NATIONAL PRESS CLUB OF AUSTRALIA

Dr Elizabeth Finkel
Wed 5 June 2019

Today at the National Press Club, Australian science journalist and author, Dr Elizabeth Finkel. Dr Finkel has written two books about the stem cell and genome revolution and will outline how researchers are approaching the issue. That's today's National Press Club address.

Sabra Lane: Welcome ladies and gentleman to the National Press Club today and the Westpac address. My name is Sabra Lane. I am the Club's President. And today's speech will be given by Dr Elizabeth Finkel who is the Australian Society of Medical Research medal recipient for 2019. And to present her with that award - and I understand it's the first time a journalist has been given this award - please welcome Professor Anne Kelso, the Chief Executive of the National Health and Medical Research Council.

Prof Kelso: Thank you very much, Sabra, and good afternoon ladies and gentlemen. May I start by acknowledging the traditional custodians of the land on which we meet, the Ngunnawal people, and pay my respects to their Elders past and present, and also acknowledge all Aboriginal and Torres Strait Islander people who are with us at this event today.

Now, throughout human history society has been guided by storytellers, people who think deeply around the world around them and then use the power of language to teach, to challenge and to inspire. Today we need those powerful storytellers as much as ever and particularly in science and medicine at a time when knowledge and technology are expanding so fast their impact on every aspect of our lives is so profound and when our society faces complex decisions about the way we use this new knowledge and technology.

The Australian Society of Medical Research has made a brilliant choice in awarding their ASMR medal for 2019 to Dr Elizabeth Finkel.

Dr Finkel received her PhD in Biochemistry - so she's a real scientist - from the University of Melbourne in 1982, and in fact, she won an award for the best

presentation of original research at ASMR's National Scientific Conference in the year before.

She then undertook postdoctoral research training at the University of California, San Francisco, investigating the genes that sculpt a fruit fly egg into an embryo.

Returning to Melbourne in 1988 Dr Finkel left research for journalism broadcasting for ABC Radio National and writing for Science, the Lancet, Nature Medicine, journals any scientist here would be pleased to have on their CV, and New Scientist, The Age and The Monthly. She cofounded the science magazine 'Cosmos' and served as Editor-in-Chief from 2013 to 2018.

Dr Finkel has authored two books, one of which won the Queensland Premier's Literary Award in 2005, 'Stem Cells: Controversy at the Frontiers of Science' and the other 'The Genome Generation.'

She's been recognised with many awards for her journalism and in 2016 was appointed a Member of the Order of Australia in recognition for her service as a science journalist and author as well as a supporter of a range of Not-for-Profit organisations. While continuing to write, Dr Finkel now serves on advisory boards of centres of excellence in Australian archaeology and in gravitational wave research as well as the Melbourne Zoo and Latrobe University Press. She's a Vice-Chancellor's Fellow at Latrobe University.

As a scientist, a thinker and a storyteller, Dr Finkel is an outstanding ASMR medallist who I know will now teach, challenge and inspire us with her address. So, it's my very great pleasure to present the ASMR medal for 2019 to Dr Elizabeth Finkel.

Sabra Lane: If you are following this at home and you want to join the conversation when Dr Finkel delivers her address our Twitter user handle is @pressclubaust and the hashtag is MPC. Dr Finkel, congratulations.

Dr Finkel: Thank you. Thank you, Sabra. And thank you very much, Anne, for those wonderful words.

It is a great honour to be the ASMR medallist especially to be the first journalist to receive it albeit one who began as a medical researcher. I guess the ASMR selected me this year because they want me to spruik the value of medical research, perhaps tell a heroic tale of what happens when research escapes its laboratory cocoon and hits the streets. And thanks to serendipity I can oblige because we have arrived at a fascinating moment. Gene therapy, for so long something that belonged to the future has indeed just hit the streets.

A couple of weeks back you might have picked up a headline alerting us to the

most expensive drug in history ever, a one-off gene therapy cure for spinal muscular atrophy. Novartis has priced Zolgensma at three million Australian dollars. This is going to be a game-changer. Traditionally a parent of a baby with spinal muscular atrophy was told "Take your baby home, love him or her, have no false hope. The baby will die, paralysed, unable to eat or talk by the age of two." What's the narrative going to be now? "There is a cure but it's going to cost $3M." I think we are in for some poignant debates ahead.

But before I launch into my gene therapy story let me tell you a bit about my journey from researcher to journalist. I did my PhD at Melbourne University analysing the Vitamin D receptor and how it shape-shifts to switch on genes. I'd like to acknowledge here my supportive and inspiring professors, Jack Martin and John. I credit them with hammering the unruly thing that I was into shape. I got hammered some more as a postdoc at the University of California, San Francisco, where I participated in the unravelling of a mystery that mesmerised Aristotle; "How is an embryo fashioned from the mush of an egg?" We discovered the sculptures, homeobox genes in fruit flies. But the same genes are now known to be at work on human embryos and they are now being used to sculpt stem cells into laboratory-made pancreases or kidneys, an amazing example of the medical translation of blue sky research.

I left the lab behind in 1988 to pursue another passion, writing. And so, the fruit fly researcher metamorphosed into a journalist. My scientific training served me well. The values of journalism - to report without fear or favour, to drill-down until you find the complex and difficult truth of a story - are familiar to anyone hammered by the rigours of the scientific method. And there has never been a more important time to broadcast the scientific method to the general public.

We have entered the post-truth era. We're back to a dark age where people seem unable to differentiate between hype and the evidence of experts. Witness the victory for the anti-vaxxers in the US measles epidemic - currently at 970 cases. Measles was declared eliminated in the US in 2000.

As a science journalist I feel a particular sense of mission to do my bit to blow away the dark, dangerous fog of our times. And I take encouragement from the past. It was the scientific method developed by Galileo, Francis Bacon, and Newton in the 17th Century, that lit the minds of the enlightenment thinkers of the 18th Century. The flowering of reason and science across Europe and North America inspired the architects of the American Constitution; people like Thomas Jefferson, third President of the United States, whose sobriquet was "The Statesman of Science." I think scientists must once again do their bit to try and rekindle enlightened thinking to show how the scientific method works through the testing of hypotheses and the limits of certainty.

But let me get back to my main thing. When the ASMR informed me of the

award in February, that I would be addressing the Press Club, I was dumbstruck. But it turns out, thanks to serendipity, I had a story ready to go, an article that I had just penned for The Monthly on the Arrival of the Gene Therapy Revolution. So, the journos here must be really impressed that I'm on top of the gene therapy story just as it's breaking. You might think "Wow! Ella really has her finger on the pulse of science" and you'd be totally wrong because I totally missed the arrival of gene therapy. It wasn't something I picked up through a news media alert or a heads-up from a scientist. The person who alerted me to the arrival of the gene therapy revolution was a mother of two sick children.

I met Megan Donnell last August at a Melbourne conference for ethical start-ups called "Above All Human." We were both speaking on a panel for Eugene, a start-up which offers prospective parents a saliva test to check 300 genes.

If you were to meet Megan Donnell what you'd see is a very vibrant, appealing person. What you wouldn't see is simultaneously her life's greatest tragedy and her life's greatest mission. Both of her children suffer from the rare genetic illness Sanfilippo Syndrome. They lack a gene for breaking down heparan sulphate, the sugar that holds proteins in place in the matrix between cells. The high levels of the sugar poison the organs particularly the brain. In the normal course of the disease the children die in their teens, paralysed, unable to talk or eat.

When Megan Donnell's kids were diagnosed at the ages of four and two she was told "Do not have false hope." She didn't listen. The one time IT business manager started the Sanfilippo Children's Foundation. She raised a million dollars and invested in Abeona Therapeutics. It was a start-up company based in Ohio that was trialling gene therapy to treat her children's disease. Part of the deal for that million dollars was that the company would conduct trials in Australia as well as in the US and Spain. So far 14 children have been treated worldwide.

Megan Donnell's story stunned me. I'd written two books about coming medical revolutions: one on stem cells, the other on genomics. But when a medical revolution actually arrived I'd missed it. It was all the more remarkable because for six years I'd been the editor of a popular science magazine, Cosmos. We scanned the media releases for hot papers each week but gene therapy never came up on our radar, probably because we'd been dazzled by CRISPR, the powerful new technique that can rewrite the DNA of everything from mosquitoes to man. But CRISPR has barely entered clinical trials. Meanwhile there are already five gene therapy products on the market and 750 of them working their way through the pipeline.

The US FDA predicts that by 2025 between 10 to 20 gene therapy treatments will be added to the market each year. Some of the gene therapies what can only be described as biblical effects. Blind children are seeing, crippled children are

walking. The star example is the Novartis treatment for spinal muscular atrophy. Untreated babies die paralysed by the age of two, but those treated with Zolgensma have now reached the age of four and some are walking and dancing. In 2017 the FDA approved Luxturna, now marketed by Roche. This gene therapy can restore sight to children suffering from a form of retinal blindness that begins months after birth. For the first time that I can recall medical researchers are using a four-letter word, "Cure" because these treatments appear to have fixed the underlying condition especially when they are given early. Indeed, as part of a global trial, spinal muscular atrophy treatment is being offered to babies in New South Wales now at a few weeks of age before their motor neurones have started to wither.

These biblical gene therapy treatments have been over 30 years in the making and the saga of their journey to the clinic reveals some common plot lines with therapies now in the making like those from stem cells. The one thing, the potential of gene therapy was obvious as soon as Marshall Nirenberg cracked the genetic code back in the 1960s. In an editorial for science he wrote "This knowledge will greatly influence man's future for man will then have the power to shape his own biological destiny." But if the end goal was obvious the pitfalls were not.

What made the dream of gene therapy was viruses. They've involved to invade our cells and sneak their DNA in next to our own so that they can exploit our cellular machinery. But now we've turned the tables on them; we're using them like tiny spaceships inserting human DNA into their payload.

Throughout the 1980s genetic engineers learned to splice human DNA into the viruses and by 1990 we saw the first attempt to change the biological destiny of humans. It was to treat two children with a dysfunctional immune system. The results were hardly miraculous but they were promising and researchers raced to bring more potent viruses to the clinic. Racing was a bad idea.

In 1999 Jesse Gelsinger, an altruistic 18-year-old, paid the price. He had volunteered to try gene therapy for his inherited condition which stopped him from breaking down ammonia, a waste product of dietary protein. He'd managed his condition through medication and watching his diet and was a pretty healthy 18-year-old. But four days after his treatment at the University of Pennsylvania Jesse was dead, a result of a massive immune storm set off by trillions of adenovirus particles introduced into his body, the same viruses that cause the common cold.

Tragedy struck again in 2003. This one involved so-called "Bubble boys." They too carried an immune deficiency which sees them confined to a sterile bubble; even a common cold could be fatal for them. This time around the gene therapy appeared effective but within a few years of treatment five of the 20 boys developed leukaemia. The virus had inadvertently switched on a cancer-causing

gene.

The two tragedies set the field back and many researchers dropped out of it finding it very hard to get funding. But the quest to alter a blighted biological destiny kept others going. The key was to keep re-engineering the viral spaceships.

There was a project that reminds me of the evolution of powered flight. From the bi-planes that the Wright brothers flew in 1903 to the epic Apollo 11 flight to the moon in 1963, took about 60 years. The virus engineers have been a lot faster. Ten years after the disaster of the leukaemia-causing viruses they had re-engineered so-called "lentiviruses" not to activate cancer genes. They had also found other viruses that did not provoke catastrophic immune responses. Instead of the adenovirus the discovered its mild-mannered partner known as adeno-associated virus. There's a whole zoo of them and some species are particularly good at targeting specific organs. It is this new generation of viruses that are responsible for the biblical results that we are witnessing. AAV9 virus, for instance, can cross into the brain, and that's the one that's used to treat spinal muscular atrophy.

Telling the story of gene therapy, this turning the table on viruses and hacking into their code, that particularly fascinates me. I'm still, at heart, a biochemist. But as a journalist there's another intriguing angle to this story. Contrary to received wisdom we are seeing big pharma galloping in to treat very rare diseases. The spinal muscular atrophy market in the US is probably just 400 babies per year. Luxturna might treat 2000 cases of blindness per year. It's not the sort of market size that would bring joy to investors yet the companies think it's worth their while. Why? Well, for one thing, the FDA has provided incentives for orphan diseases, fast-tracking their passage through the tangled regulatory maze. And there is a convincing business case. If gene therapy is a one-shot cure then it really may end up saving the health system money.

Consider this calculation. For haemophilia the cost of injecting clotting factors per year is about $250,000, so over a 70-year lifespan that's 17.5 million, so a one million dollar price tag for a one-off treatment starts to look like a good deal. But drug companies say that justifies some of the most extraordinary prices for a drug that you've ever heard of. But of course, all this relies on the treatments truly being cures that last a lifetime, and that remains to be seen. So, Novartis is offering US insurers pay-as-you-go plans as well as refunds if the treatments don't work.

And how will Australia come at such prices? Well, we have been world leaders when it comes to bargaining down the price of exorbitantly-priced cures. In 2003, when the first drug for curing Hepatitis C came out the price was around $100,000 for a 12-week course. That then was most exorbitantly-priced drug that I'd ever heard of. But in Australia the government negotiated a price of

$9000 per patient and all 230,000 of those living with Hepatitis C are being treated for what is the lowest price in the world. In the US the cheapest price is at least $26,000 per person and only 15 per cent of patients have been treated.

Greg Dore at the Kirby Institute in New South Wales who participated in the discussions over Hep C pricing believes our model will work for the new gene therapy drugs - notwithstanding their eye-popping price tags - and the fact that the patient populations for these diseases will be tiny.

But the real reason drug companies are getting into gene therapy is not to treat rare disease; it's because they realise this technology will be a game-changer for medicine. They have already entered the field of cancer with a gene therapy for acute lymphoblastic leukaemia called CAR-T Cells, and Greg Hunt announced in April that the government will pay the cost, which is a cool $500,000 per treatment.

And after cancer what next? If you have a virus that can take a gene to the brain and cure spinal muscular atrophy what else could you cure? Alzheimer's disease? Strokes?

Australian researchers are jostling to be part of the gene therapy revolution.

Ian Alexander, a paediatrician and self-described tool-maker, together with virologist Leszek Lisowski, are engineering the next generation of virus vectors in their labs at the Children's Hospital at Westmead, Sydney. They are designing them to home efficiently to specific organs and produce therapeutic levels of proteins.

Curiously, it turns out that a major bottleneck is scaling-up the production of these exquisitely engineered viruses.

Who'd have thought there'd be a problem churning out the most abundant organism on the planet, viruses?

David Parsons in Adelaide is refining methods to deliver gene therapy to children with cystic fibrosis. The key is to get the viruses past the extremely viscous mucus that lines their lungs.

John Rasco in Sydney is a pioneer when it comes to treating patients with gene therapy having been a part of the international trials to treat patients with beta thalassemia.

Elizabeth Rakoczy in Perth is developing a treatment for macular degeneration.

And Alan Trounson, Australia's pioneer of IVF, and then human embryonic stem cells, who spent six years at the helm of the world's biggest stem cell

institute in California, is back for a third tour of duty at the frontier. His company, Cartherics, based at Melbourne's Hudson's Institute, is pushing ahead with the technology to develop off-the-shelf, universally compatible, CAR-T cells to attack ovarian cancer.

One thing is for sure: medicine is set for a major disruption from the arrival of gene therapy. As we enter an era where once incurable diseases become curable be prepared for some challenging debates about how to pay for gene therapy and the value of the human life. Thank you.

Sabra Lane: Thank you very much for your speech. Dr Finkel, right at the head you talked about the need to speak truth to power and that now is an important time for scientists to speak up in this area, you know, post-truth. How can scientists speak up? For example, you know on climate change, for example, a number of scientists are saying that the evidence is clear on that, that there's peer-reviewed evidence showing the world that there is a problem and yet they're drowned-out by a cohort of people saying that they are alarmists. How do you contend with that argument?

Dr Finkel: That we can't give up. We can't give up; we keep going. And personally, when I'm asked to defend climate science I really try to make transparent the nature of climate science, and the IPCC is exemplary in the way that process has been prosecuted.

So, you know, I think using science for something to beat people over their heads with is not the right approach. And what I like to point out is that when the IPCC first convened in the 1980s they put forward a hypothesis. They said, "Look, our measurements are telling us that the world is warming. At the moment we can't tell if that's just natural variation - we know that climate goes through cycles - but we have a suspicion it could have something to do with the greenhouse effect, but at the moment we can't be sure. Let's start watching this."

The next report that came out five years later they said, "Look, the data we've gathered now, you know, we're about 67 per cent confident that it looks like this is man-made emissions."

Five years later "Looks like 80 per cent." You see where I'm going with this.

The last one they released in 2014 the confidence was 95 to 100 per cent certain. This is the way science works; it's the best method we have. That would be my answer.

Sabra Lane: Sue Dunlevy.

Sue Dunlevy: Dr Finkel, the holy grail of genetic therapy is to use it in prevention eventually.

A Monash University expert has recently costed that it would cost about $600M to genetically screen all 18 to 25-year-olds for a set of key diseases that we know are caused by genes and that could be treated. How far off do you think it is before we do introduce a mass-screening program for these types of diseases and use it in prevention rather than just treatment? And secondly, where do we draw the line between a therapy and changing the human race? Because we've already seen a doctor in China genetically engineer some babies. He wasn't stopped by his mentors. Do we have in place the sort of culture that's going to keep this under control or are we at risk of changing the nature of what it is to be a human being if we're not careful?

Dr Finkel: Okay. So, the first one, mass-screening. So, we have pilots in place. We have one in place already in Australia as far as part of the Medical Research Futures Fund which was set up, I believe, in 2016 to try to bring research out of the labs and into the public sphere. And we're releasing it as a pilot program; I believe $2M to screen I think 10,000 prospective parents, couples. And we need to unveil it quickly.

I mean Makenzie's Mission was a result of a patients' lobby group. Mackenzie Casella's parents had a child with spinal muscular atrophy, and it is a parent's worst nightmare. Unfortunately at the time there was no therapy available for their child and they had to witness the agony that their child went through. And as part of a patients' group they lobbied very hard for this wider screening for prospective parents.

And certainly you would think "This is a no-brainer; let's roll it out." Nobody should have to go through that agony, or the agony that I see Megan Donnell going through now with her two children. However, rolling this out it needs to be done as a pilot because there are things we don't anticipate. So, for Mackenzie's Mission they are going to test somewhere between 500 and 1000 genes. I think they will all be extremely severe conditions. But there are discussions that need to take place as to "Well, what next?" Once parents get given this diagnosis that "You are each carriers" for some terrible disease, well, what next? What sort of counselling will follow? What will be the next steps? All this needs to be deliberated carefully. But I think it is coming; I think it's definitely coming, in my view, and it will be a great thing.

What do we do about changing the gene pool as He Jiankui tried to do?

He Jiankui was a maverick. What he did was completely indefensible and he has been punished by it, and there is new legislation now in China that should stop any scientists who also want to be that sort of a pioneer.

I think, you know, we're becoming pretty expert at seeing futuristic new technologies. I personally closely witnessed the debate over human embryonic stem cells and then therapeutic cloning to produce - for instance, take one of

my skin cells and turn it into perhaps a spare pancreas for me, therapeutic cloning of my skin cell. I think we're getting pretty expert at deliberating these kinds of issues and crafting thoughtful legislation which gives us the benefit without the risks. So, I'm not really too worried about it.

Sabra Lane: Simon Grose.

Simon Grose: Simon Grose from Canberra IQ. My question is about a revolutionary technology about 30 years or so old. It's about health, it's about biotech, it's also about agriculture and about the US legal system, and I'm talking about glyphosate, Round-up, which has been found by a couple of US juries, Californian juries, to cause a form of lymphoma, and this process go through the courts. The underlying pressure is coming from the anti-GM lobby. I wonder if you could have a view on the state of play there with glyphosate? It's been approved by regulatory agencies across the world. Do you back those agencies or do you still think there's doubt?

Dr Finkel: I find it a remarkable situation because the evidence for the toxicity of glyphosate - also everybody should immediately stop drinking red wine, and I hope you didn't have any meat because it is the exact same level of risk that this particular United Nations body which does their regulatory evaluation in a different way. I can't go into it here, but suffice it to say that glyphosate has been given exactly the same level of risk warning as red meat and red wine. So, I expect to see the same sort of suits for lymphoma against the manufacturers of red wine and butchers.

Sabra: There's an interesting question off the back of that. Those groups that are against genetically-modified crops, they say that, you know, we shouldn't be farming this stuff; we shouldn't be producing it. What's your view?

Dr Finkel: I'm aghast because it was a legitimate view maybe 40 years ago when GM crops first came out. Now, a tremendous amount of money and resources have gone in to testing the safety of GM crops, and like glyphosate, the regulatory organisations around the world; Europe, a very tough one, Australia, have all come out with a finding after hundreds of millions of dollars' worth of research to say that "GM crops are just as safe and just as dangerous as conventional crops. No food is safe." I mean I think 70 people died from eating organic beansprouts. We haven't had a single documented illness from eating genetically-modified food. We have lots of illnesses from eating naturally-grown corn from the carcinogenic toxins and funguses that grow on natural corn.

I'm aghast that science doesn't prevail, and particularly aghast because it has ... I mean at the beginning, all right, it's just Monsanto that's making this stuff, but it's not Monsanto; it's science groups all over the world. We have TJ Higgins here - my personal hero - who's been making GM cowpea for the

poorest of the poor subsistence farmers in Africa. Cowpea is poor man's meat and it's vulnerable to the predations of Hel - one of those moths, anyway. And you know, ha, ha, he's had to struggle to get that through but I think he has got it approved.

This is a humanitarian issue and this is now an environmental issue because we're facing climate change, you know we need all the tools we can get. So, I would really like to see trusted organisations like Greenpeace be held accountable when you know they're trusted by the community, what they say counts. Greenpeace were always my heroes, but why are they so anti-science, anti-environment and anti-humane?

Sabra Lane: Tim Shaw.

Tim Shaw: Sabra. Thank you, Dr Finkel. Tim Shaw, Radio 2CC here in Canberra, Member of the Board of Directors for the National Press Club.

My listeners understand medical research; they're excited when they hear about developments in that regard but they're not particularly clear on ethics; medical ethics, research ethics. You spoke about Jesse, you spoke about Bubble Boys. We just heard from Sue Dunlevy about the out-there Chinese work that was being done there. Where are we now in 2019 in terms of science research and the ethics behind it and the work we're doing there to stay on-track? And the ethical debates, you know, the right-to-lifers back in 2003 protesting when Christopher Reeve was invited by the New South Wales State Government to come and talk about the importance of stem cell research and the work that had been done there. Are you satisfied as a scientist and as a journalist that we've come a long way in that debate regarding medical and science ethical research?

Dr Finkel: I really am. And I'm full of admiration for Australia because as I say, I was involved in and watched very closely this process when we went through the stem cell era, and the Cloning Legislation, which really, you know, captured the public very, very easily. "Cloning! Oh, my God!" You know all the tropes we've seen on the movies, "It's coming." And I think we dealt with it in a very Solomonic way. We've got legislation which has held up wonderfully, and we're getting the fruits of that research, and you know I don't see any negative consequences of it.

Sabra: David Denham.

David Denham: David Denham, Preview magazine. First of all, thank you very much for that magnificent address -

Dr Finkel: Well, thank you.

David: - that was thought-provoking and impressive with the outcomes of the research.

And I'd like to ask you a question about the balance of the government's health funding because I know it's putting an awful lot of money through the National Health and Medical Research and the Cancer Fund for specific research, but you never hear anything about the prevention and what it's investing in the lifestyle manners to which we are accustomed to that lead to diabetes and air pollution and all this sort of thing. So, the question is, is the balance right, do you think, in the government between what it's investing in prevention of diseases , it is in solving these very important sharp to define ones which you are?

Dr Finkel: So, I think, yes, the basic science funding is in a bad way; it's gone down over the last 10 years, which is a little shocking. And the funding for the National Health and Medical Research Council, which is more at the basic end of research, has flat-lined. And this basic research is what feeds the translation of researchers. I said in my talk, I used to work on blue sky research addressing this problem that has mystified us since the time of Aristotle: "How does a mush of an egg sculpt itself into an embryo?" And I never thought this was going to be used to turn stem cells into brains in a dish that are now being used to screen for drugs for brain diseases. In fact, Megan Donnell, who gave me the low-down on gene therapy, when I saw her yesterday she told me now they've got this grant they're funding to make little brains in a dish out of the stem cells of children who have her children's disease, Sanfilippo. So, they're taking those stem cells. And thanks to the Cloning Legislation that we put in place they can turn those stem cells into little brains in a dish that have the underlying disease. And then they're going to test thousands of drugs to see if any of those drugs will make a difference to the health of those brain cells in a dish. So, yes, we need all parts of the research pipeline well-filled, well-funded.

Sabra Lane: Mark Metherell.

Mark Metherell: Mark Metherell from the Consumers Health Forum of Australia, Doctor. Congratulations on your medal, and as the first journo to take the gong, well done.

From your scientific and journalistic background what advice do you offer in terms of how the public and consumers at large should best be advised in responding to this enormous and disruptive influence of gene therapy and the whole genomics revolution where now people can get phone apps which can maybe tell them, you know, whether they are genetically predisposed to a particular illness even though it may be one chance in a thousand. Are we not facing a future where we're going to have, on the one hand, a whole group of people who are unable to afford treatment, and yet another group who are misguidedly seeking expensive treatment when there may be no clear safeguards?

Dr Finkel: It's a huge challenge, and that's what we've witnessed with stem cells. Patients

are impatient and they are prey to all sorts of bogus treatments. They'll sell their houses, go all over the world to have some sort of bogus stem cell therapy. It's an enormous problem. The stem cell researchers they put a lot of resources putting information out there to the public - Megan Munsie from the Australian Stem Cell Centre does a tremendous job with putting out public information. And I think "Where will we go with gene therapy?" At the moment with genetic testing, yes, we're already beginning to see a lot of that bogus stuff out there. "Yes, get a gene test and it will tell you the best diet to not put on weight." And you know it's kind of rooted in a little bit of evidence; it might make the difference between putting on half a kilo after a year or not if you absolutely stick to what they tell you. I'm not sure what we can do about that.

I do think we are going to be in for some - talk about ethical debates. I think we're really going to be in for some very poignant ethical debates coming very soon because of the price tags of these new gene therapies. And yes, in Australia because we've got a one-stop shop with the Federal Government buying drugs and universal healthcare, we did very well bargaining down Hepatitis C drugs. Is the same system going to work? I think this is going to be very interesting to watch.

Sabra Lane: Is that a question that's left up to a Pharmaceutical Benefits Scheme type committee? Like how do you decide what will be publicly funded and what cures won't be publicly funded and will require crowd funding? I mean we've seen a debate right now about the crowd funding of -

Dr Finkel: Yes. Yes.

Sabra Lane: - difficult surgeries. How do you make that decision?

Dr Finkel: Well, I guess the Department of Health will make a decision based on ... they have complex formulas here, you know, "What's the cost of the therapy compared to the amount, number of life years you get?" And actually, you know, so, Novartis was quite careful and negotiated a lot with health providers or insurance companies when they came up with their price, which is two million US, or three million Australian. And so, they've gone through these sorts of formulae. That's what the health economists at the Department of Health do.

Sabra Lane: Misha Schubert.

Misha Schubert: Dr Finkel, Misha Schubert from the Press Club Board as well. Thank you for your address.

Can I ask you to extend a little bit more that answer in relation to Mark and Sabra's question about the architecture that millions of Australians are grateful around Medicare and how it works and the financing and the Pharmaceutical

Benefits Scheme. You've said that perhaps that architecture might not be able to ... you know, we know through this next period and the bigger price tags that are attached to this. Can you give us your best assessment of where we're likely then to land? I know you said, well, there's some further thinking to be done at that Department of Health and the Pharmaceutical Benefits Scheme governance level about how do we pay for this so that we can ensure that that access is available to everyone regardless of their means?

Dr Finkel: So, I guess the saving grace here is that these diseases so far are rare. So, Greg Hunt has approved the CAR-T cell treatment for acute lymphoblastic leukaemia - that will be half a million dollars. I don't know what price the government will pay; it's half a million dollars on the books. We'll see what they will pay for that. As far as spinal muscular atrophy there's probably only going to be 20 or 30 cases per year and if the genetic screening gets taken up there will be less. So, I think that is the saving grace so far. I should say that as of about a year ago there has been a treatment for spinal muscular atrophy, not exactly a one-off gene therapy. It's called SPINRAZA, and you need to deliver this therapy three times a year if I recall correctly. And so, so far it looks like it is keeping these children developing relatively well; they are walking and so on. So, the government is paying for that. So, I think I calculated that after six years a single payment for Zolgensma, the single-shot gene therapy, would be equal to what they're paying for SPINRAZA. So, the government is not shying away from these treatments.

Sabra Lane: Jon Millard.

Jon Millard: Thank you, Sabra. Jon Millard, freelance. Thank you very much for your address, Dr Finkel, not only as a journalist but also as a [Unintelligible 0:51:58] biochemist.

My question involves inheritability. Given the possible elimination of some inheritable diseases there comes the question of reproduction and the random distribution of genes in ovaries and [Unintelligible 0:52:13] and so forth, and gametes, we call it Meiosis. There are obviously advantages in not having these inheritable disease passed on but do you think there also might dangers?

Dr Finkel: That's right, that's a very good point. Well, with spinal muscular atrophy there's no doubt about it; you don't want to have a child with spinal muscular atrophy. But why has it been kept in our gene pool? It is possible that people who are carriers might be protected from something. So, there are other diseases like that. The most famous is with sickle cell anaemia. If you are a carrier of the sickle cell anaemia gene you are protected from malaria, and huge numbers of people all over Asia and Africa are carriers of the sickle cell gene. But if both of your parents have it and you get a double-dose then you suffer from anaemia and you're disadvantaged. Now, if we were to get rid of that gene from the gene pool, you know, then we don't know what's happening in the future, we're

seeing viral outbreaks all the time. It protects you from malaria but what else might it protect you from?

An interesting example that I came across is a gene that predisposes you to Crohn's Disease; it's called NOD2. So, if you found out that you were a carrier of this gene you might want to have IVF and make sure that your child will not carry it; you'd screen away those embryos. But it turns out that the NOD2 gene gives protection against leprosy. So, we don't know. It's one of the dangerous areas, one of the fraught areas that we have to look at going forward.

Sabra Lane: Ken Randall

Ken Randall: Dr Finkel, several previous questions have almost touched on this, but given your varying distinctions in treading both sides of the fence, what do you regard as the biggest public policy issues facing the Government after the election and perhaps the biggest two or three, in fact?

Dr Finkel: I hadn't prepared for that one. Climate. How are we going to move forward on a rational roadmap for dealing with our emissions? I happen to know someone who put forward a very good, rational roadmap. Funding of science. As I said before, basic science funding has seen its budget drop. Is it okay if I just sort of stick to health and science or do you want me to speak about the whole thing? There are some things to look at with the Medical Research Futures Fund which is very exciting and changing the landscape of medical research in Australia. But it's challenging because the traditional model of research is bottom-up where the pool of researchers come up with brilliant ideas and put them forward for a competitive assessment. But the Medical Research Futures Fund is a top-down thing where the Government, advised by experts, decides on what the priority areas are, and it's fascinating, but exactly how that is administered in a very transparent way still needs to be fine-tuned.

Sabra Lane: In the fragmented media environment that we face now in the era of social media what is your advice to young people about the value of long-form journalism given that it's what you do; you specialise in that. What is the value of it?

Dr Finkel: So, it was interesting. So, as the Editor of Cosmos, which for me was a wonderful arena to showcase what long-form journalism could be, I think after we'd been going for a few months Bill Condie, one of my editors, said, "Ella, we have to get online news happening; we've got to get the eyeballs and the hits." And "No, no, that's not what I want. You know I want every story edited to within an inch of its life and you just can't do that if you're producing five or six stories a day." So, we had almighty clashes. What can I say? Bill was right. You know, we got to a fantastic following online, you know - I can't remember - hundreds and hundreds of thousands of hits, wonderful metrics. And that's what people look at. So, even people like the Chief Scientists would

tell me "No, no, it's great. You know I want a quick-fix every day; I just want to check the Cosmos website. I don't want to do a deep-dive; I just want to know what the big stories are of the day. You know, I'll do my deep-dive some other time." So, okay, I understand the short-form, the news things, the Tweets, they serve their purpose; they're alerts, so "This is what's going on." And then you come to places like Cosmos or The Monthly to do your long-form read, and that's where long-form journalists like myself will try to put the pieces together to show you what the whole picture is.

Sabra Lane: Sue Dunlevy.

Sue Dunlevy: So, the upside of what you're talking about is the great therapies that can cure some of these diseases, but the risk is that to find out whether you may be predisposed to these diseases you need to be tested, and there have been suggestions that we should test every child at birth and read their whole human genome. And how do we deal with the fact that some people may not want to know that they're at risk of these diseases? How do we deal with the fact that insurance companies might decide not to insure you or charge you very high premiums of they get hold of the results, or that you may end up not being given a job or that your life prospects may be changed by the findings of those tests? Are we equipped to sort of tread that tightrope currently?

Dr Finkel: When was that move 'Gattaca' made? I think we've had lots of time to prepare for it. They are all very big issues and we're already seeing them played out. Just recently - what was it called - the proposal to do medical records online, your medical record?

Sabra Lane: My Health Record.

Dr Finkel: My Health Record. I think we're getting well-practiced for the day when that will come. So, yes, they're very important, and not theoretical issues - we've already seen them played out. I think we're very practiced.

Sabra Lane: Simon Grose.

Simon Grose: Simon Grose, Canberra IQ. Let's talk about an emerging GM debate. The CRISPR technology that you mentioned in your speech. You've got a national audience. Please explain the CRISPR technology and how you would assess the potential for good and the risks?

Dr Finkel: Right. Okay. So, you all use Microsoft Word and you all edit your documents. So, the beauty and the power and why it's captured the imagination, it's like the "Find/Edit" function. So, gene therapy, you package up a whole gene in your virus and you send it in and it sits alongside what's already in your DNA code and compensates for the missing or faulty gene. But the idea with CRISPR is that you would still have to package it up in a virus to get it to where you want

unless you're doing what the Chinese scientist did and was using an egg cell where you know you could just inject it directly into the egg cell. But if you're going to use it in people for treating diseases you have to do exactly the same thing that the gene therapy pioneers have made available to us: package it up, put it in a virus. And then what happens when the virus delivers its payload to perhaps, let's say, a child with spinal muscular atrophy, what it will do is it will find the faulty part of that DNA and it will edit it and it will correct the error.

So, what is so powerful about CRISPR is its precision and that you might be able to target not just one mutated site but many, because the drawback with gene therapy is you've got to put a whole gene into this payload, into the little virus spaceship, and that has been a limitation. So, in Duchenne's muscular dystrophy it's an enormous gene; it's been hard to fit it inside the viral payload. But if now you're going to use CRISPR just to fix what was missing you're going to be able to fit it in. And going forward, if we're talking about a few things you'd like to fix, well, that's all going to be possible, and that's why CRISPR has dazzled us. And its precision. Well, we thought it had enormous precision. But what we're finding now is it's not as precise as what we thought; it does have off-target effects. And that's why we need to "Whoa, slow down" before you start putting CRISPR into the clinic. So, I believe, if memory serves me correctly, that there was reason to suspect that the experiment the Chinese scientist did was likely to have effects on other genes in those children, so it's certainly not ready for prime time.

So, the potential is that going forward, I mean you've got a blank slate; you can change so many genes. And if we ever got to a point where we thought "Hey, it is all right to change human biological destiny" because look what's happening, we're not fit-for-purpose any more. I fully expect my son and his partner, Cam, to live maybe to be at least 100, maybe 110, but are they going to be fit-for-purpose? You know, we can't yet cure dementia. You know they may get osteoporosis. Sadly I've got it; I might have passed it on. I think we have to look at the ethical argument that going forward we know what genes to fix there. You know the APOE4 gene gives you enormous protection against Alzheimer's Disease. We know genes that will protect you against osteoporosis. We know the genes to protect you from cancer. So, we've got some very interesting ethical debates ahead of us. When that technology gets to the point where we believe it's safe I think there are ethical explorations worth having.

Sabra Lane: Excellent. Everybody please join me in thanking Dr Elizabeth Finkel. And on behalf of the Club I'd like to say thank you very much for coming here today.

Dr Finkel: Thank you, Sabra.

Sabra Lane: Guest membership here.

Dr Finkel: Uh!

Sabra Lane: You get free car-parking upstairs. And when you get a spare moment and you don't want to continue reading about gene therapy for a couple of hours -

Dr Finkel: All right.

Sabra Lane: - that's 'Stand and Deliver,' the history about the club.

Dr Finkel: Oh, wonderful. Thank you.

Sabra Lane: Thank you.

Dr Finkel: Thank you very much.