Senate Community Affairs Committee
Inquiry into Legislative Responses to the Lockhart Review

QUESTION ON NOTICE

Senator Gary Humphries requested Do No Harm – Australians for Ethical Stem Cell Research to provide comment on the paper "Key Recent Advances in Human Embryonic Stem Cell Research" prepared by Dr Nicholas Gough and Associates.

This paper, together with a cover report signed by Sir Gustav Nossal and Dr Graham Mitchell, was made public by the Victorian Government on October 2, 2006.

The following comments are an edited version of Do No Harm's response to this paper published as a blog at davidvangend.blogspot.com on 10 October, 2006.

Dr Graham Mitchell and Sir Gustav Nossal, trading as Foursight Associates Pty Ltd[1], a company in strategic alliances with JBWere Private Equity Fund, Challenger Biotech Capital Ltd and KPMG Melbourne, claim in their report[2] to Premier Steve Bracks and Victorian Minister for Innovation, John Brumby that: "**a broad SCNT approach** is required for stem cell-based regenerative medicine to **achieve its undoubted promise**."

The Foursight report mentions **three hurdles** to using embryonic stem cells for therapies. These are (a) transplant rejection; (b) guidance of the ES cells down the correct pathways of differentiation and (c) ensuring that cells of such great proliferative potential do not develop into cancers, even on rare occasions.

The Foursight report enthusiastically proposes SCNT (cloning) as the way to overcome the transplant rejection hurdle:

"If **transplant rejection is the biggest single concern** then this is where the **extraordinary, legislatively-constrained technology of SCNT** – somatic cell nuclear transfer- **comes into its own**. Clearly, SCNT has the potential to overcome the transplantation barrier through "personalization" of the ES cells."

The Foursight report fails to address the other two hurdles or to explain what possible reason there is to lift the legislative ban on cloning now before these hurdles are overcome in animal models. What is the point of being able to do stem cell transplants that won't be rejected but cannot be reliably differentiated into the required cell types and have a tendency to form cancers?

The Foursight report also glosses over a fourth hurdle, the **problem of abnormalities in genetic coding**, referring to two papers demonstrating equivalence between mouse ESCs from cloned mice with those from fertilised mice. However, given the very evident problem of abnormal genetic programming that is a feature of reproductive cloning of animals[3], proof that programming and epigenetic effects do not occur in

[1] http://www.foursight.com.au/index.htm
[2] http://www.business.vic.gov.au/busvicwr/_assets/main/lib60041/sti_stemcell.pdf
[3] http://newton.nap.edu/books/0309076374/html/41.html#pagetop

SCNT-derived cell lines will require much more work than this, including especially study of expression of a very much wider array of genes.

The Foursight report is a brief attachment to a longer report, **the Gough report**, prepared by Dr. Nicholas Gough of Nick Gough & Associates Pty Ltd, biotechnology consultants with a declared interest of holding options to acquire ordinary shares in the Singaporean stem cell company ES Cell International Pte Ltd.

The Gough report admits that "Whilst generation of personalised ES cells by SCNT for specific patient is a theoretical option, given the high costs and length of time involved**, it is unlikely that production of personalised therapeutic tissues by genomic replacement would represent a practical strategy**."

There you have it.

In other words, SCNT for actual therapies is "not a practical strategy".

Rather, according to the Gough report, hope lies in producing "a bank of some 150 human ES lines [that] could provide a beneficial match for 25 to 50% of potential recipients in a target population (and a 95% chance of providing a full match for at least 8% of patients". [Such a bank could be developed under Australia's existing law only no-one has got ESCs to work safely and efficaciously yet.] Oh, and in other ways, yet to be discovered, of overcoming the transplant rejection hurdle.

There is thus a blatant contradiction between the two parts of this hybrid report that has led Premier Bracks to claim[4] "While there is much to do and the road in curing these diseases is a long one it is clear from this report that our greatest roadblock is our scientists' inability to perform this work [cloning] in human cells in Australia" and his Minister for Innovation, John Brumby to claim that "SCNT remains the only tool available that can create 'tailored' stem cells that would be a genetic match to a patient."

The Foursight part of the report claims that cloning will overcome the transplant hurdle but the Gough report, whose comprehensive literature review and analysis is said to have informed the views of the Foursight team of Mitchell and Sir Gus, states that "**it is unlikely that production of personalised therapeutic tissues by genomic replacement would represent a practical strategy."**

The Gough report really only commends cloning as a means to "allow the generation of ES cells derived from individuals with specific genotypes for dissection of complex multigenic diseases, such as Alzheimer's disease, motor neurone disease, and others of unknown cause or multigenic origin. The ability to generate specific differentiated progeny cells that express aspects of a disease phenotype from ES cells of defined genotype will be invaluable in dissection of such diseases."

Minister Brumby[5] picks up on this alternative purpose for cloning – the only "practical" use according to the Gough report – in his statement that "SCNT remains

[4] http://www.premier.vic.gov.au/newsroom/news_item.asp?id=959
[5] http://www.premier.vic.gov.au/newsroom/news_item.asp?id=959

the only tool available that can create 'tailored' stem cells that … would help to **model diseases for drug discovery**."

This completely ignores the still unanswered and seemingly unanswerable challenge to the would-be cloners from Professor Alan Mackay-Sim at Griffith University in his submission[6] to the Lockhart Review:

"It is often stated that therapeutic cloning will be required to investigate the biology of certain diseases and to find cures for them by studying embryonic stem cells and their progeny derived from the patients… Therapeutic cloning is a long and laborious procedure that will require donor oocytes and will produce an inexact "copy" of the donor because of the handful of mitochondrial genes passed on through the donor egg. An alternative source of stem cells for these important investigations is provided by adult stem cells. In our lab we already have **over 40 adult cell lines derived from persons with schizophrenia, Parkinson's disease, motor neuron disease, and mitochondrial disease**. These are **relatively easily obtained**, **easy to grow in the lab** in large numbers and amenable to cell culture studies, gene expression profiling and proteomics analyses. **It is probable that such cell lines as these will render therapeutic cloning irrelevant** and impractical."

[6] http://www.lockhartreview.com.au/_pdf/201-300/LRC217.pdf