

The Game Changer Geneticist

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**BioSpectrum Lifetime
Achievement of the Year Award
2011**

Widely regarded as the man behind DNA fingerprinting in India, Dr Lalji Singh has been a pioneer in developing and introducing the technology for a plethora of applications including forensic analysis and wildlife conservation.

Dr Lalji Singh, 64, sits easy in his chair at the Center for Cellular and Molecular Biology (CCMB) in Hyderabad. When he met BioSpectrum, he was having a calm last day at work. However, his links to CCMB and to Hyderabad are far from severed. Not only his research group at CCMB continues to work under his guidance, his name is indelibly imprinted in the history of this illustrious organization. Among his most significant contributions is the setting up of the Center for DNA Fingerprint and Diagnostics (CDFD), which was an

application of his research on genetics.

Path breaking study: The origins of man

Dr Singh along with his colleagues at the CCMB undertook a unique challenge of mapping the ancestry of the Indian population and in doing so, helped elucidate the migration route adopted by man, millions of years ago. Dr Singh proudly speaks about this landmark paper published as a lead article in Nature. This paper was a culmination of years of research. “We had sequenced mitochondrial DNA of tribes in Andaman and Nicobar which showed that they were different from other population. We found that they do not resemble any of the populations in India or anywhere else. This data generated a lot of interest. Later in collaboration with the Massachusetts Institute of Technology, we undertook a project in which one million sequences were studied of selected populations in India,” he elaborates.

He had an opportunity to present this data at the World Congress of Genetics held recently, in October 2011, at Montreal. Dr Singh further elaborates, “Our findings rule out Aryan invasion theory and prove the theory of

Southern route of migration instead. It also showed India is made of a diverse population and that the research should not be limited to western populations.

Genome Foundation: Labor of love

In tandem with the findings of the study, Dr Lalji Singh had put forth the need to find solutions for India-specific disorders. Dr Singh explains the idea behind his project, the Genome Foundation, when he says, "I started this foundation with the humble aim that if each citizen of India can do a little towards it, that amount can be used to improve the conditions of people in rural areas by better providing solutions specific to the Indian rural population. This would aim to provide better healthcare and bridge the gap between scientists involved in basic research with clinicians working with hospitals and also increase awareness among the rural population."

Dr Singh has been bestowed with numerous honors including the Padma Shri in 2004 and the prestigious Shanti Swarup Bhatnagar fellowship in 2009. Forty seven years after he started his career, Dr Singh continues to have an impact on the Indian public through various roles.

In 1991, he was an officer on special duty tasked with setting up of the CDFD. However, even before the CDFD was spun-off, as an independent entity, he was working hard to make DNA fingerprinting admissible as evidence in the court of law. Operating out of the center for excellence at CCMB, he was instrumental in getting forensic evidence accepted in an Indian court in 1988 in Thalassery, Kerala. This paved the way for the common man to get justice in more than 500 cases since. The technology has provided irrefutable forensic evidence in sensational cases such as the Naina Sahni 'Tandoor' case, Swami Premananda case and many paternity cases. After that first case in Kerala, Dr Singh became the most celebrated evidence-man. He was grilled countless times by many lawyers and had to painstakingly go over and over again clinching evidence.

The progress in the field of DNA fingerprinting caught everyone's attention and won many accolades including the CSIR Technology award in 1992. It was ironical that the CDFD had to investigate the murder of the very man who supported its inception in 1991. The CDFD aided in the investigation of the assassination of the then prime minister, Mr Rajiv Gandhi, by providing strong

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pleased Dr Singh is being given this award.

Very few scientists have made as strong an impact on Indian science as him. He

revolutionized forensic sciences in our country when he developed DNA fingerprinting techniques and brought it into the realm of the common people. Also, he created history when he became the first Indian whose work was featured as a lead article in Nature. As the director of CCMB, he added new dimensions to it by always bringing forth new ideas such as LaCONES, the first laboratory of its kind. He constantly worked towards improving the technology at CCMB. Bringing him to CCMB has been one of my best decisions"

Dr Pushpa Mitra

founder director, CCMB

Dr Singh today has his hands full with the responsibility of the vice chancellor of BHU and the head of the Genome Foundation, a non profit organization, that was incorporated in 2004. His dream is "health for all" and he believes that personalized medicine will be cost effective in India. However, he feels that for this to take place, genetic testing has to be made available and affordable.

Deeply connected with his roots, Dr Singh's heart goes out for rural India. Born in rural Uttar Pradesh, in the small village of Kalwari, in Jaunpur district, Dr Singh was lucky to have a school within six kilometers from his home and a father who was passionate about education and supported his dream. However, he wasn't dreaming about becoming a scientist but a medical doctor. It was fate that he missed the entrance exam date for medicine course and went on to apply to the zoology course at the BHU. That one step became the foundation of the sterling scientific career that followed. However, nothing came easy for Dr Lalji Singh.

His interest in science had, in fact, taken root when he saw the central nervous system of the frog for the first time at the dissection class during his intermediate school. A young Dr Singh, who loved sports and mathematics, was enamored. His curiosity led him to dissect many frogs, that were captured sportingly from the village pond. The dissection lab, for him, moved at his home. So, the disappointment of not being able to make it to the medical school was huge for him. However, on his father's advise he decided not to waste time moping around but do some other course. Encouraged and goaded by his mentor and a friend of his father, Professor Nandan Lal Singh he dreamt big, went ahead and applied at the BHU. "When I applied, it was more like a pipe dream because BHU was a glorious university where only the best-of-the-best make it," recounts Dr Singh.

He had no idea how good he was, until affirmation came in the form of letter of admission from the BHU. And almost immediately, he hit his first roadblock. He discovered that, at 16, he was underage for the course by two-years. Professor

Nandan Lal Singh who taught physics at the BHU stepped in to help this bright aspirant once again, and managed to influence an exemption on merit. The year rolled-on, results came, and Dr Singh made his mentor proud by remaining on top of his class. He went on to receive a gold medal in his batch of MSc zoology in 1966.

'There is a need to change the mindsets'

How do you perceive the current situation in Indian universities?

The best people in science should be in the environment of a university. In my own experience, I found that the right mentors can make a world of difference and today's students need that kind of mentoring. The problem is that the universities are compartmentalized. There is a need to change the mindsets. The approach should be integrated. The key is to try to create centralized facilities that promote translational research. A university like BHU is very much suited to research being carried out in this manner.

How do you like your new job role as the vice chancellor of BHU?

Administration takes up a lot of time and gives me less time to focus on research. However, this job role allows me to make a positive impact on a larger scale. Improving the academic atmosphere of BHU is on my agenda.

fingerprinting on public platforms and all his efforts paid off when the government agreed to help set up a center such as the CDFD. It was his tireless efforts, which included setting up the initial protocols for the center, which made DNA fingerprinting the buzzword in India. His landmark papers on human genetics prove that he is one of the best human geneticists in India"

Dr Seyed E Hasnain

professor of Biological Sciences, IIT Delhi, and former director CDFD

While academics proved to be cakewalk for him, everything else was a task. The sudden change in environment took quite some time for him to adjust. It was during his time at BHU that Dr Singh found his life long mentor and guide in Dr Rai Chaudhari, the head of the department of zoology at BHU and a


Dr Seyed E. Hasnain

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Singh absolutely deserves this award. Despite being a scientist, he actively advocated DNA

From guiding Dr Singh on his future doctoral thesis to welcoming him into his home in Kolkata post his doctorate, to teaching him how to make tea, Dr Singh credits Dr Rai Chaudhari with being the influence that shaped his life. It was Dr Rai Chaudhari who suggested that Dr Singh pursue his doctoral thesis in karyotyping of snakes. The karyotype or the complete set of chromosomes in a species, of different species of snakes was not yet done in India, until then. Along with the scientific challenge of the project, with this Dr Singh also faced the challenge of overcoming his fear of handling dangerous snakes, such as Indian cobras, pythons, banded krait, on a daily basis in order to collect blood samples. Reminiscing about those times, Dr Singh says, "In the beginning I was afraid of snakes and would need the snake handler to hold the snake while I collected the samples. Later on, I became so adept at the technique that I would hold the snake with one hand, its tail under my foot, while I collected the sample with my other hand."

His efforts paid off when during his study, using C banding technique, he elucidated that during the course of evolution newer species showed the presence of W chromosome in females, which could be used as a marker for identifying the gender and species of any snake. His doctoral thesis set a precedent when it was published as a whole paper with full 62-page text in the international research journal Chromosoma. It was a first for any thesis to be published as it is. Path breaking in itself, the findings in his doctoral thesis was set to have even more important implications in the future, as he later discovered.

Meanwhile, Dr Rai Chaudhari moved back to Kolkata. Dr Singh applied for CSIR fellowship. Restless at the distance from his mentor, he quit his job at BHU and followed Dr Chaudhari to Kolkata, partitioned his lab into two and started pursuing the sex determination gene lead in snakes again. The infrastructure in Kolkata was not up to the mark. However, he persevered on, while also trying to find better options to pursue this research.

Skunk there are very few scientists in India as honest and kind as Dr Lalji Singh. The technology for the Universal Primers could not have been done, had it not been for Dr Singh. He not only gave me a free hand in my research but also took it upon himself to handle all the bureaucratic matters involved with patenting our technology. On winning the 2009 BioAsia Innovation Award, Dr Singh, in a magnanimous gesture, made me keep the prize money associated with it. This is just one of the incidents which exemplify his selfless character"

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Dr Sunil Verma

scientist, CCMB (former student of Dr Lalji Singh)

motivated Dr Singh to take some action. The next milestone arrived in Dr Lalji Singh's life as a Commonwealth Fellowship for nine months for his research on snakes. He informed Dr Jones that he has received the fellowship and would like to start his research. Dr Jones wrote back that there are no snakes in Britain and that Dr Singh would be his own mentor as Jones hardly knew anything about snakes. A determined Dr Singh fixed his snake tissues in alcohol and set sail for the University of Edinburgh in 1974 to work under the illustrious Dr Jones, who had become Dr Singh's guide and mentor.

Six months of his fellowship went on with little further evidence of his hypothesis of chromosome specific satellite DNA. He ran out of tissues and no further work was possible unless he got fresh snake tissues. At this crucial juncture, once again, Dr Rai Chaudhari stepped in with assistance. He sent him a consignment containing 30 live snakes to Britain.

Success came to him when late one night, using in situ hybridization he saw the evidence of a satellite DNA specific to the W chromosome. In addition to being able to demonstrate that this satellite DNA was specific to a single chromosome, he also later showed that his DNA was associated with sex determination in all organelles including humans. These studies were further used to elucidate the pathways involved in sex reversal as well.

However, just when he made such an exciting discovery, and was basking in the glory of his finding he got the rudest shock of his life, an order to return back to India within immediate effect. The Indian government wanted to stop the brain drain from the country and made efforts to bring the talent back to the country.

The fact that Dr Singh was the one of the first young scientist award winners in India, he became the first casualty of the scheme. What followed were some of the harrowing days of his life. With his passport impounded, he was caught in a situation that made little sense to him. Finally, after many visits to the Ministry of Education and intervention of the Prime Minister's Office, he was allowed to go back to his research in Edinburgh.

Crystallizing Achievements

In 1987, Dr Singh was in Hyderabad at the invitation of Dr Pushpa Mitra Bhargava, the founder director of Center for Cellular and Molecular Biology (CCMB). At the CCMB inaugural, an event marked by the largest congregation of Nobel laureates until date in India, Dr Bhargava, who was working at getting talent for CCMB, inspired Dr Lalji Singh to join there as senior scientist.

All of Dr Singh's conditions on infrastructure requirement was met. Dr Singh returned to India with his family, comprising wife and two sons, in tow to Hyderabad at the CCMB. His achievements at the CCMB are reflected in the fact that not only did he conducted outstanding research and published many papers but was also decorated with many awards. He rose to the position of director in July 1998 and took charge of the CCMB. At the CCMB, Dr Singh continued with his work on sex determination and with his colleagues and indigenously developed a probe called Banded Krait minor satellite DNA probe (Bkm-derived probe) that had applications ranging from forensic analysis to seed stock verifications.

Leveraging research

What sets Dr Singh apart from his contemporaries is that he has been using technology to help not just humans, but also the wildlife. Based on the studies of Dr Lalji Singh and his colleagues on wildlife conservation, the Government of India has set up a "Laboratory for the Conservation of Endangered Species (LaCONES), which is a unique initiative for the conservation and protection of Indian wildlife. One of the important findings of Dr Singh in this regard has been through the study of tigers from different reserves, which refuted the earlier claim that wildlife in India was genetically homogenous. Dr Singh provided evidence that there is sufficient amount of polymorphism in wildlife, such as tigers, from different parts of the country.

Another highlight of Dr Singh's work was the study of conserved sequences in mitochondrial DNA that can be used as universal primers to identify any biological organism for which he acquired a joint patent with Dr S K Verma.

During the 11 years that Dr Singh spent as director of CCMB, he spearheaded the research on the origins of man, which put

He hit a number of roadblocks in his struggle to find a lab and a mentor who would support his research and take it further until he came in contact with Professor K W Jones, reader at the Institute of Human Genetics at the University of Edinburgh, UK. He wrote to Prof Jones expressing that he wanted to continue his research under his guidance. Prof Jones informed him that he had neither a project nor any

funding for working on snakes. 'However, if Dr Singh can get his own fund he can work at Jones' lab'. That piece of communication

CCMB on the world map.

-**Manasi Vaidya**, and **Nandita Singh** in Hyderabad