Interview

WITH LOLITIKA MANDAL

Lolitika Mandal is an Assistant Professor at the Indian Institute of Science Education and Research (IISER), Mohali. Her research has contributed to a global understanding of how blood cells develop. In this interview, she shares her experiences and insights on the life of a scientist.

Tell us something about your current work.

We are interested in understanding how blood cells develop (haematopoiesis). To do this, we use the fruit fly (*Drosophila*) as a test model. The fruit fly is a small insect (a fully grown adult is only a few millimeters in size!) that gathers around very ripe/rotting fruit.

You may wonder why we use an insect for our studies – after all, insects do not have blood like we do. How can anything we learn about the process of blood formation in insects be relevant in humans?! As it happens, fruit flies (and all other insects) have a fluid - called haemolymph, which is very similar to blood. It circulates within the insect body, remains in contact with all its body tissues and is composed of cells that are very similar to the cells in our blood. What's more, the cells in both these fluids develop in very similar ways!

But, you may ask, why not just study the development of human blood in humans? The cells in human blood are short-lived. They are produced and their numbers continually replenished by the division of some special cells called the haematopoietic stem cells. The specific physical location of these cells, within the body, is called their 'niche' (pronounced *nee-sh*). Turns out, the niche has an important role in the behavior of these stem cells. Not only does it influence how often these stem cells divide, but also whether they retain what's called their 'stemness' - an inherent quality that allows them to stay less specialized themselves. The questions we are asking are: what are the signals from the niche that direct the stem cells to divide? How does the niche influence this 'stemness'? How are the maturation signals (that direct the formation of fully specialized circulating blood cells) warded off from the stem cells in the niche; and, also, by the niche?

The human niche of haematopoietic stem cells is the bone marrow. The bone marrow is the spongy part in the centre of some of our bones, like the bones at our hip and in our thigh. Studying the niche of haematopoietic stem cells within the marrows of people is not easy. In contrast, stem cells in flies are found in their lymph glands (blood forming organ). Knowing that the process of blood development in flies is very similar to humans, *Drosophila* thus becomes an attractive model to explore these questions that intrigue us.

What is a typical day at work for you like?

I use the early hours of the day with my doctoral students. We discuss experiments they've performed the previous day and examine any hurdles that require trouble-shooting. We also meet once a week for more detailed discussions and brainstorming on individual projects.

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Being part of one of the IISER system institutes, which offers (BSc/MSc integrated courses), I invest an hour and a half, every day, in teaching a class or preparing for one.

What would you say are the most rewarding and frustrating aspects of being a biologist?

The most rewarding aspect is that I get to unravel phenomena that Nature has been concealing from us! In the words of a great biologist E.O. Wilson, "Our sense of wonder grows exponentially: the greater the knowledge, the deeper the mystery."

There are two aspects of my work that bother me to some extent. The process of getting one's work published can be frustrating - especially when you see your work being tossed from one academic journal to another, without peer review (the process of examination of a paper by your scientist colleagues in the same field, from anywhere in the world). The other big constraint to research is obtaining funds for one's work. Not only does this directly affect the quality of your research, but it also slows you down scientifically.

What are some of the most important benefits of your work to society?

As I've mentioned before, how blood cells are formed in our bodies is remarkably similar to that in fruit flies, both in the distinct phases of the process and the nature of signalling molecules that are crucial to it.

Very recently, my group identified 'hubs' of haematopoiesis in the fruit fly model system. These sites are simplified versions of a vertebrate bone marrow. We hope that this discovery will establish *Drosophila* haematopoiesis as a simpler, genetically testable model to separate out normal from abnormal blood cell development. This will open up endless possibilities in the future. The fruit fly haematopoiesis model can be used to help answer questions related not only to the formation of blood stem cells, but also to their migration and their roles in immunity, wound healing, ageing, and so on.

How do your personal and professional lives influence each other?

I have always tried to balance my personal and professional life. While my profession has taught me to be logical, focused, and to some extent philosophical, my interactions with my kids after a long day's work, rejuvenates me!

What sparked off your interest in science?

I do not remember a specific time when I arrived at the decision to become a scientist. I have always been curious about the natural world. As a child, I remember spending many fun-filled afternoons, in the winter/summer school breaks, chasing insects or looking at birds, while my mother and grandmother were fast asleep. My love for science has kept me so focused on research that I have never considered any other career options.

Many people have nurtured my interest along the way. My parents have been a huge support system, and have helped me steer my course. My dad was my role model. Although he was a busy surgeon, he

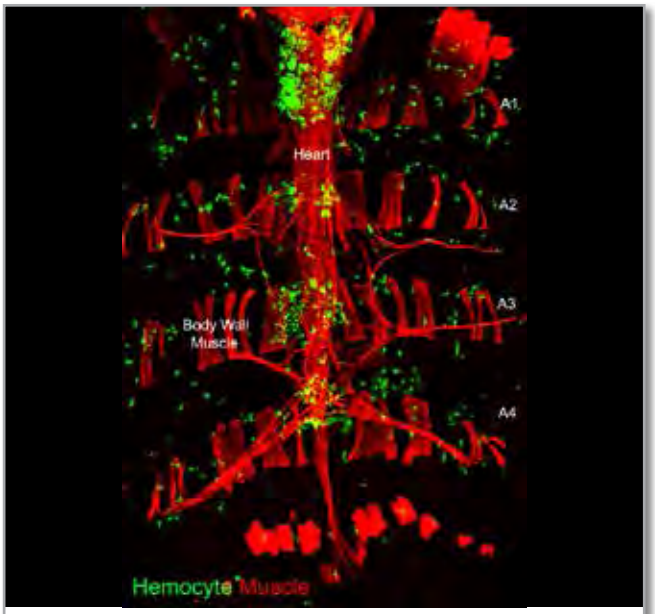

Figure 1. Haematopoietic hubs of the fruit fly: the simplest version of the vertebrate bone marrow. Haematopoietic hubs (green), containing discrete clusters of haemocytes, house progenitors and differentiated blood cells. In this image, they are seen tightly associated with fly heart muscles (red).

had a tremendous love for research. He was my first mentor—my interactions with him stimulated my scientific curiosity. In fact, it was he who inspired me to pursue a doctorate in science. My husband and brother have helped make all these years of work fun, and still keep me going!

My science teachers at school always encouraged me to ask questions, even though I would often use this opportunity to pester them with my endless curiosity. In those 'pre-internet days', we depended almost entirely on teachers and parents to guide us. But, somehow, I feel that our interactions with our teachers were warmer and more inspiring when we were not exposed to huge databases of information before we were ready for it.

During my postdoctoral studies at the University of California in Los Angeles (UCLA), I was lucky to have two fantastic scientists, Professor Volker Hartenstein and Professor Utpal Banerjee as my mentors. It was they who introduced me to my current field of work - *Drosophila* haematopoiesis.

How did you come to choose haematopoiesis in *Drosophila* as the area of your research?

My doctoral work with Prof Jagat Roy at the Cytogenetic Laboratory, Department of Zoology, Banaras Hindu University (BHU), was focussed on studying the role of a tumour suppressor gene in brain tumours in fruit flies. I started studying neurobiology to understand normal brain development, but fell in love with the subject.

Figure 2. Fruit flies – the Cinderella of Genetics.

> Neil Armstrong once said, "Mystery creates wonder and wonder is the basis of man's desire to understand.

For my post-doctoral studies, I chose to join Prof. Volker Hartenstein (UCLA), who happens to be a pioneer in fly brain development. One day, after about three weeks of being in his lab, Prof. Hartenstein stopped by my working bench, and commented on how he thought that it was during post-doctoral work that one must take risks. I was puzzled by his comment and asked him why he was saying this to me. He responded with a smile, saying, "Do something that you have never done...there is fun in doing so....." He added that while the fruit fly is famous as a model for studying immunity, its feasibility as a model for studying the developmental aspects of blood cells was still in its infancy. He would like his students to explore this aspect of fruit flies. Like Prof. Volker, Prof. Utpal too had a tremendous interest in following this field of research. The first milestone paper on blood cell genesis was, in fact, published from Prof. Utpal's lab. It seemed like there was still a lot in this field that was left to be unravelled.... So there you go - I left neurobiology, and engaged myself in pursuing the development of blood cells in fruit flies.

Are there any character traits that are a natural fit for scientific research?

Students showing curiosity, motivation, a commitment and eagerness to excel, and of course diligence, are a good fit for life as a researcher.

How important are observation and wonder in science education?

A key element that drives research is your capacity to observe. Observing a phenomena or an experiment has a profound effect on a young mind. If we hope to infect students with an enduring interest in science, we must provide opportunities for students to observe textbook concepts in action.

The astronaut Neil Armstrong once said, "Mystery creates wonder and wonder is the basis of man's desire to understand". As also beautifully pointed out by Erwin Chargaff, "It is the sense of mystery that, in my opinion, drives the true scientist; the same blind force, blindly seeing, deafly hearing, unconsciously

remembering, that drives the larva into the butterfly. If [the scientist] has not experienced, at least a few times in his life, this cold shudder down his spine, this confrontation with an immense invisible face whose breath moves him to tears, he is not a scientist." I fully agree with Armstrong and Chargaff's views on the importance of wonder in science. School science must provide opportunities for students to be awe-struck with the wonders of the natural world, and leaving them curious to unfold the mysteries that they observe.

Can you tell us some things that you think teachers could do to encourage an interest in science?

Teachers have to be the bridge between textbooks and students. I mean this in the literal sense - to instil interest in the topic, we have to be the proactive link that infuses life and our own excitement into textbook content. Instead of telling students facts straight from a book, teachers may need to involve students in the process of discovering science through experiments, or engaging with a movie or story about a discovery or discoverer.

How can researchers contribute to school science?

Researchers can inspire and fuel aspirations of eager students. Short interactive sessions with scientists can provide opportunities for the students to not only discuss the latest in science, but also get a feel for the real world of research. Another way researchers can engage with school science is by hosting students in their labs during school summer/winter breaks.

Figure 3. Dr. Mandal at work.

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IISERs (Indian Institute of Science Education and Research – a new series of institutes similar to the IITs) have 'outreach programs' that reach out to school students on a regular basis. There are five of these in India: apart from the one at Mohali, there are ones at Pune, Bhopal, Kolkata and Thiruvananthapuram. Another place that interested schools can visit is the Homi Bhabha Centre for Science Education (Mumbai).

What are some of the biggest misconceptions that school students and teachers may have about a career in science?

While it is true that it takes time to establish oneself in a scientific career, what I think may be important to remember is that a career in science does not have to be boring, draining, or poorly paid. If you have passion for science, you will enjoy the ebbs and tides of a research career.

In what ways is the practice of science as a profession evolving? And, what fields will take centre-stage in the next few decades?

A career in science today is no longer restricted to becoming an educator or Professor. We find science students adopting a range of careers - from hard-core research (in academic as well as industrial organisations) to science communication and journalism, management, and even law (related to Intellectual Property Rights and Patents). Journalists with a strong background in science can help communicate the latest in scientific research to the common man. Those who also have a flair for English can help write scientific papers. A patent lawyer with a scientific background can help steer a researcher through dilemmas of 'what and what not to patent'.

Armed with multidisciplinary approaches, new technologies, and high-end instrumentation, current researchers can reach new heights and realise things that were previously unappreciated. Therefore, predicting which fields will rule the next decade is quite difficult at this point.