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## **Review Article**

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

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#### **Abstract**

Americans live in the most democratic society in the world. When they reach adulthood, they are free to marry with whom they please regardless of race, religion, sex, or the place of origin or not to marry if they choose. They are also free to have children or not to have children or have as many children as they want. The population exploded and reached its peak of 2.09 percent by 1968 to 7.8 billion. With this rapid growth, the population expected to reach 9 billion by 2030. Then came the good news that by 2020, due to the world-wide collapse of the total fertility rate, the population growth rate declined to 1.05 percent. Now, we have conquered the Quantity Control of the Population, it is time to cautiously approach the Quality Control of the Population. Although we live in the freest society in the world, when it comes to selecting the best children or the quality control by enhancing the traits of the population by Germline gene therapy, our freedom is limited by the law of the land. You may not make any changes to improve the quality of life of the unborn children. The natural way of bringing children to this world without examining the health of Egg and Sperm present great risk. This abstract presents some suggestion to improve the quality of life of the future generation based of modern science.

**Keywords:** Genome, Gene, Mutations, Genetic toolkit, Chromosome-X and Y, AZQ

# Historical Background on the Quantity Control of the Population

More than seven and a half billion people live on Earth today. We are adding 90 million additional mouths each year to this planet. According to UN, by 2030, the population is likely to reach nine billion. Do we have enough resources to feed, clothe, and house all of them? 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, 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. Today, the population of the world is 7.8 billion and by 2023, the population would be more than eight billion. More than one third of the world population live in Asia alone which includes one billion three hundred million people live in India and one billion four hundred million live in China. It has placed

the greatest burden on our countries' resources. Our people work so hard and yet, they cannot raise the standard of living. The progress we have made since the Imperial power left Asia, more than seventy-five years ago, is enormous. It is eaten up by new mouths. At the time of independence, the population of our countries 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 of 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 and about 100 million each year to this planet. If we continue on the present trend, by year 2060, the population of the world is most likely to increase to ten billion. Our planetary resources are limited. We will not be able to feed, clothe and house adequately to all ten billion souls. Mother Nature is cruel; she takes drastic action and will crash the population explosion. She will unleash natural disasters such as cyclones, tornado, hurricanes, earthquakes, and epidemics of unusual diseases such as Covid-19, AIDS, Ebola, Dengue fever etc. If we continue to increase the population at the current rate, most scientists predict that there will be a massive starvation within the next ten years. By repeated farming on the same piece of land, we are using up Earth's nutrients. We are exhausting Green Revolution. It is time; we ask ourselves a simple 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 have to decide as a society how to educate young couple. There is no doubt that we live in a free countries. But freedom also carries some responsibility. You are free to walk in the street, but you are not allowed to walk on the highways.

Police will arrest you. Your freedom is restricted by the society. The society has a right to restrict the number of children a family could afford by increasing taxes to provide adult education in villages. We are the members of the society and we all must decide to limit the number of children per family. Once we

decide the number of children then we must decide the quality of life of those children who are likely to live. Some parents who are predispose to genetic defects still would like to have children even if they are determined to be genetically unfit to survive past their teens? For example, some middle aged couple who have Down syndrome children. Who will pay for their medical bills? Over 6,000 babies are born with Down syndrome in the United States each year. As recently as 1983, a person with Down syndrome lived to be only 25 years old on average. Today, the leading causes of death for persons with Down syndrome is Pneumonia, infectious lung disease, congenital heart defect (CHD) and circulatory disease. At the enormous medical cost, average life expectancy of a person with Down syndrome is nearly 60 years and continuing to climb. A couple with Down syndrome plans to have children, do they have a right to sequence their fertilized ovum to see if they are bringing a Down baby?

In this article, I will cover three areas: Where we began this journey, where are we now and where are we heading? 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. Like all other creatures, we left Africa in search for food, fresh water, and shelter. We became hunter and gatherers of food.

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 then collecting foods and searching for 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 plain of Africa today.

Human advanced rapidly leaving all other creatures behind. When we reached the Agriculture Age and started farming, we defied Darwin's laws of natural selection; we allowed even the most physically unfit humans to survive. We needed more children to farm the land.

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. More children provided more hands for farming and also provide security that was the old age slogan.

Today, we have two extreme points of view. First view considered that children are the gift of God and must be produced and protected at all cost. Second view is that we are technologically so advanced that we have machines to perform farming. We don't need additional hands for farming. Now, it the time to 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 20 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 our women what their sisters in the Western countries have accomplished personal freedom as their ultimate goal. They got the woman's rights and got on with their lives. Without women's consent, men cannot have a brood in our countries. 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 Asian husbands lost their power in America. Asian women, who came to America, have quickly learned their rights from their Western sisters. The divorce rate among Asian 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 who 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 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 Revolutions. 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 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. In short, our population increased 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?

Let me provide some historical background how we got here: Although science tells us that we are the result of four and a half billion years of biological evolution, our journey on Earth began over 3 million years ago in the heart of dark Africa. The place of our origin was confirmed by paleontologist, archaeologists and geneticists. Recent genetic advances indicate the existence of Mother Eve, who was the mother of us all, was born in the Afar Valley in heart of dark Africa. The first proof came from the genetic studies. We inherit a piece of genetic material called the mitochondrial DNA that is provided by our mothers only (because during our conception, only the central nucleus of our father's sperm fuses in the egg nucleus of our mother and the tail of the sperm which contains the male mitochondrial DNA, is dropped off). A study on woman's mitochondrial DNA was conducted in 150 countries, the data point to their origin to a

single woman in Africa; we may call her Eve if you wish that is where our journey began. More recent studies in geology and paleontology confirm the story of scientific genesis. It tells us that about 3 million years ago, there lived a women geneticist called her fossil Lucy, in the lush green forest in the Afar Valley in Ethiopia; she is the mother of us all. We all have descended from her. During the past three million years, we, her children, multiplied and traveled beyond Afar Valley in search for food.

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.

In the Age of Hunting and gathering, every morning, our ancestors woke up in search for food like deer and cattle in the Serengeti Plains. They said to themselves; they better run faster than the lion or we will be eaten by the lion. The lion 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.

People in that Age rarely died of old age as soon as they become weaker, they became some creatures food. The population was checked by the laws of nature for thousands of years. We traveled to different continents. In the Age of Hunting and Gathering, people were light, mobile and had small families. Large families were an impediment to moving.

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

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

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

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

How rapidly did we expand our population? The answer is very rapidly. It took from the beginning of time until 1850 for the world population to reach one Billion - then we expanded even more rapidly; it took only 80 more years for the world population to reach two billion in 1930. It took about 30 years for the world

population to reach three billion people in 1960. Then we lost control on growth; it took only 17 years for world population to each four billion in 1977. It took only nine years for world population to reach five billion, and by the middle of this decade, we have exceeded seven and a half billion. The population is expected to reach 10 billion by year 2060.

Let me summarizes below:

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

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

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

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

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

1996 through 2021, within 25 years, the population reached = 7.8 billion

If we were to continue with this rate by 2030, the pollution of the world will reach 9 billion

In terms of net gain (live births minus deaths) the world population increases by 269,000 a day. More than half of everyone who has ever lived on earth is alive today - the dead are in the minority. 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 Americas and Ebola virus in Africa, and Dengue in India that 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 our 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 Asian 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. America can afford it because it has only 333 million people who occupy a continent, a massive piece of free land trapped between Atlantic and Pacific oceans.

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. If we don't plan for population control, there will come a time when Nature takes care of things in a coldly efficient way giving us Earthquakes, Tsunamis, Tornado and now Coronavirus. If we don't practice family planning, we will be forced to control population.

Religions and Politicians will try to ignore this issue; as I said above, to them more head count means more votes. 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 up 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 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 rights 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 other people's rights away. This right will have to end soon. This is a luxury, Asia 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 Asians have fewer children. It might have been a wonderful idea at the beginning of the 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 it cannot be changed. If we accept the glut as our destiny, then we are in trouble and our nations are 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 biological 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: (1) What to do with the very ill, the brain dead who are occupying hospital beds, (2) what advice do we have to offer to women of fertile age who blame their husbands for their frequent pregnancy, and finally (3) What rights do we give to unborn 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 of dollars in the long run. The amount of money that will be spend on these contraceptives will be less than fifty to one hundred million dollars per year which is not even one tenth of one percent of our current expanse.

The third issue is that 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 a doctor makes a 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 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 Is a piece of a chemical which contains a set of instructions to make a human being. Is it alive? Contrary to common belief, the answer is no. The Human Genome Project showed that it is a piece of DNA. 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 belief is 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 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 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 live before freezing not alive after thawing because it was a piece of DNA an information molecule. 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, but when placed in the mother's womb, obeying the laws of physics, chemistry, and Darwinian evolution it organizes itself to become alive and to make a baby. Once you thaw the ovum to room temperature

and put it back into a mother's womb; it will attach itself to the wall of the uterus. Enzymes of the uterus enter the egg and signal the egg machinery to become functional. From the wall of 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 testtube baby Louis Brown who was born in 1978, she is now 43 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. Three years after the birth of Louis Brown, Mrs. Brown wanted another baby. From the frozen sample, 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 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 ethicist says, scientists have no problem in determining the three years age difference between the two sisters.

The frozen egg was never considered alive. Because the frozen ovum is not a living creature, its biological activities were minimized by lowering the 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 donating the sperm. I don't need it 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 Asian women? To avoid unwanted pregnancy, I want to share two facts with our sisters.

#### **For Informed Women**

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. As long as women maintain a high level of prolactin, they will not get pregnant. Prolactin is an excellent natural 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 technique 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.

#### For Uninformed Women

The secret of not getting pregnant is in your hands. Your husband has no control on your pregnancy. As long as 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 you will get pregnant if you wish. 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 Asian countries beyond year 2,100. By 2050, the population is expected to be nine 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. Before sequencing the Human Genome, the debate in Western countries now was, what if you want a child and the child is mentally handicapped. The medical cost of keeping that child alive is extremely high. Is there any reason to keep that child alive? A mother can have another child. It is less expansive to have another child. After the sequencing the Human Genome, the cost of sequencing Egg and Sperm is very affordable. For in vitro fertilization, we can select Egg and Sperm free from any genetic defect. For families who have a history of genetic diseases, conception in natural is very risky.

For overpopulating our countries, we blame politicians, we blame the rich; we blame the foreigners, we blame the Imperial powers such as English; we blame everyone except ourselves. Do you think having more babies is a foreign conspiracy? These are the very politicians who are responsible for giving us our democracy, our freedom, and 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 villages. There are so many good businessmen who have invested in our countries 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 Statue of Liberty, should we destroy the Statue? The answer is, of course not. How could we blame businessmen for over population of our countries?

When we walked out of Africa as Neanderthal about three and a half million years ago, I imagine that the world at that time must have been a pristine and a clean place. 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. We multiplied rapidly. Is there any need for more people now? 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, to tell 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.

We need a massive education of our people. The entertainment world has made us addicted to Hollywood films. May be 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 the people of the world 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 and if the food we eat is safe.

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 mother and destroy the happiness of the family, by informing them that we have made enormous progress around the world and yet a billion people don't have enough to eat, and 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, tsunami in Japan, Earthquake in Pakistan, Tornado in America, Volcanoes in Iceland, and Coronavirus world-wide.

#### The Quality Control of the Population

Americans and Europeans have passed the stage of the quantity control of their population. Most Americans and Europeans couples have two children. Now, they are entering into a new phase, the quality control of their population. The good news is on the way. The population exploded and reached its peak of 2.09 percent by 1968 to 7.8 billion. With this rapid growth, the population expected to reach 9 billion by 2030. Then came the good news that by 2020, due to the world-wide collapse of the total fertility rate, the population growth rate declined to 1.05 percent. If this trend continues for the next five years, we could claim victory; we have conquered the Quantity Control of the Population, it is time to cautiously approach the Quality Control of the Population. To reduce the population of prisons, mental institutions and Asylums, Quality Control of the population is essential.

Science is here to help us. We broke the genetic code and unlocked the secrets of Life. Before we bring a new life to this world, we can read its genetic book of life to ensure that the new life is of highest quality and free from all genetic defects. Within the next few years, it would be much easier for parents to decide if they would welcome a newborn in their families. The total genetic information to make a human is called the Human Genome. My Institute, NIH, was authorized to read the entire book of life that is to read our entire genome. The essence of life is information, and the information is located on the four nucleotide bases A-T and G-C. According to Central Dogma of Crick and Watson, the information on DNA is transcribed onto RNA which is translated in Ribosome to protein [1].

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

On April 3, 2003, we sequenced (read the entire script of our genome, letter by letter, word by word) the entire Human Genome that the number of letters and the order in which they are arranged (sequence) the entire Genome called the Human Genome Project. We found that less than two percent of the Gene in our Genome codes for proteins and the rest is the noncoding 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 noncoding region which could serve as markers and which has no effect, but a slight change in the coding region makes a normal cell become abnormal or cancerous. Recent studies showed that mutations in switches, promotors and enhancers which are present in the non-coding regions are also responsible for some unusual diseases. We need to go back and look at these regions more carefully.

As I said above, we deciphered all 46 chromosomes, 23 from each parent. The 46 chromosomes present in each cell of our body are the greatest library of the Human Book of Life on planet Earth. The Chromosomes carry genes which are written in nucleotides. Before sequencing (determining the number and the order of the four nucleotides on 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. The Chromosome-22 contains 56 million nucleotide bases and carry 701 genes. Finally, the sex chromosome of all females called the X-chromosome contains 164 million nucleotide bases and carries 1,141 genes. The male sperm called the Y-chromosome contains 59 million nucleotide bases and carries 255 genes.

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

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 [2-8]. 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.

As I said above, the old cells begin to die, and they are constantly being replaced by healthy cells. Why do the normal cells become abnormal or become cancerous? Damage to functional

gene called Mutations are responsible for causing normal cells to become abnormal. Mutation is caused by exposure to Radiations, Chemical/Environmental Pollution, Viral Infections or Genetic Inheritance. Mutations also occurred during DNA replication, such as insertion, deletion, relocation, multiple copying, inversion etc.

Anyone those factors will disrupts the two percent of the coding region of our genome will alter its function by slightly altering its code; an altered codon will code for a wrong amino acid and wrong amino acid will give a wrong protein and it will make normal cell become abnormal. When the functions of Codons are disrupted intentionally or unintentionally, we alter the Codon's function. For example, intentionally we alter a codon by smoking and unintentionally by exposure to environmental pollution such as chemicals pollution, viral infection, radiations, or genetic inheritance. Altered Codons have wrong information to make wrong amino acids. Wrong amino acids make wrong proteins and wrong proteins make wrong cells and wrong cells grow much faster than the normal cells and become abnormal or cancerous and they form a lump, we call these lumps, tumors. Attempts are being made to design drugs to attack cancer cells on all three level that is DNA, RNA and Protein. Herceptin, a novel class of drug, has been successful in attacking protein. Craig Milo has designed double stranded RNA to shut off gene and prevents its translation into protein. Attack on DNA was carried out by Ross. He has been successful shutting off genes using extremely toxic Nitrogen Mustard.

One of the essential component of the Quality Control of population is to treat all diseases including common allele as well as rare allele diseases. Once the bad mutation is identified on a gene which is responsible for causing diseases. There are two ways to treat these diseases either by replacing the bad gene with a good gene as in Gene Therapy or shut off the bad gene by designing drug as in Drug Therapy to attack the bad gene DNA.

#### **Gene Therapy**

Once the mutation sites and chromosome number are identified, we can diagnose, prevent, and treat the disease/cancer either by Gene Therapy if a single gene mutation is responsible for causing any of the above disease/cancers or by Drug Therapy if multiple mutations are involved. With the method of gene therapy, a functional gene is inserted into a cell to make a transgene with the intent that it will work in place of the mutated gene (i.e., Vector-based delivery). Viral, chemical, and physical methods are being explored for transferring genes. The transfer of the new gene occurs inside the body (in vivo) after systemic delivery, often using an IV infusion. The original genetic material in the chromosomes is intended to be left unchanged. This means that the mutated gene would still be there and can still be passed on to the offspring. The most successful experiment of Gene Therapy was carried out by scientists at NIH, French Anderson and his colleagues have successfully developed Gene Therapy for treating SCID (Severe Combined Immune Deficiency Syndrome), we could use the same method to cut and paste and replace the bad gene with the good gene in a virus as Victor which is used to infect the WBC obtained from the same patient. After harvesting the infected WBC, the transgenic WBC was injected back in the same patient to treat SCID. It worked and patients fully recovered. Several thousand SCID children are living a normal life. Gene Therapy works on diseases with a single gene mutation, but not if the multiple mutations are responsible for causing diseases such as cancers. We must design drugs to shut off those genes.

#### **Drug Therapy**

Gene Therapy cannot be applied to multiple genetic defects such as cancers or heart diseases. Drug Therapy could be used to develop novel treatments. The hero of Drug therapy is Ross. Professor WCJ Ross of London University was the first person who designed drugs to attack DNA for Cancer Treatment. He designed drugs to cross-link both strands of DNA that we inherit one strand from each parent. Cross-linking agents such as Nitrogen mustard are extremely toxic and were used as chemical weapon during the First World War. Hundreds of more toxic analogs of Nitrogen Mustard were developed during the Second World War. Solders exposed to Nitrogen Mustard showed a sharp decline of White Blood Cells (WBC) from 5000 cell/ CC to 500/CC. Children suffering from Childhood Leukemia have a very high WBC count over 90,000/CC. Most of the WBCs are premature, defected, and unable to defend the body from microbial infections. Ross rationale was that cancer cells divide faster than the normal cell, by using Nitrogen Mustard he could cross linking DNA and prevent cell division. Once he demonstrated that he could shut off a gene by cross-linking DNA; he could shut off any mutated gene of all 220 tissues present in a human by finding a dye that could specifically color that tissue. He could attach the Nitrogen Mustard group to the dye and attack the cancer genes in any one those tissues. Over decades, he made thousands of Nitrogen Mustard analogs.

Ross was the first person to use chemicals successfully to treat cancer. Although such drugs are highly toxic more cancer cell will be destroyed than the normal cells. Over decades, Ross made several hundred derivatives of Nitrogen Mustard as cross-linking agents. Some of the Nitrogen Mustards are used for treating cancers such as Chlorambucil for treating childhood leukemia (which brought the WBC level down to 5,000/CC) and Melphalan and Myrophine for treating Pharyngeal Carcinomas [9-15]. Because of the high toxicity of Nitrogen Mustard, new drugs could not be developed to treat other types of Cancers.

As I showed above, we sequenced our genome, our book of life, letter by letter word by word, sentence by sentence, chapter by chapter all forty-six volumes written in six billion four hundred million genetic letters (nucleotide) of a healthy human being under the Human Genome Project. We can use our healthy Genome as a Reference Sequence for comparison. It took 13 years to sequence the entire human genome. Now, we developed next generation sequencers like Nanopore technology which will sequence the entire genome cheaper and faster. Using biopsy sample, we can take a single cell from the Lung or Oral tumor of smoker, sequence its genome, and compare with the Reference sequence to identify the number and location of all mutations or damage genes caused by smoking. To identify mutations with precision and accuracy, recently, we also completed the 1000-genome project which will provide thousand copies of the same gene for comparison. We also learned to convert Analog language of Biology into the Digital language of computer. Now, we can write a program and design a computer to read and compare and transfer the sequence of any living creatures across international borders (such as Coronavirus sequence) at the speed of light. For example, if we compare the Reference Sequence with the smoker's gene sequence, it will identify all the mutations with precision and accuracy. Once the mutations responsible for causing Carcinoma are identified, we can design drugs to shut off those genes.

Using the same rationale, it has taken me about ten years to make (CB1954), a novel drug to shut off a mutated gene responsible for causing Walker Carcinoma 256, a solid aggressive tumor in Rat and about a quarter of a century to make AZQ to shut

off Glioblastoma gene in human responsible for causing brain tumor. The following example explains how easy it is to get Lung or Oral cancer by simply smoking a dozen genetically modified high Nicotine content Cigarette and how expensive, time-consuming, and exhaustive it is to find a possible cure. If we do succeed in developing a drug, the Drug must be safe and effective. After a year use, if the FDA receives an Adverse Effect Report, the Drug is withdrawn. All the effort is wasted. Detail information is provided below:

As I stated above diseases with multiple genetic defects cannot be treated with Gene Therapy but can be treated with Drug Therapy. Diseases with multiple genetic defects can be treated with highly toxic drug like Nitrogen Mustard. It acts as drug by cross linking DNA shutting off a gene. Nitrogen Mustards act as drugs and are highly toxic. On the other hand, there is another class of chemicals called the Prodrugs. They are Aziridine and Carbamate which are non-toxic. They became active in the presence of acid and then bind to a single strand of DNA shutting off the genes.

At the London University, I was a graduate student of Professor Ross. After receiving my Doctoral and then Post-doctoral Fellowship, I became his Special Assistant. For almost ten years, I worked with Professor Ross making derivatives of Nitrogen Mustard as anticancer agents. While Professor Ross was designing drugs to attack both strands of DNA which are extremely toxic, as a part of my doctoral thesis, I was assigned to design non-toxic prodrugs to attack a single strand of DNA. The prodrugs, I was designing are non-toxic when activated in acidic media become highly toxic. This class of drugs is called Aziridines and they are a novel class of drugs which attack only one strand of DNA [16-18]. I made over 100 Aziridine dinitrobenzamide (CB1954) analogs which attack the DNA of Walker Carcinoma 256 in Rat, a solid aggressive tumor.

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

I developed the same rationale to continue my work in America when I was offered the Fogarty International Fellowship Award to continue my work at the National Cancer Institute (NCI) of

the National Institutes of Health (NIH) in Bethesda, Maryland, USA. I brought the idea from London University of attacking one strand of DNA using Aziridine, but I do not want to use the same dye Dinitro benzamide. One day, I listened to a lecture at NIH. The speaker described that methylated radio labeled Quinone crossed the Blood Brain Barrier. When radiolabeled Quinone is injected intravenously in mice, within 24 hours, the X-ray showed that the entire radioactivity was concentrated in the Brain. I knew that Glioblastoma multiforme, the brain tumor in humans, is a solid aggressive tumor like Walker Carcinoma in Rats. I decided to use Quinone moiety as a carrier for Aziridine rings to attack Glioblastoma. I was pleased when I remember when 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. It worked. Over the years, I made several dozen analogs of Aziridine Carbamate Quinone. The most active analog was Diaziridine Dicarbamate Quinone, I named it as AZQ. My major concern was how toxic this compound would be to the normal brain cells. Fortunately, brain cells do not divide, only cancer cells divide. AZQ acts as a Prodrug. A Prodrug is compound carrying a chemical masking group that renders it inactive and nontoxic. Once the prodrug reaches a treatment site in the body, removing the mask frees the active drug to go only where it is needed, which helps avoid systemic side effects. 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 genes of Glioblastoma. The tumor stops growing and starts shrinking.

My drug AZQ is successful in treating brain tumor because I rationally designed to attacks dividing DNA. Radio labeled studies showed that AZQ bind to the cancer cells DNA and reduce brain tumor and normal brain cells are not affected at all. AZQ is a new generation of drugs. Not so long ago, these cancers mean death. Now, we have changed it from certain death to certain survival. The immunologists in our laboratories are developing new treatment technique by making radio labeled antigens to attack remaining cancer cells without harming normal cells.

We have cured many forms of cancer. We have eliminated childhood leukemia, Hodgkin disease, testicular cancer and now AZQ type compounds which are being developed rationally. While most anti-cancer drugs such as Adriamycin, Mitomycin C, Bleomycin etc., in the market are selected after a random trial of thousands of chemicals by NCI, AZQ is rationally designed for attacking the DNA of cancer cells in the brain without harming the normal cells. We are testing combinations of these drugs to treat a variety of experimental cancers in animals [19-21]

As I said above, I rationally design drugs to treat Brain cancer. I am the discoverer of AZQ (US Patent No. 4,146,622 & 4,233,215). I shared a 17-year royalty with two of my colleagues. The discovery of AZQ has been a quarter century long effort starting from the Royal Cancer Hospital, University of London, England and ending in the National Cancer Institute, Washington, America. Some may think that we are very lucky. The fact is that luck has nothing to do with it. It is a shear hard work. I had already made over one hundred derivatives of Aziridine drugs which tested against experimental animal's tumors and published with Professor Ross before I came to America and joined NCI (National Cancer Institute). Let me share with you how we sweated for making AZQ. To introduce one successful drug for treating one kind of cancer, over the last 25-year period, I conducted over 500 experiments, out of

which 200 drugs were tested in thousands of animals and only 45 drugs were considered valuable enough to be patented by US government and only one drug, AZQ, has recently completed a Phase-III clinical trial which showed that patients receiving AZQ live 20 to 24 months longer than the untreated patients. Glioblastoma not only stop growing, but the tumor also starts shrinking. This period gives physicians enough time to develop alternative treatment to eliminate the remaining resistant cancer cells by Immunotherapy. For the discovery of AZQ, I was honored with the "2004 NIH Scientific Achievement Award", one of America's highest awards in medicine.

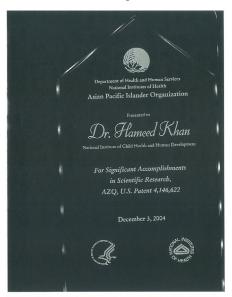
#### Exhibit #1

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

During the NIH/APAO Award Ceremony held on December 3, 2004.



Dr. Khan is the Discoverer of AZQ (US Patent 4,146,622), a Novel Experimental Drug Specifically Designed to shut off a Gene that causes Brain Cancer for which he receives a 17-year Royalty for his invention (License Number L-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,

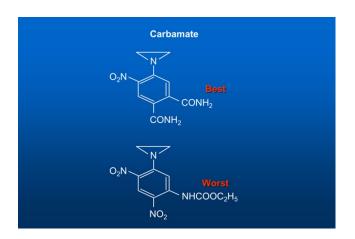


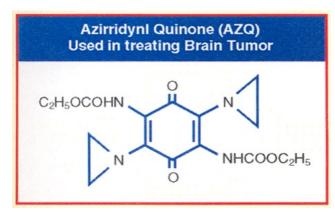
Discoverer of anti-cancer AZQ, after receiving 2004, Vaidya Ratna,

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





U.S. Patent 4,146,622

#### Exhibit #4

#### Gold Medal for Dr. Khan



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

#### **Ethical Issues**

In developing drugs for treatments, we poison bad DNA selectively. All poisons are a class of chemicals that attacks all DNA of all cells whether they are good and/or bad alike. Chemicals that cause cancer, at a safe level, can also cure cancer. Science teaches us to selectively attack bad sets of DNAs without harming the good sets of DNAs. Poisons are injurious to living creatures. There is a small class of chemical, when exposed to humans, disrupt the function of DNAs, and make normal cells abnormal and they are called cancer causing chemicals or carcinogens. I must confess, we still use surgery to cut off a cancerous breast; we still burn cancer cells by radiations; and we still poison cancer cells by chemicals. The largest killer of women is breast cancer. After all the treatment, the remaining cancer cells return as metastatic cells and kill breast cancer patients in three years. A decade from now, these methods could be considered as brutal and savage, but today that is all we have. We hope to develop new treatment for Breast Cancer. Hopes means never ever to give up.

The completion of the Human Genome Project has provided us toolkit to read the script or sequence of the genome of Egg and Sperm at the minimum cost. Eggs and Sperms carry heredity information which is passed on the future generations. When we decoded the Human Genome and learned that the language of Life, we found that all Life forms is written in DNA which is made of four genetic letters called nucleotide bases and they are A (Adenine), T (Thiamine) and G (Guanine) C (Cytosine). The chapter of the book of life that describes the script of Egg is called Chromosome-X which is made of 164 million nucleotide bases and carries 1,141 genes while the Sperm called the Y-chromosome is made of 59 million nucleotide bases and carries 231 genes. We have ABI computer that reads a thousand nucleotide bases per second and can identify mutations responsible for causing horrendous genetic diseases. Before the conception, the parents can have read the sequence of their Egg and Sperm to see if they are free from any damage caused by radiations, chemical environmental pollution, viral infection, or genetic inheritance. Sequencing of the fertilized ovum should easily identify the markers of serious diseases

such as autism, attention deficit hyperactivity disorder (ADHD), bipolar disorder, major depression, schizophrenia. Sickle Cell Anemia, Cystic Fibrosis, Tay-Sachs, Hemophilia, Huntington's Disease, Muscular Dystrophy. Down Syndrome, Thalassemia, Huntington's Disease, and Duchenne's Muscular Dystrophy.

To reduce the population of Prison, Asylum, and Mental Retardation Institutions, is it time to encourage parents who have a family history of serious illnesses to have in vitro fertilization to have healthy babies? Is it time to permit Germline Gene Therapy for a limited time to permit Quality Control of the Population? Do parents have a right to ask if they are bringing children who will be acceptable member of human society? Because of our technology is not advanced enough, currently, we are not recommending producing gene-rich children, enhancing traits to introduce High I.Q., Athletic ability, pretty face etc. Instead, we are recommending, eliminating mutated alleles from the egg and sperm before conception.

### Genetic Engineering and Recombinant technology

It involves cutting, pasting, copying, and sequencing DNA. As I said above, in humans, less than two percent of the Genome codes for proteins and the remaining 98 percent of Genome contains non-coding regions which carry switches, enhancers, promoters, inhibitors etc. How do we know that only two percent of the Genome codes for proteins because only two percent of the Genome transcribes into RNA? The non-coding regions of the RNA is spliced out into mRNA which carry three letter Codons. It is the Codons which is translated in the Ribosome into proteins. The protein carries out our body functions as soon as it folds and becomes three dimensional. As the Central Dogma of Francis Crick describes that double helical DNA replicates (makes its own copies) in the nucleus and it transcribes into the single stranded RNA as it leaves nucleus as mRNA in the cytoplasm (splicing out non-coding sequence) which is translated in the Ribosomes into proteins. Information flows from both good genes and bad genes from nucleus into the cell keeping the organism healthy or sick. Good proteins from good genes keep us healthy and bad proteins from mutated genes produce bad proteins that make us sick. The flow of information is continuous and uninterrupted.

One of the greatest challenges of the 21st century medicine is how could we cut out and purify a single gene from the string of genes from the entire human genome and insert this single human gene into a biological system making a recombinants which serve as Vectors (such as bacteria or plasmids for smaller genes, and for larger genes using Phagemids, or Cosmids (Cosmid vectors are hybrids between plasmid and phage  $\lambda$  vectors. Cosmid vectors are designed to clone large fragments of DNA and to grow their DNA as a virus or as a plasmid. Cosmid vectors are used in homologous recombination between two different plasmids in the same cell and grown in both bacteria and animal cells).

For making their clones, we use BAC, Bacterial Artificial Chromosomes, and YAC, Yeast Artificial Chromosomes) of a single cell bacteria or yeast cell to produce large number of copies (library) of this gene. The desired gene from the recombinant library is released using restriction enzymes EcoR1 to produce large amount of highly pure protein to treat a specific disease such as producing large quantity of Insulin to treat 300 million diabetics around the world. Genetic Engineering and Recombinant technology are the answer to remove the mutated allele before conception.

We suspect that each of us carries a couple of mutated genes. Let me explain with an example how this work will help parents to make a decision to have a baby even before conception or during pregnancy. A newlywed couple gives a sample of eggs and sperms for genetic analysis before conception. Detection kits (gene chip) 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 newborn a color blind or give him MS (muscular dystrophy). Doctors will inform the parents whether the child will be incurable blind, or carry a gene for defected heart, kidney, or liver. How many parents will love to have a blind or permanently sick child in their families? Not many. We must run the census among 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 defect 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 our medical system. After completing the Human Genome Project, we have already developed over 1500 test to identify mutated genes, we can provide in-vitro fertilization (IVF). Instead of having children in natural way, 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 or surrogates. This way we can control the quality of the babies we bring into this world.

Different overpopulated 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 (population over 1.4 billion) where government controls population and on the other extreme is India (Population over 1.3 billion) where nobody does anything to stabilize the over population.

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. 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. 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 rule China. They have adapted an undemocratic system to control over population. In Western countries China's policy on newborn is considered eugenic and repugnant and for that reason most Western countries refused to send their delegates to attend a conference on population control in China. Now, China has relaxed the restrictions.

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

make a decision when and if parents would like to have children. Only 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. Parents 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 Egg Banks (cryopreservation) at an early age to be used when they become well-established. Parents have to 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. The question is, should we add physically handicapped or mentally retarded people to our future gene pool. Or should we require a couple to sequence their fertilized ovum before conception to eliminate unacceptable members to our society. 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 science. In the light of the collapse of the fertility rate which decline the population growth rate to 1.05 percent, if it continues for the next five years, is it time to allow Germ line gene therapy for a limited time to eliminate genetic defects passing on to the future generations. Is it time to develop new ethical principle to deal with problems created by advances in science?

If you look at our distant future, we are certain that human destiny lies in other star system. We are trapped in a middle age dying solar system. Our Sun has been burning for the past four and a half billion years. It has used up more than half of its energy. As the Sun burns all the Hydrogen, it will collapse on itself and explode as a super nova. Before the Sun explodes as super nova, we have enough time to find a new home for humanity.

If we wish to send human to colonize Mars and to use Mars as a base to launch city-size spacecrafts on a one-way travel to the nearest exoplanet, we need to redesign humans to cope with the deep space environmental conditions. We must control our own evolution. Our evolution on Earth as a Homosapien is the result of four and a half billion years of biological evolution. Space travelers don't have the luxury of time. To accommodate the space travel conditions, we have to become more than human. Germline Engineering will give us the power to manipulate the Human Genetics of our next generation to alter their biology to control Human evolution in meaningful predictable way.

Using the genetic toolkit developed during the Human Genome Project, it is time to select and alter human embryo to introduce new traits to survive for long space travel. These developments culminating in Germline engineering beginning from mice to men. The manipulating of Egg and Sperm to modify future generations. Direct Germline manipulation in human may be a decade away. Since we plan to land men on Mars by 2030, it is time to start thinking about conducting some basic experiments in our Labs such as prolonging the age of Mice. We cannot send space travelers on a one-way journey if they die on their way within a hundred year. The Human Genome Project showed that our Aging is a combustion process. The tail end of each chromosome carries a set of a six-letter code called Telomer. Aging is related to the loss of Telomeres, the six-letter code (TTAGGG) that shorten our DNA and shorten our lifespan. During replication, each Chromosome loses about 30 Telomeres each year. If we slow down the loss of Telomeres by using the enzyme Telomerase Reverse Transcriptase (TRT), we could slow down the aging process. We have already demonstrated in the worm C. Elegance that by using TRT gene, we have increased its lifespan by several folds. Now, we could translate this work first in mice then in human embryo; we could try by making a Vector, a virus, carrying TRT gene when infected the embryo and harvested to eight-cell and sequence to confirm the presence of the trans gene. The TRT gene would have been inserted in the entire genome of every cell of the growing embryo. By sequencing a single cell to confirm that the TRT transgene is spliced, we could implant TRT gene carrying embryo in the mice womb. We could monitor its development by frequently taking three dimensional MRI (22). If MRI show any abnormality, we could discard the embryo and use a new one. If this transgenic experiment in mice is reproducible and verifiable, we could try in human embryo. Suppose this experiment conducted in humans is successful and also suppose the sequence show that at each replication only 15 Telomeres are lost instead of 30 Telomeres. Since the longevity treatment with the TRT transgenic virus is safe, inexpensive and would be easily available to human. Should we provide the treatment to every man, woman, and child on the face of the Earth or make it available to long distance space travelers only?

The study of Down Syndrome patient show that they carry in their Genome an extra copy of Chromosome-21. We learn that human being can survive with 47 chromosomes. Now we can introduce an artificial synthetic chromosome with new genes to enhance the human ability. Paving way to human genetic engineering and the beginning of the human biological design. The father of molecular biology, James Watson said, If we could make better human being by adding better genes why shouldn't we. We will not only succeed, but also, we will succeed gloriously. We must overcome the ancient fears. By deciphering the Human genome. we have spent billions of dollars to unravel human biology, not for idol curiosity but in the hope of improving our lives, we are not about to turn away from this achievements. HGP is the only beginning, we are deciphering the codes of codes and reading the book of life of hundreds of living species. The technologies developed during the sequencing allow us to move the genes around from man to mouse to monkey to microbes. The products of these species will provide us new food, new fuel and new medicine to treat every disease known to mankind. Thousands of Labs around the world conducting hundreds of gene therapy trials. In the same century, we have moved from observing human nature to understanding human nature, to engineering human nature. Now, we are ready to enter in the forbidden areas of germline gene manipulation because the changes we make in egg and sperm will be passed on to our future generations. Comprehensive germline engineering is required for two reasons: first to sequence Embryo to identify any deleterious mutations to prevent diseases and second, to introduce genes to enhance the individual performance. The arrival of safe germline engineering will signal the beginning of human sub-design. We don't know where this development will

ultimately take us, but it will transform the evolutionary process for drawing reproduction into a highly selective social process. We need to debate and discuss this issue now and draw some guidelines 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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