Speeches / Lectures

Address at the Inauguration of the 39th Annual Meeting of Indian Society for Human Genetics and International Conference of Human Genetics

[Ahmedabad, Jan 22 2014]

No one should approach the temple of
science with the soul of a money changer.

Friends, I am very happy to participate in 39th Annual Meeting of Indian Society for Human Genetics and International Conference of Human Genetics. This Conference has the mission of ***"bringing together internationally and nationally renowned scientists to discuss the latest developments, trends, technologies and clinical applications in various areas of human genetics. Furthermore, various workshops will be accomplished by eminent scientists on subjects such as FISH, flow cytometry, array-Comparative Genomic Hybridization, UCSC Ensemble genome browser and PCR for early career researchers".***

Genomic medicine is a promise that is at the cusp of changing the way healthcare is delivered around the globe. It has grown by leaps and bounds since the completion of the Human Genome Project in 2003. It is the largest collaborative biological project to date running into billions of dollars. Whilst it provided the most detailed view of the fundamental biological molecule, it has also become a prime example of capturing public interest and the role of science in economic output.

Friends, in 2007 I visited Greece. I spent many hours at the Acropolis Museum and interacted with the knowledgeable curators who told me several stories from Greek Mythology carrying important messages for the mankind. One such story was about the prophet of Thebes. His name was Teiresias. One day Teiresias accidentally came across Athena, a Goddess while she was bathing in a lake. The infuriated Goddess cursed Teiresias with instant blindness. Later at the pleading of people about the great intellect and kind heartedness of Teiresias, Athena gave Teiresias the gift of visualizing the future as a compensation for the curse that she herself could not undo. A year later when Athena visited Teiresias, she found him very sad. When she enquired about the reason of his sorrow, Teiresias said, "O Goddess why did you curse me twice?" Athena told Teiresias that the curse was only given once; the second was a boon and not a curse. Teiresias then told the Goddess that there cannot be a more severe curse than knowing a future that you cannot change.

When I met Prof Jayesh Sheth in last September and learned from him his work on Foundation for Research in Genetics and Endocrinology (FRIGE), this story resurfaced in my mind. I spent many hours reflecting on the rationale of genetic research. Why are we searching the hidden future? Would not genetic testing open up ethical and psychological problems? Why to know something that cannot be corrected? I requested Prof Jayesh Sheth to send me some of his research papers. I learnt from the papers that genetics is

not only about forecasting; it is about knowing the reasons behind our present existence and a quest about how to mitigate the negative outcomes in distant future by acting now. I also learnt from those papers, how low protein diet, low Vitamin B12 and other gene-nutritional interaction is more likely for the error which occurs in chromosome transfer during pregnancy and how birth of a healthy child can be ensured by taking good care of the pregnant mother. So, I selected the topic ***"Passion for Science: Commitment for a Better World"*** to share with this august gathering of genetics scientists and medical experts.

Link to our past and future

Friends, it is very important that right understanding of genes is percolated at every level of our education and professional training as a new era in medicine is ushering in. Let everyone realize that we live in an intelligent and self-regulatory universe and genes are the connection that binds us with both of our past and future. The information in genomes provides the instruction set for producing each living organism on the planet. While we have a growing understanding of the basic biochemical functions of many of the individual genes in genomes, understanding the complex processes by which this encoded information is read out to orchestrate production of incredibly diverse cell types and organ functions.

We now recognize that inherited or acquired variation in DNA sequence and changes in epigenetic states contribute to the causation of virtually every disease that afflicts our species. Scientists across the world are doing active investigation of genetic and epigenetic regulation of development, molecular genetics, genomics and cell biology of stem cells. In addition, they are engaged in the biochemistry of micro RNA production and their regulation of gene expression and genetic and genomic analysis of diseases including cancer, cardiovascular and kidney disease, neuro degeneration and regeneration and neuropsychiatric disease. I am indeed delighted to be here today in this gathering of genetic scientists because you are holding in your mind the picture of medicine not yet known to even the medical practitioners.

Reverse Genetics

I will now discuss the possible directions that the science of Genetics can give to the practice of medicine.
Researchers are now able to alter the genes in plants to produce different types of plants with special characteristics, such as an increased resistance to diseases and pests or the ability to grow in difficult environments. I have recently visited International Crop Research Institute of Semi Arid Tropics in Hyderabad. I was shown a number of Genetically Modified Plants tolerant to not only pests and insects but also to draught. I inaugurated their newly constructed greenhouse containment facility of the Platform for Translational Research on Transgenic Crops (PTTC).

Gene therapy is a promising new field of medical research. Researchers try to supply copies of healthy genes to cells with variant or missing genes so that the "good" genes will take over the physiological function. Viruses are often used to carry the healthy genes into the targeted cells because many viruses can insert their own DNA into targeted cells. But there are problems with gene therapy. Unlike in plants, scientists still do not quite know what every gene in the human body does. Huge scientific efforts like The Human Genome Project and related projects have completed mapping of the entire human genome. But it will take many more years to find out what each gene does and

how they interact with one another. Probably you scientists have to accelerate the pace of the work.

For most diseases, scientists do not know whether and how genes play a role. Also, there are major difficulties in inserting the normal genes into the proper cells without causing problems for the rest of the body. The concept of gene therapy has been around for 25 years but we are not advancing beyond adding copies of genes that are defective. We must insert a corrected copy of the gene exactly where it should be. That means it is properly controlled and switched on and off as it should be.

During my recent visit at LV Prasad Eye Institute, Hyderabad, my friend Professor D Balasubramanian explained to me the new technique, called genome editing. In this new type of genetic engineering, DNA is inserted, replaced or removed from a genome using artificially engineered nucleases, or "molecular scissors." It holds promise against a group of illnesses that run in families and are caused by faults in genes that underpin the healthy working of the immune system, bone marrow and liver.

The power to edit genes is as revolutionary, immediately useful and unlimited in its potential as was Johannes Gutenberg?s printing press. And like Gutenberg?s invention, most DNA editing tools are slow, expensive, hard to use and a brilliant technology in its infancy. I propose Indian Society for Human Genetics to form a consortium in this meeting to develop genome-scale editing tools as fast and easy as word processing, to rewrite the genome of living cells.
Some emerging research fields which have potentials to revolutionize medical practice, need special attention of Genetics Researchers. These include: Pharmacogenomics and Synthetic Biology. In Ayurveda practice, personalized medicine concept already exists. Type of medicines and its dosage may be varied depending on the Prakriti of the patient. Studies at the Institute of Genomics and Integrative Biology (IGIB) have illustrated a good correlation between Genomic profile with Prakriti. Pharmacogenomics is based on this concept which needs to be validated through more research efforts and introduced in clinical practice.

Similarly, Synthetic Biology, a major offshoot from Genetics has opened up many new possibilities to find novel cure through synthesizing new molecule, enzyme or even a gene. Predicting susceptibility to disease early in childhood can provide early intervention and even possibility of prevention of diseases.

Research challenges

Children are born with mentally challenged conditions. There could be various reasons for this. By the theory of Darwin, the evolution is a continuous process of adjustment to the environment. If so why can't we identify those genetic elements responsible for the mentally challenged conditions, at least in certain cases? Sometimes, mentally challenged children are born of the mentally challenged parents. But at times, such children are born from apparently normal parents? What is the role played by genetics in this? Or is there a Gregor Mental?s law coming into picture in making some mentally challenged and the others normal? Or are there environmental factors like the food habits, fast food, alcohol, drug and some medicines and social stress on parents leading to the birth of mentally challenged children. If there are mentally challenged cases, purely because of parental genes, can there be any switching on and off mechanism where the good genes can take over the faulty genes? If the environment is playing a

role into a genetic induction and mutation (environmentally induced mutation) how to identify the environmental factors and to check them? If there are environmentally induced genetic mutation for the worse, why can't there be environmentally induced, mutation for the better? What are the possibilities in this line? If the environmentally induced mentally challenged situations occur, can there again be switching on/off possibilities by gene scissoring or gene insertion? Ultimately what all could be the genetic triggers, which could be clinically or otherwise used, to make a better variety of humans immune to hardships and prone to higher contribution in the right sense.

What motivates a scientist?

Friends, I will now share with you some of my personal experiences on why some people give away all comforts and pleasures of their lives and pursue hard and difficult scientific pursuits. I have worked under the guidance of some truly great scientists and institution builders, namely Prof Vikram Sarabhai, Dr Homi J Bhabha and Prof Satish Dhawan. I worked with hundreds of brilliant scientists and engineers who gave shape to Satellite Launch Vehicles, Guided Missiles, Nuclear Weapons and also developed countless devices that were denied to us by the developed countries. They were all very passionate and selfless people. Most of them could have gone abroad and earned millions of dollars for themselves and their families but they stayed back and contributed to the science that was more relevant in their situations. When I met Prof Jayesh Sheth and Prof Frenny Sheth and experienced their self-less passion, I thought of articulating on what motivates a scientist and that I share with you today.

There could be three motivators - 'gold' (financial rewards), 'ribbon' (reputational/career rewards) and 'puzzle' (intrinsic satisfaction). My observation based on my interaction with thousands of Indian scientists is that many do science for reputational and intrinsic reasons and that financial rewards play a relatively small role. Many young scientists are attracted to research for the sake of curiosity, the hunger to learn more and understand more, to step out into the unknown. "I research because I believe it will make a difference to the natural environment," said young Isha, working at Computer Science laboratory at JNU. "I like to think that I shall make a difference, whether it be now or in the future," she felt.

Typically, research teams comprise post docs, graduate students and research assistants, individuals who have different career goals and are highly intelligent and want autonomy. Managing such teams can be very difficult at times. It is very important that primacy of scientists' self-motivation must be supported with a broader mix of motives to include the social and affective aspects of intrinsic motivation. I suggest' Indian corporate sector to encourage commercial engagement of scientists and support their reputational and intrinsic motivation with financial security.

Now I come to the most difficult problem that the scientific community is facing in today's globalized world. Multinational pharmaceutical companies are one of the most profitable industries in the world and finance most clinical research in medicine. In contrast to governmental funding, the industry's share in clinical research has been growing. While drug companies are responsible for much of the innovation in medicine, their role and influence in running clinical trials need to be carefully examined. And this responsibility rests on your shoulders.

Commercialization of clinical research

Pharmaceutical companies develop drugs in their own laboratories and have traditionally sponsored academic health centers to carry out clinical testing. Drug companies carry out clinical testing with academic health centers for three main reasons: these centers can provide, a pool of potential participants, academic researchers who can design the trials and publications in prestigious academic journals that could help market drugs. As a result of these benefits, most drug studies by pharmaceutical companies in the Western World have been affiliated with academic researchers and medical schools.

Based on my exchange of thoughts with researchers worldwide, I have seen seven requirements for ethical research: (1) value (2) scientific validity (3) fair subject selection (4) favorable risk-benefit ratio (5) independent review (6) informed consent and (7) respect for enrolled subjects. I will now elaborate on each of them and request you to take it forward.

Social or scientific value: Research must enhance health or scientific knowledge in order to prevent the exploitation of subjects and wastage of resources.

Scientific Validity: Research must use rigorous methodology to produce reliable and valid data. This prevents the exploitation of subjects and wastage of resources.

Fair subject Selection: Subjects should not be selected based on privilege or vulnerability in order to assure justice for participants.

Favorable Risk-benefit Ratio: Risk must be minimized and benefits must be enhanced in order to prevent exploitation and unnecessary harm to participants.

Independent Review: Unaffiliated individuals must review the research and approve, amend or terminate it if necessary in order to minimize conflicts of interest and to foster accountability.

Informed Consent: Individuals should be informed about the research and provide voluntary consent in order to respect subject autonomy.

Respect for Enrolled Subjects: Participants should have their privacy protected, the opportunity to withdraw from the experiment and have their well being monitored in order to respect subject autonomy and welfare.

Private industry will be the main player in drug development for the foreseeable future. We must carefully examine the role the commercial entities play in clinical research. The pharmaceutical companies cannot remain just a products company. To their understanding of disease, they must also add some services. I feel it is very important to set up network of patients. Pharmaco-Vigilance and Post-Marketing Surveillance mechanism need to be strengthened at national level. We also must contribute to create a repository of new treatment modalities and nutrition management and involve scientific institutions and their students in such community oriented activities. We have chosen science as our career. Is it not by choice that we took upon us the commitment to do hard work, dedication to the job at hand and the determination that whether we win or lose, we would apply the best of ourselves to the task at hand in return for God's blessings to ourselves and our families?

Conclusion

The most challenging problem of human civilization right now is that science is gathering knowledge faster than society is gathering the wisdom. Since the time of Hippocrates,

the history of medicine has been one of ever more sophisticated phenotyping: these are the signs of diabetes; those, the symptoms of Alzheimer disease. Medicine's ability to understand and treat disease has hinged on this careful phenotyping of patients.

Modern genetics now has historic opportunity to complete the symmetry of this equation by bringing genotyping to the traditionally phenotypic endeavor of clinical medicine. And while the complexity of this information is a barrier to its implementation, medical geneticists and genetic counselors are well positioned to deal with this emerging volume of information, ensuring our relevance to medical practice.

You also bear the additional burden of safeguarding ethics and moral values surrounding the work done outside our country. From sequence analysis to microarrays, unprecedented amounts of medical information are being generated which will soon directly pertain to patient care. It is high time that Indian medical geneticists demonstrate to clinicians and policy makers that their activities are necessary to patient care and genetics must emerge as part of medicine's mainstream. With these words, I am glad to inaugurate the 39th Annual Meeting of Indian Society for Human Genetics and International Conference of Human Genetics and wish all its members a fulfilling scientific career in mitigating the human suffering.

May God bless you.

By Dr. APJ Abdulkalam
www.abdulkalam.com

Printed on:3-Aug-2015 5:23:12