Australian Government

BIOBREAKFAST – BIOMELBOURNE NETWORK

KEYNOTE ADDRESS:

CAN AUSTRALIA AFFORD TO FUND TRANSLATIONAL RESEARCH?

PROFESSOR IAN CHUBB

30 MINUTES SPEECH PLUS 20 MINUTE Q & A

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Can Australia afford to fund translational research?

Good morning and thank you for inviting me to be here this morning.

I've been invited to speak about funding for Australian research, and in particular whether Australia should prioritize translational research.

As with many new concepts, and translational research has only come onto the scene in the last decade or so, if you were to ask ten people what it means, you're likely to get ten different answers. My favourite description is 'the bridge across the valley of death' where on one side of a great divide, you have doctors and medical practitioners, and on the other are the basic researchers. In between them you can draw what you like to emphasise the issue… But the essence of the analogy is that there is a gap between basic research and clinical applications, and it is to the detriment of our health care options.

We need some sort of link to facilitate a pathway from discovery to health. We need to take the research from bench to bedside and transform basic-science breakthroughs into clinical applications on an appropriate scale. Because when it comes to biomedical research, we have two main priorities:

The first is to ensure that Australia continues to contribute to the world's stock of knowledge through basic research. We punch well above our weight, producing 3% of the world's research with only 0.3% of the population. As a developed and rich country in a rapidly changing world, we have a responsibility to continue to strive to be a world leader in research. It is important that we contribute the knowledge and our skills to the world's stock. It is important that we be an anticipator and not just an adaptor. Just yesterday I was asked to comment on a view that Australia can't afford to do all this research (and I presume all this training); we should just buy-in what we need and adapt it – somehow by also buying-in the talent we need to do so. What a sad and narrow view of Australia's role and Australia's place.

The second priority is to improve the lot of the Australian people. Every time a researcher receives funding for a study into a certain gene, or a protein, there is an underlying hope that it will matter in a big way. That it will change the way we treat patients. That it will improve the health of our citizens. It is not necessarily about making money and filing patents, although they help, but most taxpayers want to see results that will help them and their loved ones.

Today, Australian biomedical research shares the tale of two cities: it is the best of times, and the worst. In some ways, the field is experiencing a golden age: the amount of basic research being conducted is sky high and budgets are far larger than they were in the 1980's or 90's.

A friend of mine is the editor of the highest-ranking journal in its field. He receives over 1000 papers per year, but can only publish 3% of submissions. According to him, the avalanche of outstanding research is overwhelming. I quote: "The amount of fundamental discovery is staggering and medical journals are choked with quality science."

That being the case, why is this the worst of times? Because, paradoxically, research advances (in quality and quantity) have not led to a marked increase in new cures. Much of what we now use to treat many common ailments is based on research from years ago.

Two examples come to mind – depression and obesity[1].

Depression is the second cause of disability. Suicide, which is mostly a consequence of depression, is the eleventh overall cause of death; it is the third cause of death in the age group of 15–24 years and the fourth cause of death in the age group of 25–44 years. Australia alone has spent $140 million on scientific research into depression in the last ten years.[2]

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[1] Licinio, J. 2001. Editorial: Why does the United States need a national centre for new cures? Molecular Psychiatry (2011) 16, 882–884;

[2] NHMRC expenditure by funding purpose 2002-2011

And yet most patients are treated with antidepressants such as the selective serotonin reuptake inhibitors, the second most widely sold class of drugs in America. But the action of the majority of antidepressants is based on a scientific principle elucidated in 1961. In essence, the sheer multitude of scientific discoveries over the last 40 years has shown little improvement for patients with depression[1].

In obesity, the story is similar. Two-thirds of Australians are overweight or obese. In the last 20 years, there has been an explosion in the science underlying the genetics, basic biology and neuroscience regulating food intake and satiety[1]. In the last ten years, we have spent almost $200 million on research[3]. And yet such knowledge has not been translated to any new drugs that decrease weight safely and effectively.

The paucity of new treatments is not restricted to obesity or depression—it cuts across most human diseases. And largely the cause of that is the valley of death.

It hasn't always been this way. In the 1960s, there were fairly strong links between basic and clinical research. Medical research was largely done by physician-scientists who also treated patients. But as molecular biology exploded, clinical and basic research started to separate. Nowadays, the majority of biomedical research is done by highly specialized PhD scientists who have never seen a patient before.

Likewise, many (not all) clinicians who treat patients have little time and sometimes little inclination to keep up with an increasingly complex basic literature, let alone do their own research. "At the same time, genomics, proteomics and all their cousins are generating such a volume of potential drug targets and other discoveries that the pharmaceutical industry is having trouble digesting them"[4]. With pharma spending more on research but delivering fewer products, it is no longer in a position to take forward most academic discoveries. Since 1996 in the US, pharma companies have increased their expenditure by 75% but their molecular entity output has fallen by 25%[4].

Today, it takes a minimum of 6.3 years for evidence to reach reviews, papers and textbooks. On average it *then* takes an additional 9.3 years to implement evidence from reviews, papers and textbooks into clinical practice[5].

Translational research is heralded as the answer. It has a key part to play in improving our lives and also in justifying taxpayer dollars. Because the underlying question *is always* 'is the country gaining the greatest possible practical benefit from its research investment?'

Academics often resent this question, longing for an era when the pursuit of knowledge was supported for its own sake. But to expect to do research 'just because' with no questions asked, is unacceptable in a climate where competition for funding is fierce.

By comparison to the investment in basic research, relatively little government funding or private capital is available for translational research. Since 2002, the NHMRC has increased its funding for translational research from 0.5% to about 4% - around $30 million in 2011[6].

By contrast, the US and Europe have invested heavily in translational research. In the US, the NIH have invested $480 million in its Clinical and Translation Science Awards, and another $500 million in a National Centres for Advancing Translational Sciences. And in the UK, they have recently invested 900 million pounds setting up a system similar to the US.

The organisers asked me to address the question of whether Australia can afford to fund translational research. The cogs have already started turning. This year the NHMRC has

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[3] NHMRC expenditure by funding purpose 2002-2011
[4] Butler, D. 2008. Translational research: Crossing the valley of death. Nature, 452, 840:842
[5] Balas and Boren, Yearbook of Medical Informatics, 2000
[6] NHMRC Research Funding 2002-2011 Annual Expenditure by Funding Purpose

committed $52 million to the cause in support of partnership programs and research grants. One particular success story is the Translational Oncology Research Collaborative Hub, bringing together pharmaceutical giant Pfizer with university and public funds[7]. But let me say that the economic situation in the US and UK is a catastrophe compared to Australia. But they have prioritized translational research. And on a broader international level, the consensus is that no matter how bad the economy is, this is something we need to invest in.

This isn't a case of cutting one particular area and transferring funds to a new area. Competition for grants and programs is already fierce, and no-one wants to see less funding in any one area. But we also know that squeezing money from governments can be like drawing blood from a stone right now, especially in these times of fiscal constraints. In the UK, they 'cut' their budget by a measley 0.9%, not something people can get *too* upset about, but returned it to the budget by making that 0.9% available for competitive grants for translational research. An innovative idea, and perhaps one for consideration here in Australia.

But let me go back to a point I made earlier. Funding research is all about return on investment. By funding basic research, we have seen that there is usually little return, certainly very little *immediate* return. Basic research is rarely developed in a practical way for doctors, hospitals or pharmaceutical companies (and it leaves the door open to those who might argue that we should just buy-in what we need).

But if we invest in translational research, the wealth of knowledge available will be amplified since it all of a sudden has clinical applications. A small investment in translational research, could lead to huge outcomes stemming from the basic research. Translational research, economically speaking, has a multiplier effect. Investing in translation leverages the investments made in biomedical science.

Of course for the moment, all of this is fairly hypothetical. There have been a few translational research success stories, but mainly, we are biding our time, waiting for our US and UK leaders to make the case. The National Institutes of Health began funding their translational research centres in 2006 in a progressive rollout, with the last round of centres receiving their funding only last year. It's too early to tell how successful they will be, and the onus is on the investigators to come up with success stories.

Measuring success however, always a tricky beast, becomes even more difficult in the face of long time frames and an audience beyond collegial experts. Surely, the traditional yardstick of publishing in highly ranked journals and being listed as one of the top academic institutions in the world is not enough. In fact, "one might even claim that the aim of publishing high-profiled papers is antagonistic to a successful translational process— publication rewards number and high visibility, whereas translational research is slow and the number of new therapies that make it to the clinic is very small"[8] . Describing a new compound that is the basis for drug development is not likely to make it into the 'high-profile' journal like nature or science, but confined to specialised literature instead.

Stemming from this is the obvious quandary of how to encourage scientists to set their careers towards translational research. How will we reward the work of researchers who embark on translational projects? Are we ready to go beyond the cult of prestige and impact factors when evaluating translational researcher? And what weight should we give to patents and intellectual property generation?

It may very well be the case that we need an entirely new evaluation system that recognises the links between academia and industry. From my time as a vice-chancellor I can see this may very well be a problem. There is a sort of anti-entrepreneurial culture that still prevails in

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[7]Carr, K. 2011. Opening of the Peter Maccallum Pfizer Translational Oncology Research Collaborative Hub transcript. Australian Government.

[8] Bornstein, S. and Licino, J. Improving the efficacy of translational medicine by optimally integrating health care, academia and industry. Nature, 17, (12): 1567-1569.

many places within the academic world that is recognised by others, not only myself[8]. But future leaders of translational research might require additional time to be evaluated for tenure, funds specifically aimed at paying for the less exciting aspects of translational research (toxicology or legal paperwork quickly come to mind) or time off the lab to work with industry scientists[8]. Even if Australia can afford to fund translational research, as a culture we need to be able to support it.

This culture must also cut across the silos of government research institutes, academia, hospitals and health care. In Australia and around the world, there are strict revenue streams for hospitals on the one hand and research organisations on the other. It doesn't help that the two report to different departments – Health for the former, and Education for the latter. These silos need to be broken down, and the NHMRC should be congratulated on their current work in setting up a network of Advanced Health Science Centres to do so.

So to conclude, can Australia afford to fund translational research? Funding is not a matter of 'well we've spent all our money, we will not fund anything from this point on'. Funding is a matter of prioritizing. Translational research is a priority, and the more our international competitors invest in it while we lag behind, the more challenges face us in the future. But as I argued earlier, funding is not enough. We need to change the way we recognize research, the way we engage between silos and the way we encourage future scientists. For translational research in Australia to be fully effective, we need more than funding, we need cultural change.

And we need to ask whether, given our commendable research strengths, Australia can afford **not** to fund translational research.