Trevor Lithgow joined the ASBMB as a student member in 1991, won an ASBMB Progen Student Fellowship in 1993 and was awarded the Roche Medal in 2004. We asked him to reflect on his experience as a molecular biologist and for his opinion on the future of the discipline in Australia.

From time to time, the students who work with me (pictured) are subjected to discussions on the lessons from the first stages of my career as a scientist. But a thousand word essay steeped in personal experience? I'm not sure how well these lessons will come across in print; something like a fireside reminiscence by grandfather laced with locker room pep-talk, I suspect.

I majored in animal physiology at La Trobe University. At high school I became more and more interested in science broadly, and biology in particular. Unfortunately, I didn't know any scientists and, in fact, didn't know anyone who'd been to university. So my choice to study biological sciences was totally uninformed, and I never actually chose to be a biochemist. I was a high school kid curious to understand how cells function. **Lesson number one: if you let curiosity and interest drive your decisions, your choices will probably be good ones.**

George Stephenson in Zoology at La Trobe was doing very cool things with fluorescent proteins from jellyfish. This was the eighties, the proteins weren't expressed – they were harvested from critters caught from under the Portsea pier. Thinking about his work, it seemed to me that doing cell biology and understanding subcellular structures was going to require skills in protein purification. Instead of starting in the Zoology department, I talked to Gideon Polya about doing an Honours project to learn protein purification. In his lab, this meant purifying protein kinases from silverbeet. Not exactly what I had in mind originally, but skills are skills. **Lesson number two: however lofty your long-term aspirations might be (how cells work, curing cancer, understanding the basis of memory), your Honours project should give you a set of new and relevant skills, and the topic itself matters less.**

I was never really convinced that I was a scientist, and didn't want to rush into a postgraduate degree. After honours I worked for Dick Wettenhall as his research assistant, helping him finish the complete sequence of ribosomal protein S6 – this was still the eighties, we purified the protein and pieced together the entire sequence from a jigsaw of tryptic and chymotryptic peptides, purified by HPLC and individually sequenced! But I still wasn't so sure that I was cut out to be a scientist, so after two years I quit and spent six months back-packing. **Lesson number three: avoid the path of least resistance, and spend as much time as possible critically contemplating any position you take in science.**

When I came back to Melbourne, I took a part-time job with Nick Hoogenraad working on rat liver mitochondria. I spent three months watching and learning "molecular biology" from Robyn van Heeswijck; these first experiences of plasmid building (*wow*) and DNA sequencing and mutagenesis (*no really, wow*) left me in no doubt that these were things I wanted to learn more about. Robyn convinced me that I should sign on for a PhD and that Nick and Peter Høj were the best choice I could make for supervisors (she perhaps should have disclosed that she was married to Peter before those conversations ….). **Lesson four: seek out mentors, senior lab-mates as well as official supervisors. Be sure to find good ones and then trust their advice.**

I (wrongly) believed I was reading very broadly in order to find a potential post doc position: this is a crucial thing to be doing as a student and I didn't really do it well. I was fortunate that it worked out for me anyway. I had a short list of three people whose work I liked: Jeff Schatz working on protein targeting, Hugh Pelham working on protein targeting and Tom Silhavy working on, you guessed it, protein targeting. It's very common that your postdoctoral position ends up being not far removed from your postgraduate work. But this stage, from PhD to post doc, is likely to be the last easy chance you have to change subject areas and experimental systems. **Lesson five: any aspirations you have about investigating cancer or memory or anything else, might best be acted on directly after your PhD. This will also be the last chance you have to work overseas, at least without the fetters that come with running a lab at home as well. One of the greatest aspects of doing science is how international an enterprise it is. Working as a scientist overseas, intensely and in the right environment, is a rare and truly cross-cultural experience. So, lesson five is a big one.**

Research funding in Australia can be hard to come by: this makes setting up a new lab a difficult job and it is becoming more and more likely that scientists finishing post-doctoral positions will join established research programs rather than start something new. It's a situation that needs some case-by-case consideration, because there are benefits to be had in working collaboratively within a large group. But it is also true that post-doctoral work (ie. the first few years after the

The Lithgow lab in 1996.
Left to right: **Traude Beilharz, Peter Cartwright, Trevor Lithgow, Travis Beddoe, Rebecca Lucattini.**

PhD) generates excitement, vision and opportunities that might be best used to initiate and energise new research programs. This last 'lesson' for me, in returning from overseas, was complex and I'm still not sure I have everything in perspective.

Finding a position is tough. Although I had succeeded in getting a fellowship from the Human Frontiers Science Program to work as a post doc in Basel, and was subsequently awarded as one of the best ten postdocs in the program's history, I wasn't successful in getting a fellowship from the NHMRC to come home. The job I did come back to was in fact the only one I found that I could apply for. It seems that both the funding bodies and departments/institutes have improved things somewhat, making more fellowship-based opportunities available to new returnees. The society has a role in facilitating this crucial career transition, and the ASBMB Online Position Database is an excellent move, especially as a portal to be visited by young researchers overseas (and out of the loop). We, the prospective employers, should be making more use of this.

Setting realistic objectives for a new lab can also be tough. Experimental systems need to be established, preliminary data need to be gathered, research funding needs to be secured. What worked for my lab was to start in a not-too-sexy niche; we worked on how translation kinetics and ribosome-associated factors can influence protein targeting. It wasn't exactly the problem I wanted to work on, but it served to establish key techniques in yeast genetics and molecular biology in the lab, gave us a rationale to develop some protein expression and purification capabilities, and was attractive enough to be funded by the ARC and to elicit invitations to some key international meetings. After a few years of moderate success in that area, the lab had a critical mass and we have now moved into more fundamental (and harshly competitive) areas of protein targeting and organelle biogenesis. But this, again, was not a cunning plan perfectly executed by me alone. The strategy worked because of two factors built into the way universities do science.

Firstly, I had the selfless support of colleagues in the department I moved to (in my case, Biochemistry at La Trobe). I was given space to grow, a gradual induction into teaching, and my senior colleagues 'advertised' me to potential postgraduate students. Not just because they were nice folks, but because the duty of care that universities have for students requires promoting new and interesting areas of science as good environments for postgraduate training (lessons one and two). Secondly, I was given the benefit of 'early career researcher' status when my internal and external grant applications were read. With current financial pressures it must be getting harder and harder for the ARC and NHMRC to be generous to first-timers going up for grants, but the first grant is the thing that will make or break a new lab, and this philosophy needs protection.

So, what can ASBMB do for the future of our discipline? We need to recognise (and say loudly) that science is not technology, it is an aspect of culture. The future of molecular biology in all its guises relies on new inductees being trained to think creatively about problems, learning how to recognise key biological questions, and having the skills, confidence and resources to address them. Unfortunately, funding has become the rate-limiting step in being an effective scientist in Australia. That might be a necessary fact of life, and might be true in many other countries too, but I think we are in danger of making some serious mistakes here, and we need to take care. It is by no means doom and gloom, and an encouraging move by the ARC increased the proportion of the total budget that funded Discovery Projects (by my calculations from ~13% in 2001, up to ~22% in 2005), including a rise in the total number of Discovery Projects funded and an increase in the average size of the project budgets. ASBMB has a role to play in constructively assessing funding trends, to ensure that the quality of science done in Australia can be maintained at a level of excellence.

There is a slow but determined push to assigning research funding into larger and larger dollops, to be spent on programs, centres and networks which usually have very short-termed goals. A lot of money, in the hands of very few people, who need to justify themselves

The Lithgow lab in 2001. ***Left to right:*** ***(Back)*** **Vasyl Demchyshyn, Travis Beddoe, Traude Beilharz, Trevor Lithgow, Diana Macašev, Ian Gentle** ***(Front)*** **Kip Gabriel, Peter Walsh, Billie Egan, Yinchern Law.**

in a very short time. It will be the greatest of shames if we look back on this period to find that many of these entrepreneurial ventures have left only Qintex-legacies to science. Don't get me wrong, some problems can only be tackled by big programs of research and some of the big programs recently funded incorporate excellent science. But a large slice of science funding needs to be maintained, as an investment in the future, in small enterprises where talented students are supported and encouraged to develop independent careers. This will almost always be in small labs in university departments. This can't easily be justified if the argument is reduced to a purely economic one. But there is a limit to how far any aspect of culture can be economically rationalised, and an essential role for our society is to guard against this limit being broken. There would be but a dim future for biological science in Australia if too many of our students become seduced by economically-driven, applied problems, instead of developing both the creative and the analytical skills that come with a full education in science.

The last week of my postdoctoral time was spent in Davos at the 1st European meeting of the Protein Society. On the bus, on the way back to Zurich airport, I enjoyed two hours with Max Perutz, as he talked about Nobel prizes and stories from the early days of the Cavendish lab in Cambridge. He also shared his worries about how readily science can be justified in economic terms, and whether excellent science can be done in the context of goal-driven experiments associated with whole-genome and high-throughput research programs (this was the nineties, genome-scale analyses were more a promise than a reality, but the writing was on the wall). I subsequently read in his book *I wish I'd made you angry earlier. Essays on science, scientists and humanity.* [Perutz, M.F. (1998) Cold Spring Harbor Laboratory Press, New York], and I often cite, **"Discoveries can not be planned; they pop up, like Puck, in unexpected corners... Science has changed the world, but the scientists who changed it rarely foresaw the revolutions to which their research would lead."** There is a need for some of us to focus on big pictures. But there is an equal need to maintain the laboratories that train people to discover and critically analyse the small details that give meaning to the big pictures.

The Lithgow lab in 2004.
***Left to right:* Trevor Lithgow, Dejan Bursac, Lena Burri, Michael Dagley, Katherine Vascotto, Nickie Chan, Joanne Hulett, Ian Gentle.**