

AN INTERVIEW WITH...

Oliver Smithies



March
of Dimes®
Saving babies, together®

The March of Dimes developmental biology prize is in its tenth year. This time, the developmental biology community has decided to award the prize to two outstanding scientists, Professor Oliver Smithies and Professor Mario Capecchi, in recognition of the importance of gene targeting — a

virtually ubiquitous technique, which they developed independently, some 20 years ago. Magdalena Skipper talked to them to find out their perspective on the achievement they were being honoured for, how they saw the future and to shed light on some lesser known facts about them. Below is an excerpt from a conversation with Professor Oliver Smithies. Oliver has made his name as an inventor (he has developed starch electrophoresis and, of course, gene targeting) and as an accomplished human geneticist. Hypertension has been a particular focus of his work.

An interview with Professor Mario Capecchi will appear in the June issue.

You trained as a physiologist, then as a physical chemist, only to become a molecular geneticist later. Did these changes influence the questions you were interested in?

I think it was in some ways the other way around. Trying to answer the questions that I got interested in was very much easier for me because I was comfortable with the biology and with the physical chemistry, and that's still true today. I find I can't bear students or postdocs talking about something unless they can write its chemical formula. My old thesis advisor's, insistence was that you should understand what you are doing.

What or who has been an inspiration in your scientific life?

Without any doubt it was Sandy Ogston, who was the physiology and medical student tutor in Balliol (Oxford). He was the person I did my Ph.D. work with in the end. He had some marvellous characteristics. He was really quite a humble person in some ways and not in others. He would solve a problem and be rather ashamed of the fact that he'd done it easily. He was made a fellow of the Royal Society because of something that he said only took him 15 seconds to think of. And he had it written up the next day.

But I was lucky, even my high-school teachers were inspiring and my tutors in Oxford were marvellous. In Oxford, each week you had to write an essay and you'd read it to your tutor and he'd critique it. One week, which I remember very well, I was given a marvellous topic — to discuss the Periodic

Table and Pauli's exclusion principle. I had a grand time writing my essay, and I probably wrote 12 pages. We only got half way down the first page, because somewhere in there I'd written something down I could not justify and I didn't understand. My tutor took an hour to teach me that you never write down anything you don't understand and you can't justify.

Your laboratory books are impeccably organized — is this a reflection of a systematic mind?

My wife tells me that I'm organized and disciplined in some things, but my lab bench is an absolute mess; it looks terrible. But I always say that the inside of my test tubes are clean, even if the outsides are not. I found that I have learnt to keep notes better and better as time goes on. And I have evolved a notation that helps people to go between each other's notebooks that turns out to have been very valuable.

I have all my notebooks right back to when I was a graduate student, so I've probably got nearly a couple of hundred of them. Those notebooks to me are my life. It's a diary of my life, to have them and look at them and open them and go back to them....

What gives you greatest pleasure in science?

A long time ago, I decided I didn't want to be a chairman of anything and so I've continued what I like most — working at the bench. And the consolation is that I've still produced things that have been worthwhile. For the gene targeting, for example, most of the experimental work was mine and it was published after I was

60. So it means you can go on being productive; the idea that a person ceases to be productive at the age of 35 is complete nonsense. Artists and composers go on much longer than that. Scientists are no different.

It seems that there is at least one other passion in your life — flying....

I still fly a great deal. I had a good day [recently], it was one of our first [flying] days of this year; I managed to get my glider to stay up an hour.... It is quite enjoyable to be able to glide at 5,000 feet of altitude without power, seeing birds.

As someone who has worked in chemistry and biology, how important do you think interdisciplinary research is?

I have two conflicting thoughts on this and I can't really completely resolve them: definitely you need to bring several types of skills together in a lot of the problems. And yet, I worry about the tendency for science to become big science; ideas are not generated by groups, ideas come from individual people.... So we have to still find a way that individual scientists can still work without having necessarily to be part of a huge group....

“...it means you can go on being productive; the idea that a person ceases to be productive at the age of 35 is complete nonsense.”

Human genetics has been accused of promising a lot but delivering very little in terms of tangible cures of disease. Do you think that this opinion is justified or are we too impatient?

I think that both these things are right. People are impatient, but they are made impatient by over-exaggerative claims. All of us would like our work to be recognized.... When talking to a news person about what we've been doing, we tend to make it sound better than it really is, that it will solve this and that and the other. Well, often enough it is going to make a contribution, but it probably won't do all that we hope. Combined with the fact that news persons have to write something that looks exciting... it feeds on itself and leads to things being promised too soon.