Genome Editing – A Novel Business Opportunity for India as a BRICS Country to Excel in Global Genomics Enterprise

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Abstract

The revolutionary method of Genome Editing by CRISPR/cas9 was invented recently (Cong et al.,2013, Jinek et al., 2012). Replacing defects of DNA sequences with synthetic corrections is already an award-winning tool. Further, it resulted in a new Informatics-based industry (Alex and Caroline, 2016). Borrowing the words of Wired magazine "Easy DNA Editing Will Remake the Word" (Sara, 2016., Maxmen, 2015) . Hence, in the spirit of the brewing revolution, leading US genomics experts traveled to India (Richa, 2012, Gandhi 2015, and Pellionisz, 2012) to facilitate the inevitable unfolding of India's potential to play a major role in global genome industry, based on the excellence, affordability and relative freedom from undue regulations in the process of transfer of informatics-based results into clinical applications (Pellionisz, 2012). To edit genomic DNA in cells and organisms is relatively simple for disorders caused by single nucleotide polymorphisms. However, for complex diseases caused by genome regulation malfunctions, to edit out errors in the genetic code, first we must understand the pristine code determined by the underlying mathematics. Genome Editing is presently in its infancy, focusing on animal models. Non-coding DNA and non-coding RNA, along with other "fractal defects" have not yet been replaced by "spell-checked" sequence-snippets, to the knowledge of FractoGene inventor Andras J Pellionisz, US Patent, 8,280,641. The question is inevitable "What code are we editing?" Simply put, with very few exceptions aside, those highly skilled in the art of genome editing do not really know the mathematics of the code they are about to edit. Furthermore, massive funds are invested in generating Big Data - and now Genome Editing is unstoppable to sift through the genome, particularly of its regulatory system, and to replace fractal defects with pristine sequences. The full mathematical underpinning of the Noncoding DNA and Noncoding RNA will take time to find what are the fractal defects in these regions and a thorough understanding of the not so junk "Dark matter" of the genome. The approach, however, promises an avenue to edit sequences by CRISPR technology. In cancer, thousands and thousands of mutations have been reported since it is a virtual melt-down of the genome. Identification of the fractal defects in early stage of cancer paves the way to Genome Editing with precision and accuracy-with efficiency. Synthetic Genomics to manufacture sequences of any design in an eminently affordable manner – if we are sure we know "what the pristine syntax of the code is". Inserting the edited correct version to replace Fractal Defects first calls for animal models (Gibson et al, 2010). We now have Whole Genome Sequencing, Synthetic Genomics and Genome Editing. A triad can be put together even for non-coding DNA segments of a) The protected intellectual property of FractoGene to compute Fractal Defects b) Synthetic genomics to cheaply manufacture an edited replacement-sequence, and c) Genome editing. Though editors must first know what is e.g.. the mathematical (fractal) language of non-coding regulatory DNA. Our studies are aimed at providing an insight in to the regulatory non coding DNA, and how they play a role in disease mechanisms and progression. If deployed with the highest possible priority, India with US and European cooperation could claim a fair share of the global market of Genome Editing estimated by 2019 at $3.5 Billion (Rohan 2016). Indian prowess in informatics, mathematics combined with genome enterprise, could be a key factor to elevate the Indian participation in the global genomics and genome engineering industry.

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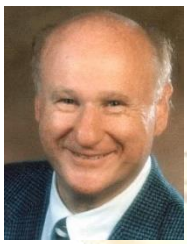

As a domain expert in Genome Informatics, **Andras Pellionisz PhD** is a cross-disciplinary scientist and technologist. With Ph.D.'s in Computer Engineering, Biology and Physics, he has 45 years of experience in Informatics of Neural and Genomic Systems spanning Academia, Government and Silicon Valley Industry. Dr. Pellionisz played a leading role in the paradigm shift from Artificial Intelligence to Neural Nets, including the establishment of the International Neural Network Society. Today, his work is foundational to HoloGenomics, the integration of 100+ years of Genetics with 60+ years of Epigenetics. In 2005, he combined interdisciplinary communities of Genomics and Information Technology when he established the International HoloGenomics Society (IHGS). Pellionisz founded HolGenTech, Inc. as a Genome Analytics company to leverage defense-validated high-performance hybrid computer hardware with a novel, fractal algorithm-based approach for genome analysis and recommendation. Based on sound genome informatics, his work sets forth new mathematical principles for proceeding soundly with full exploration of the whole genome. Dr. Pellionisz' fractal approach to genome function is now corroborated by recently published findings about the fractal folding of DNA structure by Presidential Science Adviser Eric Lander. Dr. Pellionisz put forth the first theory of full genome (hologenome) recursive fractal iterative function, as the mathematical basis of genome regulation, **presenting in Cold Spring Harbor Labs, 2009.** He correctly **predicted that genome regulation includes recursion in 1989**. His work, since 1989, precedes by many years what is considered today's cutting edge in genomic science. For years, Dr. Pellionisz published his research in direct opposition to mistakenly held assumptions (Junk DNA and Central Dogma) that held sway for decades. In 2002, just one year after The Human Genome Project acknowledged that a decade of research and billions of dollars failed to produce the expected 140-300 thousand "genes" in the highly repetitive genome, Dr. Pellionisz conceived FractoGene and filed US patents since 2002 (his first issued patent dated 1984). He formally published this work in **2006 before the US NIH DECODE concluded** with a disposition consistent with Dr. Pellionisz' findings: In 2008, his breakthrough research: "**The Principle of Recursive Genome Function**" superseded the misnomer "Junk DNA", a term widely used for 30+ years to define intergenetic material, was as widely misunderstood and dismissed until HoloGenomics. As now widely admitted, the material is critical to understanding DNA, and Dr. Pellionisz' algorithmic formulations represent rare methods of discovery and application of the material. Pellionisz' US career started in 1973 with a Stanford Post Doctoral Fellowship followed by a position taken in 1976 as a Research Professor of Biophysics at New York University Medical Center. Anticipating the Internet boom, he moved back to Silicon Valley to work for the US government at NASA Ames Research Center as a Senior Research Associate of the National Academy. Dr. Pellionisz was the first to provide a blueprint instruction for automated landing an F15 fighter on one wing with the Transputer parallel computer neural network. He subsequently participated in the government handover of Internet development to private industry. From 1994, he served as Chief Software Architect to several "dot com boom" Silicon Valley companies. Over the decades, Dr. Pellionisz successfully pioneered the geometrization of biology, first in neuroscience resulting in early industrial neural net applications and later in genomics, manifesting today in industrial applications for personal genomes.

M. V. Ramanujam (Ram) is currently Strategic Advisor and President of Clevergene Biocorp Pvt. Ltd, Bangalore, India. Ram has 25 years of experience and a seasoned biotech professional. He is a functional biologist having worked on Enzymology, Protein Chemistry, Microbial physiology, Nucleic acid enzymology and Genomics. Ram also has worked on Biologics, RNA Biology, and Genome informatics. Ram completed his M.Sc. from Bharathiar Univ., and M. S. Molecular Biology from New Mexico State University and also attended University of Kansas USA. Ram has work experience from global leaders spanning four countries US, FRG, Japan and India. **Ram discovered a procaryotic TGase from B subtilis cells and is widely cited for this work in late 80s**. His name is listed in Icons websters sporulating time line history 2007. Ram also invented a technique for Rz diagnostics, in which he used FRET to monitor Rz reactions in real time. He also is a RNA specialist worked on Rz kinetics. Ram worked in 90s with Regeneron USA and Biocon India. He also spent time at University of Kiel FRG and NAIR Univ of Tsukuba Japan. He was a first generation Bioinformatician at DSQ and Satyam India

and later continued as an intrapreneur at many start ups including V Clin Bio labs India and currently a stakeholder, and Strategic advisor in Clevergene Pvt Ltd. India. Ram was guided by Dr James H Hageman and Dr Glenn D Kuehn of NMSU USA who hail from Dr Daniel Atkinsons lab in UCLA and mentored by Dr Paul D Boyer. Ram's Nucleic acids Enzymology advisor Dr Peter A Gegenheimer comes from world's leading labs Dr Sid Altman and Dr David Apirion and John Abelson. Ram's Genomics mentor and advisor is Dr Andras J Pellionisz a triple doctorate, in Genomics, Biology and Computers science from USA and informatics coach is Dr E G Rajan PhD., is a World leader in Signal Processing and Image Processing. Ram is currently also commercializing his discoveries like Transglutaminase from Bacillus subtilis cells, for various Food and Industrial applications. Ram is also looking at Commercial ventures involving Genomics and Genome Informatics, concentrating on Fractal Genomics and Cancer Genomics with Internationally Renowned Figure Dr Andras J Pellionisz, his collaborator from silicon Valley USA. Ram has current responsibilities as a global business development, Strategic planning and development, organizational development, Techno commercial activities, and fund raising activities. Clevergene is poised to become a world leader in Novel Genomics and Genome Analytics Technologies, and Ram is currently deeply involved in its development into a global leader. Ram has taught and lectures in various Universities including NMSU USA, KU USA, and offered Genomics lectures as Visiting faculty in many Universities and Private Colleges in India. Ram is a committed individual, with perfect combination of Biology and IT having worked in Various types of organizations like Product and service sectors, and blessed with the skill eye for the detail and exceptional in timely executions of Projects and succinct performance. He organized 2012 ICSCI conference life sciences track as a convener, And ICETT 2012 Life sciences conference in India and now is the Chief Coordinator & convener for the Genomics, Genome Analytics and Precision Medicine track of the ICSCI conference being held in Hyderabad by 2017 March 9-12.

Prof. Dr. E. G. Rajan **B.Sc., D.M.I.T., M.E., PhD, FIE** is the Founder President of the Pentagram Research Centre (P) Ltd., Hyderabad, India. He is an Electronics Engineer and a Professor of Signal Processing having about 42 years of experience in teaching, research and administration. He has a number of publications to his credit. He has been a professional member of ACM and an editor of the journal of AMSE, Royal Academy of Doctors, Barcelona, Spain. He received his Ph.D degree in Electrical Engineering, (Signal and Image Processing), from Indian Institute of Technology (IIT), Kanpur, U.P., M.E. degree in Applied Electronics, from Madras University, the then famous DMIT in Electronics Engineering from the Madras Institute of Technology, Chromepet, Madras and B.Sc degree in Physics from Madras University. His contribution to the state-of-the-art of Electronic Warfare and Support Measures has been well recognized in the Government and industrial sectors. He was a noted teacher in the department of Electrical Engineering of the Indian Institute of Technology, Kanpur. He received Distinguished Scientist and Man of the Millennium Award from Who is Who Bibliographical Records, Cambridge, 2000. He authored many books like, Symbolic Computing – Signal and Image Processing, Electronic Order of Battle Records of Military Radars, Computers and Information Technology and Foundations of Information Technology. He is the father of a novel paradigm Symbolic Computing In the Framework of Markov's Constructive Mathematical Logic. His contribution to Computer Vision, Pattern Recognition, Modeling and Simulation, Artificial Intelligence and Machine Learning Could be seen in his research publications. Two of his sixty five Ph.D scholars were involved in the design of digital circuits using organic molecules and some of them are working in the area of Big Data Analytics pertaining to Genome Data Base, Biometrics Data Base, Medical Data Bases like MRI and CT Scan imageries of Breast Cancer, Geospatial Data Bases like Multispectral Satellite imageries and Subsurface Three Dimensional Radargrams obtained using Ground Penetrating Radars. He has brought out more than 25 original patentable concepts. One such concept is Codon Space, which advocates the theory of Life Forms as Subspaces of the Information Space called Codon Space. Another concept is a Mathematical Transform, which goes by his name as Rajan Transform. On November 15, 2015, he was awarded the prestigious Dr APJ Abdul Kalam Gold Medal for his life time achievement in Teaching, Research, Industrial Development and Corporate Social Responsibility.