Mike Sheetz: “Basic research has the possibility to go back and understand these biochemical mechanisms and find answers”

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Professor Mike Sheetz, Mechanobiology Institute of Singapore and professor at Columbia University, USA.

*Professor Michael Sheetz, one of the pioneers in the field of Mechanobiology, is the director of the Mechanobiology Institute of Singapore and professor at Columbia University in the USA. Michael Sheetz has been working in the biomedical field for more than 40 years and has been one of the biggest promoters in the study of molecular motors. His achievements led to the discovery of the kinesin motor protein and revealed the steps by which molecular forces convert chemical energy into mechanical work. His discoveries, for which he was awarded the Lasker Award in 2012, permitted the discovery of drugs for both heart problems and cancer, among other illnesses. Professor Sheetz participated in the VI edition of the CNIC conference called "**Mechanical forces in physiology and disease**", a scientific event organized by the CNIC researchers Jorge Alegre-Cebollada, Nadia Mercader, Maria Montoya and Miguel Á. del Pozo and by Martin Schwartz, from the University of Yale (USA).*

- You were one of the first people to use this type of mechanical techniques in biological research. Why did you center your research in this field?

- Thanks to the help of bioengineers, we can access extremely useful tools to investigate and get in depth knowledge on these forces that influence the cellular environment. The context is the following: our cells interact with other cells and with the extracellular matrix, and have the information inside them to associate in the right way and in the right quantity. For example, in twins, all these forces and all these biomechanical factors are working on the two twins essentially in the same way, but independently. And that makes the final result almost the same. Our big challenge is to determine why and how these events are produced. And for that we need to work in collaboration with bioengineers, biochemists and biological physicists. In the past, this whole process had been overlooked because the biologists were dominated by biochemistry. Now we are trying to go into detail about these biophysical and mechanical elements because until now we have been unable to understand how these physical forces are produced.

- Are these factors involved in all the diseases?

- Yes indeed. Cancer is the first in which we are certain, but little by little we have seen that these mechanical forces are involved in the development of cardiovascular disease, among others. Mechanical forces play an important role in the cell´s biology, including the processes that provoke its death.

- What can we expect in the future of this field of research?

- It seems risky to talk about short-term results. That's why we have so many problems with politicians. They are only willing to finance research that offers short-term results, one year, for example. But one of the reasons why I continue in this field of research, in addition to the fact that I really enjoy it, is because I'm not entirely sure what I'll be doing in the next six months. Asking questions and finding answers in this field is very exciting. Actually, I only know what we already know now but it's not what I'm interested in at this moment. I want to ask myself more questions and find out more. I don't think that we can go forward until we have a more global knowledge of all the structures that are involved in the integration of the mechanical forces; and this is a long way. We have to gradually construct a structure of knowledge from the bits, of the blocks of information that we find out, in order to be able to advance in this knowledge.

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- When did you decide to research in this field?

- For many years, I have worked in the field of biochemistry and biochemical physics. I started to become interested in the physical controls and their influence on biological activity and when I started to investigate this field in more detail, it became clear to me that the physical promotors were critical elements in understanding the classical biochemical model, which biophysics had not incorporated until now. This makes it necessary to go back and ask the same questions and investigate the same issues already analyzed like, for example, how the cell relates with its surroundings and with the cell matrix, to determine what is going on in individuals.

- Do you remember any important or especially discouraging moment in your career?

Rather than an important discovery, which our laboratory makes quite frequently, from a personal point of view it was very relevant to understand that we were not working or researching in the right way. This happens sometimes when you are conducting an experiment and the results are different from what you had thought at first. It's on that occasion when you have to find someone to confirm that what you are doing is not correct. And it's precisely in these circumstances that you truly understand why the results are not what you had predicted in the first place.

- Is it about learning from your mistakes?

- They are not exactly mistakes, but rather it is nature itself that is signaling the right way to obtain new information that is correct.

- What is, in your opinion, the one quality that a young researcher should have?

Curiosity. Their decision to be a researcher and to follow this career must be marked by their desire to truly discover how certain events occur and develop in the most detailed and precise way possible. Only if they are curious and ask the right questions can they be good researchers.

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- How important is the figure of a mentor in research?

- I'm going to tell you an anecdote about an old German teacher whom the students demanded his attention. One day he threw a fish at them and told them: "come back in two years with what you have learned and tell me about it". It's certainly not, the best way to act as a mentor. What we try to do at our center in Singapore is for physicists, chemists and biologists to work together, in the same space where there are no walls or separation of any type, therefore the laboratories are together, so they can speak amongst each other and share what they are doing, what they are seeing, in their different scientific languages. We all know how difficult it is for physicists to explain their findings to biologists, and the same is true with physicists, biochemists, etc. And this interrelationship is very valuable because it makes the researchers go back to some issues that were already assumed, and it is possible that they may have to reconsider them and look at them in another way. It's a challenge.

- Is it similar to what occurs between clinical researchers and basic researchers?

Right. However, one aspect must be taken into account. Doctors and clinicians have one basic principle: not to cause any type of harm. That is why they work with methods that have been proved no to provoke any harm, despite the fact that in some cases they don't generate a real benefit for the patient either. If you analyze the research rationally with some drugs, these are very fragile. However, basic research has the possibility to go back and understand these biochemical mechanisms and find answers. It is the first step, to understand the most basic mechanisms, in order to advance in the design of treatments.

CNIC Conference: 'Mechanical forces in physiology and disease'. 4 y 5 de noviembre de 2016. Invitada por Jorge Alegre-Cebollada, Nadia Mercader, María Montoya y Miguel Á. del Pozo (CNIC) y por Martin Schwartz, de la Universidad de Yale (EEUU).

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