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EMPOWERING TIMES



THINKING ALOUD

The unending quests in science
Jay

PODIUM

Dr. Viloo Morawala Patell
Founder & CMD
- Avesthagen



WE RECOMMEND

Xiaomi
Jayadevan P.K.

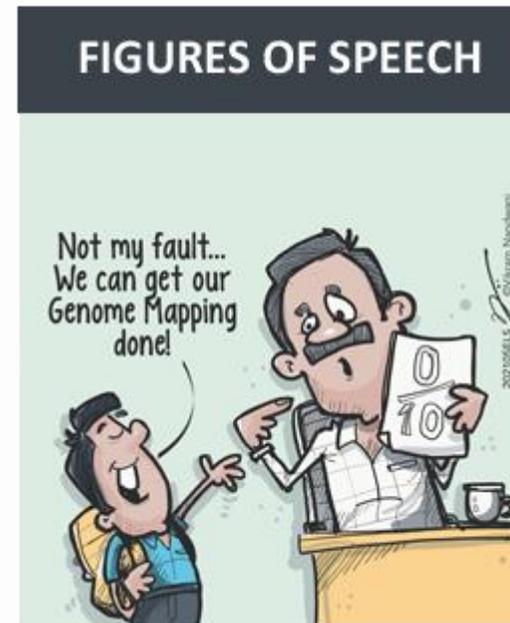
Dear Reader,

Genetic science has come a long way, making significant contributions to the society since the 20th century. From exploring avenues of pest resistant crops for higher productivity to the management of vector-borne diseases in public health, genetic science has improved the way we live.

Another breakthrough in this field is genome mapping to better understand disease profiles across generations. Several countries have embarked on genetic mapping of their population to understand disease profiles. Case in point is UK which undertook the sequencing of 100,000 whole genomes of cancer patients and other rare diseases in 2013. The project was extended to 1 million in 2018. India too is not far off in this regard. The Department of Biotechnology initiated their ambitious Genome India Project in January 2020 aiming to collect 10,000 genetic samples from citizens across India, to build a reference genome. This would aid in advancing personalized medicine while paving the way for predicting health and disease outcomes.

Genetic technology is questioned and debated upon very often. However, the implications of not applying genetic technology when it has proven potential in making human lives better should not be on the back-burner.

ET this month looks at the '**New frontiers in Science: Mapping the Genome.**' On the **Podium**, **Dr. Viloo Morawala Patell** - Founder of Avesthagen, delves into what genome mapping is all about and the progress made in this field so far.



In the **Thinking Aloud** segment, **Jay** reflects on how far the human civilization has advanced thanks to power and possibilities of science. In the **We Recommend** section, we review **Xiaomi** authored by technology enthusiast, **Jayadevan P. K.**, who traces the journey of the Xiaomi brand of smartphones from a start-up in China to a serious contender across the globe.

In **Figures of Speech**, **Vikram's** toon's 'exceptional' performance goes way back!

Please also [Click Here](#) to check out our Special issue of ET, which is a collation of selected themes that were featured over the years highlighting the changing landscape of the business world. This special edition has been well received and can be [Downloaded Here](#) for easy reading and is a collector's item.

As always, we value your opinion, so do let us know how you liked this issue. To read our previous issues, do visit the Resources section on the website or simply [Click Here](#). You can also follow us on [Facebook](#), [Twitter](#) & [LinkedIn](#) - where you can join our community to continue the dialogue with us!

THINKING ALOUD

The unending quests in science

Jay

When we speak of the rise of human civilization, we refer to the world that has over centuries seen the growth and demise of kingdoms, empires and nations. The caveman gave way to the pastoral man and over centuries we have moved from agriculture to industry and now we aspire to touch the sky. Not only did we watch with awe the movements of the helicopter, Ingenuity, on Mars last month but the sound of wind on Mars and discovery of water on the moon has already excited some people with fat wallets and brave hearts to book tickets on Branson's Virgin Galactic or get ready to board Bezos's Blue Origin (for which bookings open soon). What is the common thread underlying all the above transformation in man's journey on earth? The answer: the power of science!

What we have taken for granted over the years is actually the key driver of universal change. Whether it is the journey to the stars, the quest to build big monuments of human vanity or ameliorating the pains of human condition, the role of scientists has not been appreciated enough. Rather, there have been periods of human history when the early scientists who tinkered with natural elements and discovered new knowledge were punished as sorcerers or charlatans because their brilliance was under-appreciated. The mysteries that scientists have set out to solve in various arenas are the ones that have offered us the most benefits that we luxuriate from now in our world.

New frontiers continue to challenge mankind as mysteries abound in nature's creations, one of which is our own body. While broad physiology has been studied quite well (though not completely still) the elements that go in to making a human body into a person still fascinates scientists, and I am not even referring to the psychological dimension involved. As much as the telescope enabled man to view the stars, the microscope and the stethoscope

has enabled us to peer deep within the body. The invention of new tools has been an on-going series all meant to decipher the functioning of the inner systems with the object of not only fixing whatever has gone wrong but also in the quest for understanding what we do well and thereby creating a better prototype. Don't get me wrong, I am not referring to the ethical debates around cloning or taking any moral postures but suffice it to say that in a world of evolving ideas, boundaries are being pushed at an increasing rate than before.

Consider that the first in vitro birth happened in 1978 (Louise Joy Brown) and Dolly (the Sheep) was cloned in 1996. Both had its share of controversies in their time but today in vitro fertilization is a standard procedure that raises no eyebrows but instead generates happy smiles from new parents who had lost hope. Yet, new science has its abundant share of critics. When the Chinese scientist, Dr. He Jiankui, claimed in November 2018 to use CRISPR technology to bring to the world twin babies with genetic changes to enhance resistance to HIV by disabling a gene, there was uproar after an initial applause in the scientific world. Who knows what is in store in future for Lulu and Nana (the twins in this case) as the discredited scientific team is in prison now and their work has been reportedly shelved. Nevertheless, cutting edge work is always controversial in nature which is why it is argued that science is too important to be left to the scientists alone. Take cloning for instance where the global consensus is that therapeutic cloning is permissible not reproductive cloning with its 'Brave New World' connotations. Yet, to quote a genetic engineering writer about the Chinese scientific project, 'The 4-minute mile of human genetic engineering has been broken. It will happen again.'

As I mentioned, the argument about good and bad science is not really in the scientific realm. The reality that we find today is that the scientific community is a vibrant group of people that is inherently both competitive and collaborative in nature. The latest vindication of this is the battle to save the planet from the ravages of the Covid-19 pandemic. Much to the relief of the politicians and the religious leaders who lost support from the common man, it was a band of scientists who shared resources and ideas and pivoted their work to tackle the scourge. While good fortune is always at play, commercial might (with governmental support) has also contributed to ensuring limitless resources to fight a common enemy.

Will we see more of this in the coming days? First of all the battle against the Covid-19 virus has not been won yet. Secondly, while scientists as a class were galvanised this time around, whether they would agree to a common agenda of future challenges to tackle is a moot question. What should we focus on as the Top Ten priorities for

the future: hunger (farm productivity), malnutrition, water and sanitation, climate change, diseases of the masses in the developing world or should it be efforts for increasing longevity, cancer, Alzheimer's, dementia, etc. (often seen as first world problems)? And, who will decide these priorities?

Let the debate continue. For now, let us agree that with moon-shot projects like the Human Genome Project, mankind has opened fresh doors of enquiry which potentially offers staggering benefits in multiple fields (medicine, agriculture, etc.) that can help us evolve more. By understanding human beings at a molecular level can science make us a better civilization? That to me is an open question still!!

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Podium

Dr. Viloo Morawala Patell Founder & CMD - Avesthagen



Dr. Viloo Morawala Patell, Founder and CMD of Avesthagen Limited and The Avestagenome Project® is an innovator, and serial entrepreneur involved in international biotechnology development, academic and corporate leadership with a longstanding interest in global development leading to establishment of global networks and alliances with academia and industry. She is an experienced deal maker having raised capital from PE and strategic financing with firms and foundations globally.

Dr. Viloo Patell is the recipient of many awards of international and national acclaim as a scientist and as an entrepreneur including the French National Order "L'officier du Merite", 'Karmaveer Puraskar' award, "Parsi Entrepreneur par Excellence Award" from Bombay Parsi Punchayat, from WZCC and many other awards. Her academic research experience spans research work at highly reputed institutions globally, including ICRISAT, IBMP-CNRS, Strasbourg, University of Ghent, NCBS-TIFR. She has been the recipient of grants from many prestigious institutions like the J.N. TATA, Rockefeller Foundation, IFCPAR, USAID (US Agency for International Development), DFID (Department for International Development, in the United Kingdom), World Bank.

Dr. Viloo Patell's international biotechnology experience coupled with her longstanding interest in global development from building international networks and alliances with academia and industry led to her founding Avesthagen Limited. Avesthagen Limited is built around the convergence of food, pharma, environment-adjusted

agriculture, and population genomics, leading to predictive, preventive, and personalized healthcare driven by a systems biology approach to population genetics and food security.

ET: What is Genome Mapping and what are the challenges in this process?

VP: Genome mapping also called linkage mapping can offer firm evidence that a disease transmitted from parent to child is linked to one or more genes. Mapping involves assigning/locating a specific gene to a specific region of a chromosome and determining the location of and relative distances between genes on the chromosome. Mapping also provides clues about which chromosome contains the gene and precisely where the gene lies on that chromosome. Genetic maps have been used successfully to find the gene responsible for relatively rare, single-gene inherited disorders such as cystic fibrosis and Duchenne muscular dystrophy. Genetic maps are also useful in guiding scientists to the many genes that are believed to play a role in the development of more common disorders such as asthma, heart disease, diabetes, cancer, and psychiatric conditions.

ET: Technology has made it possible for early detection of genetic diseases. What are some of the innovative and digital/analytical tools that has made genome mapping insightful today?

VP: While majority of the innovations in the genome mapping field have focussed on the development of tools for generating high-quality genome sequences in the form of Next Generation Sequencers, innovations currently focus on analytics and deep mining of complex genome data from prokaryotic and eukaryotic genomes. Recent innovations like Hi-C is used to identify complex DNA interactions in the cell to ascertain DNA binding sites and new developments in mining and interpretation of structural variants like deletions, duplications, inversions, translocations, mobile element insertions, and complex alterations that span tens of thousands of bases.

ET: Your recent study - The Avestagenome Project® - has made it to the headlines. Can you tell us about the project, its focus areas and objective?

VP: The Avestagenome Project® is a unique and proprietary biobank of the endogamous Zoroastrian-Parsi samples and personalised medical data founded in 2007 to first, preserve the biological heritage of the endogamous Parsi

community and secondly, for this biobank to be used to control population utilising a systems biology & big data mining approach to accelerate discovery of novel biomarkers and advanced novel therapies for Precision medicine.

The project plan envisages to sequence 10,000 samples from the Zoroastrian Parsi community in India and UK. Preliminary data from our cohort collection of 4,700 Parsis showed that the community overall has an increased median life span characterized by markedly higher incidence of ageing associated musculoskeletal disorders, neurodegenerative conditions like Dementia, Parkinson's disease and Alzheimer's disease, auto-immune conditions like Rheumatoid arthritis, cancers and metabolic disorders like G6PD deficiency. The community has been on a decline in numbers due to infertility, reproductive disorders and neo-natal conditions manifesting in the form of heritable rare genetic disease conditions. A higher prevalence of metabolic disorders like diabetes, cardiovascular conditions in the community have been linked to their lifestyle and dietary habits.

Genomic, transcriptomic, proteomic and metabolomic analyses of breast cancer samples from case-control individuals have been initiated. Whole genomes of 11 individuals (breast cancer cases + controls) have been sequenced, and their analysis is underway. Metabolomic analysis for breast cancer case-control samples have led us to 17 putative unique and novel metabolic markers that have been detected within patient samples that do not occur within the control samples.

Since collection from 2007, and recent added collection, we have secured the samples, paid for cohort protection, isolated genomic signatures from sequenced pilot cohorts (n=109) Whole genomes and cfDNA/cfRNA (n=580) for liquid biopsy based analysis of Ultra low frequency variants for lung cancer risk from a newly collected case/control cohort, designed gene panels for hybrid capture of cfDNA fragments for genes correlated to cancer and neurodegenerative conditions, set up ethics review board for expansion with the Government of India while bolstering our technical and analytical capabilities.

We have received interest from other large genome sequencing projects across the globe that have identified the Zoroastrian Parsi cohort collection to be of significant interest for the study of ageing, lifestyle and inherited disorders mentioned above, as well as enhancing the genomic diversity of the existing global genomic repositories.

ET: Can you please throw some light on the current scientific landscape in India? How does India compare with the rest of the world specifically for research in genetics?

VP: The completion of the Human Genome Project and the exponential advances in genome sequencing technology has radically altered the study of human diseases. Given the diversity of cultures and endogamous groups in India, it offers formidable potential for novel discovery in medicine using population genomics. The Avestagenome Project® is a large vision project and effort to harness the genomic potential of the endogamous communities of India for understanding human disease and development of the next generation of omics-led precision medicine and diagnostics.

The Indian Genome Variation (IGV) consortium started in 2003, aims to provide data on validated SNPs and repeats, both novel and reported, along with gene duplications, in 15,000 individuals drawn from Indian subpopulations. In 2009, IGV reported the first genome sequence of an Indian citizen. More recently the Government of India completed the sequencing of 1,000 Indian genomes as a public health initiative titled the "Indigen Project". While India encompasses more than 17% of the world population with extensive genetic diversity, it remains under-represented in the global sequencing datasets in the context of representation of Indian and south east Asian diversity. With its diverse human biodiversity and numerous endogamous population groups, India offers a formidable laboratory for genetic and genomic studies for understanding human diseases. For example, consanguineous unions are prevalent in the states south of the Narmada, with the highest rates reported in Andhra Pradesh, Karnataka and Tamil Nadu.

Many different types of genetic disorders have been reported to be more common among consanguineous progeny, for example congenital disorders, including neural tube defects and congenital heart defects. Autosomal recessive hearing loss disorders and visual defects such as early-onset retinal dystrophies primary congenital glaucoma and anophthalmos also are present at increased prevalence.

Except for few well-established hospitals or clinics which are active in research, our primary health centres where most patients get treatment are not equipped to capture this important information. This limits the application of current computation tools and statistical methods from a deeper analysis combining genotype and phenotype data. Models like UK Biobank are good examples that can be followed in India.

ET: As a scientific entrepreneur you have had an interesting journey. Can you tell us about your company, Avesthagen and some of the notable breakthroughs it has achieved? Under your leadership, what are your future plans for the company?

VP: Avesthagen Limited is a company was built as a grid of verticals of biodiversity and horizontal of "omics" Platforms leading to the development of novel, innovative pipeline of products and technologies. It is an international, integrated, diversified life sciences company based on a systems-biology approach that facilitates Scientific Discovery, Technology Development and new Products for Predictive Preventive Precision Healthcare and Agriculture. Avesthagen's corporate mission is to develop and commercialise new products and technologies for Nutrigenomics and Precision Medicine, with the aim to develop to support its proprietary predictive, preventive and personalised ("PPP") healthcare platform. The convergence of food, pharma and population genetics and the development of new products, offers a unique pathway to address the high unmet need in understanding and treating chronic disease as well as addressing nutrition and energy and environment limitations around the world. Avesthagen Limited has had long-term collaboration with global companies like Limagrain, Nestle, AstraZeneca, Novartis, Cipla and bioMerieux, to develop superior technologies for the Indian and global markets.

The Avestagenome Project has finished sequencing 200 Zoroastiran Parsi (ZOPA) Whole genomes and we are shortly releasing the publication and we are proceeding with the sequencing 4,500 Genomes and published a major paper on 100 Mitochondrial Sequenced ZOPA genomes. The Publication is extremely detailed and tracks the various Haplogroups of Indian Zoroastrian Parsis and linked the data with the Iranian genomes and their ancestry. The company has released the Reference Standards Publications for the Zoroastrian- Parsi, Mitochondrial, Whole Genome and Epigenome of Zoroastrian-Parsi population and these are all landmark papers. We are well on the way on The Avestagenome Project® and are now initiating partnerships worldwide for biomarker and drug development. As an application of the work done so far, we are launching our new Strategic Business Unit, AVGEN Diagnostics, offering Point of Care genetic diagnostics®.

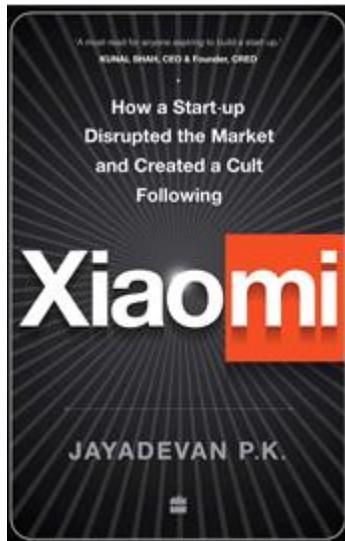
Avesthagen Limited, India's pioneering genomics company, will launch a new SBU, AVGEN Diagnostics in 2021, the first fully integrated end-to-end personalized genetic testing centre using the latest sequencing technology and advanced analytics to provide diagnostic testing services for individuals, hospitals, private clinics and health insurers. AVGEN Diagnostics offers the broadest range of genome based diagnostic testing services with the ability

to detect a broad portfolio of cancers, infectious and non-infectious diseases and genetic disorders. The portfolio includes tests for common diseases, customized panels for different disease conditions and comprehensive disease risk panels, interpreting all genes associated with the patient's phenotype. AVGEN Diagnostics will be uniquely supported by the R&D outcomes of flagship, The Avestagenome Project[®], which will provide accelerated and continuous innovation to create a pipeline of novel diagnostic tests, enabling best-in-class patient care.

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We Recommend

Xiaomi
Jayadevan P. K.



Think Xiaomi and what comes to mind is a smartphone brand that captured the hearts of its customers through its unique selling point - value for money.

In 2020, Xiaomi was the number one smartphone brand in India, with a 31% market share. Xiaomi has been successful in capturing the hearts of its Indian consumers for the last seven years. What began as a humble start of offering mobile phones, has now emerged as a brand that also offers earphones, Bluetooth speakers, fitness bands, power banks and air purifiers!

How did this start-up reach this feat? Tech journalist, Jayadevan P.K. looks at the journey of Xiaomi and how it became the youngest company to be a part of the Fortune 500 list in a short span of time.

Xiaomi, founded by Lei Jun, entered the Chinese market by offering a smartphone OS, called MIUI, for free, amid the competition from domestic brands - Huawei & Lenovo - and international players - Apple & Samsung. Being an outlier (till date), instead of competing, Xiaomi offered users free software and eventually built a full-fledged online community to engage and understand which features they craved for.

The company eventually entered the competitive smartphone market in 2010 and upon its listing on the Hong Kong stock exchange in 2018, Xiaomi raised \$4.7 billion at a valuation of \$54 billion. The capital was directed at

expanding its network and presence in India, as well as fund local start-ups in the software and mobile tech space. Within seven years, Xiaomi transformed into the world's largest consumer IoT firm by 2020, with its revenue surpassing \$37 billion and more than 210 million IoT devices (excluding smartphones and laptops) sold in over 90 countries.

To effectively expand into categories outside Xiaomi's expertise, the company implemented a unique process for identifying and developing partnerships. One important benefit Xiaomi offered to its partners was "incubation" - it assisted them with R&D by sending in teams of its own engineers, and it helped its partners identify key suppliers and negotiate contracts. Xiaomi's investment and operational involvement brought brand awareness. To maximize returns on its brick-and-mortar stores, Xiaomi leveraged online sales data, using analytics to establish its e-commerce platform.

With anti-Chinese sentiments running high amid the current pandemic, Xiaomi has been actively promoting its 'Made in India' stance to convey that the company is not only a global brand, but is one which is building a local company in India. Mi India, Redmi India and Poco India - the sub-brands under Xiaomi India - has one thing in common: an Indian upbringing.

While the power dynamics between consumers and companies have shifted over the years, Xiaomi continues to pay close attention to users' needs and continues to build its products accordingly. It has taken over 10 years and many hits and misses for Xiaomi to build up to this moment and there is no holding back now. The "Apple of China" has a long way to go.

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THROUGH THE LENS



Bird watcher, **Rupesh Balsara**, spots the Rufous-fronted Bushtit, which is largely found in the eastern and central parts of the Himalayas in Bhutan, China, India and Nepal. These birds very social and are often found in large flocks in temperate forests, primarily eating insects or plant material such as berries or seeds. The species in this family are generally not migratory.

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