

Chancellor, Vice-Chancellor, distinguished guests.

It is a great pleasure to be here. I want to begin by offering my congratulations to those who have graduated with their PhDs and won prestigious awards. It is a particular pleasure to be here at the University of Melbourne because our universities have several things in common including a shared former Vice-Chancellor and a number of collaborations. It was my pleasure today and yesterday to be able to talk with my collaborators, Geoff Donnan and David Howells. Our universities have staff exchanges through the Manchester-Melbourne Mobility fund and today I met members of the University of Melbourne who hold some of those mobility grants. We even have the same initials

When Glyn asked if I would deliver the Menzies Oration, I was enormously honoured and I considered how I could deliver something to a mixed audience that was of relevance to higher education. I proposed three areas to Glyn on which I'd given earlier talk:- the similarities and differences between Science and Arts, a summary my career including public communication, and our research. I was surprised when he replied to say, "Yes please, can you do all three? And you've got thirty minutes."

So if this doesn't work, it's Glyn's fault. I hope to be able to give some of my thoughts and comments on higher education throughout the next half hour. Let me begin with something that is extremely important to me, a matter of heroes, those who you revere, respect and learn from. A great hero of mine is Sir Peter Medawar, an immunologist and Nobel Prize winner who worked on transplant rejection. Sadly, his career was cut short by a series of strokes which is my own area of research, but more important to me were his writings on science. I would urge you all to read a small book called 'Advice to a Young Scientist'. You don't have to be a scientist and you don't have to be young to appreciate it. It includes many thoughtful comments. I begin with this, "One does not need to be terrifically brainy to be a good scientist. Most people who are in fact scientists could easily have been something else instead." I think we tend to feel that we are born a scientist or an artist. While that may be true for some, it isn't necessarily the case. I certainly wasn't aware of what I was going to become early in my studies.

Perhaps unusually, as I'm a professor of Physiology and very much a biologist, I dropped Biology at the age of 14 because I didn't find it particularly interesting. This is a good illustration of the importance of inspirational teachers whether it's at primary school, secondary schools or in university. Almost everybody I know chose their discipline because of a teacher who inspired them. I had inspirational teachers in Maths, Physics and Chemistry and in Art. Hence, to the dismay of my traditional girl's grammar school in the North of England, I chose to take those subjects for 'A' level. My choice of subjects didn't fit with what was expected of pupils, it didn't fit with the curriculum and it didn't even fit with the exam schedule. So, I attended the local Art School in the evenings.

Aside from the joys of studying art, there were three other important outcomes from attending art school. Later, when I was a poor PhD student, I earned some money from drawing cartoons for a company. Second, my art qualification gained me some credibility amongst those in the humanities when as a scientist, I became vice-president for research at the University of Manchester. Thirdly and perhaps most importantly, one of my fellow students at Art College was a handsome young man with a nice sports car, and we're still together today.

We ask young people to specialise rather early in their careers, which often means making a choice between sciences or arts because they are considered to be very different. C.P. Snow described 'The Great Divide' between arts and sciences, suggesting that he was among two groups who had almost ceased to communicate at all. This was not always the case. Another of my great heroes, Leonardo Da Vinci, was a great artist, a very accurate engineer and a biologist in his anatomical drawings. In fact, it surprised me to learn that apparently, the term "scientist" was first coined in 1833, relatively recently. It is often assumed that arts and science are intuitively different and that it's very difficult to span the two disciplines. Indeed, the arts we think of as being personal, reflecting about individual feelings, unconstrained by dogma, subjective, unique and even focussed in a different part of the brain to science which requires consistency, objectivity and replication. I have no doubt about the fundamental difference between objectivity and subjectivity, but I do think there are a number of things in common between the science and arts and many of the most talented people I know do manage to achieve both.

There are a number of similarities, between science and arts particularly in subjects such as photography, architecture, dance and music. One important barrier to working across disciplines is communication and even dialogue between the scientific disciplines can be limited by technical terms and jargon. So that's why an important job of universities, of students, and of academic staff is communication within their university and indeed, with the external world.

There are some aspects of science and arts which, I believe are very similar, one of which is creativity. Science is commonly taught as fact and theory in which intuitive leaps, imagination and creativity played no part. Yet most great scientists used their creativity, intuition and their imagination in making major discoveries. Creativity which we think of as being something new, originality of thought, inventiveness applies as much to the sciences as it does to the arts.

There is also a problem in public perception of scientists because many opinion polls suggest that while musicians are esteemed, novelists are hip, film directors are cool, scientists are unfortunately nerds. There is also a sense that we are born to be one or the other, in contrast to Medawar's views described above. Picasso said "Every child is an artist," I would add, "and a scientist." Every young person I've met has a curiosity about the world around them and how it works. Medawar also described what the diversity of scientists: "Among scientists are collectors, classifiers, compulsive, tidiers-up. Many are explorers, some are artists and others are artisans."

My choice of later study was based on the good advice of my art teacher who suggested that I might not have the talent necessary to make a living at art, so it would probably be wise to go into science. That I did and I went to study Physiology in London with no idea about my future career, until I began a research project in the final year of my degree. Science is about doing and discovering things, and as such research is a fundamental part of science education.

I was inspired in my final year to undertake research and I'll briefly tell you about some of the areas of my research. Initially, I studied the regulation of body weight, trying to understand why some people stay slim and others don't; why some people struggle not to lose weight while others seem to pile on the pounds with great ease. Body weight regulation is at its

simplest level about physics- energy balance. As described by the laws of thermodynamics, any energy we (or any other organisms) take in as food or drink either is largely burnt off as heat generated through the normal metabolic processes or through physical activity. When the energy taken in equals that which is expended, the energy content of the body-mainly fat and protein will stay the same. But if intake and expenditure are not balanced, the energy content of the body will change. Most of the energy we expend is produced as heat, mainly from normal body processes that continue even when we are asleep. Apart from in extremely active people physical activity is a relatively small part of total expenditure. As we are growing, most of the energy deposited in the body is as protein but unfortunately as we get older, the changes in energy content are almost all fat. A relatively small excess of energy intake will gradually result in excess fat deposition and obesity, whereas if energy intake is less than expenditure, body energy content and hence body weight is reduced.

My research was trying to understand which of those components of energy balance are regulated. At the time, it was assumed that it was the amount of food that was eaten that was the regulated component and that obesity results from excess intake or low physical activity, often referred to as "gluttony and sloth". Our research during and after my PhD contributed to a growing realisation that many animals and probably humans are also able to regulate their metabolism without consciously changing physical activity. We showed that animals can burn off extra calories using a specialised tissue called "brown fat" which helps small animals and babies to keep warm. We tried to understand whether or not humans can activate this brown fat to stay slim so stimulating brown fat might be a treatment for obesity.

Like all good physiologists, we did experiments on ourselves and our colleagues. I was a subject on an experiment which required eating an extra 3,000 calories a day for four weeks. I gained one kilogram. One of my unfortunate colleagues gained 14 kg and only managed to lose 2 kg after the experiment, so unfortunately is still quite obese. It was during this time that I first became passionate about communicating science because a Horizon Program was made about brown fat called the 'Fat in the Fire', when I took a routinely used drug called ephedrine to stimulate brown fat and demonstrate "hot spots" on my back using thermal imaging. We suggested that this might be brown fat. This was many years ago. Today modern PET imaging techniques are being used to more accurately identify brown fat in humans and aid the search for treatments for obesity.

A few years later, I relocated from London to Manchester. I was fortunate enough to have a Royal Society Research Fellowship which allowed me to establish an independent research career. I remained in the field of energy balance regulation, but rather than continuing research on obesity, I studied cachexia. This is the wasting condition that is associated with many diseases such as cancer and severe injury and can be the direct cause of death. Cachexia results in part from reduced food intake but is also associated with increased metabolic rate and raised body temperature, fever.

Increased energy expenditure (metabolism) in patients with severe burns, serious infection or multiple fractures contributes to serious weight loss, and we showed the brown fat is activated in many of these conditions. The next step was to try to discover what was causing the activation of brown fat and hence the increase in metabolism. As is so often the case, the clues came from a completely different field-immunology.

This was a very exciting time in immunology because of emerging discoveries of whole families of new molecules that contribute to the activation of a number of immune processes. These molecules were called cytokines and the first to be discovered, interleukin-1 (IL-1), was identified as a major driver of fever and its associated increase in metabolism. At the time, a colleague and I were working on the increased metabolism seen in stroke (damage to the brain caused by reduced blood flow and oxygen supply). We had a hypothesis that the cytokine IL-1 caused the increases metabolic rate and temperature after stroke.

We were fortunate that there is a naturally occurring blocker of IL-1, known as IL-1Ra which is also produced by the body in disease to prevent excessive actions of IL-1. We found that the IL-1 blocker did indeed prevent the increased metabolism and temperature. So our hypothesis was right and we were almost ready to publish our findings, with just one last “control experiment” to finish. We had to make sure that blocking IL-1 was specifically reducing the metabolic response to the stroke and not affecting the brain damage. To our surprise IL-1Ra dramatically reduced the extent of brain damage caused by the stroke.

This was quite a fundamental discovery and an example of what is relatively common in science-making new advances as a result of chance rather than planning. I had to then make the choice between staying in the field in which I was successful and reasonably expert, metabolism and cachexia, or completely change to the field of neuroscience to pursue our new findings. Against the advice of many of my colleagues I changed fields and since then, we have been working on brain diseases, stroke, brain injury and Alzheimer's, trying to understand how cytokines like IL-1 and inflammation contribute to these devastating diseases. The choice turned out to be a good one, as changing fields can be very stimulating. As one of my colleagues Andre Geim has said, “if you take the trodden path, you may find that all the grass has been eaten!”

Inflammation is a well-established cause of arthritis, asthma, psoriasis and inflammatory bowel disease. We are now starting to recognise that inflammation is also a major contributor to disorders like diabetes, obesity, atherosclerosis and diseases of the brain, and that the cytokine IL-1 is a key player in these conditions. We found that there is very rapid production of IL-1 in the brain after an injury and that when IL-1 is increased, it makes the injury worse. More importantly, blocking IL-1 reduces the extent of damage in a number of experimental brain disorders.

IL-1 has many complex actions on numerous cells in the brain. It acts on the endothelium, the barrier round the blood the vessels on the edge of the brain, and stimulates glial cells in the brain to produce toxins that kill neurones (nerve cells). It also has effects outside the brain the activate the liver, the bone marrow to produce immune cells that then travel to the brain to make damage worse. It's one of those vicious cycles in disease where one trigger seems to activate a cascade of events that can be catastrophic.

So intervening to block IL-1, for example with IL-1Ra (which is already used to treat arthritis) may indeed be an important treatment for brain disease. We have carried out a small clinical study to test the effect of IL-1Ra (compared to placebo) in patients with stroke. The results are promising because IL-1Ra is very safe and there was an indication that the patients who received the IL-1 blocker fared better than those that received placebo. We have just finished a larger trial of the IL-1 blocker in patients with subarachnoid haemorrhage and we are conducting a much larger trial in stroke. If the results are positive, we would be in

a position to conduct very large multi-centre trials which could lead to a potential treatment for stroke. This research has also taught me a great deal about patents and lawyers since the primary patent for IL-1Ra was held by an American biotechnology company while we filed a patent for the use of IL-1Ra to treat brain diseases such as stroke.

There are several reasons why I've been so passionate about a career in science. The first is solving problems and discovering things, secondly these discoveries could have real human benefit, but also because science is a very social activity which involves working with others, often with very different backgrounds. Certainly in science, and perhaps also in humanities, the lone individual academic is much less common and more academics are working in complimentary teams bringing together different skills. Several decades ago Peter Medawar noted that 'synergy and collaboration' are key to success in science and to moving up in a scientific career.

Medawar had much more to say about careers in science. He described senior scientists who served on "committees of grey heads, all confident on the rightness of their opinions and all making pronouncements about the future development of scientific ideas." I vowed I would never be one of those grey heads serving on numerous committees. Indeed, in an interview in 2002 for a New Scientist magazine about my career, I said I had three career aspirations: one was to be a professor, another was to become a fellow of the Royal Society and the third was to develop a new treatment for brain disease. When asked about taking on more senior roles, I said, "Yes, my ambition is that I will never take on an administrative role within a university."

That went badly wrong, largely thanks and to Alan Gilbert who moved from Melbourne to Manchester in 2004 when the two universities in Manchester, UMIST and Victoria University merged and he became the inaugural president and vice-chancellor. Within a few weeks of arriving in February, he persuaded me to become vice-president for research which meant overseeing research in humanities, in business, in physics, in nursing, in engineering. Sadly, as many of you know, Alan became really quite unwell from 2009 onwards and tragically died in 2010 when I took over as president and vice-chancellor.

The University of Manchester has much in common with the University of Melbourne. Each has many international students and staff, studying a similar range of disciplines and a very large alumni community. We have also both faced challenges of changes in the policies and funding from our respective governments and the increasing globalisation of universities.

A particularly important feature of the University of Manchester, in addition to our focus on research and education, is our commitment to social responsibility - 'making a difference'. This includes recruitment of a very high proportion of our students from disadvantaged backgrounds, an emphasis on volunteering and a commitment to wider communication of our research. When I joined the University of Manchester, most of the windows faced inward, our local communities around could not access much of the campus and knew little of what went on behind those 'ivory towers'. Alan Gilbert contributed significantly to changing our campus and developing our public spaces such as our museum, art gallery and Jodrell Bank and we greatly value public communication. Some of you may know one of our more famous staff, Professor Brian Cox who will be giving a series of major public science lectures in Australia.

One of the proudest activities of my career was delivering the Royal Institution Christmas lectures for the BBC in 1998. Many of my PhD students took part and one was subjected to a bath of freezing cold water so children from the audience could make measurements and better understand how we control our body temperature. It also allowed me to meet another of my heroes, Sir David Attenborough and many years later a little girl here who attended the lectures, came to study at the University of Manchester. Her mother sent me a photograph as she graduated with the first class degree in Chemistry and wrote me a short note to say, "You inspired me."

So my attempt to present here some of our research findings, a little of my career and the importance of communication, all in half an hour, may not have worked well, though as I said I say I blame Glyn for that. I hope I did manage to convey some of the things that I think are important in an academic career: passion, creativity, taking the unexpected path, choosing good mentors and heroes and communication, and that science and arts actually have much in common. My final thought "Still aspiring to be a famous scientist".