

# GREAT EXPECTATIONS



Phil Marley.

*I never wanted to be a lumberjack: I always knew I was going to be a scientist. The only real question was, what flavour?*

I grew up surrounded by science. My home town, Abingdon, was equidistant from the UK Atomic Energy Authority's laboratories at Harwell, the Rutherford high energy physics laboratories at Culham (where the Joint European Torus nuclear fusion project now is) and Oxford University. My school was full of kids from scientific parents and I was one. My father was a physicist, but I never really knew much about his research because his PhD was examined under the Official Secrets Act – even he was not allowed to keep a copy – but it was something to do with explosions and his time at Los Alamos during the war, which was pretty exciting. With an older brother and twin sister into genetics and maths, I was destined to be a scientist.

But when I finished school, I went to Germany to play chess. My school had an unusual connection with a nuclear research centre near Karlsruhe whose director was chess-mad and each year sent a chess-playing student to work there before going to uni. Not quite child labour, but in 1975, I found myself dividing my time between playing chess, learning bad French from my supervisor (to this day, my French has a Breton dialect) and doing my first research project – on the efficiency of air monitoring for leaks of radioactive materials – americium, plutonium, californium. Surreal.

I went to Cambridge University in 1975 to study chemistry, but doing a bit of everything in the Natural Sciences degree exposed me to all sorts of biological sciences I had not experienced at school. I was instantly hooked.

Big influences back then were two tutors at Trinity College: Mike Berridge, of IP<sub>3</sub> and Ca<sup>2+</sup> signalling fame, and Tom Jessell, who was doing his PhD with Les Iversen at the MRC Neurochemical Pharmacology Unit (NCPU) – he found his research sufficiently unchallenging he was learning Japanese in his spare time. Together with Les, a brilliant and inspiring lecturer in neuropharmacology, they were

*"...we know there are some things we do not know"  
– Donald Rumsfeld*

*"Nothing worth knowing is accessible to the mind"  
– Woody Allen (Manhattan)*

*Phil Marley tells his story of the lab and beyond.*

## Gut Feelings

responsible for opening my mind to the addictive attraction of research. They taught me my first two rules: **Rule 1 (the Rumsfeld Rule): The unknown is infinitely fascinating;** and **Rule 2: Do something that really switches you on.** Their excitement about their research was palpable and infectious, yet for every question I asked them, they said they didn't know the answer. Tantalising stuff!

I graduated in Pharmacology in 1978 totally besotted with neuropharmacology. After a summer working with Brian Richardson on pancreatic beta-cells in Swiss drug company Sandoz in Basel, I returned to Cambridge to do my PhD (after resisting persuasive arguments that I should go to Oxford to become Phil D. Marley, D. Phil.). My initial project, on the pharmacology of dorsal root ganglion cells using intracellular electrodes, did not go well – in part because my lab was next to a lift which caused local earthquakes every time someone used it and due to a falling out with my supervisor. So after completing a Masters, I joined Piers Emson at the NCPU and started studies on the gut peptides vasoactive intestinal peptide (VIP) and cholecystokinin (CCK) as potential neurotransmitters in the brain. It would be over 20 years before I returned to electrophysiology.



*Phil's first research experiment, testing the efficiency of air monitoring for radioactive particles in front of a 'hot cell' at the Euratom centre near Karlsruhe, 1975.*

NCPU was research heaven: it was really humming. It had been set up to research schizophrenia. Les Iversen scoured the world recruiting the best postdocs with the latest techniques and bringing them to Cambridge, and many

other outstanding people came on sabbatical. NCPU students got exposed to the best-of-the-best by way of people, ideas, technologies and resources. Everyone worked long hours and weekends. It was an extended family – we worked, ate and partied together. One day the whole unit was in a mesmerised, catatonic state after seeing the newly-released *Apocalypse Now* the night before.

I remember my first NCPU paper because it was accepted by *Neuroscience Letters* without change – I naïvely thought this was normal, but it has not happened since with my 101 other papers. Everything at NCPU was done in front of world class researchers: bad logic in research questions, poorly designed experiments, low quality data and over-interpreted results were instantly, publicly and ruthlessly exposed. It was invaluable training for the competitive life of medical research ahead and taught me **Rule 3: Do it well**. Quality matters.

I came to Australia by accident. After my PhD, I continued my neurochemical studies on the molecular forms of CCK and gastrin in the brain for six months with Jens Rehfeld at the Rigshospital in wonderful, wonderful Copenhagen. This was filling in time before going to Montreal for a postdoc with Bruce Livett. I had met Bruce at the 1981 International Society for Neurochemistry meeting in Nottingham where, still a PhD student, I gave a symposium talk. Bruce attended my talk and subsequently offered me a place in his lab at McGill (to this day, I don't think he knows I missed his own symposium talk the day before mine). But while I was in Denmark, he contacted me to say he had accepted a position back in Melbourne and would I go to Australia instead of Canada. I had a vague feeling Montreal and Melbourne were about the same distance from the UK and said yes. I accepted a Royal Society Stothert Research Fellowship, took a one-way ticket to Melbourne and flew straight into a firestorm.

I arrived here the day before Ash Wednesday 1983. Instead of swapping the -1°C in London for the -25°C of Montreal, I came to +43°C in Melbourne. And Melbourne was burning.

What followed were 10 years in the Department of

Biochemistry at the University of Melbourne, a move from the central to the peripheral nervous system and from gut peptides in the brain to the role of neuropeptides in regulating adrenaline release from the adrenal medulla. But after years of intense study, I was bugged if I could work out what adrenal opioid peptides did. With my partners-in-crime in Bruce's lab, Steve Bunn (now in Dunedin), Jane Ward (now in Pharmacology, University of Melbourne), Ken Mitchelhill (unfortunately passed away recently), and Zeinab Khalil (still at Melbourne), we drafted a template for our papers with the title "Lack of effect of opioid peptides on XXX in bovine adrenal chromaffin cells" and just completed the blanks. The best part of Bruce's lab was the 'cake-and-chatter' lab group meetings – so long as the cake we made was good, nobody minded that the chatter only presented more negative data.

It was Ian Chubb who convinced me to apply for an NHMRC Research Fellowship. He simply pointed out that the worst thing the fellowship committee could do was say no. So in 1985, I applied for my Research Fellowship (equivalent to the current R.D. Wright), John Funder took me under his wing and tutored me for the interview, and I got the fellowship. I had switched to a Queen Elizabeth II Fellowship in 1984 and moved onto my NHMRC Fellowship in 1986 – at three years postdoc. Chubb taught me the Nike rule, **Rule 4: Just do it**. Have a go, get involved.

Three activities based on the Chubb Rule had enormous significance for me in future years. I became department seminar coordinator – something I did for the next 18 years. I became convenor for regular meetings of Victorian NHMRC research fellows (although largely social, we did talk real science: I clearly remember a serious talk by John Ludbrook on the cardiovascular consequences of crucifixion at one Easter gathering). And I joined the second messenger journal club run by Stella Clarke, Phil Robinson and Marjorie Dunlop. These networking activities introduced me to literally hundreds of terrific researchers from all disciplines, outstanding people who I drew on to help me in my research and, subsequently, in my decision to leave lab science.



Above: Bruce Livett's lab in the Department of Biochemistry, University of Melbourne. From right: Bruce Livett, Elaine Kekorius, Steve Bunn, Jane Ward, Phil Marley, Zeinab Khalil, David Small and unknown, c.1986.

Left: Radioimmunoassay of CCK in 900 rat brain samples: PhD at the MRC Neurochemical Pharmacology Unit, Cambridge, 1980.

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After 10 years hiding my lack of biochemistry knowledge by being the token pharmacologist in a biochemistry department, it was time to move on. OK, it was only 50 metres to the Pharmacology Department, but my 1993 move was not without hiccups: the week before I moved, the ceiling in the lab opposite my future lab collapsed under the weight of dried rat droppings, which had accumulated over many years from feral rats in the ducts and swelled with water from a leaking pipe.

My research refocussed on the pharmacology of cell signalling in neurones, using cell-permeant drugs to interrogate the roles of kinases in receptor-evoked exocytosis in chromaffin cells. My 13 years in Pharmacology brought two key developments. One was an invitation

from Elspeth McLachlan in 1996 to become National Secretary of the Australian Neuroscience Society – a role I held for six years, the maximum permitted. The other was a strong relationship with Peter Dunkley in Newcastle. Although Peter had adopted chromaffin cells as a model for his kinase research and we shared many collaborative studies, for me his key influence was as a mentor. Bruce and Peter were my sounding boards, advisors and guides throughout my lab research life and many was the time I depended on them to keep me going. **Rule 5: Get a mentor.** Open, frank, fearless, trustworthy.

In 2004, I needed an exit strategy. After 18 years in the NHMRC fellowship scheme and having been promoted to PRF in 1998, I wanted to move on from the lab. I was 48 and felt I had gone as far as I could in a research career. At the time, my lab was getting increasingly empowered with siRNA techniques to knock down trimeric G proteins and patch-clamp electrophysiology (the first cell patched on my rig was by Bert Sakmann, Nobel Prize winner as co-inventor of patch-clamping). However, I was getting more satisfaction from other activities: influencing policy on fellows' careers, being a member of the Mental Health Research Institute's scientific advisory committee, assessing grants on NHMRC review panels, managing the Australian Neuroscience Society and organising conferences. So in December 2004, I announced publicly that I would close my lab in December 2005 and walk away from lab science. I have never regretted my decision.

I spent 2005 fact-finding. What could life outside the lab offer? After 22 years in the lab, I knew nothing of the real world. With guidance from a career counsellor, I drew on the generous advice and experiences of a wide range of people, many from the contacts I had made from my extensive networking activities: COOs and Directors of research institutes, CEOs of research collaboratives and commercialisation companies, CEOs and CSOs of biotech companies, partners in venture capital firms, directors of research administration offices, associate deans and DVCs of research, MDs of recruitment companies, government executives, consultants and others. And I found there were fabulous opportunities out there for someone with



Back to electrophysiology 25 years on: Pharmacology in 2003. From left: Damian Wallace, Amanda Donald, visitor and Phil Marley with our patch rig.

experience in medical research. It was an enormous relief and greatly energising.

I duly swapped my lab coat for a suit in December 2005 and moved to the dark side to become a public servant for the Victorian Government – Manager of Biomedical Research and Technology in the Department of Innovation, Industry and Regional Development. My role is to facilitate medical research in Victoria through developing policy that supports medical research and translation of research into health and commercial benefits, and through delivering programs that develop new facilities (such as the Parkville Comprehensive Cancer Centre and extensions to the Walter and Eliza Hall Institute and the Burnet Institute) and assist research institutes with indirect costs. It's a very different world from the lab, one captured with frightening accuracy by *The Hollowmen*, but it uses my knowledge of the players and the game of medical research, and the need for advanced technologies and skills. It also uses communication skills in educating and persuading my department and government to adopt certain positions or actions. It is a very good fit for me.

My career has had no grand plan. I have not mapped where I am going, but have just followed my interests and gut feelings. I did my PhD at the same uni I did my undergraduate studies (unusual in the UK), came to Australia by accident and moved 50 metres between departments as the sum total of my travels in over 22 years in the lab. I have often followed the path of least effort and this has taken me where it has.

In reflecting on my times in the lab, I am particularly proud of two papers, both reviews that highlight what we don't know and question the evidence for what we think we know. To me this is what research is all about. So perhaps I should add a Julius Sumner Miller rule: **Rule 6: Ask why is it so?** Assess, evaluate, ask big questions, ask the right question.

My rules continue to guide me in my new lab-less life.