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# Virulence profile

## Dipshikha Chakravortty

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### Tell us about your early days

I was born to my mother, Mrs Bani Chakravortty, a homemaker and my father, Shri Santosh Kumar Chakravortty, an engineer. My birthplace was Jabalpur, one of the major cities of Madhya Pradesh, India. My father served in a government job with frequent changes in service locations. So immediately after my birth, we moved to Bombay and I completed my schooling there. My mother came from a family of doctors and my paternal side had a legacy of practicing Ayurvedic medicines. I was born when she was 18 and hence our relationship is more of a friendship. She has shaped my career and played a very instrumental role in making me what I am today. My early days were very happy days: going to school, playing around with friends, making mud houses in the garden and mock-cooking with my brother Sanjoy and our friends in the garden. We used to collect all the leaves from the garden and cook using wood fire to discover the color of the resultant broth! My parents never inhibited me from doing anything and hence I opened up all faulty stuff in the house from fan to transistor. I was 7, I think, when I mixed some milk cream with talcum powder and named it as my special cream. Ignorant enough, not knowing the science of microbes! My mom to her horror saw black stuff in a corner and threw it away! Strangely, at an early age I felt the presence of an invisible strength. I always thought that there is some invisible strength in this universe, though never shared with anybody.

### Did you have a particular career wish as a child?

I think my wish got modulated by several factors. As a very small child, I played with my great-grandmother's medical kit. My great-grandmother completed her degree in medicine in 1939 at Kolkata Medical College and she was one of the very few lady gynecologists of her time way back in the 1940s. Her dynamic life story is fit for picturization. She was known as Lady Doctor Kiron Chatterjee, just not Dr! My great-grandmom gave the kit, which was imported from Germany, to my mother. I grew up playing with the kit. It contained long scissors, pair of tongs, glass syringes, and very beautiful spatulas. As I have heard the story of my grandmom, the only dream I had was to become a doctor.

### When did you first get interested in science?

With a very strong mindset of becoming a doctor, my crazy ideas were about how I would very finely cut open any damaged part and correct it. I used to like math, physics, and chemistry a lot and was good at them. However, the dream of becoming a doctor overpowered everything. As such I had no idea about what "science" was.

### How did you get interested in science?

My dream of becoming a doctor was shattered when I could not secure my place in medical school by just one mark! Then I thought that I should do my bachelor degree in chemistry and microbiology. Strangely, my mother introduced

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that subject to me. I don't know from where she got to know it. In those days, microbiology was not a very common subject. Getting admission to graduate school with microbiology was a cake-walk for me. When I went to the college first day, one of my zoology teachers (I took zoology as my third subject instead of botany, because I thought botany would not help me to at least get near what I wanted—so-called human science) Dr Majumdar told me “Dipshikha, don't be sad, you have 5000 medical doctors and just 15 microbiologists each year,” in those days, seats in microbiology were very few, “so you will do something different, just try!” That advice boosted me up and I was again all myself. My teachers in microbiology, Dr Anuradha Desphande and Dr Kulkarni, were really great teachers and from then on there was no looking back. My real understanding of science came to me during my graduate and post-graduate studies when we started doing experiments. In our college, we performed very interesting experiments, such as playing with soil samples, milk samples, and even trying to make wine from grape juice.

**When did you decide to become a scientist?**

I took microbiology as my major in my master degree and I knew I wanted to pursue a PhD. As I was very adamant about doing a PhD, I never took any other liking or any other jobs. I struggled for around half a year to get a position and succeeded. I already saw myself as a scientist, even before I joined a PhD program. Somewhere, my sadness about not being able to become a great doctor got buried in the world of science. I always thought that science is not just doing experiments. I was doing my PhD in India (National Center for Cell Science, Pune) and was working on the role of endotoxins in pathogenesis. I felt that science has a soul; it is more than just doing some mechanical experiments. I used to take care of my cells, actually feel for them, and once I remember that my cells got contaminated and I cried the whole night! My feelings for things that cannot communicate is much more than for the ones that can. I always felt that science is a way of life, an integral part, like blood, silently flowing through our arteries.

**Were there any people who influenced your decision?**

In fact, I myself am not very clear about how I had made the decision. It was never a conscious decision; I actually did not leave a choice for myself. The decision factor comes when you have three different choices! In my life, I have never provided myself with options, so getting into a PhD program was the only goal. However, my parents and my mentor Dr KS Nandakumar taught me some very valuable principles in life. I would say that there were many key players in my life, but no one such person who influenced my decision.

**Tell us about your education and experiences at university**

I took admission to graduate studies known as Bachelor in Science (BSc). The college was a girls' college, L.A.D. College, affiliated with Nagpur University. Nagpur is a very important city in Maharashtra and is central to India. We had a great group and discussed our subject, went for project work, caught butterflies as a part of zoology project and dissected earthworms soaked in formaldehyde. Our few teachers in zoology, chemistry, and microbiology were excellent and they taught us in different ways. Our course curriculum was quite intense. We had classes, practical sessions, and discussions. Teachers used to give us notes. I never liked their notes. Hence, I became a member of the university library and dug all the books by Pelzcar, Reid and Chan, Stanier, Lehninger, and Alberts and made my own notes only from those books. I still recall that sometimes I did not understand anything I was reading, but I read and read and tried to understand. Nagpur is a hot city with temperatures soaring up to 47 °C. In that sultry and hot weather, I used to travel by my school bus to our college. In my post-graduate course, where I took microbiology as my major, our group and seniors were worth appreciating. It was a very small group of 10—two boys joined the course and both of them left and we were left with again an “all girls course.” Post-graduate course was very rigorous with long hours of practical. We took seminars, had discussions, and were lucky to have a few very good teachers, like Prof Khandwekar, who taught us industrial microbiology, or Prof Ingle, who

taught our enzymology class. I continued with my habit of making my own notes and this time more in depth as I was in a sea of knowledge with great textbooks in our own library. I made wonderful notes (maybe it could have been published as a book!) but one fine day I came to find that my 1000 pages of hard-earned notes made on industrial microbiology were stolen. Anyway, with exams coming, I had no choice but to read the class notes. We had access to good books and a moderate lab with basic microbiology facilities. There was a burning desire to do experiments and to learn a lot and then time came for the final exams. I did very well and stood second in the university! I never came first.

**Where did you perform your PhD and postdoctoral studies?**

I was admitted into the PhD program in National Centre for Cell Science, then called the National Facility for Animal Tissue and Cell Culture, a great vision created by Dr UV Wagh. At NCCS, my journey of research in animal cells and tissue culture began. My first introduction to the cell culture systems, preparation cell lines, preparation of fastidious cell culture, cryopreservation of cells, etc. made me actually go crazy. I could not sleep at night and thought of ideas that might sound very crazy. Dr Wagh was very well organized with systems and management of the organization and administration. He took utmost care that we young graduate students were happy and got good support from the institute. We research students had an organized laboratory, excellent cell culture rooms, and an efficient instrumentation facility. Our training program began with washing glassware. Dr Wagh used to tell us if you cannot wash your own glassware to get it clean and sterile, you will never be able to do good experiments and get wonderful results! I know now what he meant. Though we had an automated glassware washing machine, we washed the glassware, test tubes, beakers, conical flasks, plugged the pipettes with cotton, baked the glasswares, autoclaved, dried, and put them back in the racks. Ours was a very new institute and mine was the second batch of graduate students. We were just three students in our batch. Hence, we

never had very intense coursework that we see in institutes these days, like in my present institute (Indian Institute of Science). A few of the scientists however started an experimental course and there I got a first glimpse of how to grow phage cultures and check for lysis. Dr Yogesh Shouche and Dr MS Patole were instrumental in teaching us molecular biology techniques. How can I forget the wonderful teaching of Mr Powar? He was a lab technician and taught us chicken embryonic fibroblast cultures, the first cell culture technique I learnt from him. However, the research program for my PhD degree could not be finalized for some time, although we are busy with various experiments. Real research came to me when I was introduced to a very young scientist, Dr KS Nandakumar, who joined the Institute. He came with a background in bacterial pathogenesis, and with him, I had my real first scientific interaction on the topic of bacterial adhesion and colonization. From him I learned about ethics in science, how to write research projects/research synopses with clear objectives, plan experiments, maintain data books, make and label reagents, document the results, and importantly how to present the work. The first lesson he taught me was the lesson of independence in doing research work. He taught me how to become an independent researcher, and believe me, that is not so simple. He never gave me a problem to solve, he only discussed with me some interesting facts and experiments and told me to design my own problem and solve it. That is how I got into the world of beautiful science and marvelous experiments. He also taught me that science is not just bench work; it is something more than that. I was so lucky to have him as my mentor. I realized the importance of these facts in research when I stepped out for doing my post-doctoral work. I slogged for my research findings, failed, and finally succeeded in my work. From him, I learned the hard and true way of doing science. The essence of science, power of scientific communication, and writing skills that he taught me will be with me throughout my life. During my PhD, I worked on the endotoxin-mediated cellular response in human lamina propria small intestinal fibroblasts. My work involved culturing small intestinal

lamina propria fibroblasts from aborted human fetuses due to medical termination of pregnancy and then studying the response of lipopolysaccharide (LPS). Our work gave some very important leads in the field of bacterial pathogenesis and also attributed important functions to the so-called ubiquitous “fibroblasts.” Finally, I received my doctorate degree in December 1999 from the University of Pune, which recognized the NCCS for degree course work. Thereafter I left India and set out for my first post-doctoral studies with Prof Takashi Yokochi at Aichi Medical University in Japan. Prof Yokochi is a pioneer in endotoxin research and was the second wonderful mentor in my life. Prof Yokochi’s sense of giving independence to students to carry out research was appreciable. We called him Sensei. Sensei is a fun loving person who played ice hockey during his young days and he had his MD and PhD. His lab was very well-funded and I was able to elucidate the signaling mechanism induced by LPS in macrophages. My post-doctoral days were very joyful; however the only thing I dreamed and did was to develop newer ideas and get them to work. I learn to speak Japanese and enjoyed the social life of Japanese people, had very great friends, and did a very successful two years of post-doc work. During my days in Japan, I thought that what I was working with was just one molecule (i.e., LPS) from the entire bacteria. I also thought that the progression of pathogenesis and diseases cannot be attributed to just one molecule and from there my interest began to evolve around two life systems—i.e., the host and the pathogen. I chose a bacterial system because from the beginning, bacterial diseases interested me and made me curious enough to investigate as to why there are very poor vaccine candidates against bacterial diseases. One fine day, I replied to an advertisement in *Nature* about a position in Prof Michael Hensel’s lab in Erlangen and packed my bags for Germany. Prof Hensel was the third important mentor in my life. A very composed and sharp person, Michael introduced me to the world of bacterial secretion systems and more so overall bacterial pathogenesis. Michael was a hard core molecular microbiologist and a geneticist. We complemented each other and I began

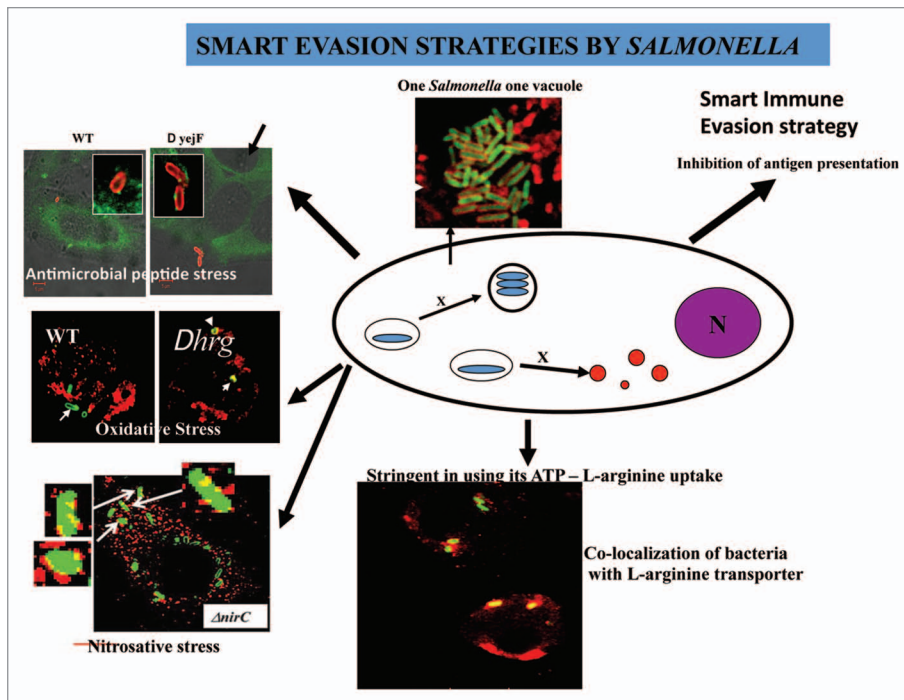
our study on the host–pathogen crosstalk using *Salmonella* as a system. Michael encouraged me to apply for the prestigious Humboldt foundation fellowship, which I did, and I received it. This fellowship is so unique that if you have not experienced, you will not be able to understand. Michael, along with his post-doc mentor Prof David Holden, was instrumental in discovering the SPI2, another island coded by the type three secretion system in *Salmonella*. I always thought that everything is fine in vitro, but what about when the bacteria is inside the cell? Does such a kind of secretion system indeed exist? I was very adamant to answer this question, and with the help of a very great and excellent electron microscopist, Dr Manfred Rohde, affectionately called Mannie, we showed that indeed the vacuolar bacteria project these so-called structures at the intracellular level. In Michael’s lab, I got introduced to Jonathan, an MD student, Cedric, Volker, Imke, and Dani. We had untiring discussions, especially Jonathan, Cedric, and me about our experiments, shared ideas, performed experiments and had a very successful two years! In every lab from the beginning, I used to teach and guide undergraduate students, post-docs, and MDs, and I thought, I am a very good teacher and I would like to have my own group now. The moment this idea got inside me, I applied for a position at the Indian Institute of Science. This is not only a very prestigious Institute but has a very rich genesis and excellent history. I got the position and returned to India! It was a very tough decision but I could not resist the offer from IISc. I came to IISc in 2004 and joined the Department of Microbiology and Cell Biology.

**What was your first position after university?**

My first position was a junior research fellow (JRF) followed by a Senior Research Fellow (SRF) position, both at NCCS, Pune.

**When and where did you start your own lab?**

I started my own lab and research group after getting my faculty position at the Department of Microbiology and Cell Biology, at IISc, India in the year 2004.



**Figure 1.** A summary of Dr Chakravorty's work.

**How many people work in your lab?**

Nine students already graduated from my lab and are elsewhere in the world doing their post-doctoral work. Currently there are 6 students at various stages of their doctoral work. Two of them are expected to submit their theses in 2014. At any given time I have around 15 young colleagues working in my group.

**What is your function in your institution?**

I have a wide array of different functions in my Institute and sometimes some of the functions vary depending on the requirement for the department and the institute. (A) Mentor: I mentor the young graduates toward getting their degree and publications. I mentor the short-term summer trainees who come to my lab through various competitive programs. I teach two courses, namely, essentials in microbiology and host-pathogen interaction, for a given semester to the graduate students and one course in practicals for the undergraduates. (B) General Administration: I am one of the honorary hostel wardens and my function is to oversee the smooth functioning of the hostel allotments and safety/security of the girls' hostel, decision making abilities with the hostel matters, etc. (C) Scientific:

Whenever required, I am part of the panel responsible for setting various national and institutional entrance and other competitive exams, part of the interview committee for selection of students for various courses in my own department and also in other collaborating departments. I have a responsibility to take care of a few instrumentation facilities, from both departmental and divisional units of the institute.

**What areas or topics does your lab currently focus on?**

Our lab focuses on the various strategies which bacterial pathogens employ to defend the host (Fig. 1). Our intense research work has contributed tremendously to understanding the pathogenesis of *Salmonella* infection. We work on various strategies that are unique to the cell type and these show how dynamic and smart the pathogen is! We try to answer and relate our findings to the physiological aspect of pathogenesis. We mainly use *Salmonella* but are also getting into other bacterial pathogens.

**Do you have partners that are important for your research projects?**

Yes, partners are extremely important for the research work. I have three major

partners with whom we are doing some wonderful work. Prof Jagadeesh, from the aerospace department, and I have made a shock wave-mediated vaccine delivery device. We have shown that this device can be also used for transformation and the efficiency is better than the expensive electroporator. Prof Ashok Raichur of materials engineering and I have developed an excellent delivery system for drugs and tested them in our infection model. Prof Narendra Dixit from chemical engineering is a pioneer in simulation and prediction models, and we are trying to understand the host-pathogen relationship using this knowledge. These partners play a very instrumental role in our science and I am really lucky to have them.

**What are your main goals for the next five years?**

In the next five years, I want to concentrate on getting our vaccine strain, which got patented, into trials. Results from our preclinical experiments with the typhoid vaccines are excellent and I feel that this vaccine will do wonders. We would like to develop the transformation unit and market it. Our very intense research on the role of gut microbiota in bacterial infection will be the major focus in coming years.

**Tell us about the most important stages of your professional career**

The beginning of my professional career started with my getting admitted to a PhD program and interacting with my mentors. Getting experiences in different domains of research both from Japan and Germany was a turning point in my professional career. Getting into the wonderful Indian Institute of Science was the determining factor in my career. Another important stage of my professional career was setting up my research lab, as well as guiding and training graduate students in various research programs. I was and I am very lucky to get vibrant and bright graduate students with different capacities that make a big difference in my science. This institute is unique and several peers I met here, such as Prof CNR Rao, Prof G Mehta, Prof P Balaram, Prof R Nayak, Prof V Nagaraja, Prof MS Shaila, Prof U Varshney, and Prof U Vijayraghavan, and

my colleagues Prof U Nath and Prof KN Balaji played an important role in my professional career. I have learned a lot from each one of them.

#### Who were your mentors?

Dr KS Nandakumar (India), Dr UV Wagh (India), Prof Takashi Yokochi (Japan), and Prof Michael Hensel (Germany).

#### What makes a good mentor?

A good mentor should be very sharp, witty, and compassionate. The mentor must have an unbiased approach and a very positive attitude, and should be a good listener. It is an additional boon if the mentor is a good psychologist and understands the behavior and temperament aspects of students or mentees. A good mentor will never generate followers but leaders. This says it all!

#### What are your research interests?

My research interests lie in understanding the mechanism of bacterial infections, and developing antidote and vaccine strains with excellent memory. I am also trying to understand the strategy that bacteria use to inhibit the process of antigen presentation. The literature is extensive but equally dark!

#### What was your most significant scientific accomplishment?

There are a couple of accomplishments that I feel made a mark and will continue to do so. During my PhD I showed that the so-called quiescent intestinal fibroblast is indeed very vibrant and can modulate the response in other cells. The establishment of culture from the human small intestine was adopted by many labs across the world. In *Salmonella* pathogenesis, we showed that SPI2 is responsible for the inhibition of trafficking of the iNOS containing vacuole to the *Salmonella*-containing vacuole. This study is still highly cited. We further demonstrated the SPI2 structure within the cells and this gave direct demonstration that the secretion system indeed functions in intracellular bacteria. Coming to *Salmonella*, the



**About Dr Dipshikha Chakravorty.** Dr Dipshikha Chakravorty studied microbiology at Nagpur University (Nagpur, India), and completed her PhD in Biotechnology at the National Center for Cell Science at Pune University (Pune, India) in 1999. She performed her postdoctoral studies in the labs of Takashi Yokochi at Aichi Medical University in Japan, and Michael Hensel at the Institute for Clinical Microbiology, Immunology and Hygiene at the Friedrich-Alexander University in Erlangen, Germany. In 2004 Dr Chakravorty returned to India to take a position as Assistant Professor in the Department of Microbiology and Cell Biology at the Indian Institute of Science in Bangalore. Since 2009, she has been an Associate Professor at this institution. Her research revolves around infectious diseases and host-pathogen interactions, with a particular interest in the pathogen *Salmonella*. Her research has resulted in over 80 publications in international peer-reviewed journals and chapters in biomedical books, as well as patents related to *Salmonella* diagnosis and vaccines. Besides her research, she teaches graduate students at university, actively participates in national and international committees and societies, and serves as editor and board member for several journals, including *Virulence*. During the course of her career Dr Chakravorty has received numerous honors and awards, including the Fellowship for the National Academy of Sciences, India in 2012.

development of the excellent vaccine strains DV-STY and DV-STM is actually a major accomplishment. Trials are awaited and we are very optimistic about its success rate. In our studies on bacterial pathogenesis we aimed to understand how the pathogen uses evasion mechanisms to establish itself in the host. We found that *Salmonella* resides in a single vacuole and the division of *Salmonella* happens along with the vacuole. The moment this strategy is jeopardized, *Salmonella* meets with a dead end.

#### What were your “highlights” in recent research performed in your field?

1) *Salmonella* resides in a single vacuole and its division happens along with the vacuole and this lifestyle is important for its pathogenesis.

2) *Salmonella* can recruit cationic amino acid transporters to its SCV and quench host arginine.

3) *Salmonella* differentially channelize arginine toward arginase and inhibit NO output

4) The excellent protection provided by the vaccine strain DV-STM in typhoid model and in pregnant mouse models shows that absence of this gene may be important for developing long-term memory.

5) Shock wave-mediated vaccine delivery system is an excellent needle-less system that provides wonderful protection in animal models.

#### What do you think you would do if you were not a scientist?

If I were not a scientist, I would have become a cheese-maker! Cheese and microbiology always fascinated me and still I would like to do apprenticeship in Greece or France about cheese-making.