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[I AM A SCIENTIST]

Physical exercise encourages cells to grow

Mechanobiology Institute's head explains significance of his field of research

Carolyn Khew

Q: What are some examples of your speciality, which is called mechanobiology?

Mechanobiology describes a cell's ability to detect, measure and respond to mechanical forces and geometry during normal functions, disease, regeneration and development.

The cells in our bodies, as well as single-cell organisms such as bacteria, are constantly exposed to mechanical forces. Major health problems of cancer, ageing and cardiovascular disease are mechanobiological problems and need to be understood as an interplay between the cell mechanics and the biochemistry.

There are many examples in our bodies of cells being exposed to mechanical force, including all the movements we make and the bumps that we encounter. Similarly, inside the body, the heart is pumping and the lungs are expanding and contracting.

If you look at blood vessels in particular – they provide circulation to tissues for survival while being subjected to the physical constraints of a pump (the heart), changing pressure and the need to accommodate rapid changes in flow rate and volume to specific organs.

There are hundreds of individual machines, or cellular components, working away at any one time to detect, measure or respond to the mechanical force over a range of times.

Q: You head the $150 million Mechanobiology Institute (MBI) at the National University of Singapore. This Research Centre of Excellence (RCE) has 220 engineers, physicists, chemists and biologists working together. How is being a director of the institute different from being a researcher?

As director, I feel that it is my job to create an atmosphere where people of different backgrounds will come together and solve important problems. Innovative solutions require new ways to look at old problems, and bringing engineers, biologists, physicists and chemists together provides for many different possible ways to approach issues.

To get them to discuss problems is difficult because they come from different cultures with different scientific languages. We mix them in an open lab, assigning writing desks on a lottery basis, and that helps.

We also provide central facilities with state-of-the-art tools in microscopy, nanotechnology and molecular biology so that when they get an idea, they can readily test it even if they weren't trained in the technology needed to test the idea.

RCEs in Singapore provide an excellent opportunity to develop this concept. The students, post-doctorates and young faculty, who do the research, find that it drives their research in new, productive ways.

Q: Was it always your dream to be a research scientist?

As a child, I was always curious about science and regularly contributed projects to the science fairs in my hometown of Midland, Michigan. I liked to tinker with things and built devices to measure the light scattering and the surface area of soap molecules.

My first science project was to measure the area of a single soap molecule in a soap film on water. By measuring the area of the film and by knowing how many molecules were in the film, it was easy to calculate the area per molecule.

I was fascinated by how things worked and loved books that showed the inner workings of things.

Q: You did a study last year about the stretching of cells, which may explain why exercise may be important for people. What is the significance of this finding?

We have found that mechanical stretching of cells such as what you and I do every day through normal physical exercise encourages cells to grow.

This is expected because we know that there is a "use it or lose it" problem with many tissues, such as muscle.

The fact that we can produce growth in cells maintained in laboratory cell culture outside the body, in environments that would normally not support growth because they are too soft, means that we can better understand the factors that promote cellular growth through exercise.

Q: You were awarded the prestigious Porter Lecture Award last month for your contributions to research in cell biology and mechanobiology. Could you elaborate on your work?

Initially, my success was in building a way to measure cellular motor functions in the test tube. Those assays defined new motor proteins and we now understand how those proteins can convert energy from the biochemical substrate ATP into mechanical work.

Since then, we have shown that mechanical forces per se influence important disease processes, particularly with regard to cancer.

My lecture was about our latest findings that bring together a mechanical assay of cellular motility with the processes that enable cancer cells to grow in the wrong environment. There are many different cancers but some show dramatic changes in their mechanobiology that provide new approaches to possible treatments.

Q: You also published a paper discussing how small institutes may address the problems faced by biomedical researchers?

There are many new opportunities for biomedical researchers with new technologies and, yet, the need to fulfil obligations for lab, animal and chemical safety is taking professors' time away from research. A single professor's lab is often unable to access new technologies readily, but small institutes can help a lot.

As for regulatory burden, a small institute can hire and manage technicians to effectively handle those matters, freeing the professors for research. The faculty can also oversee the new technologies and see that regulatory issues are effectively satisfied.

In a larger institute, it is harder for faculty to change direction as new research directions arise, since they have less control over the facilities and they are often still saddled with regulatory burdens.

Q: What is one area in cell biology that you feel is understudied?

At this time, we know the protein compositions of many cells and we know how many of those proteins distribute within cells.

However, we understand relatively little about how many cellular functions actually occur, and this is particularly true of mechanical functions that shape the cell in the tissue and are responsible for the form plus many functions of the tissue.

The reason that this area is understudied is that most cell biologists do not like physics or physical approaches to cells, and most physicists do not understand the biological complexity or dynamics of cells.

Traditionally, cellular functions were believed to result solely from biochemical reactions without understanding how they were altered by mechanical factors.

Q: Singapore has been pumping a lot into the biomedical sector. Do you think it is working?

Yes, there are many benefits to Singapore beyond the simple issue of patent income and new industries.

Singapore has gained a reputation for supporting biomedical research that will serve it well.

Although the research has not delivered any blockbuster financial successes, no one expected that this could be done in 15 years, since it takes nearly that long to bring a single drug or product to market.

What this investment has established is that Singapore cares about biomedical research and has built a large community of highly trained biomedical researchers. In the future, Singapore is likely to anchor many of the companies involved in supporting health-care delivery through new technologies.

kcarolyn@sph.com.sg

ST FILE PHOTO

Mechanobiology Institute head Michael Sheetz, recipient of the Porter Lecture Award for contributions in cell biology and mechanobiology, says Singapore has gained a reputation for supporting biomedical research that will serve it well.

A PIONEER IN HIS FIELD

Professor Michael Sheetz, 68, is the director of the Mechanobiology Institute (MBI) at the National University of Singapore (NUS).

With more than 40 years of experience in cell biology and biomechanics, he is a pioneer in the emerging field of mechanobiology, which looks at how mechanical forces are controlled in biological systems at a molecular, cellular and tissue level.

Prof Sheetz was instrumental in the discovery of a novel family of motor proteins called kinesins.

For his contributions to the biomedical sciences, he was awarded the 2012 Albert Lasker Award for Basic Medical Research, the 2012 Wiley Prize in Biomedical Sciences, the 2013 Massry Prize and the Porter Lecture Award last year.

Set up in 2009, the $150 million MBI is one of five Research Centres of Excellence here.

It trains 10 graduate students each year and hosts 50 postdoctoral fellows at any one time, and its researchers have published more than 350 papers in major journals.

Prof Sheetz is married to Professor Linda Kenney, a research scientist at NUS who focuses on understanding the pathways of bacterial infection in mammalian cells.

He was raised in Midland, Michigan, the home of Dow Chemical, where his father was a research chemist.

"He encouraged my interests in science but was a great believer that one should be independent," said Prof Sheetz.

He and his wife are avid bird watchers and have done bird watching at Sungei Buloh and in Penang.