IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the matter of:

Reexamination Control. No. 95/000,154	Art Unit: 3991
U.S. Patent No. 7,029,913	Examiner: Gary L. Kunz
Issued: April 18, 2006	
Inventor: Thomson	
For: PRIMATE EMBRYONIC STEM CELLS	

DECLARATION OF DR. ALAN O. TROUNSON, PH.D.

SIR:

I, Alan O. Trounson, do declare and state:

My Education and Experience Related to Human Embryonic Stem Cell Research

1. I received a B.Sc. (Hons II) in 1968 and a M.Sc. in 1971 from the University of New South Wales, Sydney, Australia, a Ph.D. in 1974 from the Faculty of Agriculture, Sydney University, Australia, and a Doctor Honoris Causa in 2003 from the Faculties of Medical Sciences and Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium.

2. I am currently Director of the Monash Immunology and Stem Cell Laboratories (MISCL) and founded the Australian Stem Cell Centre in 2003. In addition to my current

appointments, I have held numerous university, Australian government and other professional appointments, including Director of the Centre for Early Human Development, Faculty of Medicine, Monash University (1985 – 2002), Director of the Master of Clinical Embryology Course, Faculty of Medicine (2003 – 2005), Member, Prime Minister's Science, Engineering and Innovation Council Working Group on New Fields of Medicine (2000 – 2002), Director, Victorian Endowment for Science, Knowledge and Innovation (VESKI Ltd) (2003 – present), President, Australian Society for Reproductive Biology (1993 – 1995), Board Member, International Society for Stem Cell Research (2002 – present), and Chair, Government Affairs Committee, International Society for Stem Cell Research (2006 – present).

3. Since receiving my Ph.D. in 1974, I have performed extensive embryonic research, including research specifically related to embryonic stem cell derivation and culture. For example, from 1977 – 1995, I pioneered the development of human in vitro fertilization and embryo transfer for the treatment of human infertility, human embryo freezing, oocyte and embryo donation, micromanipulation of human oocytes and embryos, including sperm microinjection procedures, embryo biopsy for diagnosis of genetic disease, and in vitro maturation of human oocytes. From 1992 – 1995, I established an Animal Research Program involving embryo multiplication and transfer (EMT) in cattle involving oocyte maturation, enucleation, cell fusion, development of embryonic stem cells and nuclear reprogramming, had a continuing research interest in molecular biology and in vitro culture techniques and also initiated research on the development of human embryonic stem cells for studies on differentiation, transplantation and gene therapy.

4. From 1996 – 1999, at the Institute of Reproduction and Development, Monash Medical Centre, Melbourne, Australia, I led research programs involving stem cell biology, which included the control of stem cell renewal, Oct IV expression of embryonic stem cells, molecular manipulation of embryonic stem cells, and human pluripotential cells, which included development and characterisation of human embryonic stem cells, factors monitoring undifferentiated embryonic stem (ES) cells in vitro.

5. I have achieved significant development of human embryonic stem cells, including controlled differentiation of human embryonic stem cells into pure nerve cells in culture and directed differentiation of human embryonic stem cells into respiratory and prostate tissues.

6. A copy of my curriculum vitae is attached hereto as Exhibit 1.

Reexamination of the '913 Patent

7. I am familiar with U.S. Patent No. 7,029,913 to Thomson titled, "Primate Embryonic Stem Cells" ("the '913 patent").

8. I am aware that the Foundation for Taxpayers and Consumer Rights, through its counsel the Public Patent Foundation, requested reexamination of the '913 patent, that the U.S. Patent and Trademark Office granted that request and issued an Office Action on March 30, 2007, and that the owner of the '913 patent submitted a Response to the Office Action on May 30, 2007. I have reviewed the '913 patent, the Office Action and the Response. I have also specifically reviewed the '913 patent's claims as amended by the Response.

9. I am aware that the initial application leading to the '913 patent was filed on January 20,

1995.

Robertson '83 and Robertson '87

10. I am familiar with Robertson, et al., "Isolation, Properties, and Karyotype Analysis of Pluripotential (EK) Cell Lines From Normal and Parthenogenetic Embryos," *Teratocarcinoma Stem Cells*, Cold Spring Harbor Laboratory, Cold Spring Harbor, volume 10, pp. 647-663 (1983) ("Robertson '83") and Robertson, Elizabeth J., "Embryo-Derived Stem Cell Lines," *Teratocarcinomas and Embryonic Stem Cells; A Practical Approach*, Oxford: 1RL Press, Ch. 4:71-112 (1987) ("Robertson '87").

11. Robertson '83 and Robertson '87 each describe a method for deriving pluripotential mouse ES cells. The process detailed in Robertson '83 and Robertson '87 and the claims of the '913 patent differ only in that Robertson '83 and Robertson '87 isolated mouse ES cells while the '913 patent claims human ES cells. In January, 1995, it was obvious to me and others in the art of ES cell derivation that the process taught by Robertson '83 and Robertson '87 for isolating mouse ES cells could be used to isolate human ES cells. The motivation to do so came at least from the general understanding in the field of the applicability of mouse studies to human research. It was also common sense that methods successfully developed for deriving mouse ES cells could be expected to work to isolate human ES cells, because one of the most important reasons for performing mouse research is to apply the results of that research to humans.

Piedrahita

12. I am also familiar with Piedrahita, et al., "On The Isolation Of Embryonic Stem Cells:

Comparative Behavior Of Murine, Porcine And Ovine Embryos," *Theriogenology*, 34(5):879-901 (1990) ("Piedrahita"). I have reviewed Piedrahita and specifically its teaching regarding the isolation of ES cells for several different mammalian species.

13. Piedrahita described a way to isolate murine ES cells and putative porcine and ovine ES cells. Piedrahita and the claims of the '913 patent differ only in that Piedrahita attempted to isolate murine, porcine and ovine ES cells while the '913 patent claims human ES cells. However, in January, 1995, it was obvious to me and others in the art of ES cell derivation that the process taught by Piedrahita for isolating mammalian ES cells could be used to isolate human ES cells. The motivation to do so came at least from the general understanding in the field of the applicability of mouse, pig and sheep studies to human research. It was also common sense that methods successfully developed for deriving murine, porcine and ovine ES cells could be expected to work to isolate human ES cells, because one of the most important reasons for performing murine, porcine and ovine research is to apply the results of that research to humans.

Robertson '83, Robertson '87 and Piedrahita

14. At the time the first application leading to the '913 patent was filed, one of ordinary skill in the art would have combined the teachings of Robertson '83, Robertson '87 and Piedrahita, as they each relate to the derivation of mammalian ES cells. Further, Robertson '87 was written by the same author as Robertson '83 and both Robertson '87 and Piedrahita expressly cite Robertson '83.

15. Robertson '83, Robertson '87 and Piedrahita combined teach virtually the same method

for isolating ES cells of various mammalian species. They only differ from the '913 patent claims in that they isolated mouse and putative porcine and ovine ES cells while the '913 patent claims human ES cells. However, in January, 1995, it was obvious to me and others in the art of ES cell derivation that the process taught by Robertson '83, Robertson '87 and Piedrahita for isolating mammalian ES cells could be used to isolate human ES cells. The motivation to do so came at least from the general understanding in the field of the applicability of studies on the mouse and other mammalian species to human research. It was also common sense that methods successfully developed for deriving murine ES cells and putative porcine and ovine ES cells could be expected to work to isolate human ES cells, because one of the most important reasons for performing murine, porcine and ovine research is to apply the results of that research to humans.

Bongso et al.

16. I am also familiar with Bongso et al., 9 Human Reprod. 2110-17 (1994) ("Bongso et al."). I have reviewed Bongso et al. and specifically its teaching regarding the isolation of human ES cells. The human ES cells isolated and cultured by Bongso et al. are identical to those of the claims of the '913 patent except that Bongso et al. cultured their cells using LIF and not feeder layers, while the instant claims use feeder layers and not LIF. Bongso et al, 2110.

17. Two of the authors of Bongso et al. and I recognized by 1995 that using feeder layers with or without LIF would work to successfully maintain isolated human ES cells over an extended period of time. We made this recognition well before Dr. Thomson published the results of his work, as it was obvious to us at the time that, had Bongso et al. simply not dispensed with the

feeder layer in the passaging step, they would have successfully developed the claimed invention. A successful result of such an obvious modification was entirely predictable to us.

18. We co-authored Reubinoff et al., 18 Nature Biotech. 399-404 (2000) ("Reubinoff et al."), in which we discussed this recognition:

> Since [Bongso et al.] did not use embryonic feeder cell support (required for proliferation of pluripotent human EC and nonhuman primate ES cells) but relied instead on LIF supplementation of the culture medium, these cells eventually underwent differentiation or death. Therefore, we subsequently employed a culture system incorporating embryonic fibroblast feeder cell layers to derive human ES cells from blastocysts. While this work was in progress, Thomson and coworkers reported the derivation of ES cell lines from the human blastocyst.

Reubinoff et al., 399. I also cited our work in Trounson, *The Derivation and Potential Use of Human Embryonic Stem Cells*, 13 Reprod. Fertil. Dev. 523-32 (2000) ("Further studies (A. Trounson, A. Bongso and C.Y. Fong, unpublished data) used 35 human blastocysts in an attempt and establish human ES cells in the period 1995-1998.").

In Closing

19. I have not been compensated by either the Foundation for Taxpayer and Consumer Rights, the Public Patent Foundation or any other party in exchange for this declaration, nor do I have any financial interest in the outcome of the reexamination of U.S. Patent No. 7,029,913.

20. I declare that all statements made herein of my own knowledge are true and that all statements made herein on information are believed to be true. I further declare that these statements were made with knowledge that willful false statements and the like are punishable by fine or imprisonment or both under Section 1001, Title 18 of the United States Code.

27.6.2007

Date

ALAN O. TROUNSON, PH.D.

EXHIBIT 1

CURRICULUM VITAE