AN INTERVIEW WITH...

Cliff Tabin

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The 2008 March of Dimes Prize in Developmental Biology has been awarded jointly to **Cliff Tabin of Harvard Medical School and to Philip Beachy of the Institute for Stem Cell Biology and Regenerative Medicine at Stanford University and the Department of Developmental Biology at Stanford University School of Medicine. The prize recognizes** researchers whose work has contributed to our understanding of the science that underlies birth defects. Patrick Goymer talked to the winners about the influences that have shaped their scientific careers. The interview with Philip Beachy appeared last month. This month we feature excerpts from a conversation with Cliff Tabin.

You did your Ph.D. with Bob Weinberg, studying viral oncogenes. How did you move into studying development and evolution?
The year I started graduate school (1976) was the end of a year-long moratorium on recombinant DNA. [...] When it was lifted there were initially only a few places in the world capable of doing recombinant DNA, and MIT [Massachusetts Institute of Technology], where I happened to be, was one of them. At the time, the most exciting work applying this technology was the sort that Bob Weinberg and David Baltimore were doing. I focused on cancer as a grad student for that reason. But that's different from the direction one wants to go with this powerful new technology over the course of a career. [...] I took a step back and asked, what are the really big questions in biology? At least from the point of view of this rather naive grad student they seemed to be: where do babies come from? And where does diversity in nature come from? At the core of both of these is how one regulates morphogenesis within an embryo, and differentially between different species.

How important is evolution for developmental biologists, and what are the barriers to integrating the two fields?
I've always had a serious interest in evolution, which was part of the reason for choosing development in first place, and I've always tried to have at least one person in the lab from a real evolutionary background. There are people in the evolutionary community who are very excited by the new information we're able to bring, but at the same time you can read critiques of some of Sean Carroll's essays, for example, that argue that evo–devo people are naive when we talk about regulatory cassettes and forces of selection, and are ignoring the vast population genetics literature. There's some truth to both. The impact of developmental biologists has been very important and has been well integrated into thinking within with the evolutionary community. [...] Evo–devo insights from individual developmental experiments have been very well received. It is only when we have extended our models and speculations on a grander scale that we have run into problems with a subset of people in the field.

Your landmark 1993 paper on sonic hedgehog was accompanied by two papers from other groups. Was there competition there?
Our labs were closely collaborating, not competing. My lab had become interested in trying to clone vertebrate homologues of Hedgehog, which was known to be an important signalling molecule in flies. [...] At dinner one day [during a conference in Germany] Phil Ingham, Andy McMahon and I happened to be sitting together. Phil, a leader in studying Hedgehog signalling in *Drosophila*, was very open and said he'd be happy to talk to me about Hedgehog, but added "I should be upfront with you and tell you that our lab is also trying to clone vertebrate homologues". And Andy, next to Phil, piped up with "we're trying to clone them too" — I wondered if everyone down the table was trying to clone them! It turned out that we each had different interests and worked with different organisms ... so by the end of dinner we'd decided we should be working together. It was the most fun collaboration I've ever had — literally every other day we were updating each other on what was happening, and each lab contributed to pushing the thing forward in a very fundamental way. The first person to get a vertebrate hedgehog clone was Andy — his lab pulled up what we now call desert hedgehog in mice. We each pulled out desert equivalents from our species but Andy said "I hate to tell you that the only place it's expressed is in testes". That was disappointing — we didn't work on spermatogenesis, we worked on limb. And it was even more disappointing for us: in mice and fish you can easily study testes, but we get chick eggs in cartons; for chicken testes you're talking about roosters! My postdoc Bob Riddle went to a slaughter house and brought back a couple of live roosters, and sure enough desert hedgehog was expressed in testes. But we were disappointed if after all this work that's all we'd got. So Bob designed PCR primers and the next e-mail was "guys, there are three bands". Phil then used the chick PCR sequences to pull out the fish genes and e-mailed back saying "drop everything you're doing with the first clone, clone three is the one you want", and he sent an expression pattern showing activity in the midline of the embryo. We knew that the notochord and neural tube were important signalling centres so we knew we were probably onto something....

How did sonic hedgehog get its name?
My original concept was to give them names of vertebrate hedgehog species. For example, desert hedgehog is a species from Algeria. Bob had a little girl named Annie, and a friend of his in England sent them a Sonic the Hedgehog colouring book. This is before Sega had brought the computer game to the US and I'd never heard of it, but sonic hedgehog sounded good, looked like a vertebrate hedgehog, so vaguely fitted my scheme, and Bob played in a rock band so 'sonic' appealed to him. [...] The funniest part involved a colleague whose husband was driving home from work. We submitted the papers in October and they were published in the last issue of December; in November Sega started promoting Sonic the Hedgehog in the US, including at McDonald's. The husband saw the big sign, slammed on the breaks and went to a pay phone to call his wife — "you're not going to believe this, McDonald's is doing a promotion on Cliff's gene!"

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