MARILYN ANDERSON nee HULETT: PROFESSOR OF BIOCHEMISTRY, ORDER OF AUSTRALIA 2016

Background

I was born in Deer Park, a suburb that was established in the 1870s as a site for the manufacture of explosives for the goldfields in Ballarat and Bendigo. It was located exactly 12 miles from the centre of Melbourne so management could make the trip from the city centre to the factory and back in a day, a distance that could be comfortably covered by horse and carriage. Imperial Chemical Industries (ICI) took over the factory in 1928 and the factory expanded during World War II and over the following years as Australia's mining industry grew.

My father worked at ICI and even though he wasn't a scientist he was involved in the manufacture of chemicals and explosives. During my childhood, most of the people who lived in Deer Park worked for ICI and their children expected to find employment there when they finished school. My brothers were sent off to do apprenticeships and learn a trade, an option that was not available to a girl. I did not know any women who stayed in the workforce after they were married. I thus had freedom to study whatever I liked during my education at primary and secondary school as I was not expected to have a career. But when I came to the decision in secondary school of whether to do history, art or science, my father encouraged me to take the challenge and do science.

My father was an inspiration. He was born with a heart defect and his family was told he wouldn't survive childhood. He missed primary school and had only a couple of years at secondary school, but he was smart and made his way up to the level of engineer in ICI without a university degree. He used to sit at the kitchen table with my two brothers and ask questions like what's the area of a circle? I remember on my first day of school I went to the teacher and said "The area of a circle is Pi r squared." I thought you needed to know that to be successful at school.

I did well at school, driven by natural curiosity and quite a bit of boredom when I was home. I collected tadpoles and nurtured them until they turned into frogs and I learnt to love plants as I followed my mother around the garden. I gathered some concepts from Sunday school that I could not understand. They still bother me. Just how long is eternity and how far is infinity? I enjoyed the broad range of subjects at school and found humanities and science of equal interest. I started at the St Albans High School in 1962 and went through to 1967. The first big decision that set me on the path to becoming a biochemist was when I had to choose between the science and humanities stream at the end of year 10. My father, inspired by his career in the chemical industry, encouraged me to take the tougher option and do science. How strange when he did not encourage his own sons to do the same.

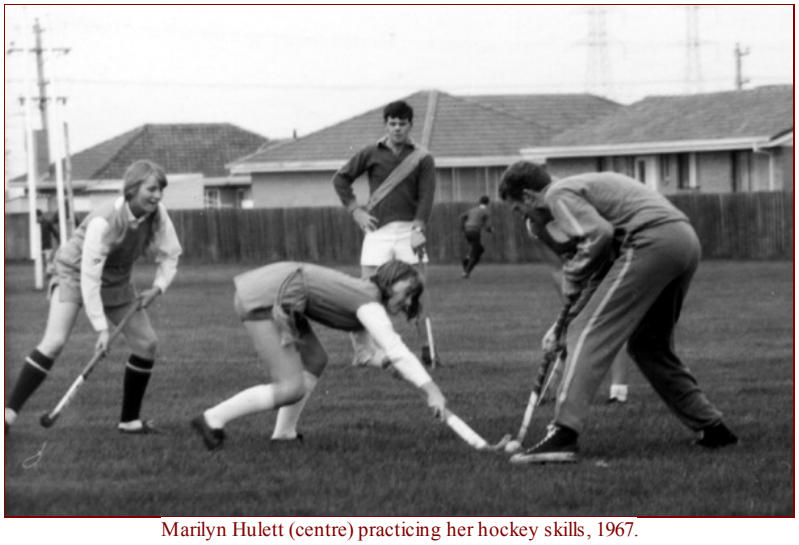
In the final year at St Albans High I was a prefect as well as being on the school magazine committee and playing in the girl's hockey team. The magazine was a challenge because an official school magazine had not been published for several years. Mr Ziemelis, one of the senior teachers who taught German and was the school's unofficial photographer, was our guide and mentor; other students on this group included Maija Svars, Leo Dobes, Joachim Simovic and David Beighton. I'm happy to confirm that Alba was definitely published that year.

Alba team: Leo Dobes, Maija Svars, Joachim Simovic, Marilyn Hulett, David Beighton, 1967.

As I approached the end of secondary school my teachers encouraged me to apply for University entrance. This was truly foreign ground to me, because no one in my family had been to university and I didn't imagine I would go to because I didn't know anyone who had been to university. But my school friends were children of immigrants who had been displaced from northern Europe after the war. Most of their parents had been tertiary educated but their qualifications weren't recognised in Australia. This made them heavily committed to getting a good education for their children. My best friend was Latvian and practised piano and violin for five hours a day. It made me realise I could aim for more than I had been exposed to in my non-immigrant household.

Marilyn Hulett (front left) and other prefects with Alison Gliddon, Brian Torpey, Ivan Matthews, 1967.

I was familiar with the University of Melbourne campus because I often played hockey there. We had a good hockey team at St Albans High in 1967: we went through the year undefeated and beat the winning team of the other section in the final. The team members included Lila Smith, Maija Svars, Elizabeth Prince, Ronda Wheelhouse, Gina Kosiak, Helga Fuchs, Olga Susko, Judith Barnes, Bridget Deutsch and Brigitte Linhart. I also went to Melbourne Uni for the German poetry competitions and oral exams, so I dared to dream of going to university. This shows the value of bringing young students onto campus.



Marilyn Hulett (centre) practicing her hockey skills, 1967.

Marilyn Hulett (far right) with the undefeated hockey team and coach Mr Maplestone, 1967.

I did have the opportunity to go to university and signed up for a science degree because I never dreamt that anyone like me could do medicine or law. I got into science and I absolutely loved it. I started my science degree at the University of Melbourne in 1968. My first year there was one of the best years of my life. I remember my first lecture on biology when Dr Gretna Weste introduced cells. I was enthralled. I ran over and bought my first text book "The Cell" by C.P. Swanson and devoured it over the next few days. Peering through the microscope at cells in my first practical class I drew my first cell with great attention to detail and was terribly disappointed when Dr Weste informed me that I had drawn a perfect air bubble! Looking back I think that was the most life-changing year for me. I still thought I was going to fail because I was from the western suburbs and almost everybody else was from a private school. I was stunned when I did well in my first-year exams. After that I immersed myself in university life and moved into Janet Clarke Hall for the full university experience.

When I started at university I was going to do chemistry because that's what I did at ICI for my summer jobs. First-year biology opened up an entirely new world but I did not think it would lead to a career. I just assumed I would be a chemist and go back to work for ICI or become a secondary school teacher. Growing up in Deer Park and being part of the "ICI family" had been handy because I was given summer work in their chemistry laboratories from the end of high school to the end of my undergraduate studies at University. I started in the ammunition factory working out the copper content in the brass used for the casings. The following three years I spent my summers in the laboratories at the urea-formaldehyde plastics factory and in my final year I moved onto the Central Research Laboratories for ICI. This institute housed about 100 research chemists and was one the major employers of PhD

chemists in Australia at the time. I joined the team that was working on the synthesis of a new nematicide for sheep called tetramisole. I spent the summer immersed in organic synthesis and was rigorously trained in safety procedures. Indeed, I dropped to the floor immediately when we had our only incident. The coffee pot had exploded!

But then I was introduced to biochemistry. It was a relatively new subject in those days and I found it really exciting. At the end of third year I had the choice of doing honours in chemistry or biochemistry and decided to do biochemistry. Biochemistry was a better environment for women than chemistry in those days. The lecturers and tutors were inspiring - Mary-Jane Gething was my tutor when I was in college and I thought she was fantastic. In those days there were strict quotas to get into second year, third year and honours biochemistry. Not everyone could get in, so you felt privileged if you did. When I went on to do honours with Bruce Stone, he handed me Elizabeth Blackburn's and Mary-Jane Gething's laboratory books from projects they had done in his lab a couple of years earlier. That was what I built my honours project on.

It's pretty amazing now to look back and think I was following on from a future Nobel Prize winner. In 1971 when I was an honours student I joined the Australian Biochemistry Society, which is now the Australian Society for Biochemistry and Molecular Biology (ASBMB). Attendance at the annual conference was part of our honours program and Syd Leach had run a course to prepare us for the plenary lecture on protein folding by Harold Sheraga. The whole honours class travelled to Brisbane by train, which took two days!

I applied to do a PhD at Melbourne University with Bruce Stone. At the end of my honours year he accepted the position as inaugural Professor of Biochemistry at La Trobe University. He moved his lab out to La Trobe and we all followed. Bruce trained several successful biochemists who have been members of the ASBMB for a long time, including Geoff Fincher, Tony Bacic, Adrienne Clark, Robert Henry and Robin Anderson. My PhD project was focused on polysaccharide chemistry and the specificity of the enzymes that break them down. That was in the days before 'molecular biology', although Bruce insisted that we had always been molecular biologists.

Then I went overseas to do a postdoc and took up molecular biology. In those days almost every PhD student who wanted to continue in science would look overseas for a postdoc. I wanted to continue in carbohydrate chemistry so I went to The School of Medicine at the University of Miami where there was a big cluster of carbohydrate chemists in a unit headed by Bill Whelan. He started The Miami Winter Symposium, which is now in its 47th year. It was at those meetings that I first heard about the newly emerging field of molecular biology from scientists like Francis Crick, James Watson, Paul Berg and Phil Sharp. They inspired me to move fields from carbohydrate chemistry to molecular biology. It was the mid-1970s, just as scientists in the USA called for a national moratorium on DNA cloning. For the rest of the time that I was in Miami, no cloning was done whilst this voluntary group of scientists evaluated whether gene cloning was safe. We still did a lot of work with DNA but we weren't cloning. I was trying to use SV40 virus to create an immortal line of insulin-producing pancreatic cells. I met and worked with William Rutter, who had developed techniques for isolation of RNA from pancreas. This technology was very useful later in my career.

Joe Sambrook, who was deputy director at Cold Spring Harbour Laboratory, came to Miami for a student symposium. He heard my husband talk and offered him a job, so I went with my husband to Cold Spring Harbour and continued working on oncogenes in adenovirus, another DNA tumour virus. Many people worked on adenovirus and SV40 virus in the early days of molecular biology.

When we got to Cold Spring Harbour, the moratorium on gene cloning was lifted. My husband Bruce Anderson was working with James Watson and Joe Sambrook, firstly on the cloning of middle T (later renamed p53) and then on the cloning of plasminogen activator. I was working with Bill Topp in the same building.

It was an amazing environment to work in, but there was a complication because I had had a child - so when I turned up at Cold Spring Harbour I had an 18-month-old child. At that time there were very few women working in science who had children. I knew Barbara McClintock well and we talked a lot. The advice she gave me about how to succeed as a woman in science was not to get married or have children. Times were just starting to change, and I got a job at Cold Spring Harbour. But even though I worked every day and all weekend I was still, relative to men, regarded as not as serious. In some way that gave me more freedom because the men were under a lot of pressure.

In 1982, when our son was four years old, Bruce and I decided to come back to Australia. We had been away for seven years and my mother was very sick. Bruce got a job with Ian Gust at the Fairfield Infectious Diseases Hospital to do virology research, set up molecular biology there and cloned the hepatitis A virus.

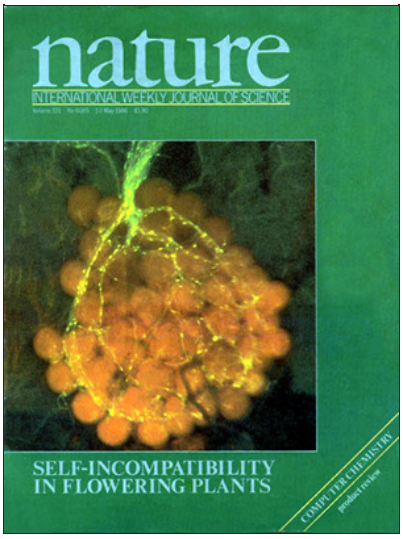
I decided to work with Adrienne Clark, who had received funding from one of the first rounds of ARC Centres of Excellence. Adrienne could guarantee me five years of funding and the stability that offered us was one of the reasons we came home. I think I would still be in the US if that hadn't happened. I had a green card - in fact, James Watson was my referee for the green card. So we decided to come back for two years, and then our green cards would still be valid, and I could head back to the US and pick up where I had left off if things did not work out.

I came back to work with Adrienne and hopped right into plant biology. People often think I am a plant biologist but I hadn't really worked with plants before. My work with Bruce Stone had been focused on carbohydrate chemistry and enzymes. Adrienne had a fundamental and important biological question and James Watson had said to us: "If you are going to do basic science ask a big question, don't just tinker on the edges."

Adrienne's question was on self-incompatibility in plants; that is, how do most flowering plants recognise and reject self-pollen so they are forced to outbreed? This question had been posed by Charles Darwin 100 years earlier. He wrote a book on it and used this phenomenon as evidence for the requirement of outbreeding for hybrid vigour and survival of the fittest. Although people knew the genetics behind it, the genes and the proteins that were responsible had not been isolated.

Even though I'd been working with viruses and oncogenes, Adrienne thought somebody from an entirely different field with new technology might help solve this problem. Very fortunately, we cloned the gene that controlled self-incompatibility within two years. It turned out to be one of the first major and important plant genes to be cloned - we published in Nature and got the front cover. We discovered that the female tissues rejected self-pollen by making a ribonuclease that could enter the self-pollen and kill it by breaking down the RNA.

The scientific community around the 'Parkville Strip' really contributed to our success. I was a bit of a gypsy when I first returned from the US. I would walk over and talk to people at the WEHI, the Howard Florey and Ian McKenzie's group in the Pathology Department at Melbourne University, and they would invite me into their labs to work. We would share techniques and they gave me access to their resources. Without that we would not have cloned the gene. I look back at it and think what amazing times they were. I wouldn't have been prepared for it if I hadn't worked at Cold Spring Harbour in the early days of molecular biology.



We followed that first paper with another two Nature papers. It shows the advantages that special research centres can offer. I stayed there for about 13 years. With regard to switching from working in animals to plants, what was so coincidental was that I made RNA from the female tissue of the flower using the same methods that I had used for pancreas when I was working with Bill Rutter. Pancreas is full of ribonucleases that break down RNA so we had to take extra precautions to inactivate them.

When I was working with flowers, they turned out to be full of ribonucleases like the pancreas. So I used the method I had learnt in the animal field. That was the big breakthrough that enabled us to isolate the good quality RNA that we used for cloning. When we first sequenced the gene we didn't know it was a ribonuclease. We found that out because our collaborator, Richard Simpson, was working with a colleague from Japan who had just cloned a ribonuclease gene from a microorganism. When he lined up the sequence of his gene with the sequence of ours we could see regions of homology, and that led us to ask whether it was a ribonuclease and it was!

Once we cloned the self-incompatibility gene we attracted a series of very good postdocs to the lab and we had a lot of very good questions to pursue. We had excellent facilities in Melbourne and we had international recognition for our work. Furthermore, my husband had managed to clone the hepatitis A virus so he was enjoying his work as well. We decided to stay in Australia.

Adrienne Clark and I establish the agribiotech company Hexima in 1998. Hexima has existed in different forms, but it really started in 1997 when we had our first employees. We now have 36 scientists and about five administrative people. We floated on the ASX in 2007 and raised $40 million. We delisted because the climate is too volatile for a small biotech on the ASX.

We became involved with investors and patents very early on. In the first year that I was back in Australia, Adrienne Clarke had received funds from one of the world's first plant biotechnology companies, Agrigenetics, for the self-incompatibility work. Agrigenetics was founded on venture capital money from Hollywood actors who formed an investment group called the nematodes in the early 1980s. They had a couple of business people who chose the projects to bring into Agrigenetics, such as the first transgenic plants with the insecticidal gene, Bt Toxin, agrobacterium-mediated transformation and our self-incompatibility work, amongst others. Some of the most valuable patents in plant biotechnology came from that original company.

When we were working on pollen and how it grew, we realised that female plant reproductive tissues were rarely infected by microorganisms, even when the rest of the plant had an infection. I applied for an ARC research fellowship to look at molecules that protect the flower from invading microorganisms and damage from insects. I identified some molecules, we put some patents in and it's really from that work that Hexima was founded. It started off with protease inhibitors. We found that they are good insecticidal molecules that protect the female flower from insect damage. Then we found some potent antifungal molecules and the work has broadened.

Most of the Hexima work that has generated commercial interest has been our antifungal technology. We've had a five-year program with DuPont Pioneer to enhance disease resistance in corn by applying this work. We've just signed a new five-year contract with them to go back and start working on insects. We have generated plants with enhanced resistance to some of the major corn diseases and the seed is now going through field trials in the US.

About three years ago we moved just about everyone from Melbourne to La Trobe University. My memories of La Trobe began before I was a student there. When I was a first year student at Melbourne University and my boyfriend Bruce Anderson had his first car we drove all the way out to La Trobe which seemed to be the end of the world to me to have a look at this exciting new campus. This had been in the late 1960s so coming back in the 1990s there had been a lot of change in the meantime. We built a large greenhouse at La Trobe for production of transgenic corn with our antifungal molecules. We have a very efficient system for generating and testing the plants. We can make and test 10,000 transgenic plants per year.

Now we have gene constructs that make two or three different proteins so they can hit different targets to control levels of resistance and provide more broad spectrum control - the aim is to give plants resistance to all the major fungal diseases. We are going to keep working at making Hexima successful. We are now looking at human applications for some of our technology.

I think it is really important for scientists to learn business skills as we are asked more and more to focus on translation of our research. We are training people who can span business and science. We are still very interested in basic research because we are university based. It is important to us that we get academic publications and we are still writing grant applications to support basic research.

Our students do basic research but they get to see how a company runs, they get some training and understanding of IP, how contracts work and so forth. Nicole van der Weerden, who is now our COO, was a PhD student with us. She went off and did an MBA and has come back.

I feel very honoured to be the 2014 Lemberg medallist, 43 years after I attended my first meeting as a starry-eyed honours student. Syd Leach's preparation and Harold Sheraga's plenary lecture started a love of proteins that has stayed with me throughout my career. Fortunately, I will be flying to Canberra and will not have to travel on the Brisbane Limited Express.

Note: The Lemberg Medal is awarded to a distinguished member of the Australian Society for Biochemistry and Molecular Biology who will present the Lemberg Lecture at the ComBio meeting. The Medal is presented in memory of Emeritus Professor M.R. Lemberg who was the Society's first President and Honorary Member. The award is made to an individual who has demonstrated excellence in Biochemistry and Molecular Biology and who has made significant contributions to the scientific community.

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Professional affiliations include:

- Fellow of the Australian Academy of Science (FAA);
- Fellow of the Australian Academy of Technological Sciences and Engineering;
- Chief Science Officer of Hexima Ltd (since 2009);
- Founder and past Director on the Board of Hexima Ltd;
- Fellow of the Australian Institute of Company Directors (FAICD);
- Director on the Board of City West Water Ltd (since 2008);
- Past Director on the Board of South East Water Ltd (1998 - 2008);
- Served on the Biological Sciences Study Panel of the Australian Research Council (1999 - 2000).

Comment:

"My personal philosophy is what I am now trying to talk to my daughter about, who is considering doing a PhD. I tell her don't do it unless you love it and feel passionate about it. I think the best time in my life was when I was in the dark room by myself and I developed the x-ray film and as I was looking at it a spot appeared on it, and that spot told me that I had cloned the gene. That's probably my career highlight."

Marilyn Anderson, 2014

Marilyn Anderson was inducted to the Victorian Honour Roll of Women in 2014.

Dr Sylvia Walton AO and Prof. Marilyn Anderson, 2014.

Bruce Anderson, Barbara, Helen, Marilyn Anderson, Nick, Alex, Lindsay, 2004.


Marin Gunew, Marilyn Anderson, Cathy Alexopoulos, Stefan Czyz, Luba Uwarowa, 2004.

Marilyn Anderson with colleagues at 50th school anniversary, 2006.

OFFICER (AO) IN THE GENERAL DIVISION OF THE ORDER OF AUSTRALIA

Professor Marilyn Anne ANDERSON, Vic
For distinguished service to science, and to higher education, particularly to biochemistry and molecular biology, as an academic and researcher, and to professional associations.

Service includes:
La Trobe University:
Professor, Department of Biochemistry, since 2004.
Member, Real Estate and Infrastructure Committee, since 2011.
Council Member, 2011-2012 and since 2014.
Chair, Genetic Manipulation Supervisory Committee, 2002-2008.

University of Melbourne:
Principal Fellow, School of Botany, since 1995.
Member, Professorial Promotions Committee for the Science Faculty, since 2006.
Founder, Molecular Biology Field, Plant Cell Biology Research Centre, 1982.

Chief Science Officer, Hexima Ltd, since 2009 and Director since 2010 and 2001-2007 and Founder, 1998.

City West Water:
Non-Executive Director, 2008-2013.
Chair, Occupational Health and Safety Committee, since 2012.
Member, Risk and Audit Committee, since 2012 and Member, Environmental Committee, 2008-2012.
Non-Executive Director, South East Water, 1998-2008 and Chair, Environmental and Occupational Health and Safety Committee, 2003-2008.

Fellow, Australian Academy of Science, since 2011 and Chair, Sectional Committee for Plant Sciences, 2014-2015.
Fellow, Australian Academy of Technological Sciences and Engineering, since 2010 and Committee Member, Victorian Division, since 2013 and Member, Agricultural Forum, since 2014.

Australian Representative, International Plant Molecular Biology Society, since 2009.
Member, Biological Sciences Study Panel, Australian Research Council, 1999-2000.
Member, Institutional Biosafety Committee, Austin Hospital, 1992-1997.
Member, Institutional Biosafety Committee, Monsanto Ltd, 1992-1997.
Member, Editorial Advisory Committee, The Australian Journal of Plant Physiology, 1992-1996.
Member, Australian Society for Biochemistry and Molecular Biology, 'no dates'.
Member, Australian Society of Plant Biologists, 'no dates'.
Member, Australian Biotechnology Society, 'no dates'.
Member, American Society of Plant Biologists, 'no dates'.
Member, Society for Growing Australian Plants, 'no dates' and Secretary, Keilor Plains Group, 'for many years'.
Fellow, Australian Institute of Company Directors, since 1998.

Awards and recognition include:
Lemberg Medal, Australian Society for Biochemistry and Molecular Biology, 2014.
Named in the 2014 Victorian Honour Roll of Women.
Co-Recipient with Professor David Craik, Ramachiotti Biomedical Research Award, 2015.

Marilyn Anderson, Officer (AO) in the General Division of the Order of Australia, 2016.

Reference: Marilyn Anderson "How I became a biochemist" in IUMB Life, Vol 62 Issue, 7 July 2010
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Reference: Susan Williamson, Lab+Life Scientist, 15 October, 2014.
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School photographs courtesy of John Simovic.