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PEOPLE & IDEAS

Tamas Balla: Leading the way with phosphoinositides

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Balla investigates how phosphoinositides control trafficking and signaling.

A sanatorium for curing respiratory diseases in a mountain resort area of Hungary was home to Tamas Balla as a child. According to his parents, both medical doctors, Balla was very observant and spent a lot of time outdoors collecting insects and reading about them and other animals. His first real encounter with science, however, was studying physics in sixth grade. It quickly became his favorite subject, an enthusiasm he continued by attending a math and physics-specialized high school. Balla picked up astronomy as an extracurricular activity with a fantastic math teacher who led the astronomy club and taught deductive thinking. At the same time, a biology teacher introduced his class to the processes by which DNA is transcribed and the resulting RNA translated into protein. Although not part of the curriculum, Balla found the molecular biology fascinating and emphasizes that "teachers are very important in shaping our interests." Although he initially wanted to become an astrophysicist, this wasn't written in the stars for Balla and he ultimately specialized in physiology and molecular biology. His research group at the National Institutes of Health (NIH) seeks new ways to shed light on where different phospholipids localize in cells and how they control membrane trafficking and cell signaling. We contacted Balla to find out more.

Where and with whom have you studied?

My mother talked me out of pursuing astrophysics as a career, arguing that Hungary did not offer great opportunities for graduates of that discipline at the time. I am not even sure she was right, but I went to the Semmelweis Medical School in Budapest. In my second year, a very charismatic instructor in medical physiology (Dr. Andras Spat) invited me to work in his laboratory and I was a student researcher with him for the rest of my medical studies. Dr. Spat introduced us to the basics of how to conduct research and we were able to run our own experiments under his supervision. He was responsible for my choosing research as a profession and I joined the Department of Physiology at Semmelweis to begin my PhD under his guidance after finishing medical school. I came to the NIH in the United States in 1985 for a postdoc with Dr. Kevin Catt at the National Insitute of Child Health and Human Development. The research conditions and opportunities were such a stark contrast to Hungary (a difference that has shrunk a lot since), that I just could not have enough of it. The place was vibrant and full of energy and I was ready to learn anything necessary to pursue my research ambitions. Dr. Catt let me follow my own interests and supported wherever I wanted to take my research. I learned a lot from him about writing manuscripts, dealing with reviewers, and how to navigate the hurdles and frustrations associated with publishing research. He definitely helped me mature as a scientist.

> "Research requires a lot of tenacity, patience, and high frustration tolerance."

What drew you to study phosphoinositides?

I was introduced to phosphoinositides during my studies on the signaling pathways triggered by angiotensin II receptors in the adrenal gland while still back in Budapest (1). These signaling lipids turned out to be critical for almost anything that happens in a eukaryotic cell. What fascinated me most was how the permutation of various phosphorylations on the inositol headgroup of these phospholipids can control so many cellular processes. A big turning point in my research was when we developed tools to see where these lipids are located in living cells and how they change during cellular responses to environmental cues (2, 3).

Tamas Balla in his new office at the NIH. IMAGE COURTESY OF TAMAS BALLA.

What are you currently working on? What is up next for you?

I am still working on new research tools to expand the list of phospholipids that we can visualize by fluorescence. I am intrigued that the enzymology of lipid biosynthesis has been largely defined, but the exact cellular locations where these reactions take place are still poorly understood. This includes how lipids move from one organelle to another, which makes me particularly interested in the membrane contact sites where many of these lipid transfer steps take place (4).

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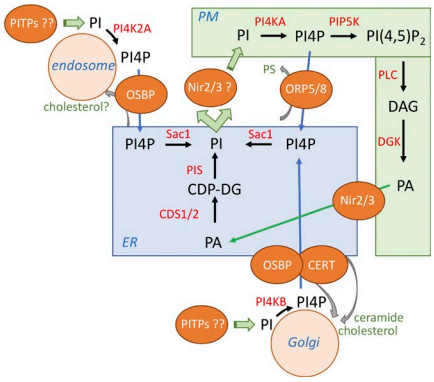

The intricate world of phosphoinositide signaling and its place in lipid metabolism. IMAGE COURTESY OF TAMAS BALLA.

What kind of approach do you bring to your work?

I think research requires a lot of tenacity, patience, and high frustration tolerance. In an ideal world, I would do research to understand the fundamental principles that govern very complicated regulatory pathways instead of focusing too much on how to publish in top journals. I think humility is one of the most important traits in a scientist and large egos often hamper rather than help scientific progress. Also, science should be enjoyable and curiosity driven and not be done under pressure. I like to keep these principles in mind when running my research group.

What did you learn during your own training that helped prepare you for being a group leader?

The student research system at Semmelweis, and particularly in the Spat laboratory, placed a lot of emphasis on mentoring the younger students still in medical school. This was extremely good training in how to work with others and to effectively teach and supervise. Moreover, we taught the whole curriculum of medical physiology and that gave me a very solid foundation in every aspect of human physiology. As I mentioned, during my postdoc in the Catt laboratory, I also learned how to pursue my own ideas and how to communicate with collaborators, journal editors, and reviewers. I also had the chance to communicate my research in scientific meetings in English. At the NIH, I worked with other postdocs from all over the world and learned to appreciate diversity. I was unprepared for how much a principal investigator has to rely on data produced by others in the laboratory. This is still the greatest challenge for me, especially when it comes to microscopy images; therefore I continue to produce these together with my fellows.

What has been the biggest accomplishment in your career so far?

There are a few manuscripts that I consider my best scientific works. I feel that our imaging and techniques to artificially alter phosphoinositide lipids in living cells had the biggest scientific impact. Still, I feel that our biggest impact overall as group leaders is through the people we train. This does not have to be measured by how well they do as researchers themselves, as some do very well whereas others chose different paths. So, I consider mentoring almost as important, if not more so, than the actual scientific discoveries made along the way. I just hope that the people who worked with me feel the same way.

"Humility is one of the most important traits in a scientist and large egos often hamper rather than help scientific progress."

What has been the biggest challenge in your career so far?

During my postdoctoral years, the biggest challenge was to balance my work and family life. I did spend a lot of time in the laboratory but I wanted to make time for my wife and children. Settling in a new country and finding my way through various career steps was challenging. As a group leader, the biggest challenge is to publish our work at highly regarded journals so our fellows can move on with their own careers. Scientifically, the biggest challenge is to break with the scientific consensus and see things differently.

Who were your key influences early in your career?

In addition to the teachers and mentors I already talked about, my work was inspired by scientists whose contribution to this field has been enormous. Robert Michell, Michael Berridge, and Lewis C. Cantley are names that I would like to mention, but there were many others who come close to these three that I had the privilege to personally know.

What is the best advice you have been given?

I can summarize this in three quotes. One comes from the Nobel Laureate and French writer Andre Gide: *"Admire those seeking the truth; beware of those who claim to have found it."* Two more come from my mentors: *"If you swim among sharks you cannot afford bleeding"* and *"Never victimize yourself."*

What hobbies do you have?

I like live music concerts, theater, and art. I love to travel and explore different countries and their history, cultures, and cuisine.

What do you think you would be if you were not a scientist?

I would probably be a medical doctor.

What has been your biggest accomplishment outside of the laboratory?

Definitely my family. My wife has always been on my side and I think I also helped her toward her goal of practicing medicine in this country. Our two children are our biggest pride and we must have done something right for them to become such wonderful adults.

Any tips for a successful research career?

I do not believe in golden tips. I can only say what worked for me. I think people should stick to who they are and not try to become something they do not feel comfortable with. Having said that, I think one has to examine themselves to determine if they have the curiosity, the patience, the tenacity, and the passion to choose research as a career. One has to be prepared to handle lots of unsuccessful experiments before finding the satisfaction of learning something new.

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Tamas Balla and colleagues in Budapest as a young scientist in 1984. From left to right: Laszlo Hunyady, Peter Enyedi, Tamas Balla, and their mentor Andras Spat. IMAGE COURTESY OF TAMAS BALLA.