

## A geneticist par excellence

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*From plant genetics to bacterial genetics, from molecular biology to neurophysiology, Dr Obaid Siddiqi's vast areas of research only projects his love for science, a thirst for individuality and a never say never attitude*



What would one do when a hailstorm destroys wheat crops sown for a year? May be. But, Dr Obaid Siddiqi moved ahead, he had learnt enough of molecular biology. Not just here, but throughout his life, Dr Siddiqi

is a researcher and has over five decades of research in fields such as plant molecular biology and his contribution to the enrichment of modern science is

Dr Siddiqi is the Director of National Centre for Biological Sciences, Bangalore, with the Life Sciences Research Group working in the fields of microbial genetics and neurogenetics. He is known for his work on *Drosophila* (fruit fly), first on their paralytic mutations and then on the genetics of the eye. Dr Siddiqi's early research on DNA transfer and recombination in bacteria, particularly in *E. coli* are some breakthrough contributions.

Dr Siddiqi is a Fellow of the US National Academy of Sciences, considered the highest honor in science. He initially focused on plant genetics and later in University of California, Berkeley, worked on microbial genetics. In the late 1960s he started working on *Drosophila* and in 1976 his research shifted to molecular biology. For the past ten years, Dr Siddiqi has been more interested in the

Dr Siddiqi, son of a bureaucrat, became interested in science towards the end of his school days when he was studying botany at the Aligarh Muslim University, where one of his teachers was a geneticist. Despite learning only conventional genetics, like Mendel's Law, Dr Siddiqi got involved in this branch by self-study and eventually decided to take up plant genetics. While, still at university, he went to the Indian Agricultural Research Institute (IARI) to study wheat genetics, where destiny had different plans for him.

"As luck would have it, at the end of the year, in a hailstorm, my crop was destroyed, all the crosses we had made from wheat were destroyed. So, I was faced with this problem of having to wait for one more year and repeat all my work. But, people at IARI advised me that as I have learned all I want to, I can move to a different lab to pursue other interests. Then, I decided to move to Glasgow," reminisces Dr Siddiqi.

At the University of Glasgow, he chose to do his PhD in genetics. The place, because of its contribution to the genetic structure, was a scientific hub of geneticists. Thus here, Dr Siddiqi met some of his future colleagues and also gradually got into molecular genetics - the subject of his first breakthrough research.

### 'Nonsense' research

In 1960, Dr Siddiqi moved to the US and started working with Dr Alan Garen at Massachusetts Institute of Technology (MIT), who was working on the connection between genes and proteins. Their experiments on the suppression of 'nonsense' mutation in *E. coli* was an important step in the understanding of chain termination in polypeptide synthesis. Building upon Dr Francis Crick's research on the existence of sense and nonsense mutations, Dr Siddiqi and Dr Garen started working on the mutations of alkaline phosphatase.

"I noticed that there were many mutations which abolished the protein, that is, no alkaline phosphatase was made in those mutants and yet those mutations could be suppressed, which would cancel the effect of the original. As I had worked on suppressors, before, I clearly recognized that many of the mutations, which cancel the effect of the nonsense mutations, were located outside the gene and yet they changed the structure of the enzyme," says Dr Siddiqi.

Late in 1961, Dr Siddiqi exchanged data on the same suppressors with Dr Seymour Benzer, another molecular biologist with whom he would soon work, it became clear that mutations terminate the making of the protein and suppressors restore the completion of the chain. This gave rise to the idea that there were codons that terminate the chain and stop its synthesis. As a result, the three codons for all the nonsense mutations - UAA, UAG and UGA were found within a year or so.

### Back on home ground

Having made up his mind early that he would return to India, Dr Siddiqi did so in 1962, after five years of research abroad. Through his acquaintance with Leo Szilard, a nuclear physicist, Dr Siddiqi landed a job at Tata Institute of Fundamental Research (TIFR), Mumbai, under the aegis of Homi J Bhabha. He was asked to set up a molecular biology group at TIFR, from scratch.

"There was no molecular biology group at TIFR and that was a very attractive situation for me, because I knew that if you

go to a university where biology groups were already there, then you have to fit into whatever existed. Whereas here, I had to develop my own laboratory, which is actually what I wanted. This was in a sense, god sent,â€? recalls Dr Siddiqi.

After setting up the lab, it was a time of transition for this researcher. The research areas he was already working on needed to be let behind so as to give way for fresh topics of experiments, which would later turn out to be his most pioneering work ever.

â€œWhen I look back at it, this was scientifically the first phase in my work. I had worked on molecular and microbial genetics, genetic code, protein synthesis, structure of gene, suppression and things like that. But, two-to-three years after setting up the lab, I realized that many other people in the world were already doing the things we were trying to do, and sooner or later bacterial genetics would no longer be an area where we could compete, because we were likely to be left behind,â€? says Dr Siddiqi.

He was extremely attracted to the ideas his friends were advocating that one should turn from molecular genetics to neurobiology, because in studying the brain of animals you could use genetics in the same way as it was used in molecular biology. Thus, started the research on *Drosophila Melanogaster*.

### Tales of the fruit fly

Dr Siddiqi decided to work with Dr Seymour Benzer on neurobiology and so, took a two-year sabbatical from TIFR. With no knowledge on the subject or on *Drosophila*, he went to MIT, where he was visiting professor, to learn about neurophysiology and electrophysiology. After a year, he moved to California Institute of Technology, where he worked in Dr Benzer's lab on temperature-sensitive paralytic mutations of fruit fly. For a year-and-half, he was interested in and worked on genes, which control the function of the insect's nerves and muscles.

### First Person



â€œDr Obaid Siddiqi is a deep thinker, a scientist who has made major contribution in bacterial genetics and in behavioral neurobiology and an outstanding institution builder. India is very fortunate to have him, first in ushering in molecular biology at the TIFR, then in developing developmental biology and neurogenetics there and later in establishing the National Center for Biological Sciences of TIFR. He is a role model for scientists and colleagues, but one who is impossible to emulate! All of us at NCBS are ave this award conferred on Prof Siddiqi.â€?

**an**, director, National Center for Biological Sciences, Bangalore



â€œDr Obaid Siddiqi was a strong influence in getting non-biologists, especially young researchers, interested in molecular biology and genetics during 1960s & 1970s. One of his talks to physicists in 1963 on the nature of the genetic code was so lucid & exciting that it got many of us interested in molecular biology. He influenced the research scene in Indian molecular biology during its infancy. A very good example of such a case is that of Prof K Vijay Raghavan, the director of NCBS. Over a period of three decades when Dr Siddiqi was at the helm, he has been able to put the world map. He has been one of its chief architects.â€?

**-Dr Padmanabhan Babu**, Biotools Technologies, Bangalore

â€œWe found a set of genes, which cause temperature-sensitive paralysis and what these have to do with the channels in muscles and nerves, through which ionic current is conducted and signaling of nerves take place. By electrophysiology, we found that *drosophila*'s muscles and nerve conduction were blocked. I consider this as the first significant discovery and many other labs started working on this paralytic mutations,â€? says Dr Siddiqi.

Later, when he returned to India, Dr Siddiqi realized that many people started working on the same topic and he understood that it was difficult to compete with them sitting here in India. Deciding to retain his individuality, he started to work out the connection between olfaction, immunology and neurobiology. Soon, he was working on sense of smell of *Drosophila*, discovering the mutants, and since then he has remained in that field.

His first paper on olfactory mutants of *Drosophila* was published in 1978 and in two years he discovered the first olfactory mutants. His team initially worked on molecular biology of olfaction looking for olfactory receptors, mechanisms and later combined behavior genetics. These discovered mutants were later sequenced. His ongoing research focuses on learning and memory of *drosophila*, which like humans, can be trained to be attracted or repelled by chemicals.

â€œOnce you train the fruit fly, then you can ask the question, how long it can remember its training. Just like higher animals, they have memory of various kinds like short-term and long-term memory and that is what we do now,â€? says Dr Siddiqi.

Dr Siddiqi and his team's work has led to a lot of other sciences. They were the first to develop methods for measuring

olfactory response and methods for doing electrophysiological recordings from *Drosophila*'s brain. Their work has had many technical implications, been used by other people and has influenced various other research.

Dr Siddiqi is married to Dr Asiya Siddiqi, a historian, and they have four children - two sons and two daughters. One of his sons has followed Dr Siddiqi's foot steps to become a geneticist and, he now works at Centre for Cellular and Molecular Biology, Hyderabad. Dr Siddiqi loves to spend his free time listening to Indian classical music. In his early days, Dr Siddiqi

wanted to be a professional photographer and despite life having different plans, he is pursuing his passion for photography.

## 'GM crops need objective examination'

*Dr Obaid Siddiqi, founder director, National Center for Biological Sciences, Bangalore*

### Q How are the US and India different as research bases?

What is lacking in India is not money or support. There is a shortage of good talent here. It is easier to get people in the US because people from all over the world are ready to move there. But, here it does not work that way, we have to look for good talent and then convince them that if they come here they can work more or less in the same way as in the US.

### Q What is your take on genetically modified (GM) crops?

I believe that plant and animal genetics can make a difference to agriculture and its production. As a geneticist, I think one cannot say all GM crops are good or all GM crops are bad. Things should be examined more objectively and see what is good for the society, environment, even economy and biodiversity. On one hand, the problem is those who want to sell GM crops do not worry about these things and on the other hand, those who oppose it claim everything that is genetically engineered, is bad. I think there has to be something in between.

### Q What are your views on the Indian biotechnology industry?

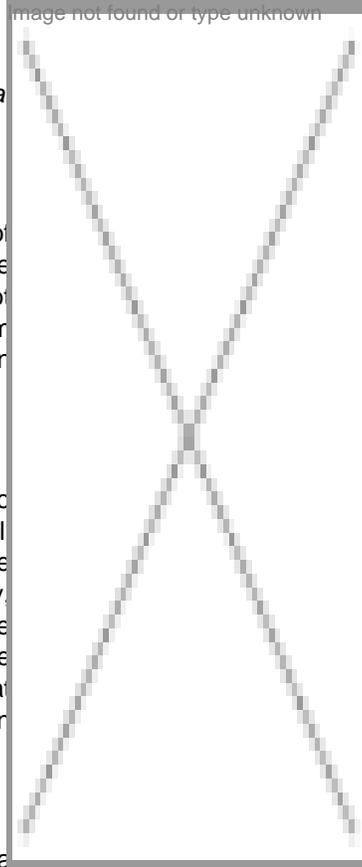
Biotechnology industry is growing fast. Apart from the big companies, a number of small companies, those started by people who were working in research institutes, are also doing very well. These small companies have developed their own research labs. People keep complaining that the existing research labs do not do things which can be used by the industries. I think, it is important for them to be close to the industry, so that they each know what the other is doing. And this connection is visibly useful in the pharmaceutical industry.

### Q Currently, what kind of students do you train?

I have just one or two degree students. I have 8-10 visiting scholars and post docs. Many universities in South India, such as VIT, SASTRA, are smart enough to see that they do not have necessary facilities for teaching students, how to do experiments. So, they freely give them six months or so to go out and work at other institutions and I get many such students. From my point of view, if I get four-five such persons, it allows me to see how they are and how they work and if some are good, I ask them to come back.

### Q Are students coming to NCBS interested in a research career or in industry?

People coming to us are more interested in teaching and research or they want to go abroad after their PhD. A majority of those here go to research institutes. Now this might change, as I hear people say that lot of them are coming back to India. My hope is more and more people who are learning to do research will continue to do it here. Right now, it is not a pretty situation, because we are not able to retain the people we train.



Shruthi Ram in Bangalore