From Caterpillars to Childhood Cancer

Michelle Haber.

As a child, I loved studying anything to do with nature and would often be found catching caterpillars or insects in the garden. For a while there, I think my family thought I was going to be an entomologist… but my path ended up taking quite a different direction.

Born in England, I was almost five when my family emigrated to Australia. It was a great adventure for me, my brother, Phillip, and sister, Stephanie, spending five weeks on an ocean liner. We were very excited to be starting a new life in a country we knew hardly anything about.

A Budding Scientist

One of my first memories is of wandering around the garden with a furry caterpillar in my hand. I was always fascinated by living things, and I loved studying science at school, where I was extremely fortunate to have an absolutely inspirational science teacher, David Ellyard. I vividly recall my first forays into scientific research: writing major projects in high school on the structure of DNA, on radioactivity, on lasers… all still fresh in my mind, more than 40 years on! I was completely enthralled.

For my HSC I studied first level biology, which I did very well in. Then came crunch time – I had to decide what to study at university. It was 1973 and women's liberation was just starting. Both my brother and sister had studied science at university, but it may surprise you that I had no intention of having a full-time career. No, I was going to study, then work part time and focus on being a mum. I had a steady boyfriend, and assumed I'd get married and have kids, then spend most of my time cooking, sewing and bringing up a family, just as my own mother had done.

I embarked on a Clinical Psychology degree at the University of NSW. Pretty soon, though, I found that the courses I thought I would particularly enjoy were those I had most trouble engaging with, and I found myself gravitating towards the more evidence-based, scientific subjects.

For my Honours degree, I committed to doing physiological psychology, then had a last-minute change of heart and signed up to do animal learning instead. I was soon studying taste aversion learning in pigeons, and finding it fascinating! After being awarded the University Medal, I decided to go on and do a PhD in animal learning.

It was three or four months into my PhD that for the first time I began to question if I had made a wise career choice. I felt well suited to biological research – being able to ask a question and design an experiment to test it was deeply satisfying for me – but I began to imagine what it might be like to do research in a more medical area, and make a tangible difference to people's lives.

The Turning Point

One Friday afternoon, on a bit of a whim, I wandered over to the Faculty of Medicine to see if I could talk to someone. I remember looking at the noticeboard of the Wallace Wurth School of Medical Sciences, seeing which departments were on which level of the building, and deciding to try Pathology.

To this day, I think providence must have been shining on me. I was shown to the office of then Associate Professor Athol Lykke, who spent a good 90 minutes in conversation with me. Looking back, he truly made me appreciate the value of people who take the time to listen and to guide young people and act as their mentor. Having recently been appointed Head of School, he was keen to attract bright PhD students, and gave me the names of three people I could talk to as potential PhD supervisors.

One of these was Professor Bernard Stewart, who was studying chemical carcinogenesis. I met with Bernard and, long story short, took up his offer of joining his lab. From day one, I never regretted my decision to change to a career in biomedical research. I have never once looked back.

On the Right Road

I was still living at home at the time, and was extremely grateful that both my parents were very supportive of my career change, and encouraged me actively to follow this new path that they felt would make me happy. It was decided by Professor Lykke that I would need to do a transitional 18 month study program in Biochemistry and Pathology, and in parallel, I started practical work in the lab straight away. I was also bringing myself up to speed with Anatomy and Histology, and I found these new areas of study exhilarating. I will never forget the day I first saw ethanol-precipitated rat liver DNA being spooled onto a glass rod – this was one of the most exciting moments of my young academic life. These were the earliest days of molecular biology. I heard magical-sounding ideas about being able to cut DNA into precise pieces – and I so wanted to be part of this new world of discovery.

This time was not without its difficulties. Coming into a Biochemistry course without any lab training was particularly challenging, and in the first week I made a couple of near fatal errors, including leaning over a spinning bench-top centrifuge and almost scalping myself as my hair caught in the rotor.

Michelle on the day of her PhD graduation in 1984. She is standing next to the fraction collector and 'home-made' chromatography column she used to separate single-stranded from double-stranded rat liver DNA after carcinogen exposure.

At my first Pathology tutorial, Professor Lykke invited me to sit at the front table with him, where we were joined by a medical student who came in late… a young man, who it turned out, was my husband-to-be. Subsequently, we found out that Paul had followed some friends in to the tutorial and was actually in the wrong place. Once again, fortune had smiled upon me.

The following year, at the end of 1980, Paul and I married. Having loved my studies in the Medical course, I thought about transferring to Medicine, but we decided that one clinical practitioner in the family was enough. My PhD studies progressed well, and I published a couple of papers along the way. It was not until the final months of my PhD, though, that my future path started to become clear.

A Brand New Lab

It was 1982, and we had decided to go to Israel for three months, for Paul's medical elective term. I was fortunate to get a position in the lab of Professor Yechiel Becker at the Hebrew University in Jerusalem, and it was here that I discovered the extraordinary new technology of DNA-mediated gene transfer. While in Israel, I heard from Bernard Stewart that he'd been appointed Research Director of a new childhood cancer research lab at the Prince of Wales Children's Hospital in Sydney. Would I like to be his inaugural postdoctoral scientist, he asked. Would I ever! Here was my opportunity to make a tangible difference, and I accepted the offer with glee.

In January 1984, I submitted my PhD and began work. Funded by the Children's Leukaemia and Cancer Foundation, which had been established by the doctors and parents of children with cancer, the new lab was purpose-built, but completely empty. I armed myself with catalogues and set about ordering everything from test tubes to ultracentrifuges.

I was itching to put into practice the new skills I had learned in Israel, and set my sights on isolating and characterising genes that could confer resistance to anti-cancer drugs. My only companions in the lab at this time were PhD student Murray Norris and pathology technician Maria Kavallaris. Today, 28 years later, Maria, Murray and I continue to work together at Children's Cancer Institute Australia (CCIA) – Murray for the past twelve years as Deputy Director and Program Head, and Maria, subsequently my first PhD student, now as full Professor and also a Program Head. Developing CCIA with these long-time colleagues has been one of the greatest joys of my life.

Life as a Postdoc

I submitted my first grant application to the Leo and Jenny Leukaemia (now Cure Cancer) Foundation and, to my amazement, was successful. This was followed by my first NHMRC Project Grant, and my life as a postdoc was off and running.

In 1986, after the birth of our first child Adam, I took six months of maternity leave. I returned to work part time and was soon back in the swing of things. Two years later, I had our second baby, Anna. Ours was now a family with two children, and two parents set on careers in the biomedical field, with Paul having recently passed his FRACP exams. How could we balance all this? We weren't sure, but we were determined to succeed.

Paul completed his MD by research, and then chose Mount Sinai Hospital, New York, as the place to do his postdoc, leading to two of the most extraordinary years of my life. I was delighted to secure a Union for International Cancer Control Fellowship to work at the Albert Einstein College of Medicine in New York. Here I did research on antimitotic cytotoxic drugs in the lab of Professor Susan Horwitz, but I also had to deal with the challenge of already being responsible for grant-funded staff and PhD students in Sydney. We made the decision that I would share my time between Sydney and New York, travelling with the children, then aged 5 and 7, who had the excitement of being enrolled for a full term in a New York school and then returning to it for shorter periods of time on subsequent visits. By judicious choice of our trips to New York, coinciding with conferences that I would have attended anyway, and Paul's return home to Sydney for an extended summer vacation, we managed to have a wonderful two years, furthering both our careers, travelling extensively as a family in the USA, surviving financially, and remarkably, not being apart for more than six weeks over the whole two year period.

Michelle together with Maria Kavallaris (left), Michelle's first PhD student and long-term colleague, and Susan Horwitz, with whom both Maria and Michelle spent very productive periods of study in New York during the 1990s.

When I returned to Australia, my research took a new turn. A new drug resistance gene (MRP) had just been characterised, and Murray Norris and I wanted to better understand its role in neuroblastoma, the most common tumour of infancy. It quickly became apparent that the MRP gene was key to the drug-resistant behaviour of neuroblastoma, and our pioneering work in this field led to a major publication in the *New England Journal of Medicine*. Neuroblastoma and the MRP gene family have remained constant themes of my work ever since.

The more I learned about childhood cancer, the clearer it became that one of the main problems with treatment was the long-term side effects that could result. I wanted to develop new drugs that could specifically target key genes and proteins in the tumour – drugs that would be more effective and less toxic to the normal cells of the growing child. I became fascinated by the new technology of high-throughput chemical small molecule screening. Introduced to me by Professor Andrei Gudkov, then working at the Lerner Research Institute in Cleveland, this technology streamlines the process of finding molecules for use as anticancer agents, and has led to the development of several potential new drugs at CCIA, the first of which is now in formal preclinical development.

Working together with people like Andrei and Murray – outstanding scientists with a shared commitment to translational research – has been immensely rewarding and has highlighted to me the importance of collaboration. I simply could not have achieved what I have without it.

My Dual Role

In 1998, Bernard Stewart left the institute and I became Acting Director. Eighteen months later, following a worldwide search for candidates, I was appointed to the position of Director. This period really was a coming of age for the Institute. The Wills Health and Medical Research Strategic Review had just been released, and it became clear that relatively small research organisations like ours were just not going to survive unless they became bigger and more internationally competitive. I felt the choice was clear: we would build CCIA into Australia's, and indeed the region's, premier childhood cancer research facility.

In tandem with growing the institute as an organisation, I was working hard to grow my own research program. A NSW Cancer Council Program Grant, shared with Murray, Maria and also long-term colleague and clinical collaborator, Glenn Marshall, and later an NHMRC Program Grant shared with Murray and Glenn, allowed my team to expand, and I was very much enjoying playing the role of mentor to the bright young scientists joining my lab. Our research effort was expanding into a whole series of new areas… the only problem was a lack of space to expand into. The institute was bursting at the seams. There was no question about it – we needed a new home. A big one.

As a new building became the top priority, I found myself in the role of fundraising advocate, spearheading a community fundraising campaign to raise $35 million. CCIA entered into a partnership with the University of NSW, and in 2009, the Lowy Cancer Research Centre was completed. This wonderful, world-class facility provides CCIA with the space it needs to grow, and I do believe we are now positioned as the leading childhood cancer research facility in the southern hemisphere.

Michelle with long-term colleagues and friends, Glenn Marshall (centre) and Murray Norris. The trio was awarded an NHMRC Ten of the Best Research Project 2012. Photo courtesy NHMRC/James Braund.

The Power of Collaboration

From the mid-2000s, the value of translational research (previously regarded by funding bodies as 'soft science') began to be recognised. I felt the whole focus of the medical research effort in Australia shift. This suited my research, and that of CCIA in general, very well. My vision of working in a field that really made a difference was coming to fruition.

Linkages with clinicians had always been key to CCIA's research, and were now becoming even more important. I had been fortunate to work closely for many years with Glenn, who, as well as heading a research program at CCIA, also heads the Children's Centre for Cancer and Blood Disorders at the Sydney Children's Hospital. Glenn well understood the importance of clinical input in ensuring that our research would translate into clinical outcomes. A perfect example of this is a long-term collaborative project on PCR-based detection of minimal residual disease in children with acute lymphoblastic leukaemia, the commonest childhood cancer. This project, developed over two decades by Murray, Glenn and me, has resulted in dramatic increases in the survival rates of children at highest risk of dying from their disease.

With my joint commitment to translational research and clinical collaboration, I was thrilled when an opportunity arose for me last year to drive the formation of the Kids Cancer Alliance, which brings together all childhood cancer research and clinical care in NSW into a single entity. Clinicians and scientists, working together and all focused on a single vision… it has been a great pleasure to see this alliance come to fruition, and I regard it as amongst my proudest achievements.

The Juggling Act

My taking on the role of Acting Director of CCIA had coincided with the birth of our third child, Daniella, ten years after Anna, and with Paul a very successful and busy clinician/scientist, it became clear that we would not continue to get by without the help of a full time nanny.

No matter how hard we worked during the day, we had always made sure that we had dinner with the family

every night – a tradition that continues today. We had also committed to regular family holidays… the kind with no work, no mobile phones and no computers. I believe this protected shared family time has been the key to preserving our sanity as a family, while allowing our professional careers to flourish.

I thought we had put our children off a career in medicine or biomedical research, but I'm delighted that our son Adam, who is currently doing his PhD in artificial intelligence is now looking to apply his skills to systems biology of cancer, while our eldest daughter Anna, with an undergraduate degree in Art Theory, has made an unexpected decision to study postgraduate medicine! So it seems that at least two of our children will follow in our footsteps.

As I look back on my life, I feel exceptionally blessed to have had the joys of a wonderful family life, as well as a fulfilling professional career. My research continues to go from strength to strength, and seeing CCIA become so successful gives me a tremendous sense of satisfaction. To have been able to choose a career in medical research has been a great gift and a privilege, and I feel that life has been very good to me.

The Habers on a recent family holiday in Israel. From left: Michelle, Daniella, Adam, Paul and Anna.