Cell PRESS

An interview with David Sabatini

(sabatini@wi.mit.edu)

David Sabatini is a Member of the Whitehead Institute for Biomedical Research, Senior Associate Member at The Broad Institute Massachusetts Institute of Technology, and Member of the Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology, as well as a Professor of Biology at the Massachusetts Institute of Technology. He is also Investigator of the Howard Hughes Medical Institute.

David and his laboratory at the Whitehead Institute study the basic mechanisms that regulate cell growth, the process whereby cells and organisms accumulate mass and increase in size. These pathways are often deranged in human diseases, such as diabetes and cancer. A major focus of the laboratory is on a cellular system called the target of rapamycin (TOR) pathway, a major regulator of growth in many eukaryotic species. Work in David's laboratory has led to the identification of many components of the pathway and to an understanding of their cellular and organismal functions. David is also interested in the role of metabolism in cancer and in the mechanisms that control the effects of dietary restriction on tumorigenesis. In addition to the work on growth control and cancer, David's laboratory has developed and is using new technologies that facilitate the analysis of gene function in mammalian cells. The laboratory developed 'cell-based microarrays' that allow one to examine the cellular effects of perturbing the activity of thousands of genes in parallel. David is a founding member of The RNAi Consortium (TRC) of laboratories in the Boston area that is developing and using genome-scale RNA interference (RNAi) libraries targeting human and mouse genes.

David received his BS from Brown University *magna cum laude* and his MD/PhD from Johns Hopkins University in 1997. He completed his thesis work in the laboratory of Dr Solomon H. Snyder in the Department of Neuroscience. Later in the same year, David was appointed a Whitehead Fellow at the Whitehead Institute for Biomedical Research. This was followed in 2002 by a dual appointment as a Member at the Whitehead Institute and Assistant Professor of Biology at the Massachusetts Institute of Technology. David has received numerous distinctions, including being named a W.M. Keck Foundation Distinguished Young Scholar, a Pew Scholar, a TR100 Innovator, a recipient of the 2009 Paul Marks Prize for Cancer Research, The 2012 Earl and Thressa Stadtman Scholar Award from The American Society for Biochemistry and Molecular Biology (ASBMB), and most recently the 2013 Feodor Lynen Award from Nature.

Did you always want to be a scientist?

No, not really. Despite my father being a cell biologist and my mother a pathologist, I did not decide on science as a career until I was in college at Brown and I worked in Al Dahlberg's laboratory on ribosomal RNA in bacteria. It was there that I fell in love with the laboratory atmosphere and the feeling of freedom of just following my curiosity. Earlier I had wanted to be an architect (although I showed no particular skill and my parents told me I would end up designing bathrooms for condos).

What do you think are the most important traits for a scientist to have?

I think that good scientists are distinguished by their capacity to pick good problems and solve them. So, in my view the most important trait to have is creativity, being able to see things differently and connect observations in new ways. Of course, being creative does not guarantee success and one also needs to work extremely hard and be able persevere and try again in the face of the many experiments that fail and 'great' ideas that turn out to be wrong. In my laboratory, those who have had the most success have combined all these traits.

In your laboratory, when someone has a new idea, how do you go about determining whether to pursue it?

Often, I will not be told about an idea and will only hear about it when experiments have worked out! When I am told, we try to ask ourselves what would or would not change if the idea were actually true. Would it change how we think or would it be an incremental step forward? Would it open up new areas for investigation or would we land in a field or subfield that is already heavily studied? Our desire is to always do something new that matters and we don't always succeed but we try to set the bar high.

Do you have a favorite paper (yours or someone else's)?

My favorite paper in the past few years is the one where we identified the first components of the pathway that signals amino acid levels to mTOR. I think this paper proposed interesting new concepts that have since been validated and opened many new research directions. It also took us a bit closer to finding the elusive amino acid sensor for the pathway and since my days in medical school I have been fascinated by how we sense our environment.

Cancer researchers differ tremendously on the question of whether there will ever be a 'cure' for cancer. What is your opinion?

Fighting cancer is like fighting evolution so although I do hold out the hope for a true cure in the future I think for

some time we will have to be content with converting cancer into a chronic disease. Of course, huge progress in early detection could lead to many cures but for cancers that have metastasized I think a stalemate will be the best we can attain for some time.

What's the best piece of advice you've ever been given?

Two pieces of advice: one from my graduate advisor Dr Solomon Snyder who fostered the attitude that is was okay to just try out ideas even if there was a huge chance of failure. The other is from Dr Susan Lindquist, who hired me to the faculty at the Whitehead Institute when she was Director. She emphasized how useful it had been to live close by to work when she was a junior PI. I have found this to be absolutely true and the only way I can imagine successfully balancing, on occasion, my work and family life.

Tell us something from your work that is exciting for you right now.

As I mentioned above, I have always been interested in sensing and I am very excited about ongoing work chasing the amino acid sensor for the mTOR pathway. We are far from succeeding but we are making many cool observations along the way and having fun.

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