide sequence of the entire genome, the couple make the decision by consulting with their physicians and their priests if they would like to terminate the pregnancy or bring this child to the full term taking the full responsibility of bringing this child into this world. Parent make the decision with their own free will and will pay the cost. The couple will have an option to conceive by in vitro fertilization using previously sequenced egg and sperm free from any deleterious mutations.

The Impact of Sequencing on our Origin

Over three million years ago, our journey began in the Afar Valley in Ethiopia, in the heart of dark Africa that is where the fossils bones of our first human ancestors were discovered. Professor Johansson and his team discovered the oldest pro-human fossil of an 18-year-old woman and they called her Lucy. Her fossil was unearthed in the Afar Valley in Ethiopia in 1974. Radio-active dating showed that she died 3.18 million years ago. The damage to the fossil showed that she must have died of injuries suffered in a fall from a tree. Lucy must have developed rudimentary Cerebral Cortex. It is the area of Brain which is a center of Cognitive function, the essence of what made her pro-human different from her ancestors. Our pro-human ancestors lived a violent life. She could have died in a violent episode. We are learning that human brain carries specific neural circuits which are responsible for Aggression and human Consciousness. A region of the brain called Amygdala carries Information Processing Center. This region sometimes unleashes intensely violent emotions. It appears that over three million years of evolution, by learning to control anger, we learn to control the function of Amygdala. Like all other creatures, we left Africa in search for food, water and shelter. We became hunter and gatherers of food.

According to Darwin's Theory of Evolution, life evolves, and nature selects. Darwinian laws of natural selection teach us the survival of the fittest. Only those species, who are fit to survive, will live and those unfit will die? Darwinism was applicable when we were hunters and gatherers of food at the dawn of our beginning, when we were on the move collecting foods and searching for fresh water and shelters. The older, the weaker, and the sicker were left behind. In animal kingdom, rarely creatures die of old age, they are mostly eaten by other creatures. This happens with all other creatures in the Serengeti plains of Africa today.

Human advanced rapidly leaving all other creatures behind. When we learned to farm, we seized to be hunter and gatherer; we settled down and our wondering is over. When we reached the Agriculture age and started farming, we defied Darwin's laws of Natural Selection; we allowed even to the most physically unfit humans to survive. During Agriculture age, we needed more children to farm the land. Even during hunting and gathering age, we needed to have more children because of the endemic diseases less than half of the children would survive their early years. Every family used to have six to eight children. Children provided security that was the old age slogan.

Three hundred years ago, in the Age of Enlightenment our distant Scientists and philosophers from Galileo to David Hume has the courage to standup for the intellectual principles and reasons. The rational science they pioneer, has given us enormous benefits. We received every comfort of life from Antibots to Electricity resulting in increase life expectancy; health and leisure provided by modern medicine. Industrial technology has given more people more time which they never had before to educate themselves about creativity and to ponder their existence.

Today, we have two extreme points of view. First view consider that children are the gift of God and must be produced and protected at all cost. Second view is that we must set the limit on the number of children and must control the world population. We must be pragmatic, some say, and others ask, "Is 20 billion population in the next century enough?"

Over population creates social unrest. As you look around the world, every major city which has reached the population exceeding 10 million, the overcrowded population explodes in violence from time to time. Civil laws begin to break down. Should we call the women of our countries to rise up, educate themselves, control their lives and take the proper place in the society? Should we tell women in the developing countries what their sisters in the Western countries have accomplished personal freedom as their goal. They got the woman's rights and got on with their lives. Without women's consent, men cannot have a brood in this country. Compare to our women, most women in Western countries are educated. If divorce rate is high, so what, may be some men deserved to be kicked out of their homes. Some men will never learn to respect women. The dominant Indian husbands lost their power in America. Indian women, who came to America, have quickly learned their rights from their Western sisters. The divorce rate among Indian families is rising rapidly in Washington Metropolitan area because women are receiving the first-rate education and getting first rate jobs while men are refusing to change and remaining arrogant and paying the price. Like American women, our women have also refused to have as many children as men want. They also believe like most American women do, not to have more than two children; more children mean; they are burden and one cannot carry much luggage in active life.

In Western countries, people have lost faith in the following three major organizations to control population: First, they know for centuries that religions will never help control population because most religious leaders believe that more head counts mean more followers, more contribution to their budget and more power. Second, no politician will vote himself out of office by reducing the potential voters. In other words, more head counts mean more votes; more votes mean more contribution and longer stay in the office. Third, people in West realized that it would be ridiculous to expect any help from the industries to control the population, because industries' main slogan is that to expand economy, population must expand.

The 16th century British economist, Thomas Malthus, in his now famous Malthus Theory predicted that while our population increased exponentially, our food grows arithmetically. Excess population will die of starvation. This theory was also defied by Industrial and Green Revolution. Using industrial machines, we started producing larger quantities and better-quality food than we needed. Most industrialized nations have three months of surplus foods in their stocks pile these days.

The single most important medical discovery which defied mother-nature's control of population and Darwinian principle of survival of the fittest is the discovery of Antibiotics for which Alexander Fleming was awarded a Nobel Prize. The discovery of penicillin has saved millions of people over decades from their certain death. Saving lives by use of antibiotics increased population further exponentially while our food grows arithmetically.

To conserve food, we are controlling every species on this planet except our own. We are the only conscious species that is increasing in numbers so unconsciously. Some philosophers wonder, if humanity is on their way to hell or is there anything we can do to help them to get off on their way to hell? How we started on this path? Where we are now and what could we do to prevent the population explosion?

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 and iPads.

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 say to themselves; they better run faster than the lion or we will be eaten by the lion. The lions wake 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. Darwin's Law of Natural Selection confirms the survival of the fittest. 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 and survival.

Then came the Agriculture Age, people began to discover the advantage of 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 food such as 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 and grow more food. 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 Industrial Age, this primitive mind set has carried over into the present age - especially in third-world Agricultural countries of Asian continent.

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 seven and a half billion today and we settled down in all seven continents and 200 countries and populate 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, 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 world population to reach three billion people in 1960. Then we lost control it took only 17 years for the world population to reach 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 2050.

Let me summarizes below: The fossil of the first human/chimp called Lucy was unearth about three million years ago.

- Lucy: evolved 3 million years ago = by 1850 = we reached 1 billion
- 1850 through 1930 = our number increased to 2 billion = within 80 years
- 1930 through 1960 = our number increased to 3 billion = within 30 years
- 1960 through 1977 = our number reached to 4 billion = within 17 years
- 1977 through 1990 = our number reached to 5 billion = within 13 years
- 1996 through 2021 = 7 and a half 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.

To accommodate this enormous increased population, we are now clearing land for farming and for development, land that normally could have remained untouched for countless years. Unknown diseases have literally risen from swamps in the jungles that have been uncovered. For example, we found Hantavirus in South Americas and Ebola virus in Africa, and Dengue fever and a rise in Mucor-mycosis a rare and potentially deadly infection also known as Black fungus. Black fungus in India has killed many people and for which we have no cures. We don't know what else will be uncovered as bulldozers plow through lands in forests, mountains and valleys that have remained untouched for millennia.

Ninety-seven percent of the world population lives on three percent of the landmass. We tend to live where everyone else does. One major way to attain breathing space in your life is to move out into a less-crowded area. Most Indian population lives in villages without proper sanitary conditions. What if the city dwellers decide to move in prime places in villages where most farming is done? In major cities around the world including America prime farming land is used to build highways, shopping malls and car parking lots.

The biggest detriment to population planning is narrow-minded name-calling. Any person commenting about the need for population planning, is labeled with epithets; geneticist, racist, God-player. However, farsighted she might have been, the former PM, Mrs. Indra Gandhi's effort was unsuccessful in India because she never prepared our people, never educated them, nor informed them in a democratic way. If we don't plan for population control, there will come a time when Nature takes care of things in a brutally efficient way giving us Earthquakes, Tsunamis, Tornado Covid-19 etc. If we don't practice family planning, nature takes over and we will be forced to control population.

Politicians will try to ignore this issue; In India, they know what happened to Mrs. Indra Gandhi. She was sent to Jail for trying to control the population in India. Unfortunately, not to decide is to decide. We call this decision by no policy. You need a license in any country to get married, to learn to drive or buy a car, to make an addition to your home, to open a beauty salon or to vend on the sidewalks, but you don't need a license to have children. Some fake leaders might scream, what do you mean; do we need a license to have children? Isn't it a free country and aren't we the largest democracy in the world and don't our people have an inalienable right to breed? Yes, ours is a free country. Yes, we are the largest democracy in the world, but freedom carries responsibility. Yes, we still have a right to have as many children as we want. By exercising, your rights, you are taking away other people's rights. This right will have to end soon. This is a luxury, India cannot afford. Look around your neighborhood; it is the poor who have too many children. They cannot afford to provide them with proper education. Educated and well-off Indians have fewer children. It might have been a wonderful idea at the beginning of Agricultural Age, and it might have been several hundred years ago, but can we now afford

to retain this right? You have heard the argument: your right to smoke ends where my nose begins. Soon it will be an individual's right to have children against the rights of other individuals - our species has come to that point.

It seems to me that we are beginning to accommodate this "glut of people" - as if it is a foregone conclusion and that population explosion cannot be changed, slowed down or stop. If we accept the glut as our destiny, then we are in trouble and our nation is in big trouble. This is not necessarily our fate. Our collective vision must be a world in which everyone has breathing space, a world in which we feed our current populations. We need to envision a world in which we manage the space we have. We are not here forever and ever. Trapped in the layers of rocks is the history of our four and a half billion years of evolution. Fossil records show that no species survived more than ten million years except dinosaurs. Within three million years of our existence on Earth, our number exceeded more than seven and a half billion. Comparing to other species, we may not even past half their time.

You know the history, now you know the problem and let us discuss the possible solutions: The problem should be solved by focusing on three areas: First, What to do with the very ill, the brain dead who are occupying hospital beds, second, what advice do we have to offer to women of fertile age who blame their husbands for their frequent pregnancy, and finally What rights do we give to unborn fetuses who are genetically defected and are unlikely to survive past their teen.

First, let us consider the brain-dead patients who are kept alive by artificial means. Many hospital beds around the country are occupied by these patients. They include both rich and poor. The medical insurance companies in America will tell you that use of the most expensive drugs should be saved for younger patients and should not be wasted on too old or brain-dead patients who are unlikely to live forever, the use of expansive drugs should be forbidden to this group of people.

Second issue is that the fertile women should be asked to limit the size of the family at the replacement level or preferably below the replacement level. They should be given the French contraceptive pill (RU486) or free Methotrexate and prostaglandin mixture. This combination of drugs was found to be effective against pregnancy. Methotrexate does not allow the fertilized egg to multiply and to grow while prostaglandin causes contraction and ejection of the fertilized egg. Even if we give this drug combination to young mothers free of charge, we will still save billions in the long run. The amount of money that will be spend on these contraceptives will be less than fifty to one hundred million per year which is not even one tenth of one percent of our current expanse.

The third issues: what should we do to the unborn genetically defected fetuses or say a prematurely born genetically defected child. In premature intensive care units of many hospitals, those children are kept alive at an enormous cost. Within the next few years, a genetic test kit will be available to most expectant mothers to see if their babies are free from all known genetic defects. The expected parents will have to make the awful decision if they would like to continue the pregnancy or opt out for abortion. The existing situation is bad where doctors make decision on behalf of parents. I am asking our elders to draw some guidelines for the doctors. Under what circumstances, a pregnancy should be terminated.

Abortion has become a major issue in western countries. Most common folks don't know when a life begins. At least, our social workers who perform an incredible job in villages should be informed to teach villagers. Villagers must be told that we are the result of the loving union of our parents. We are conceived when our father's single sperm is fused in our mother's egg. The life begins with that single fertilized cell. Although life begins with a single cell, by the time we grow up that single cell has divided over 100 trillion times. A single fertilized ovum is not a human being. It contains a set of instructions to make a human being. Is it alive? Contrary to common belief, the answer is no. A fertilized egg is not alive. Let me share a few facts before describing an actual experiment. Science deals with facts. Knowledge is power. Science gives this power to rich and poor alike. No nonsense ideas are acceptable to scientists. Authority is always suspected. Science takes power away from authority and places in the hands of common folks. A housewife may be far more knowledgeable than your community or religious leader.

In science there is no authority. Only expert's views are considered. They have mastered their skills over years. For example, a scientific fact is that water boils at hundred degree centigrade and freezes at zero degree. No matter whatever an authority says, you should all be able to repeat that simple experiment. To test if the fertilized egg is alive, there is a simple test that can separate living from non-living. Take two glass test tubes. In the first glass tube place a fertilized ovum of a worm and in the other glass tube place a live worm. Start cooling both glass test tubes simultaneously; cool them down to zero degree. You can cool below zero by adding liquid gases such as Liquid Nitrogen. Liquid nitrogen will cool the tube down to 70 degree below zero. If both creatures in the two glass test tubes were alive; they should both be freeze to death. No living creatures can survive at 70 degree below zero at any length of time and certainly cannot survive for a week, a month or a year. Now,

after some time, you may thaw gently both tubes to room temperature. The worm will die, and you see no change in the ovum. After thawing, you can implant this ovum in another live worm; it will grow and give birth to a baby worm. This experiment proves that the living worm when frozen will die, but the frozen egg was not alive before freezing and not alive after thawing. It became alive after implanting in the womb. Eggs contain a set of instructions to create live worm, but it is not a worm. One can keep the frozen ovum for years at 70 degree below zero. Nothing will happen to it. Similarly, human ovum is not a living creature; it has no spirit, no soul, no heart, no head, and no tail. It contains nothing but a bunch of organic molecules carrying a set of instructions, obeying the laws of physics, chemistry and Darwinian evolution to make a baby. Once you thaw the human ovum to room temperature and put it back into a mother's womb; it will attach itself to the wall of the uterus. It draws nourishment, grows and replicates. Enzymes of the uterus enter the egg and signal the egg machinery to become functional. From the mother's womb, the ovum will draw its nourishment, it manufactures its essential organs and becomes a baby in nine months. We found this experiment to function exactly right in case of human ovum. You might recall the story of the first test-tube baby Louis Brown who is now around 50 years old. In case of the first test-tube baby, several fertilized eggs of Mrs. Brown were stored in liquid Nitrogen at below 70 degree centigrade. The Catholic Church declared that the child was conceived outside the bed room; it has no soul. After the birth of thousands of in vitro children, the Church has gone silent. Three years after the birth of Louis Brown, Mrs. Brown wanted another baby. One of the fertilized stored eggs was thawed and implanted in Mrs. Brown. Nine months later, she gave birth to another normal beautiful girl. An ethical question was raised if both girls were of the same age or both girls were of different ages because they were fertilized at the same time but implanted in their mother's womb at different times. Whatever the ethicists say scientists have no problem in determining the three years age difference between the two girls.

The frozen egg was never considered alive. Because the frozen ovum is not a living creature, its biological activities were minimized by lowering their temperature. Western women have learned a terrific lesson from these experimental facts. They learned that they are the sole owners of their bodies. Their bodies are not factories for making babies. Men have no role to play for making babies. Most women are saying thanks for sperm banks. I don't need sperm anymore. I will buy one when I need one. Sperm banks are flourishing around the world. Under these circumstances what advice do we offer to Indian women? To avoid unwanted pregnancy, I want to share two facts with our sisters.

During breast feeding, nursing mothers produce a hormone called Prolactin in their blood circulatory system. A mother's nipple is linked with the brain via a nerve which passes through the spinal cord. Human brain is a big organ; it truly represents you. All your body parts can be replaced except brain. Brain receives a signal from a mother's nipples; it sends the signal to a part of the brain called Hypothalamus which in turn stimulates pituitary gland. In 1971, Schally and his group isolated three important hormones from pituitary gland namely LHRH, FSH and RH (Luteinizing hormone, follicle stimulating hormone and releasing hormone) establishing for the first time a link between brain and reproductive activity. (Schally was awarded a Nobel Prize for his work). These hormones are released from the brain in our blood circulatory system. When the blood carries the hormones to the ovaries, the hormones stimulate ovaries causing menstrual cycle (women have their monthly periods) and produce many eggs, but one is matured which is carried to the uterus. If the father deposits sperms when the egg is present, a baby is conceived. Once we find a link between brain and the reproductive organs; it is possible to control fertility by disrupting the menstrual cycle and by preventing the ovulatory cycle. The most fascinating discovery was that during breast feeding, nursing mothers produce a large quantity of hormone prolactin which produces milk. Prolactin is the most powerful hormone and in its presence women neither menstruate nor ovulate. If women maintain a high level of prolactin, they will not get pregnant. Prolactin is an excellent contraceptive. We learn this fact, not from women in the Western world, but from the Kalahari Bush Women of Africa. From puberty to menopause, Western women have 300 to 400 menstrual periods which causes early aging in most women, while the Kalahari Bush women have less than ten menstrual periods. The secret is in the breast feeding of their babies. Kalahari Bush women carry their babies on their back while working in the field. They breast feed their babies every half an hour for 24 hours a day for less than a minute. The babies get used to their feeding times. Every half an hour, the nipples send signal to the pituitary gland to produce the hormone prolactin. In the presence of prolactin, women do not produce eggs and will not get pregnant. The Bush women feed their babies for four to five years and will not get pregnant during breast feeding. They get pregnant once they stop breast feeding every four to five years. This is the safest and the best way to plan a family.

The secret of not getting pregnant is in your hand. Your husband has no control on your pregnancy. If you breast feed your babies every half an hour for less than a minute, you will not get pregnant. You can avoid unwanted pregnancy for four to five years and even longer. Anytime you want to have a baby, stop breast feeding every half an hour. You will get your menstrual periods back and

will get pregnant. Don't blame your husband, please. You must control your bodies and your life, and you must make the decision when is right time to have babies. You must avoid premature aging and must avoid unwanted pregnancy. After every birth, your biological system is shocked and hormonal systems disrupted. It takes long time for the hormonal system to recover. Some of you get old overnight. Look around the farms and fields. Those plants that bloom early produce flowers and fruits early and they die early. This is the law of nature. On the other hand, evergreen plants bloom late, produce fruits late and stay young for a long time that is why we call them evergreen. I propose a debate and a discussion on the population control because we must draw guidelines to decide what should be the population of India beyond year 2,100. By 2050, the world's population is expected to be nine to ten billion. The guidelines must be relevant to the need of our people. If we do nothing, we have a bad habit of copying other nations. The Western countries criticize us for not being a creative people. It may hurt our ego; there is some truth in their thinking. Our people never discover electricity, we never discover airplanes; we never landed men on moon and brought them back safely. We copy from West and even that is bad. Japanese copy better than we do.

Let us move our discussion from unborn fetus to the newborn child. It is our utmost responsibility to take care of all children who are here whether they are healthy or handicapped. The debate in Western countries now is about the rights of unborn children. How much right the unborn fetus has? What if you want a child and all the genetic tests show that the fetus is severely defected? The medical cost of bringing this child into this world is extremely high. Is there any reason to bring this child into this highly competitive world? A mother can have another healthy fetus. It is less expansive to have another child. If the couple is the carrier of the same bad mutations, they could have children by in vitro fertilization. It is the safest method to have healthy children.

We all feel very uncomfortable talking about handicapped children whether they are physically or mentally handicapped. Western countries have taken care of their handicapped, we have not. We are all altruists on this issue. We want to feel sorry for all those handicapped children who are begging in our streets. Of course, some of us so generous, we throw some coins before them. We all tell mothers they must take care of their handicapped children. That's where our sympathies end. Have you adapted a handicapped child? No, sorry cannot take that responsibility. That is too much for me. I am too busy. I don't have time.

For over populating our country, we blame politicians, we blame the rich; we blame the foreigners, we blame the English; we blame everyone except ourselves. Do you think having more babies is a foreign conspiracy? The progress we made during the past 70 years is enormous. It is better than many countries of the world then you might ask why our people don't have decent jobs, decent houses and decent food. There are so many good politicians, but there are some bad apples too. How could we blame all politicians, Mahatma Gandhi was a politician, In India, Pundit Nehru was a politician, Sardar Panel, Maulana Azad were all politicians. These are the very politicians who are responsible for giving us our independence. How could we blame politicians for over population? How could we blame businessmen for over population? In fact, they are so busy making money; they don't have time to make more babies. They have far lesser children than an average family in the village. There are so many good businessmen who have invested in our country and raised our standard of living. We are grateful to them for their farsightedness. Of course, there are some bad apples too. Because you see some structural defects in the Taj Mahal, should we destroy the Taj? The answer is, of course no. How could we blame businessmen for over population of our country? For some, businesses expand when population increases.

Who do we blame for our population explosion? Should we blame the English. East India Company came to India in 1600, and the British Government took over the direct control and ruled India for almost 150 years. Like all imperial powers, they also came to beg, borrow and steal. When our leadership got independence, they did not demand a nasty divorce from Britain. On the contrary, our separation was friendly, and we stayed as a member of family in the British Commonwealth. We appreciated them for sharing with our people, their knowledge, and skills and for introducing Western technologies in our country. Today, we are just as good, and some of us are even better than our English teachers. We learned their technology and we are ready to compete with them in all business ventures.

Some of our scientists went on to get the highest honor in science, such men like Dr. Ramakrishnan, Dr. Khorana, Dr. Chandrashekar, Dr. Raman, reached the pinnacle of achievements and were awarded with Nobel Prizes. But they had to come to foreign lands and learned the foreign technologies. When we came here, we found that the very same foreigner who we accuse of all our ills, are intellectually some of the most generous people on Earth. How could we think that the over population of our country is a foreign conspiracy? Shakespeare said well, "The fault my dear Brutus is not in our stars, it is in us." or Pogo said better, "We found the enemy, it is us."

Let us blame where the blame lies, in us. Let us blame mothers-in-law who demand to know why their 18-year-old daughters-in-law are not yet pregnant

after three months of marriage. I heard the jokes years ago, but they are so fresh in my mind. Older men, telling newly married men, are you not man enough? See a doctor or get a new wife or she is no good; she is barren; old women telling young brides, may God grant you a dozen children. How come you still don't have children? I don't want to die without seeing grand-children. From these silly comments, it becomes very clear that our people need massive education at all level.

One of the greatest challenges for our society is to change the ways of our thinking. Since our independence more than 70 years ago, everything has changed except our mind set. Our ways of thinking are the same ways of thinking of the time of Lord Buddha almost five hundred years before Christ. I imagine that the world at that time must have been a pristine and a clean place to live at that time. There must had been trees loaded with fruits, fertile land waiting to be plowed, clear lakes with fresh water loaded with fish, clean air, clean water and clean land. Everything was aplenty except people. We must have been encouraged to produce and reproduce. The policy of encouragement continued even up to the 1930 and 1940s, even these days French women would receive additional allowance for producing additional children, but they are reluctant to have many children. The population growth has slowed down. In spite of these precautions, we continued to multiply. Today, we are over seven and a half billion. Ill-legal immigration has become the biggest problem in both Europe and in America. Is there any need for more people now? The answer is not anymore. How do we change the ancient mind set is the greatest challenge we face today? If prayers might help, go ahead and pray for it. If you believe in miracles, ask for one or perform one or if you think magic could help, ask a magician or consult a mystic. I don't know of any other way except one, the TRUTH. Tell them the truth and tell them straight. Bringing additional unwanted children to this world would be disastrous to your health, to your family, to your city, to your country and to your world.

Our ability to grow food is controlled by our unique weather system. Do you know India is one of those unique countries in the world that has a strange weather system? Let me explain in simple language our weather system. Consider the land mass from Kerala to New Delhi and at the back of the land mass, there is a huge wall, the chains of Himalayan Mountain. The front plane leads in the ocean. In the month of March, April and May, the scorching sun heats up the land mass, the summer heat waves instead of spreading hot air evenly push upward towards Himalayan mountain range after colliding with the mountains, the heat waves rise. The cool air from ocean loaded with water rushes in from Trivandrum and goes towards Delhi. We call this weather system Monsoon. It rains for three months, June, July and August. The water loaded clouds takes about a month to travel from Trivandrum to Delhi. What if a couple of Monsoon fails? The environmental pollution may affect our weather systems. This could affect in many different ways, such as not hot enough summer, not enough water in the clouds. God forbid, there could be a massive starvation in our country where 20 percent of the world's population lives. We must ask ourselves; how many countries will come to help us and for how long? In time of crisis, nations protect their own people first. This is the simple and bitter truth we must tell our people and tell them now. Foreign countries may give us token help, but real help is unlikely to come on time unless we help ourselves and get this simple fact in our heads.

We need a massive education of our people. The entertainment world has made us addicted to films. Maybe we need them to use film media and bombard our people with the new and latest information about the health of our planet Earth. We must tell our people the truth that mother Earth is very sick and getting sicker every day. We have polluted the air; we have polluted the water and we have polluted the land and the over population is the worst pollution of all. Today, we wonder if the water we drink is safe and the air we breathe is safe if the food we eat is safe or 90 million additional new mouths to feed each year is enough.

How can we help our people to plan family or to control population, by launching a massive educational program, by telling them that our ability to create wealth is limited and our planet's resources to supply that wealth is also limited; by telling them that we cannot continue to have as many babies as we want; it will ruin the health of the mothers and destroy the happiness of the family, by informing them that we have made enormous progress since independence, but our gains were eaten by too many mouths, by informing them that we could never become truly independent if we continue to rely on imports, by confronting them with the truth about the worst pollution of our planet by over population and by providing the accurate facts about the fragile nature of our environment, our food supply, and the limited resources of fresh water, by educating them that we cannot continue to have more children indefinitely, by advising them that the time has come to set a limit.

If we ignore these warnings and continue to go on living as business as usual. We will have a rude awakening, when the population bubble will burst. Nature has a cool, cruel and efficient ways to fix her problem by unleashing her fury such as tsunami in Japan, Earthquake in Pakistan, Tornado in America, Volcanoes in Iceland and Coronavirus pandemic worldwide.

My purpose of writing these articles is to bring our people up to date with the discoveries made in the Western world to control the population. Americans and Europeans have passed the stage of the quantity control of their population. Most Americans and Europeans couples have two children and have succeeded in the quantity control of the population. Now, they are entering a new phase, the quality control of their population. The good news is on the way. Science is here to help them. Within the next five years, the sequence Genomes of egg and sperm would be available at a very low cost. It would be much easier for parents to decide if they would welcome a new born in their families. At a cost of $3 billion, we completed the greatest single biological experiment ever conceived in the history of humanity. We call this the Human Genome Project, to read our book of life.

In 1990, the US Congress has authorized us, NIH, three billion dollars to decipher the entire Human Genome and to decode and to map the location and function of all 24,000 genes present in human being. We completed this project in April 2003. Out of 24,000 genes, at least six thousand defected genes known to occur in humans which are responsible for causing all diseases.

The Impact of Sequencing Human Genome on the Quality Control (QC) of the Population:

On April 3, 2003, we sequenced the entire Human Genome that the number of letters and the order in which they are arranged (sequence) called the Human Genome Project. We found that less than two percent of the Genome codes for proteins the rest is the non-coding regions which contains switches to turn the genes on or off, pieces of DNA which act as promoters and enhancers of the genes. Using restriction enzymes (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 abnormal or cancerous.

A single cell is so small that we cannot even see with our naked eyes. We must use a powerful microscope to enlarge its internal structure. Under an electron microscope, we can enlarge that one cell up to nearly a million times of its original size. Under the electron microscope, a single cell looks as big as our house. There is a good metaphor with our house. For example, our house has a kitchen, the cell has a nucleus. Imagine for a moment, that our kitchen has 23 volumes of cookbooks which contain 24,000 recipes to make different dishes for our breakfast, lunch and dinner. The nucleus has 23 pairs of chromosomes which contain 24,000 genes which carry instructions to make proteins. Proteins interact to make cells; cells interact to make tissues; and tissues interact to make an organ and several organs interact to make a man, a mouse or a monkey. In every cell of our body, we carry sixteen thousand good genes, six thousand mutated genes responsible for six thousand diseases and two thousand Pseudo-genes that have lost their functions, during evolutionary time.

Our entire book of life is written in four genetic letters called nucleotides and they are A (adenine), T (thymine), G (guanine) and C (cytosine). These four chemicals are called nucleotide and they are found in the nucleus of all living cells including humans, plants and animals. Instruction in a single gene is written in thousands of AT/GC base pairs that are linked together in a straight line and we call them DNA (Deoxyribose Nucleic Acid) - Nobel prize was awarded to Crick, Watson & Morris Wilkins [1] for discovering the double helical nature of the DNA structure which is transcribed into a single stranded RNA (after splicing out the non-coding nucleotides, the RNA is converted to mRNA in which the less water soluble methyl group in Thiamine, T, is converted to more water soluble Uracil, U, by replacing Methyl group with a Hydroxyl group) which leaves the nucleus into Cytoplasm where it is translated in Ribosomes into Amino Acids leading to proteins). When thousands to millions of AT/GC base pairs contain information to make a single protein, we call that portion of AT/GC base pairs a gene (Nobel Prize was awarded to Khorana & Nauenberg for making a functional gene).

The starting Codon for a gene is AUG which codes for the amino acid Methionine after several thousand Codons for different amino acids, comes the stop codon. There are three stop Codons and they are UGG, UGA, UAG. After the stop Codon, no more amino acids are added, and DNA synthesis stops. If we count all the AT/GC base pairs in a single cell of our body, we will find that there are 3.2 billion pairs of bases present in every cell. The entire AT/GC sequence of 3.2 billion base-pair is called the Human Genome or the book of our life which carries total genetic information to make us.

As I said above, we deciphered all 46 chromosomes. What surprise us most was that our genome contains six billion four hundred million nucleotides bases 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. 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 the following genes on each chromosome:

We found that the chromosome-1 is the largest chromosome carrying 263 million A, T, G and C nucleotides bases and it has only 2,610 genes. The chromosome-2 contains 255 million nucleotides bases and has only 1,748 genes. The chromosome-3 contains 214 million nucleotide bases and carries 1,381 genes. The chromosome-4 contains 203 million nucleotide bases and carries 1,024 genes. The chromosome-5 contains 194 million nucleotide bases and carries 1,190 genes. The chromosome-6 contains 183 million nucleotide bases and carries 1,394 genes. The chromosome-7 contains 171 million nucleotide bases and carries 1,378 genes. The chromosome-8 contains 155 million nucleotide bases and carries 927 genes. The chromosome-9 contains 145 million nucleotide bases and carries 1,076 genes. The chromosome-10 contains 144 million nucleotide bases and carries 983 genes. The chromosome-11 contains 144 million nucleotide bases and carries 1,692 genes. The chromosome-12 contains 143 million nucleotide bases and carries 1,268 genes. The chromosome-13 contains 114 million nucleotide bases and carries 496 genes. The chromosome-14 contains 109 million nucleotide bases and carries 1,173 genes. The chromosome-15 contains 106 million nucleotide bases and carries 906 genes. The chromosome-16 contains 98 million nucleotide bases and carries 1,032 genes. The chromosome-17 contains 92 million nucleotide bases and carries 1,394 genes. The chromosome-18 contains 85 million nucleotide bases and carries 400 genes. The chromosome-19 contains 67 million nucleotide bases and carries 1,592 genes. The chromosome-20 contains 72 million nucleotide bases and carries 710 genes. The chromosome-21 contains 50 million nucleotide bases and carries 337 genes. Finally, the sex chromosome of all female 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. A gene codes for a protein, not all 24,000 genes code for proteins. It is estimated that less than 19,000 genes code for protein. Because of the alternative splicing, each gene codes for more than one protein. All the genes in our body make less than 50,000 protein which interact in millions of different ways to give a single cell. Millions of cells interact to give a tissue and hundreds of tissues interact to give an organ and several organs interact to make a human [2-6].

Not all genes act simultaneously to make us function normally. Current studies show that a minimum of 2000 genes are enough to keep human function normally; the remaining genes are backup support system and they are used when needed. The remaining genes are called the pseudo genes. For example, millions of years ago, humans and dogs shared some of the same ancestral genes; we both carry the same olfactory genes needed to search for food in dogs. Since humans don't use these genes to smell for searching food, these genes are broken and lost their functions in humans, but we still carry them. We call them Pseudo genes. 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.

We all carry 220 different tissues in our body and yet we have a single genome, that is the same DNA in every cell. How can all cells carry 24,000 genes and have the same DNA made of AT and GC nucleotides and yet they function in all 220 different tissues? The answer is not all 24,000 genes function in every cell of our body at the same time. Epigenetic answers one the most important questions in the cellular evolution. Small fraction of genes function in different organs and the rest are turned off by either Methylation or Acetylation which serves as Epigenetics agents. For Methylation and Acetylation, the common reagent in the Lab is Dimethyl sulphate or Diazomethane in Sodium Hydroxide for Methylation and Acetic Anhydride in Sulfuric Acid for Acetylation. The common Epigenetic agents in our body are Folic Acid responsible for Methylation and Acetyl Choline acts as Acetylating Agents. They can Alkylate or Acetylate both DNA or Histone proteins shutting off genes either temporarily or permanently. Methylation is a common and widely used mechanism for Epigenetic modifications in cells. Abnormal mutations in the Epigenome have been shown to be correlated with many human diseases, including different cancers, autoimmune disorders, neurological disorders (Fragile X syndrome as well as Huntington, Alzheimer, and Parkinson diseases including Schizophrenia).

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 does it means to be human; what is the nature of our memory our conscientiousness; 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 and microbes are all made of the same chemical building blocks and yet we are so divers that no two individuals are alike, even identical twins are not identical; they grow up to become two separate individuals.

Genome Based Diagnostic Technique:

Once we sequenced the genome, we thought that we can compare the entire genome of a healthy person with the genome of a sick person and easily identify mutated nucleotides responsible for causing diseases. We called GWAS: Genome Wide Association Studies. It is not as simple as we thought. We found that while some people having the mutated nucleotide come down with the disease, others with the same mutation do not show any signs and symptoms. We have no idea if other genes are protecting them. In some cases, we found the presence of a single copy of the mutated gene responsible for causing the disease called dominant gene while in other cases both copies of the mutated genes, called the recessive genes, do not cause any disease. The only way to solve this problem is to have as many genomes sequenced as possible and compare them using computers to identify the mutated nucleotides responsible for causing the disease with precision and accuracy. To pin point a specific gene responsible for causing a disease, we need to compare the genome of a healthy person with the genomes of hundreds and thousands of genomes of sick persons. The cost of sequencing is high, but the next generation of sequencers bring the cost of sequencing down to $100 per genome, it would be less expensive to sequence the egg and sperm to identify specific inheritable diseases in the family. To develop the next generation of DNA sequencers, my institute, NIH, provided enormous funds to Dr. Leroy Hood and his group. They accomplished miracle. The next generation of DNA sequencers uses nanopore technology that electrically pushes DNA fragments through tiny pores of proteins to read their content with the fastest speed. The faster we read the genome; the cheaper sequencing becomes. Presently, we could sequence the entire genome in one day at a cost of $700. Further improvement could bring the cost down to $100 per genome.

Many nations are providing large sum of money to sequence as many genomes of their population as possible. For example, United Kingdom launched a 1000-Genome Project. My own institute, NIH, in America launched a ten-years project at a cost of one and a half billion dollars to sequence a million genomes. The Chinese government is launching the most ambitious project; they committed $9 billion to sequence millions of genomes. Eventually, we will have to sequence the genome of every man, woman and child on Earth and use this data as a part of the medical record.

Now, we have digitized the entire Human Genome that is we converted the analog language of biology that is from A-T to G-C nucleotides bases to digital language of computer that is zero and one. Once the genome is digitized, it could be uploaded on the internet and could be moved around the world with the speed of light. Once the genomes move to the distant part of the world with the speed of light, the recipient countries will have convertors to convert back from the digital language of computers to analog language of biology. The great advantage of this conversions is that if a new deadly virus appears in one part of the world, its genome would be sequenced and sent to distant labs with the speed of light. For example, the recently identified Black Fungus in India could be sequenced and send it to Labs around the world. Identifying lethal genes on its chromosome, we could prepare its vaccine which would be readily synthesized on large scale and within days it could be made available to everyone around the world.

Mutations also occur in normal or somatic cells. Normal Cells grow and their DNA replicates to make copies. During replication, if DNA is exposed to radiations or chemical environmental pollution or viral infection or genetic inheritance, the replicating DNA is damaged causing mutations resulting the autosomal diseases. Mutations also occurred during replication. Replication is a rapid process causing mistakes by insertion of a piece of DNA, or deletion, or inversion, or translocation of DNA resulting in the formation of abnormal or cancerous cells.

As I said above, the Human Genome Project identified 24,000 genes in our book of life of which 16,000 good genes, six thousand mutated genes and two thousand Pseudogenes. In normal cells, double stranded DNA is transcribed to a single stranded RNA which is converted to mRNA by removing the uncoded region. It is the mRNA which is translated in the Ribosome into Protein. As the proteins fold, the two-dimensional linear Proteins is converted to three-dimensional Proteins, it becomes functional and perform the normal body function. A gene is a piece of mRNA segment, a unit of inheritance which codes for a protein and which has one start Codon AUG which codes for amino acid Methionine and it has three stop codons which are UAG, UGG and UGA. Six thousand mutated genes produce six thousand bad proteins which are responsible for causing six thousand different diseases.

As I said above, replication is a rapid process. It also occurs in germ cells. Mistakes also occur in genetic cells like eggs and sperms during replication. In his lifetime, a man produces enough sperms to populate the entire world. Most sperms are damaged and broken and unacceptable for breeding purposes. A sperm carries a single string of 59 million AT-GC nucleotides bases which carry 355 genes. On the other hand, a woman produces a single mature egg each month. The egg carries 164 million AT-GC nucleotides and 1,144 genes. Of course, T (Thiamine: the more fat-soluble methyl group in DNA is replaced by a water-soluble Hydroxyl group in RNA) in DNA, T is replaced by U (Uracil) in RNA. Because a Woman produces one matured egg per month, she has a right to make her own

reproductive decision. The choice to reproduce or not to reproduce; with whom to reproduce; and how many times to reproduce. In a pregnant mother so many genes are turned on to provide growth hormones and nourishment to the fetus. Once the baby is born, those genes are not turned off immediately. Her body faces havoc produced by hormones. Soon after the baby is born, she is euphoric due to the production of a high level of Oxytocin, a kind of opioid. Once Oxytocin is depleted, she undergoes sever depression. She sees herself fat, ugly, sick and no good. This is the worst time of her life. Some women suffer quietly, others behave violently.

By examining and comparing the sequences of thousands of abnormal and normal genomes of egg and sperms, we can identify all mutated genes in a genome. Each of us carries a single copy of half a dozen mutated genes. We are a carrier of one copy of the bad gene, if we marry closely related person who is bringing the other copy of the same mutated gene; the fetus is affected. Related couples in which both parents are the carriers of the same mutated gene; they are most likely to have children who inherit both recessive copies of the same genes. Such couple is most likely to have a baby which come down with horrendous genetic diseases and they are most likely to terminate the pregnancy. Although it is a painful decision, it is better than watching their children suffer and die of a terrible disease.

If the fetus carries both bad copies, it will be severely sick. Let me explain with an example how this work will help parents to decide to have a baby even before conception or during pregnancy. A newlywed couple could either conceive a baby either in the bed room or in the test tubes. If there is a family history of a disease, it is advisable to have in vitro fertilization. The couple gives a sample of eggs and sperms for genetic analysis before conception. Detection kits for several hundred genes are already being developed. The test result may show that the sperm is carrying a genetic defect on Y-chromosome that will make the baby a color blind or give him MS (muscular dystrophy). Doctors will inform the parents whether the child will be incurably blind, or carry a gene for defected heart, kidney or liver. During the ancient times when Eugenic was at its peak, the authority makes the decision about the fate of the fetus. These days, Parents make the decision to bring this child into this world. How many parents will love to have a blind or permanently sick child in their families? Not many. We must run the census among our people to get the results. It seems reasonable to assume that most parents will not be able to care for that fetus. We may not be able to correct that defects tomorrow, but day after tomorrow may be or in some distant future. We will be able to correct that defect at an enormous cost. Is there any reason for poor parents to keep that fetus alive and grow to full term at an enormous medical expanse? I am sure some rich parents will love to have children at all cost. Such children of rich families will not be burden on society or on our health care system. Since completing the Human Genome Project, out of six thousand mutated genes, we have already developed over 1500 tests to identify mutated genes, we can provide in vitro fertilization (IVF) of fertilized egg free from all genetic defects. Instead of having children in the bed room, couples will be able to select out the very healthy eggs and sperms and fertilized them in the test tube and implant them in the mothers. This way we can have the quality control of the babies we bring into this world. The quality control of the population could be accomplished by in vitro fertilization. About 25,000 Mendelian diseases (single gene defects) have been identified and approximately ten thousand are confirmed to specific genes. Developing novel drugs to treat those diseases is expensive and time consuming.

Different over-populated countries are practicing different methods to stabilize the world population. Let us see if we want to adapt any of those methods. I doubt it if you would accept them, but I will explain to you anyway. On one extreme, we have China where government controls population (now they permit three children per couple) and on the other extreme is India where nobody does anything to stabilize the over population. You can have as many children in India as you want whether you could afford them or not.

Most of our people live in thousands of villages across the nation. How many villagers understand the difference between "Family Planning" and "Population Control?" China practices population control. Now, they have relaxed the rule. For almost a decade and a half, the Chinese government has mandated the insertion of Intra-Uterine Devices (IUD) for all those mothers who have one child. Mothers are forced to undergo sterilization after two children. The third child is aborted without the consent of mothers. (now they permit a third child). China has the largest population in the world. We are number two. China does not have a democratic system of government. A handful of strong men rules the country. They have adapted an undemocratic system to control over population. In Western countries China's policy on new born is considered Eugenic and repugnant and for that reason most Western countries refused to send their delegates to attend a conference on population control in China over the years.

In South America, Mexico follows Chinese policy. Mexican women will receive an IUD without their consent or knowledge after the third child. In Peru, a mother gets a fifty-pound free food if she agrees to Tubal Ligation which could be removed later if a mother decides to have children. The government is also putting heat on doctors. If they want to practice medicine in Peru, each doctor must provide Tubal

Ligation to six women per month or loose privilege to practice medicine.

On the other hand, America is one of the most democratic countries in the world. Also, being the richest country in the world, America provides the best information to her people to decide when and if parents would like to have children. Only 3 to 4 percent work force is unemployed, the lowest in the world. Both parents go to work. None of the parents has time to take care of children. Parent delay having babies until their carriers are well-established. When women have children at later age, they tend to accumulate genetic defects. If mothers decide to take a year off from their work to have babies, they would like to have healthy babies.

They want to make sure before conception if it would be a healthy baby. They are saving their fertilized eggs in frozen Eggs in Cryo-Preservation Banks at an early age to be used when they become well-established. Parents must make that awful decision when to abort. People in West are wondering if we should have an acceptability test for all newborn children. To see if they are born healthy and that they are acceptable members of human society. Most people in the West believe that we have a moral obligation to take care of all those children who are already here. But we are talking about children who are not here yet. What rights do they have?

The completion of the Human Genome Project helps us follow the selective genetic breeding by discarding defected eggs and sperms. Some conservatives' members of our society will not accept the new discoveries. The question they must ask is should we add physically handicapped or mentally retarded children to our future gene pool. Or should we develop a series of medical tests on the fetus to eliminate unacceptable members to our society. How could we accomplish this goal? There are various biomarker tests (very expensive), we could conduct on the unborn fetus, such as examining the functioning of brain, nervous system, lungs damage, incurable blindness, kidney defect and liver malfunction. Shouldn't we check before birth if the heart and blood pressure is functioning properly? All those children who fail these tests, will place severe burden on our medical and financial resources. Should we allow the nature to take its course and let them die or should we bring them into this world by providing medical intervention and prolong their life, even though they will not live a quality life. Do you know that some handicapped children in America are suing their parents for bringing them into this world where they become burden on society? Simple economy works here. The cost of medical treatment is unaffordable. May be some handicapped children will have to sue their parents in our country that will teach their parents a lesson. For example, what should we do to Mongolian babies (Down Syndrome) who don't survive past thirty years? Should we set up committees to draw guidelines for medical professionals so that they will make a rational judgment to determine if child A will receive the precious treatment and will live and child B will not receive the treatment and therefore will die. We need new ethical principles based on modern science. This is the main thrust of my arguments. The old ethical principles also came from people's head, but they were based on the information available to our elders hundreds of years ago. Most ethical principles we used today were developed by Socrates about 2,500 years ago and everything that is written in philosophy since then is a footnote to his work. Although we have made a little progress in philosophy, we have made tremendous progress in genomic science. We are developing genomic medicine to keep people alive past one hundred years. Based on the genetic make-up, we are developing novel drugs to treat old age diseases such as Alzheimer, Cardiovascular diseases and Cancers.

Once the diagnostic tests confirm the location of mutated genes for either monogenic or poly genic diseases such as cancers or cardiac diseases or Alzheimer; we could design drugs to shut off those genes. The greatest challenge is to shut off genes that are responsible for causing cancers.

How to design drugs to shut off genes that Cause Cancers?

We design drugs to shut off genes that cause cancers. Professor WCJ Ross is one of the most distinguish English Scientists in the world. He is a Professor of Chemistry at the London University and Head of the Department at the Royal Cancer Hospital, a post-graduate medical center of the University of London. I am honored to be his graduate student, post-doctoral fellow and a special assistant and spent almost ten years in his Laboratory.

It was Professor Ross who worked on the development of anticancer drugs. An extremely lethal chemical called Nitrogen Mustard was tested against experimental animal tumor as an anti-cancer agent. We used the same method to make Nitrogen Mustard as was developed by German scientists during WWI. Nitrogen Mustard are the deadliest class of chemicals. It was extensively used during WWI. It is believed that more than 20 million people died during WWI. In 1919, there was an epidemic of Flu. It is believed that the use of Nitrogen Mustard during WWI mutated a normal Flu virus to become a deadliest strain. People have no immunity against this strain. The flu killed more people around the world than the people died during the hostility of the WWI.

Historical Background for Using Nitrogen Mustard for Treating Cancer

Fitz Heber, a German Army officer, worked on the development of Chemicals as a Weapon of War. He was responsible for making deadly Nerve gases and Nitrogen Mustards. Before the WWI, he was honored with a Nobel Prize for capturing Nitrogen for making Nitrate fertilizers directly from the atmosphere by burning the element Magnesium in the air forming its Nitride. Upon hydrolysis, Nitride is converted to its Nitrate. Using this method, we could make unlimited amount fertilizer. Nitrate is also used for making explosive. Soon after the WWI, Heber was charged with a crime against humanity for releasing hundreds of cylinders of Chlorine gas on the Western front killing thousands of soldiers in the trenches. When Allied forces reached his residence, his son shot himself and his wife committed suicide. Heber went in hiding in Swiss Alps. After the War, German Government got his release as a part of the peace negotiations. Heber returned home to hero's welcome. Although he promised never to work on the chemical weapons again, secretly he continued to develop more lethal analogs of highly toxic chemicals like Nitrogen Mustards. It was Heber who first made the notorious Bis-dichloro-ethyl Methyl Amine. Because it smells like Mustard seeds, it is called as Nitrogen Mustard. During the next 20 years, before the beginning of the WWII, hundreds of more toxic analogs of Nitrogen Mustard were developed. The bad news is that they are highly toxic, and the good news is that they shut off genes.

Nitrogen Mustard was mercilessly used during the WWI by both German and Italian Armies against Allied forces. Most soldiers exposed to Nitrogen Mustard were freeze to death. Their blood analysis showed a sharp decline in White Blood Cell (WBC). Since patients with the cancer of the blood called Leukemia, showed a sharp increase in WBC, Professor Ross and his group at the London University wondered if minimum amount of Nitrogen Mustard could be used to control Leukemia in cancer patients. It was a success. During the following 30 years, Ross developed hundreds of derivatives of Nitrogen Mustard to treat a variety of cancers. His most successful drugs are Chlorambucil, Melphalan and Merophan [7-11].

Over ten-year period, I made for Professor Ross dozens of analogs of Nitrogen Mustards. The deadliest among them was the Phenylenediamine Mustard. We use these compounds to check the sensitivity of the Tumors in the Tumor Bank. If tumors in the Tumor Bank become resistant, we must replace resistant tumor cells with fresh more sensitive tumors for testing other compounds.

Rationale for Developing Nitrogen Mustard Analogs as Anti-Cancer Drugs

As I said above, I made several Nitrogen Mustards for Professor Ross. I will describe you how to make the Nitrogen Mustard by using Haber's crudest method. Haber reacted Methylamine with Ethylene oxide to make 2-bis dihydroxy ethyl methyl amine. It was chlorinated by heating with Phosphorus Penta Chloride in the Phosphoric Acid. If you noticed a faint smell of Mustard Seed, Congratulations, you got Nitrogen Mustard; you cool the solution and diluted with ice cold water, the oil floating in the aqueous solution was extracted with Chloroform. The solution is dried, and Hydrogen chloride gas is passed through to make its Hydrogen-Chloride salt. Nitrogen Mustard Hydrogen Chloride salt is separated. No matter how much precautions you take, after the experiment, if you would take an alcohol swab of walls, doors, knobs and run a mass spectra of alcohol extract, you find a spectral line corresponding to Nitrogen Mustard. If you are exposed to Nitrogen Mustard and cross the threshold level, your WBC drops sharply and the energy providing Mitochondria die and you are most likely to freeze to death. Someone in the Defense department may make it, now a day, will anyone approve this study in the University Research Lab, probably No one. Your IRB (Institutional Review Board) and the safety committee will reject your proposal; and who will provide the funds for such an expensive study. The drug sensitivity between normal cell to cancer cell gives a ratio of toxicity called the Chemotherapeutic Index (CI). The larger the ratio the drug is more toxic to cancer cell. When tested against Walker Carcinoma 256 in Rats, most Nitrogen Mustards analogs cross-link both strands of DNA and give a CI of ten.

Rationale for Developing Aziridine Analogs as Anti-Cancer Drugs

Radio labeled study showed that Nitrogen Mustard shut off genes by binding to DNA by cross-linking both strands. We also discovered that radio-labeled Nitrogen Mustard does not bind to both strand of DNA simultaneously. First, one arm of the Nitrogen Mustard binds to a single strand of DNA, the Carbonium ion of the second arm is so reactive, it attacks its own Nitrogen atom forming a three-member intermediate ring called the Aziridine ion. Aziridine is extremely unstable in the acidic medium. As the living cells grow, they use glucose as a source of energy. Glucose breaks down to Lactic Acid which opens the Aziridine ring generating a Carbonium ion which attacks the second strand of DNA by cross-linking both strands. Once cross-linked, the two strands of DNA do not replicate. The cancer cell dies. On the other hand, Aziridine binds to a single strand of DNA. During cell division, the two DNA strand separate and the cell replicates. We thought that Aziridine analogs would be less toxic to normal cells and more toxic to cancer cells. It is indeed found to be true. We made a series of Dinitro Phenyl Aziridine compounds to test against the experimental tumor Walker Carcinoma 256 in Rats. One compound the benzamide of Dinitrophenyl Aziridine (CB 1954) gave the CI of 70 highest ever recorded [12-16].

As I said above, in the Laboratory of Professor Ross, I had worked with the deadliest Nerve agents making their derivatives such as Nitrogen Mustards, Carbamates and Aziridines developed during Hitler's time for evil purposes. We converted the evil chemicals into good chemicals. These agents easily pass-through various layers of our skin from Ectoderm to Mesoderm to Endoderm. They easily enter the cell nucleus destroying the beta and gamma cell which develop immunity. Then they enter the nuclear membrane where they find the stem cells. Stem cells differ from say skin cells. In Stem cells all 24,000 genes are functioning, cells have not yet differentiated. On the other hand, differentiated cells like skin cells which are differentiated, the Epigenetic groups such as methyl group or Acetyl group have shut off all other genes except the skin cell genes.

While Professor Ross worked with the Nitrogen Mustard by cross-linking both strands of DNA, as his Doctoral student, I was assigned to work with Aziridines which binds to a single strand of DNA. As a part of my Doctoral Thesis, I attached alkylating Aziridine to dyes like Dinitro Benzamide to attack the DNA of an experimental animal tumor called Walker Carcinoma 256. As I said above, the cancer cells grow faster than normal cells, they use more Glucose as a source of energy. Glucose breaks down to produce Lactic Acid. The Aziridine moiety is unstable in acidic solution. The Aziridine breaks down to open its ring to produce a positive Carbonium Ion. The Carbonium ion is extremely reactive; it binds to a single strand of DNA. It preferentially binds to N-7 of Guanine killing the tumor cells. Professor Ross and I have demonstrated the attack on N-7 of Guanine using the radio labeled studies. As a part of my Doctoral and Postdoctoral studies, over the years, I made 120 Dinitro-Benzamide derivatives for testing against Walker Carcinoma 256 in Rats [14-16].

From our Labs at the Royal Cancer Hospital, University of London, England, I had sent NIH (National Institutes of Health) over 120 drugs for NCI (National Cancer Institute) screening program. NCI honored me with the Fogarty International Award to come to America to continue my work with Aziridines translating the animal work in Humans. As I said above, NIH is the largest biomedical center in the world. It has unlimited facilities (chemicals, equipment and personnel). Twenty-one thousand best and brightest scientists selected from Ivy League schools work in 26 institutes in more than three thousand labs. I was honored to join this group at NCI.

I developed the same rationale to continue my work in America. I brought the idea from London University of attacking one strand of DNA using Aziridine, but I do not want to use the same dye Dinitro benzamide. One day, I came across a paper which described that methylated radio labeled Quinone crossed the Blood Brain Barrier. The entire radioactivity was concentrated in the Brain. I knew that Glioblastoma multiforme, the brain tumor, is a solid aggressive tumor like Walker Carcinoma in Rats. I decided to use Quinone moiety as a carrier for Aziridine rings to attack Glioblastoma. I was delighted when I realized by introducing just one Aziridine and one Carbamate moiety to Dinitro Benzine ring, I produced so toxic compound against tumors that its toxicity could not be measured. With the Quinone ring, I could introduce two Aziridine rings and two Carbamate moieties and could create havoc for Glioblastoma. My major concern was how toxic this compound would be to the brain cells. Fortunately, brain cells do not divide, only cancer cells divide. To grow, cancer cells use glucose as a source of energy. Glucose is broken down to produce lactic acid. It is the acid which activates the aziridine and carbamate generating Carbonium ions attacking Glioblastoma.Over the years, I conducted over 500 experiments which resulted in 200 novel drugs which were tested against experimental animal tumors. Forty-five of them were considered valuable enough to be patented by US Government (US Patent 4,146,622 & 4,233,215)). One of them called AZQ acts as a silver bullet. Glioblastoma was not only stop growing, but also 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 and I was also honored with the "Vidya Ratna" a Gold Medal, one of India's National Medal of Honors. (Exhibit # 1, 2, 3 & 4).

Exhibit # 1

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

Dr. Khan is the Discoverer of AZQ (US Patent 4,146,622 & 4,233,215), a Novel Experimental Drug Specifically Designed to shut off a Gene that causes Brain Cancer for which he receives a 17-year Royalty for his invention (License Number L-0I9-0I/0). To this date, more than 300 research papers have been published on AZQ. The award ceremony was broadcast live worldwide by the Voice of America (VOA). Dr. Khan is the first Indian to receive one of America's highest awards in Medicine.

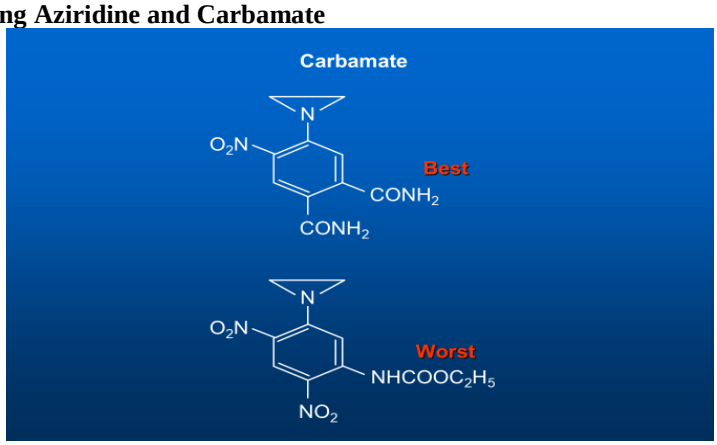
Exhibit # 2

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

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

Exhibit # 3

Single Strand DNA Binding Aziridine and Carbamate



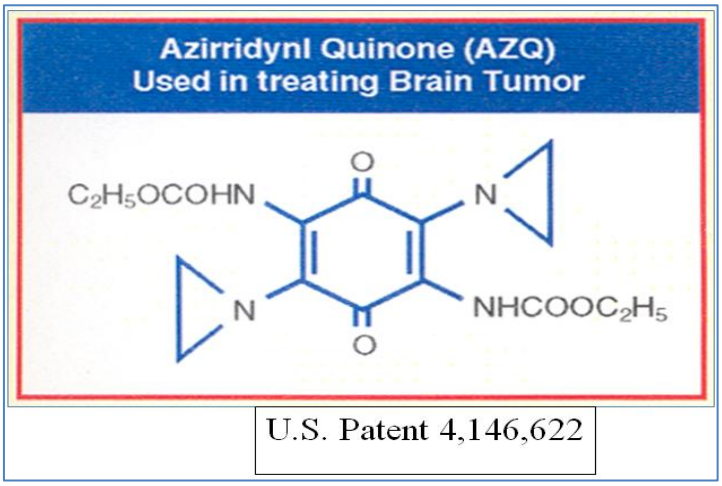


Exhibit # 4

Gold Medal for Dr. Khan

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

The Impact of Genomic Science on Society: Ethical Issues

New knowledge creates new ethical problems; knowledge is always superior to ignorance. We need new ethical solution based on modern science. We need to debate and discuss these issues among communities to provide guidance to all scientists. The purpose of life is to serve humanity; and to protect preserve and spread

healthy humans, healthy plants, and healthy animals and clean environment.

This section highlights many unsolved ethical problems and particularly the mistakes we made and lessons us learned. We are not allowed to make Human Clone, or conduct Germ-line Gene Therapy, nor we are allowed to work on Stem Cell. We need debate and discussion on these problems and we need to provide guidelines to scientists and researchers in the field. We have a history of bad decisions made by bad characters and they gave a bad name to the Science of Genetics. Now, the bad characters are dead and gone. We have some real problems before us and we need to think carefully. We not only have to think about the near future, but also distant future.

To begin with, it was Francis Galton, who coined the term Eugenics, meaning "well-born" to improve human race by selectively breeding individuals who have "desired" traits. Eugenics is a bad philosophy that has promoted a bad social movement. Well educated and well-meaning men who did not know full well the developing science of genetics, believed that it is impossible to breed out undesirable traits through systematic or medical processes and by discouraging reproduction by people with undesirable qualities and by enforcing involuntary Sterilization, killed thousands of unborn children. Hitler used this excused to slaughter six million innocent Jewish people. Now the couple not the authority makes the decision to have children. If the family of a couple has a history mental retardation, they could still have children by in vitro fertilization by selecting egg and sperm free from any defect.

The next problem is the population explosion. By producing new food, new fuel and new medicine, we ask ourselves what are the unintended consequences of our work, for example, of over food production? Do we destroy excessive amount of food as the American farmers do each year or do, we control the world population? By 2050, the population of the world will reach nine billion. By that time, we would have developed new food, new fuel, and new medicine to treat every disease known to mankind to protect, preserve and prolong human life beyond one hundred years, what would be the unintended consequences of development in Science on Society. The most nutritious vegetarian food containing all eight essential amino acids, will make world population lean healthy and long-lived. Besides new food, we would have new generations of plants which will serve as factories for producing new medicine based on the genetic make-up of the plants called the Genomic medicine which will treat specific disease based on the specific individual genetic make-up. These class of personalized medicines will further increase human lifespan. As the food supply increases, the population also increases. For example, at the time of India's Independence in 1947, the population of India was 400 million less than 75 years later, the population has increased to one Billion three hundred million. Global Warming has disrupted our regular Weather pattern. What if a single Monson fails to arrive on time?

When we succeed in shutting off genes of all three old age diseases that is Cancer, Cardiovascular disease and Alzheimer, most people on genetically engineered food will live longer and happier life. It raises several additional questions. What happens after we achieve that goal of reaching human lifespan to 100 years? What would be the quality of our life? By exercises and good nutrition, if the body mass is not retained, the Centenarians are most likely to be fragile and weak. They need the help of caretakers to perform the daily routine. By 2050, if we increase the age of about a hundred year of about a billion people, we need another billion caretakers. Will the society be happy with this achievement? I doubt it. The society is hardly likely to accept such a proposal.

After completing the Human Genome Project in 2003. We made dramatic progress to improve health of our planet and all living creatures on it. We not only understood life, but we also created synthetic life which will carry instructions not only to clean up our environment pollution, but also to create new food, new fuel and new medicine to treat every disease known to humanity. Thousands of scientists around the world are conducting amazing experiments to convert analog language of Biology into the Digital language of computers (that is from A-T/ GC to Zero and One). Once we succeeded in digitizing our genome, we could upload it on to our internet and send to any part of the world or any part of the Universe with the speed of light. Once transported our genome to anywhere, by using a convertor, we could convert our genome back to its biological form.

We are creating unusual life-forms. For example, the book of our life that is our genome is written in four nucleotide which are A-T and G-C, now we have introduced two additional nucleotide which are X and Y. This new creature is functioning and producing new protein. We have no idea the new protein from a six-letter genome is good or bad for us. In our Laboratories of Science and Technology we are conducting experiments which are unsurpassed in the history of mankind. Should we be allowed to create a new life-form? The appearance of Coronavirus is fresh in our mind. It has created havoc world-wide.

In the light of current scientific knowledge, we need to develop new ethical principle based on modern science to deal with problems created by advances in science. We need to debate and discuss these issues now and draw some guidelines for the scientists in the field and for the society. One person cannot provide answers to all these questions, we need input from experts from all over the country, but what I want to do

is to raise these questions in your mind and my aim will be fulfilled if I have made you think along these lines.

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Cite This Article: A.Hameed Khan (2021). The Impact of Genomic Science on Society & the Discovery of AZQ (US Patents 4,146,622 and 4,233,215) rationally Design to attack Glioblastoma, The Brain Tumor. *EAS J Biotechnol Genet*, *3*(3), 63-82.