

“There is a strong pressure on scientists to do some translational research”

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Singapore: His breakthrough discovery, for which he was acknowledged with the Nobel prize, were the key regulators of the cell cycle, which he terms as 'Cyclins'. It is a protein that controls the progression of cells by activating cyclin-dependent kinase.

Today, cyclins are considered as key players in regulating and controlling cell behavior and several functions including tumor suppressor genes. His discovery of Cyclin helped in explaining the behavior of cell growth in a disciplined and controlled way and in a right time, at the right pace, thus, broadening the study of cancer cells and their uncontrolled growth tendency.

Born in 1943 in England, Sir Hunt received a PhD from the University of Cambridge in 1968 and conducted research at the Albert Einstein College of Medicine in New York. He later taught at Cambridge (1981-90) and in 1991 became principal scientist at the Imperial Cancer Research Fund (now Cancer Research UK).

Sir Hunt was elected a fellow of the Royal Society in 1991 and a foreign associate of the US National Academy of Sciences in 1999. In 2006, he was awarded the Royal Medal for his work on cell cycle control and was knighted by the Queen in the same year. He is a member of the Advisory Council for the Campaign for Science and Engineering.

Sir Hunt was recently in Singapore to speak at the Global Young Scientists Summit 2015, a five-day international booth camp for eminent scientists and technology leaders to mentor global young scientists and inspire them to continue to pursue their

scientific dreams. In an interaction with BioSpectrum Asia, Sir Hunt shares his journey as a basic researcher and his perspective on today's scientific research in translation prone environment.

You have always been a basic researcher. What is your opinion on the take of pharmaceutical companies on research activities that are more directed towards translational research? Is there a gap between pharmaceutical companies and basic researchers?

My interaction with pharmaceutical companies has changed over the years. In my early research, when I discovered that RNA was a powerful biological inhibitor of protein synthesis and a byproduct, bizarrely of penicillin, it was appreciated by a company producing RNA. It was considered to be a cure for cancer. In mid 70s I first met a pharmaceutical company who was thinking to make it into a therapeutic product and was interested in my research. The impression of my first interaction with the pharmaceutical company was that they would have a closed door interest, with an insecurity to share information with anyone outside the company.

In my next experience, during a meeting with Astrazeneca in Manchester, it was again a closed door agenda with a high security interaction. My conclusion was that it was not an effective way to interact with academics where most of the ground level takes place and without whom, understanding of disease and drug development cannot be successful.

But now things have changed a lot. Two or three years back when I visited the same Astrazeneca facility, I discovered they have really opened up. They shared their unique perspectives of containing the confidentiality of their research from leaking outside and safeguarding it by all means. But now since the pipeline is so thin, they realize that academic research is a good way of scanning the horizon. I feel this is a healthy development in the mode of communication between pharmaceutical companies and basic researchers.

Pharmaceutical companies are good at finding the application or side effects of a potential drug molecule but they are not good at finding the targeted treatment. So, in the last three to four decades, there is a quite a big shift in the mindset of pharmaceutical companies.

When a researcher is progressing towards a possible breakthrough, what is the acceptance level in the scientific community?

A human body is such a complex mechanism that we still do not know many of the functions. Many breakthroughs just happen by accident. When I started working on cell cycles, I never imagined that study of cell division would be a major activity because it is so fundamental to biology. But when I discovered the cell cycle behavior, it was unbelievable, thrilling. I just stumbled upon cell cycle character and protein degradation and realized it is extremely important for the control of cell cycles. This was something that nobody, even theoretically had proposed. It was a fundamental principal that to continue cell development, we have to get rid of something, and nobody had suggested it because it seemed so impossible. Initially, there were some apprehensions but the acceptance from the fraternity came gradually.

You have spent decades observing the cells and their behavior. How has it been?

I don't interact with cells I crush them. If I see a cell, I want to break it open to study protein character (he laughs).

What is your message to young researchers who are taking up a project or area of research? Should a subject be taken with a targeted approach?

I like to emphasize to young people that the biggest drivers to fuel research is to identify problems. In biology, having a problem is an indication for finding something new, a problem which is sufficiently important to engage you for a significant period of time. Another set of targets are taking bigger puzzles like how to eradicate cancer or how brain works. But these are too complicated to get a solution. The trick is to find a nice, well defined problem that you can solve in a reasonable period of time and you can make measurable progress.

What were your initial problems in basic research?

My first problem was to find how the synthesis of protein globin coordinated with that of the prosthetic group haem which carries oxygen. It was already known that haem controls globin synthesis but it was very difficult to see how it works. While solving the problem, we realized that there are many other conditions that engage same kind of phenomenology and sometimes, the result is derived just by changing the perspective. This helped us in collapsing complicated problems to simplified ones. Every research goes through a cycle of clarification and complexity and it could be depressive.

What is the role of cyclins in understanding the behavior of cancer?

In my very basic fundamental study of cell cycle, the most important explanation is that cell, of the nose for example, does not shrink or expand but stays at its commanded size. But at the molecular level, they are turning over all the time. So they keep changing but never lose their character. But, in the cancer of nose, the cell grows abruptly and you cannot differentiate the cell and there is a disorganization. So it is not correct to say that cancer can be stopped by stopping cell division. The problem in cancer is how to stop the cancer cells from dividing and growing uncontrollably. It is a very different pattern. There is nothing wrong in cell division, but when it is out of control, it is alarming. Also, when we talk about controllers of cancer cells it becomes very difficult to understand because every tumor has a different cell behavior.

What is your opinion on personalized medicine and if it is a right approach for cancer therapy?

People have found a particular cancer genome but the problem with personalized medicine is that people expect to define common signatures in different cancers. For example, in breast cancer, there could be thousand different types of mutations and some of them would be in common, but not all. Gene therapy is not at the stage where you can correct these mutations, or repair loss of functions. There could be 25,000 different mutations and you cannot fix it.

Do you think there is a pressure on scientists to strike a breakthrough research for justifying the investments today?

Well, there are more scientists coming in to the business today than ever in my lifetime. In my opinion, there is a strong pressure on scientists to do some translational research. This implies when you already understand human biology well and I suspect that though we have progressed in discoveries, but we don't know how far we have gone. The pressure to translate is not intelligent because if you stumble on something which is translational, like discovery of penicillin, you can develop wonder drugs. But it was not translational research, they came upon it and found it by chance. If you stumble upon something which is going to cure cancer, it is absolutely thrilling but we are not at that stage. We are still finding the basic mechanisms.

Do you think the stress on the translational approach in drug research is a hasty attitude?

I think it is a mistake to take such an approach. Problems in biology really do not get solved with a straight formula. We are working in a field where principals are not known and we still do not know how things work. It is pretty difficult to translate not knowing what is going on.