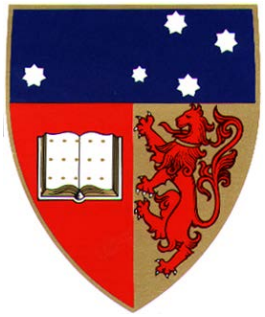

Emmanuel College

THE UNIVERSITY OF QUEENSLAND

Can doctors change the world?

By

Professor Ranjeny Thomas

EMMANUEL PAPERS
NUMBER 7 – AUGUST 2009

Emmanuel College
The University of Queensland
Enriching lives since 1911

Emmanuel College is Australia's ninth, and with St John's College, The University of Queensland's first residential college to gain affiliation. It was founded by the Presbyterian Church of Queensland in 1911 with the first students taking up residence in Wickham Terrace in 1912. As the Presbyterian Church moved towards partnership with other religious denominations during the 1970s, Emmanuel College also came under the auspices of the Uniting Church. Upon its inauguration, Emmanuel College was an all male residence but this changed in 1975 when women were admitted as collegians. Now, the College numbers around 340 students with half our population being female.

Further change was experienced by the College when it moved in 1955 from its original site in Wickham Terrace to its present location on the main university campus in St Lucia.

Since 1911, Emmanuel has stood for excellence in all round education and has had seven Rhodes Scholars during its history. Its graduates have gone on to make a major contribution to Australia in many areas, including as doctors, scientists, teachers, engineers, lawyers and judges, politicians, ambassadors and diplomats, and church leaders.

THE AUTHOR

Professor Ranjeny Thomas *MBBS WA, MD WA, FRACP*

Professor Thomas is a graduate of the University of Western Australia. She received her MBBS in 1984, and then trained in Perth as a rheumatologist. She commenced a research fellowship with Peter Lipsky at Southwestern Medical Center, University of Texas in 1990, where she first identified and characterised human circulating dendritic cell precursors. For more than ten years studying the function of dendritic cells in autoimmune diseases, she has written many articles, including several hypothetical articles on the immuno-pathogenesis of rheumatoid arthritis. She was appointed as Senior Lecturer at The University of Queensland in 1994, and promoted to Professor in 2004. Ranjeny is founder and a director of the spin-off company, Dendright, which is developing vaccines to suppress autoimmune diseases. She is Deputy Director of Research at the Diamantina Institute.

Professor Thomas' research is focused on the study of the biology and clinical use of human dendritic cells in autoimmune disease. It has explored basic mechanisms of immunity and dendritic cell function in autoimmune disease. This has given rise to several clinical applications, including:

- An antigen-specific vaccine to treat rheumatoid arthritis
- A therapeutic platform for antigen-specific immunotherapy
- A novel diagnostic test for identification of those at risk of type 1 (juvenile) diabetes
- Novel immunotherapy for type 1 diabetes
- Research projects span from understanding dendritic cell function through analysis of signalling pathways, in vivo studies of tolerance, through to clinical trials of tolerance in autoimmunity, and clinical studies of risk factors in rheumatoid arthritis and type 1 diabetes.

This paper was delivered at the Emmanuel College Medical Dinner on 28 August 2009.

Can Doctors Change the World?

It will be clear to you, many of you being members of the medical profession, that the question is a rhetorical one. Of course doctors can change the world! I'd like to start out by giving two very obvious examples of doctors who changed the world.

The first is Albert Schweitzer, who died only quite recently in 1965, at the age of 90. He was a famous theologian, musician, physician and philosopher and the recipient of the Nobel Peace Prize in 1952, for his philosophy of the reverence of life. The philosophy rejected pessimistic philosophies prevalent in his day, claiming the end of the world, where man had no particular significance and life no relevance. On the other hand, he argued that respect for life, the conscious will to live and let live, leads the individual to the service of others. To this end, Albert - already a theologian and an accomplished organist - put himself through the study of medicine, funded himself to go to central West Africa and there established a clinic, and eventually a hospital, treating patients with infectious disease, for decades. His philosophy was simple: "Therefore search and see if there is not some place where you may invest your humanity." Throughout his adult life, he continued to preach and to advocate for peace, to speak out against nuclear tests and weapons. His Nobel lecture entitled "The Problem of Peace" is considered one of the best speeches ever given… "Example is not the main thing in influencing others. It is the only thing." From these inspiring quotes you can see that Albert Schweitzer changed the world not because he was a talented physician and treated thousands of poor Africans, but because of his philosophies, his conviction, his abilities in persuasive speaking, and the way *he* invested his humanity.

The second example is Sir Macfarlane Burnett - MBBS University of Melbourne 1922 - who became a virologist and immunologist, and the eventual director of the Walter and Eliza Hall Institute for Medical Research from 1944-1965. He won the Nobel Prize in Physiology or Medicine in 1960 for the discovery of acquired immunological tolerance. He was the first to propose the concept of self and non-self in the immune system, and developed the model of clonal selection in the 1950s for how self-tolerance comes about. Amazingly, very little alteration has been made to the model since. He predicted the possibility of allografting, which was later proven by Sir Peter Medawar who shared the 1960 Nobel Prize. As he himself, stated: "My part in the discovery of acquired immunological tolerance was a very minor one - it was the formulation of an hypothesis that called for experiment." He was also involved in public health policy. The pursuit of all this quality research in Australia produced a legacy that inspired generations of Australian scientists and set a course for Australian immunology as a highly productive and effective field.

It’s great to be inspired by these Nobel Prize winners. But let’s get to the real reason I asked the question at the start. Can mere mortals like us change the world?

I’ll tell you now about my job in medical research, and then (rather than go into all the gory details about my work), I’ll talk about what it’s like to be a medical researcher, how I got into it and how others, particularly the students in the audience, might end up taking a similar journey. My job involves a mix of clinical Rheumatology practice (one clinic of general Rheumatology and one dedicated to diagnosis and care of early rheumatoid arthritis patients), teaching of undergraduate medical students and science students and supervising PhD and Masters students, and research. I research rheumatoid arthritis.

My goal for the last 15 years has been to develop disease-specific vaccines for autoimmune diseases, including rheumatoid arthritis. I also research type 1 diabetes - here undertaking basic laboratory science with application and translation to the clinic. I am an inventor of novel treatments for rheumatoid arthritis and type 1 diabetes, and a novel diagnostic for diabetes. We are currently trialling our treatment for rheumatoid arthritis, and undertaking a longitudinal study in type 1 diabetes families to determine the utility of our diagnostic test in predicting the disease.

I am also the Deputy Director of Research at the Diamantina Institute. This is a role which encompasses mentorship and facilitation of others in their careers, policy development and strategic direction of the Institute. Overall this is a pretty big job description!

Why do I do research? First, there is the excitement, challenge and stimulation that goes with the job. Working out how to answer, and chipping away at answering some of the big questions about a disease - how to treat it or cure it - is what gets me out of bed in the morning! Being the first to make a new discovery is as thrilling today as it was when I got hooked on research 20 years ago. I do still love my job and wouldn’t swap it. Second, a research unit or institute is a wonderful environment in which to work. I work with a talented and stimulating bunch of people, who by-and-large share similar values (including a desire to change the world!). Not only do I work with these people, but I travel, so as to interact with similar-minded scientists worldwide. Our competition is international and our community is international. Through research, scientists make friends and lasting relationships across many countries of the world - this is truly a privileged way to work, perhaps unparalleled in other fields, (except by musicians I suspect) in the collaborative nature of work, that is markedly enhanced by interaction with others seeking similar goals.

Finally, there is one's capacity to make a contribution through research - to be truly the agents of change in the world, the prophets of our day.

I got started in research while I was training to be a rheumatologist in my home town, Perth, and I asked my mentor for a research project. Around the same time, I was studying for my physician's exam and we had a weekly journal club. An immunologist from the United States was visiting the clinical immunology laboratory at the hospital and he was invited along to the journal club so we could learn some immunology. Along with my research project and my mentor, he proved to be my inspiration. He also provided me with a list of top US immunologists to whom I wrote in order to undertake a Fellowship, after I passed my exam. As a result, I travelled to the University of Texas Southwestern Medical Center at Dallas to do my Doctorate in Medicine with Peter Lipsky. He was also a rheumatologist and running a large and well-funded lab, and he paid me to come! My project was in basic immunology. I asked how rheumatoid arthritis starts. I'm not sure anyone has fully answered that yet, but I have contributed to the field and seen the answer evolve through my career.

It was always our goal to go to the US to study or work after we were married. My husband did a Masters in Architecture with Charles Moore in Austin, Texas while we were there. In 1994 we returned to Australia, this time Brisbane, and my academic career began at The University of Queensland.

Is this a career for everyone; would I be good at this?

I think the following characteristics make for good researchers, especially in the basic sciences: 1. Creativity, lateral thinking and curiosity; 2. Determination, grit and focus; 3. Drive, ambition and the will to succeed; 4. Intellectual ability; 5. Organisation; 6. Enjoy writing and public speaking; 7. Analytical and critical ability. If you don't have the first gift, you'll never be attracted to research in the first place. If you don't have the second and third, you won't stay the course. Research is full of ups and downs - resilience is essential to both survival of the researcher and getting the world to know about the discovery. Writing and speaking are the ways we convey our discoveries and get new ideas out there - without these skills we are no more than a pair of hands. Critical analysis underlies any great piece of work - the finished product or publication is the result of many iterations. In order to pick a research project and a team to work with, it is important to understand who you are and how you work best. It will be clear by now that mentors and inspiring figures play a large part in our development as researchers, so it's important to get this right.

Are you an introvert or an extrovert? Introverts (Albert Einstein is a classic example) are focussed on their internal world, while extroverts on their social

contacts and network (the Immunologist Polly Matzinger is a good example). While extroverts make up about 70 per cent of the population, scientific researchers are enriched in introverts. Introverts think long and hard about a problem on their own or with a trusted few before divulging their ideas, so these can sometimes seem a bit whacky when they first start to communicate them. Think of the reception Charles Darwin received when he first put forward the Theory of Evolution! Introverts work best with low levels of external stimulation eg. lighting, music, chatter. Extroverts need high levels of external stimulation for optimal function and like to bounce their ideas off others. Polly Matzinger developed the "Danger Theory" of Immunity and took her ideas on a worldwide roadshow (filmed by the BBC) where she spoke to and received feedback from many scientists in large fora.

How do you learn best? Visual/spatial learners are good with detail, learn by seeing and watching demonstrations, remember what they write down and recall the placement on the page, like descriptive writing and are deliberate problem solvers, planning solutions in advance. Auditory/verbal learners like music, poetry, dialogues, debates, learn from verbal instructions, talk to themselves aloud, and talk through problems, weighing pros and cons. They tend to be global rather than detailed thinkers. Kinesthetic/tactile learners learn by hands-on experience, like direct involvement, enjoy performing arts and athletics, like working with materials and equipment, and experiment with ideas to see how they work in the real world. They remember what they have done rather than what they have seen or read. Technological learners are mechanically oriented, pick up technology without formal instruction, obtain much information electronically, play with and work with new software, hardware, gadgets, and integrate technologies with ease. Thus it's important for both supervisors and students to match individuals to the right project!

When planning a career, my advice is to plan backwards. By that I mean, start with a big dream - one that seems very important and pretty unlikely e.g. win the Nobel Prize. With at least one other person, brainstorm possible goals around that dream eg. find a cure for juvenile rheumatoid arthritis. Now work backwards: to achieve that goal, I'll need to be a world expert in eg. pediatric rheumatology and immunology, and understand how the pharmaceutical industry works. To do that, I'll need to get the best training possible: clinical training and specialisation, scientific training in specific world-class laboratories, perhaps do a stint in biotech or a pharmaceutical company.

Plan which parts of your training will be in Australia and which in other parts of the world. Australian science has a lot going for it right now. Australia leads the world in terms of the impact of its research in medical and biological science, adjusting for relative size of science system. Australians have a reputation for

good training and are highly sought-after as overseas post-docs and fellows. Medical research has had a funding boost over the last 7-10 years, and the old problem of the "brain drain" where our best and brightest are retained overseas, is reversing, leading to a very competitive environment locally. There is a strong commitment from many sources (eg. Australian Research Council, Queensland State Government) to bring Australians back to enrich and build the Australian scientific community. Moreover, the balance for stronger scientific financial support overseas is tipping since the global financial crisis. Thus, the future is bright for intellectual pursuit and leadership in Australia.

A worrying global trend, however, is the diminishing proportion of clinician scientists amongst medical scientists. The reasons are many, but include the difficulty of trainees committing time and loss of financial security to training in research, the increase in the proportion of female medical trainees, and their competing priorities of building a scientific career and starting and raising a family, and a generally more regulated and competitive research environment. This means that it is harder for clinical trainees to "dabble" in research than previously. Nevertheless, in my experience, clinical trainees are no less inquisitive than before. To capitalise on the tremendous contribution clinicians can make to medical research, we need to find new models and processes for incorporating clinicians into medical research questions and teams. It is important that opportunities are created for involvement of clinicians at all career stages in medical research, especially through collaboration with well-resourced research teams, who can help mentor, support and guide clinicians, with access to good questions, administrative and intellectual support for grants, ethics applications and paper writing, as well as laboratory or computer (eg. microarray) technology, so that projects can be at the cutting edge.

Another advantage of building such integrated teams, is that they will include allied health and nursing support, which may be essential to get a study off the ground. Scientific teams are connected, and being part of a research team can be the means to securing a post-doc, or fellowship overseas - or a first job. Alternative to integration into research teams, collaboration with the pharmaceutical industry is another possibility for some clinicians. Finally, funding models need to rethink the financial support of clinicians through PhD degrees. With increasing costs of undergraduate or postgraduate medical degrees, it is no longer feasible for many to take a massive three year pay cut to complete a PhD on a scholarship. The Queensland Government has initiated some impressive funding schemes to address this issue.

Despite equal numbers of male and female medical students, women are underrepresented in senior academic and hospital leadership positions. How do these few make it and stay there, and balance their careers with their family?

This has indeed been my experience, with women comprising only about 20 per cent of senior academics in either the Department of Medicine or Diamantina Institute. This proportion has not changed in the 15 years since my first academic appointment. While it may appear that child-bearing substantially impairs women's careers, senior women with children had a high overall degree of satisfaction with their careers when surveyed. Thirty percent felt they would have had more children if they had their time "again", and 30 per cent felt that children had enhanced or markedly enhanced their career progress. Children also benefit from contented working mothers. Academic women are in the privileged position of being able to work the hours they wish, according to the stage of their career and children. I wonder how I could have coped with the on-call hours of many of my clinical colleagues.

How have I balanced my career and aspirations to change the world with raising three children? I have tried to set personal and professional goals that were achievable. I knew I needed to work to reach the goals I had set. I employed good child carers and then, as much as possible, went to work without feeling guilty. It was nevertheless important to set limits around my work time, for the sake of creating family and leisure time, and not to feel guilty about that either! For things to work out, it was crucial to choose a partner and an employer who shared these goals with me. Observing and talking with dozens of women in science, I think these supports are key to retention of women in academic careers. The most difficult time for most of them is in mid-career, as they struggle to gain academic independence while raising a family. Without the support of my mentors, employer and husband at this time, I am sure my career would have floundered.

A mentor and a "soul mate" at work are invaluable for reality checks, advice and moral support. I have found these individuals mostly in other parts of the world, after we have met at conferences or on committees. It is a great joy to meet and catch up over the years.

Finally, life does not need to be harder than it already is. It is important to arrange the essentials eg. the daily commute, the school pick-ups or public transport, the chores, the exercise and cooking routines, so that they happen easily and without unnecessary extra effort or time. It has been said that behind every great man there is a great woman, and behind every great women there is a team of great women providing support. Busy mums in my experience understand, and busy mums help each other. Create time for the important things by removing the clutter of things that don't make a difference. It is important to learn to say no, and this means focusing on what is important and prioritising time for those things.

Finally, if the research doesn't quite end up changing the world, it doesn't mean you as an individual can't. As a doctor, and as a scientist, you are a leader in society, and you should be involved in the bigger picture – from giving back to your local community, to volunteering for disaster relief work with an international aid organisation such as Medicins sans Frontières, or joining an advocacy group like Physicians for Nuclear Disarmament. "Therefore search and see if there is not some place where you may invest your humanity." Life (and research) takes you into unimagined spaces. It's about the journey, not the destination.

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