

Q & A

Peter J. Hollenbeck

Peter Hollenbeck is Professor and Associate Head of Biological Sciences at Purdue University. He did his PhD at the University of California-Berkeley with W. Zacheus Cande, followed by postdoctoral training with Dennis Bray at the MRC Cell Biophysics Unit in London. He then served on the Harvard Medical School faculty in the Department of Anatomy and Cell Biology, and later the Department of Neurobiology, before joining the Purdue faculty. His work is focused on the transport and life cycle of mitochondria in the nervous system, how mitochondrial movement and function are regulated and how this goes awry in neurodegenerative diseases. He also serves the Tourette Syndrome Association as chairman of its Scientific Advisory Board.

What turned you on to biology in the first place? Bodies of water are often involved here, aren't they? For me it was a local swamp, where I caught frogs, snakes, waterbugs, things that Mom was not happy to see arrive home with me. Biology really got interesting, though, when I received a small microscope one Christmas, and started looking at drops of swamp water. The variety of different protozoa, rotifers, and so on swimming in that water was quite a shock. I drew the different species of protozoa on index cards and looked them up in a book at the public library. I still have that little microscope on a shelf in my office! Also, like a lot of American biologists, I was greatly influenced by a superb high school biology teacher. You have to tip your hat to those folks — they have quite an impact.

What is your favourite conference? The most recent one I've been invited to! Seriously, I love the Gordon Conferences for all of the usual reasons — small size, latest science, lots of opportunity to talk informally. But the ASCB meeting will always be tops for me. It was the first meeting I ever attended as a grad student (Anaheim, 1981) and it convinced me that it was going to be really exciting to do science. All of those bright

people doing all of that cool stuff! It is the one meeting that I push members of my lab to attend. It's way too big to get your brain around, and it's a mentally exhausting week. But it brings together such a wide range of great work and great people that it is hard to beat.

What is your greatest ambition in research? To carry the questions I am interested in — of the transport and activity of mitochondria in the nervous system — into animal models of human disease. For decades cell biologists have been telling granting agencies that they should fund our studies because eventually they would be directly relevant to human health and disease. Well, guess what? In the past decade this has turned out to be absolutely right! So now I think the pressure's on us to try to use the wealth of animal models to study our basic biological questions. We want to design experiments that tell us both about a basic question like how mitochondria are distributed in neurons, and also about how defects in this process underlie neurodegenerative disease. It's pay-back time.

What has been your biggest mistake in your research career? I wish that I had moved into a genetically tractable system much earlier. Maybe with all of the genomes being sequenced and annotated, and new means available to manipulate gene expression in a lot of systems, this will become less important. But I doubt it. I would still advise any young biologist: get training in a manageable, robust genetic system — yeast, fly, worm, *Arabidopsis*, zebrafish. It puts you atop a very tall pyramid of previous work, and gives you unique tools for answering so many questions.

Do you have a scientific hero? Well, this will sound odd for a biologist, but my hero worked on electromagnetism and electrochemistry. That would be Michael Faraday, probably the greatest experimentalist in the history of science. His story is so compelling: he came up from the working class, was a bookbinder's apprentice, self-educated, real Dickensian stuff. He started as a lab grunt with Humphry Davy, but in the end he had the most extraordinary career at the bench

that you can imagine. So much fundamental work, and he did the dirty work himself — he even blew himself up several times. And he gave masterful lectures about his work to scientists and the general public. We talk a lot now about translational research, but look at what Faraday's basic research 'translated' into — most of the underpinnings of how we use energy in the modern world. I drag my cell biology students through some thermodynamics and when we come to the Faraday constant, I always take time to tell them his story. A living influence, too: my postdoctoral mentor, Dennis Bray. He is a truly original thinker who has reinvented himself scientifically twice in his career and proceeded to make landmark contributions each time.

Do you think we're on the cusp of a change in biological research and the career structure of biologists? Well, research in life sciences seems to be headed toward a place where some big discoveries will require a different sort of training background, and maybe a different kind of operator, than is typical now. Think of the increasing impact of relatively new ways of thinking: theoretical approaches to complexity, computational approaches to large datasets. But when I hear predictions that we'll all be doing 'big science' in the future, I feel the same skepticism that I did 20 years ago when a crew of 24-year-olds were telling us that soon we would all be making our living on the internet. Look, if you've spent any time in administration, you know that some of the enthusiasm for big biology involves the need for research institutions to win the very large grant awards that can be garnered by huge collaborative groups — much larger than the RO1s brought in by the likes of me. I've no doubt that some great things will be achieved by large interdisciplinary groups, assembled from above, along the lines of high-energy physics during the last century. But I suspect that a lot of great new ideas in biology will still originate in one brain, or a few sympatico brains, and that fundamental advances will still be made by small numbers of hands. I would bet on the departments or centers that can assemble a critical mass of investigators each with their own research questions and approaches, but with a rich matrix

of overlapping interests. Put them in a good physical plant with lots of shared space, and let them go to it. When it comes to the size of individual research groups, there's a value-for-money issue too — we are mostly spending the taxpayers' coin, after all. I have always had the impression that individual laboratory groups larger than about a dozen full-time workers produce less science per dollar spent than smaller groups.

We hear American academics talk about the balance between research and teaching. You're at a public university with tens of thousands of students — how do you view it? It is a tricky balance. Universities tend to reward research progress rather well and teaching success less so, at least in tangible career progress. But when you think about it, the range of activities that we carry out — doing research, training postgrads and postdocs, and teaching and advising undergraduates — is really a continuum. Research attracted most of us to this life, but in the public universities we also have an enormous, mandated public mission: to educate the students of our state, the nation and the world in science. And a great thing about being a science student in our research universities is that you are being taught mainly by active researchers: your neuroscience course is taught by a working neuroscientist, cell biology by a cell biologist, and so on. For part of the academic year I'm that guy, trying to make it seem worthwhile to hundreds of 19-year-olds to spend 15 weeks studying cell biology, trying to convey to them the excitement of this field. You can hardly fault academics who dodge a teaching assignment like that. Not everyone has the inclination or aptitude for teaching, and the incentive system can push you away from it. Still, if you take a pass on it, I think you're missing the boat. It's hard for a young assistant professor to believe, but your effect on students in the classroom will probably bring you closer to immortality than even your best paper. Our papers grow old and disappear, but, as Garrison Keillor says, "nothing you do for young people is ever wasted."

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My Word

Lysenko rising

Florian Maderspacher

When I recently unwrapped my weekly delivery of German magazine *Der Spiegel*, my fiancée thought she'd caught me ordering from the top shelf (she always had doubts about that particular magazine, despite my assurances that it is in fact one of Europe's largest news magazines). On the cover was a blond woman (it is German after all) rising from a computer-generated ocean. Around her naked breasts (it is European after all) the water was spiralling in the shape of a double helix. The headline read: "*The victory over the genes. Smarter, healthier, happier. How we can outwit our genome.*" Inside was a ten-page spread about epigenetics.

Epigenetics is of course being considered 'sexy' in vast circles of the scientific world (and has attracted the funding to go with it), but that *Spiegel* cover was a different type of 'sexy'. This kind of public attention seemed unusual: molecular biology rarely makes it to the front page. And what's more, this wasn't just some German oddity: *Newsweek* had last year a similar cover story, touting a revolution in biology in gonzo-journalism style: "*Roll over, Mendel. Watson and Crick? They are so your old man's version of DNA*". Likewise, the *New York Times* is in tune, as a news piece last year celebrated the role of the 'epigenome' in controlling "*which genes are on or off*"; nor is the hype confined to the popular press, as a recent editorial in *Nature* also noted that: "*genome sequences, within and across species, were too similar to be able to explain the diversity of life. It was instead clear that epigenetics — those changes to gene expression caused by chemical modification of DNA and its associated proteins — could explain much about how these similar genetic codes are expressed uniquely in different cells, in different environmental conditions and at different times*".

The term 'epigenetics' itself is fraught with misunderstandings (for an in-depth discussion, see an essay by Mark Ptashne, *Curr. Biol.* 17, R233–R236). Initially coined by the



'Victory over the genes': Cover of *Der Spiegel* on epigenetics. © 2010 DER SPIEGEL.

geneticist C.H. Waddington as "*the branch of biology which studies the causal interactions between genes and their products which bring the phenotype into being*", the word epigenetics has undergone one of these curious shifts of meaning that characterise language evolution and are often the source of fundamental misunderstandings. Nowadays, as evident in the above quoted *Nature* editorial, 'epigenetics' is often used to flatly refer to chemical modifications of the DNA itself (methylation) or its associated protein scaffold, the histones.

This was exactly the way epigenetics was used in the *Spiegel* piece: a graphic about 'switches in the genome' showed DNA methylation and histone modifications. A tiny blob in the bottom right corner symbolised a 'gene activating protein', otherwise there was no mention of signalling pathways or transcription factors in the entire article — the things that for half a century now have been known to be what brings 'the phenotype into being'. The article itself was mainly concerned with listing examples supporting the notion that 'genes aren't everything': on the one hand, cases where genetic predisposition, e.g. for adiposity, does not lead to the development of that phenotype, as well as the much-discussed weaknesses in genome-wide association studies to pick up causative genetic agents for common diseases; on the other hand, examples of how the environment can influence