



Stephen O'Brien

## Straight talk with... Stephen O'Brien

Stephen O'Brien joined the US National Cancer Institute as a post doc in 1971 and climbed the ranks to become head of the institute's Laboratory of Genomic Diversity, a position he held for 25 years. But, after four decades at the government agency, O'Brien was ready for something new. In December 2011, he stepped down and took up a three-year, \$5 million 'megagrant' in Russia through a program started a year earlier by the Russian Ministry of Education and Science to attract big-name researchers to work at least part-time in that country. O'Brien used his money to help launch the Theodosius Dobzhansky Center for Genome Bioinformatics at Saint Petersburg State University.

Although O'Brien is a cancer researcher, he has diverse scientific interests. He led the team that discovered the CCR5-Δ32 mutation that confers resistance to HIV, and he has helped document the remarkable genetic uniformity of African cheetahs. Recently, he and two California scientists started the Genome 10K project, which aims to sequence the genetic blueprints of 10,000 vertebrate species. On a trip back to the US, O'Brien spoke with **Elie Dolgin** about how comparative genomics and his new Russian center will help advance the search for new therapeutics.

### Why did you decide to leave the NIH?

The NIH has obviously been very supportive of me over many years. But the truth is they were looking for different leadership and directions. And some of the people in the administration had decided that the comparative [genomics] approach was less important than simply resequencing human tumors. Although I value the Cancer Genome Atlas project, it ignores the idea that we have learned just about everything in biology from animal studies. So, I didn't want to fight that battle at the NIH level anymore. I need a little more flexibility than I could get inside the constraints of a government lab. And after close to 40 years, I didn't want to die as a government employee.

### A year into the new post, how are things working out?

It's working quite well. We just moved into the laboratory a couple of months ago. It's set up with high-speed computers, and I'm leading a group of 20 or so young scientists with extremely good programming and mathematical skills. I also have international collaborations with many centers that are doing genome sequencing.

### Is your focus on comparative genomics more about animal conservation or human health?

I don't think those are mutually exclusive. I think the more we understand about adaptation and animal specializations and survival skills, the better equipped we will be to both manage the environment and ecosystems as well as to discover and then translate useful adaptations to help promote human medicine. For example, there's anecdotal evidence that sharks and naked mole rats never get cancer. One of the things I think we should try to understand is: what are the genetic adaptations that are responsible for that? Why do pelicans see so much better than we do, and can we use that to maybe improve human sight sometime in the future? Why do African monkeys resist deadly infections like HIV? The adaptations that we see in the animal kingdom are all a matter of descriptive biology, and now we have the ability to connect the dots between genomic variations and these adaptations.

### Why did you name the center after Dobzhansky?

Forty years ago when I came to NIH, I was one of the few geneticists. One fellow asked me, 'Why do you do genetics, all you get is a 1 to 23 purification?' They were thinking that if you map a gene to a chromosome that's all you do. Now, everybody is a geneticist; it's so important. Well, evolutionary biology is something that Dobzhansky recognized has to be considered in any interpretation. His famous quote is that "Nothing in biology makes sense except in light of evolution."

### The megagrants program has been criticized for its mountains of red tape. What have your experiences been navigating the bureaucracy?

I think that the initial days of megagrant, which was in 2010, were worse than what happened afterward. By the time I arrived, several aspects of the bureaucracy had already been eliminated, such as the tender system, which required a six- or eight-month delay for purchasing equipment. That all went away by the time I started. I arrived in December [2011], and I purchased a lot of equipment in a couple of weeks. Try to do that at the NIH!

### How have you found the Russian funding system?

There are advantages and disadvantages in all situations. In the United States, we have a large number of people at the prime of their careers sitting at word processors writing grants for 50–60% of their time. I was lucky in the NIH system to have a top-down funding mechanism where I was responsible for gathering the resources within the institute and the scientists were given the opportunity to just do good work. Fortunately, that's the way it is now in Russian universities, too. Basically, people [in Russia] who are motivated and talented have an opportunity to do really good research without the constant threat of writing another grant. I'm not saying the Russians have it perfect. But I think there's something to learn from the system.

### Are you still happy with your decision to go to Russia?

I felt like I'd made the right decision when [in October] Mark Zuckerberg showed up in Russia for the same reason: to look for programmers.