Exhibit 5
Part 48
To Third Declaration of
Joseph N. Hosteny

DETAILED ACTION: ***Reexamination: Granting of Request***

Procedural Posture:

The Third Party Request (dated 17 July 2006) for *inter partes* reexamination of claims 1-3 of United States Patent Number 7,029,913 (Thomson) is acknowledged.

Decision Granting the Order

A substantial new question of patentability affecting claims 1-3 of United States Patent Number 7,029,913 (Thomson) is raised by the request for reexamination.

Information Disclosure Statement

The Information disclosure statement (PTO-1449) filed on 17 July 2006 has been considered.

Ongoing Duty to Disclose

The patent owner is reminded of the continuing responsibility under 37 CFR §1.985(a) to apprise the Office of any litigation activity, or other prior or concurrent proceeding, involving Patent No. 7,029,913 throughout the course of this reexamination proceeding. The third party requester is also reminded of the ability to similarly appraise the Office of any such activity or proceeding throughout the course of this reexamination proceeding. See MPEP §§ 2686 and 2686.04.

Substantial New Question of Patentability (SNQ) Raised By the Request

For "a substantial new question of patentability" to be present, it is only necessary that:

A. The prior art patents and/or printed publications raise a substantial question of patentability regarding at least one claim i.e. the prior art teaching is such that there is a

substantial likelihood that a reasonable examiner would consider the teaching to be important in deciding whether or not the claim is patentable; and it is not necessary that the prior art establish a prima facie case of unpatentability and;

B. The same question of patentability as to the claim has not been decided by the Office in a previous examination or pending reexamination of the patent or in a final holding of invalidity by the Federal Courts in a decision on the merits involving the claim. See MPEP §2642.

For a reexamination that was ordered on or after November 2, 2002 (the date of enactment of Public Law 107-273; see Section 13105, of the Patent and Trademark Office Authorization Act of 2002), reliance *solely* on old art (as the basis for a rejection) does not necessarily preclude the existence of a substantial new question of patentability (SNQ) that is based exclusively on that old art. Determinations on whether a SNQ exists in such an instance shall be based upon a fact-specific inquiry done on a case-by-case basis. For example, a SNQ may be based solely on old art where the old art is being presented/viewed in a new light, or in a different way, as compared with its use in the earlier concluded examination(s), in view of a material new argument or interpretation presented in the request. MPEP 2258.01.

Scope of Reexamination

The following issue raised in the request:

The `913 Patent is causing significant Public Harm (see the request pages 2-3)

The reexamination proceeding provides a complete reexamination of the patent claims on the basis of prior art patents and printed publications. 37 CFR §1.906, MPEP

2658. The third party discussion of Harm caused by the `913 Patent (Request pages 2-3) is clearly outside the scope of reexamination and thus has no bearing on the raising of SNQ.

Priority

U.S. Pat. No. 7,029,913 issued from application 09/982,637, filed 18 October 2001; which is continuation of application 09/761,289 filed on 16 January 2001, now abandoned; which is a continuation of application 09/106,390 filed 26 June 1998, now Pat. No. 6,200,806; which is a divisional of application 08/591,246, filed 18 January 1996, now Pat No. 5,843,780; which is a continuation-in-part of application no. 08/376,327, filed 20 January 1995, now abandoned.

The Thomson 7,029,913 *Patented Invention*

In the Thomson `913 patent 3 claims are present, of which claim 1 is the only independent claim. Claims 2 and 3 depend from claim 1.

Independent claim 1 is drawn to an in vitro cell culture of human embryonic stem cells which possess the following four functional characteristics: (1) capable of proliferating in in vitro cell culture for over one year without the application of exogenous leukemia inhibitory factor, (2) maintain karyotype in which the chromosomes are euploid through prolonged culture, (3) maintain the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (4) are inhibited from differentiation when cultured on a fibroblast feeder layer.

Claim 2 that depends from claim1and further requires that the stem cells of claim 1 spontaneously differentiate to trophoblast and produce chorionic gonadotropin when

cultured to high density.

Claim 3 which depends from claim 1 further requires that the stem cells of claim 1 be negative for the SSEA -1 marker and positive for the SSEA-4 marker and express alkaline phosphatase.

Documents Cited By The Requester:

1. **Robertson et al.** Teratocarcinoma Stem cells, 1983, 647-683, Cold Spring Harbor Laboratory, United States of America (**Robertson et al, 1983**).

2. **Robertson et al.** "Embryo-derived stem cell lines," Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, 1987, Chapter 4: 71-112, Oxford: IRL Press, England (**Robertson et al, 1987**).

3. **Piedrahita et al,** Theriogenology, November 1990, v 34, n 5: pages 879-901 (**Piedrahita, 1990**).

4. **Declaration by Dr. Jeanne F. Loring (July 17, 2006).**

Discussion of the Cited Documents and Raising of an SNQ

1. **Robertson et al.** Teratocarcinoma Stem Cells. 1983, 647 - 683, Cold Spring Harbor Laboratory, United States of American (Robertson '83).

The Third Party asserts that the Robertson '83 reference in combination with another reference (Robertson '87 and Piedrahita) would render claims 1 - 3 of the '913 patent obvious.

Robertson '83 reference was neither cited nor used in a rejection in the application which issued as the '913 patent.

Robertson '83 teaches a step-by-step process for isolating pluripotential mammalian ES cells. The Robertson '83 process includes the steps of i) isolating blastocyst, ii) removing the ICM from blastocyst, iii) placing the ICM on fibroblast cells, iv) isolating the stem cells and v) maintaining the isolated ES cells on feeder layers. The ES cells taught by Robertson '83 are pluripotential and are maintained over a significant time period and retained a normal euploid karyotype.

The Robertson '83 reference raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Robertson '83 reference teaching to be important in deciding if one or more claims of the '913 patent are patentable. Accordingly, Robertson '83 raises a substantial new question of patentability as to claims 1 - 3, which question has not been decided in a previous examination of the 7,029,913 patent.

2. **Robertson et al.** "Embryo-derived stem cell lines,"Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, 1987, Chapter 4: 71 - 112, Oxford: IRL Press, England (Robertson et al. 1987).

The Third Party asserts that Robertson '87 in combination with other teaching (Robertson '83 and Piedrahita et al.) would render claims 1 - 3 of the '913 patent obvious.

The Robertson '87 reference was neither cited nor used in a rejection in the application which issued as the '913 patent.

Robertson '87 teaches a step-by-step process for isolating pluripotential mammalian ES cells.

Robertson '87 reference raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Robertson '87 reference teaching to be important in deciding if one or more claims of the '913 patent are patentable. Accordingly, the Robertson '87 reference raises a substantial new question of patentability as to claim 1 - 3, which question has not been decided in a previous examination of the '913 patent.

3. **Piedrahita et al.**, Theriogenology, November 1990, v34, n5 ; pages 879 - 901.

The Third Party requester asserts that Piedrahita alone or in combination with other reference teaching (Robertson '83 and Robertson '87) renders claims 1 - 3 of the '913 patent obvious.

The Piedrahita reference was cited in a rejection in the parent application 08/376,327 (abandoned) (see the request at pages 10 - 11). However, Piedrahita was not applied in a rejection to the present claims of the '913 patent, and further Piedrahita is now being presented and/or viewed in a new light or in a different way, as compared with its use in the earlier concluded parent application examination, in view of a material new argument or interpretation presented in the request.

"The existence of a substantial new question of patentability is not precluded by the fact that a patent or printed publication was previously cited by or to the Office or considered by the Office."

For any reexamination ordered on or after November 2, 2002, the effective date of the statutory revision, reliance on previously cited/considered art, i.e. "old art" does not necessarily preclude the existence of a substantial new question of patentability

(SNQ) that is based exclusively on that old art. Rather, determination or whether a SNQ exists in such an instance shall be based upon a fact-specific inquiry done on a case-by-case basis. See MPEP §2242.

Piedrahita teaches a method of isolating murine (rodent), porcine (pig) and ovine (sheep) ES cells (see page 882-883). The blastocyst are isolated and then the cells from the ICM are isolated. The ICM is then placed on embryonic fibroblast feeder layer. After plating, the growing ICM is dissociated and replated onto fresh feeder layer. ES cells are selected based on large nucleus and prominent nucleoli. The selected ES cells are cultured on fresh feeder layer to prevent differentiation. Piedrahita's ES cells are pluripotential, maintained for a significant time period and retained a normal euploid karyotype.

The Piedrahita reference raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Piedrahita reference teaching to be important in deciding if one or more claims of the '913 patent are patentable. Accordingly, the Piedrahita reference raises a substantial new question of patentability as to claims 1 - 3, which question has not been decided in a previous examination of the '913 patent.

4. **Declaration by Dr. Jeanne F. Loring (17 July 2006)**

The Third Party asserts that the Loring declaration in combination with other references (Robertson '83, Robertson '87, and Piedrahita) would render claims 1-3 of the '913 patent obvious.

The Loring declaration was neither cited nor used in a rejection in the application which issued as the '913 patent.

The Loring declaration does not raise an SNQ because this declaration is neither a printed publication nor a patent and a reasonable examiner would not consider this declaration of Loring in deciding the issue of patentability.

The consideration under 35 U.S.C. 303 of a request for ex parte reexamination is limited to prior art patents and printed publications. See Ex parte McGaughey, 6 USPQ2d 1334, 1337 (Bd. Pat. App. & Inter. 1988). Thus an admission, per se, may not be the basis for establishing a substantial new question of patentability. See MPEP §2217. "The decisions cited in MPEP 2258 and 2258.01 for determining the presence of absence of a 'substantial new question of patentability' in *ex parte* reexamination proceedings apply in *inter partes* reexamination proceedings, since the statutory language relied upon in those decisions, which is taken from the *ex parte* reexamination statue, is also found in the *inter partes* reexamination." See MPEP §2658(I.)

Conclusion

In view of the above, the request for reexamination is **GRANTED.**

A substantial new question of patentability affecting claims 1-3 of United States Patent Number 7, 029,913 B1 is raised by the present request for inter partes reexamination.

Claims 1 - 3 of United States Patent Number 7,029,913 will be reexamined.

An Office action on the merits does not accompany this order for *inter partes* Reexamination. An Office action on the merits will be provided in due course.

Extensions of Time

Extensions of time under 37 CFR §1.136 (a) will not be permitted in *inter partes* reexamination proceedings because the provisions of 37 CFR §1.136 apply only to "an applicant" and not to the patent owner in a reexamination proceeding. Additionally, 35 U.S.C. §314(c) requires that *inter partes* reexamination proceedings "will be conducted with special dispatch" (37 CFR §1.937). Extensions of time in ex parte reexamination proceedings are not available for third party requester comments, because a comment period of 30 days from service of patent owner's response is set by statute. 35 USC §314(b)(3)

Service on the Other Party (3rd Party Request)

After the filing of a request for reexamination by a 3rd party requester, any document filed by either the patent owner or the third party requester must be served on the other party (or parties where two or more third party requester proceedings are merged) in the reexamination proceeding. 37 CFR 1.903; MPEP 2666.06.

Patent Owner Amendment

Patent owner is notified that any proposed amendment to the specification and/or claims in this reexamination proceeding must comply with 37 CFR §1.530(d)-(j), must be formally presented pursuant to 37 CFR §§1.52(a) and (b), and must contain any fees required by 37 CFR §1.20(c). See MPEP 2250 for guidance as to the manner of amending.

Future Correspondence

All correspondence relating to this *inter partes* Reexamination proceeding should be directed to:

By Mail to: Attn: Mail Stop "Inter Partes Reexam"
Central Reexamination Unit
Commissioner for Patents
P. O. Box 1450
Alexandria VA 22313-1450

By FAX to: (571) 273-9900
Central Reexamination Unit

By Hand: Customer Service Window
Attn: Central Reexamination Unit
Randolph Building, Lobby Level
401 Dulany Street
Alexandria, VA 22314

Conferee:

Conferee:

Gary L. Kunz
Primary Examiner
Art Unit 3991

PTO/SB/58 (04-05)
Approved for use through 04/30/2007. OMB 0651-0033
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

(Also referred to as FORM PTO-1465)

REQUEST FOR *INTER PARTES* REEXAMINATION TRANSMITTAL FORM

66548 U.S. PTO
95000154
07/17/06

Address to:
Mail Stop *Inter Partes* Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Attorney Docket No.:

Date: July 17, 2006

64660 U.S. PTO
07/17/06

1. [X] This is a request for *inter partes* reexamination pursuant to 37 CFR 1.913 of patent number 7,029,913 issued Apr. 18, 2006. The request is made by a third party requester, identified herein below.

2. [X] a. The name and address of the person requesting reexamination is:

The Foundation for Taxpayer & Consumer Rights

1750 Ocean Park Blvd., Ste. 200

Santa Monica, CA 90405

b. The real party in interest (37 CFR 1.915(b)(8)) is: The Foundation for Taxpayer & Consumer Rights

3. [ ] a. A check in the amount of $ _____ is enclosed to cover the reexamination fee, 37 CFR 1.20(c)(2);

[ ] b. The Director is hereby authorized to charge the fee as set forth in 37 CFR 1.20(c)(2) to Deposit Account No. _____ (submit duplicative copy for fee processing); or

[X] c. Payment by credit card. Form PTO-2038 is attached.

4. [X] Any refund should be made by [ ] check or [ ] credit to Deposit Account No. _____. 37 CFR 1.26(c). If payment is made by credit card, refund must be made to credit card account.

5. [X] A copy of the patent to be reexamined having a double column format on one side of a separate paper is enclosed. 37 CFR 1.915(b)(5)

6. [ ] CD-ROM or CD-R in duplicate, Computer Program (Appendix) or large table
[ ] Landscape Table on CD

7. [ ] Nucleotide and/or Amino Acid Sequence Submission
If applicable, items a. – c. are required.

a. [ ] Computer Readable Form (CRF)
b. Specification Sequence Listing on:
i [ ] CD-ROM (2 copies) or CD-R (2 copies); **or**
ii [ ] paper
c. [ ] Statements verifying identity of above copies

8. [X] A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included.

9. [X] Reexamination of claim(s) 1 - 3 is requested.

10. [X] A copy of every patent or printed publication relied upon is submitted herewith including a listing thereof on Form PTO/SB/08, PTO-1449, or equivalent.

11. [ ] An English language translation of all necessary and pertinent non-English language patent and printed publications is included.

07/18/2006 MSALDANA 00000003 95000154
01 FC:1812 8800.00 OP

[Page 1 of 2]

This collection of information is required by 37 CFR 1.915. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop *Inter Partes* Reexam, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

United States Patent and Trademark Office
- Sales Receipt -
07/20/2006 MSALDANA 00000001 95000154
01 FC:1813 8800.00 OP

12. [X] The attached detailed request includes at least the following items:

a. A statement identifying each substantial new question of patentability based on prior patents and printed publications. 37 CFR 1.915(b)(3)
b. An identification of every claim for which reexamination is requested, and a detailed explanation of the pertinency and manner of applying the cited art to every claim for which reexamination is requested. 37 CFR 1.915(b)(1) and (3)

13. [X] It is certified that the estoppel provisions of 37 CFR 1.907 do not prohibit this reexamination. 37 CFR 1.915(b)(7)

14. [X] a. It is certified that a copy of this request has been served in its entirety on the patent owner as provided in 37 CFR 1.33(c).
The name and address of the party served and the date of service are:

Nicholas J. Seay, Quarles & Brady LLP

P.O. Box 2113, Madison, WI 53701-2113

Date of Service: July [redacted], 2006; or

[ ] b. A duplicate copy is enclosed since service on patent owner was not possible.

15. Correspondence Address: Direct all communications about the application to:

[ ] The address associated with Customer Number: [ ]

OR

[X] Firm or Individual Name	Public Patent Foundation				
Address	1375 Broadway, Suite 600				
City	New York	State	New York	Zip	10018
Country	U.S.A.				
Telephone	(212) 796-0570	Email	info@pubpat.org		

16. [ ] The patent is currently the subject of the following concurrent proceeding(s):
- [ ] a. Copending reissue Application No. _____.
- [ ] b. Copending reexamination Control No. _____.
- [ ] c. Copending Interference No. _____.
- [ ] d. Copending litigation styled:

_____

_____

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

_____ July [redacted], 2006

Authorized Signature For Third Party Requester — Date

Daniel B. Ravicher — 47,015

Typed/Printed Name — Registration Number, if applicable

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT NO.: 7,029,913

ISSUED: April 18, 2006

TO: Thomson

FOR: PRIMATE EMBRYONIC STEM CELLS

ATTACHMENT TO FORM PTO-1465,
REQUEST FOR *INTER PARTES* REEXAMINATION

SIR:

On behalf of the Foundation for Taxpayer and Consumer Rights ("FTCR"), a nationally recognized not-for-profit organization that represents the interests of taxpayers and consumers, the Public Patent Foundation ("PUBPAT") respectfully requests *inter partes* reexamination under 35 U.S.C. §§ 311 – 318 and 37 C.F.R. § 1.913 of every claim of United States Patent No. 7,029,913 ("the '913 patent") issued April 18, 2006, to Thomson because they are all invalid under 35 U.S.C. § 103 and their existence is causing significant public harm.[1] FTCR, the real party in interest, hereby certifies that the estoppel provisions of 37 C.F.R. § 1.907 do not prohibit this request for *inter partes* reexamination.

1 A copy of the '913 patent is attached hereto as Appendix A.

THE '913 PATENT IS CAUSING SIGNIFICANT PUBLIC HARM

Human embryonic stem ("ES") cell research possesses great promise to be the next frontier of medical advance. Scientists already believe that human ES cell research will produce new ways of not just treating, but preventing, a wide range of diseases, including AIDS, diabetes, Parkinson's, Alzheimer's and heart disease. Although the federal government has limited its funding of human ES cell research, many states, including most notably California which created a $3 billion state taxpayer-funded institute for stem cell research in November 2004, have chosen to provide the support that is needed to foster such research here in America.

To achieve the promise of human ES research, however, scientists need to not only be funded, they also need to be free of unjustified restraints on their work. Unfortunately, human ES cell researchers are currently being restrained by the '913 patent and two other related patents, U.S. Patents Nos. 5,843,780 ("the '780 patent") and 6,200,806 ("the '806 patent"). These three patents, which broadly claim any primate or human ES cell, are being widely and aggressively asserted be their owner against every human ES cell researcher in the United States. *Licensing Fees Slow Advance of Stem Cells*, Nature 435:272 (May 19, 2005).

By demanding significant financial consideration before allowing research to be performed, the owner of the '913, '780 and '806 patents is impeding, and in some cases literally stopping, domestic human ES cell research at its infancy. *Id.* This not only harms scientific advance here in the United States, it also has a harmful economic impact on Americans by diverting taxpayer dollars meant for research to pay for licensing fees. In the words of one

industry insider, this aggressive patent assertion is "stifling industrial research and investment." *Id.*

Although these scientific and economic concerns are admittedly not grounds to grant this request for reexamination, FTCR respectfully requests that they be considered when determining whether questions regarding the validity of the '913 patent merit review by your office. As set forth more fully below, FTCR believes that the '913 patent is invalid and, as such, should be eliminated as an impediment to American human ES cell research.

THE SUBSTANTIAL NEW QUESTIONS OF PATENTABILITY

The substantial new questions of patentability raised by this request are whether all 3 claims of the '913 patent were obvious in light of 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, 10:647-663 (1983) ("Robertson 1983"), 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 1987") and Piedrahita, et al., "On The Isolation Embryonic Stem Cells: Comparative Behavior Of Murine, Porcine And Ovine Embryos," *Theriogenology*, 34(5):879-901 (1990) ("Piedrahita"), either separately or when viewed together.[2]

These are substantial new questions of patentability because neither Robertson 1983 nor Robertson 1987 was of record during prosecution of the '913 patent and Piedrahita was not of record during prosecution of the instant application that led to the '913 patent. A detailed

2 Copies of Robertson 1983, Robertson 1987 and Piedrahita are attached hereto as Appendix B.

explanation of the pertinency and manner of applying Robertson 1983, Robertson 1987 and Piedrahita to every claim of the '913 patent is set forth below.

ROBERTSON 1983, ROBERTSON 1987 AND PEIDRHITA, EITHER SEPARATELY OR TOGETHER, RENDERED OBVIOUS THE CLAIMS OF THE '913 PATENT

Robertson 1983 was published in 1983, Robertson 1987 was published in 1987 and Piedrahita was published in 1990. The earliest application to which the '913 patent claims priority was filed January 20, 1995, more than a year after Robertson 1983, Robertson 1987 and Piedrahita were each published. Therefore, Robertson 1983, Robertson 1987 and Piedrahita are each prior art to the '913 patent under 35 U.S.C. § 102(b).

Robertson 1983 and Robertson 1987 Rendered the '913 Patent Obvious

More than a decade before the initial application leading to the '913 patent was filed, Robertson 1983 taught a step-by-step process for isolating pluripotential mammalian ES cells. Robertson 1983's process included the steps of: (i) isolating a blastocyst, (ii) removing the ICM from the blastocyst, (iii) placing the ICM on fibroblast cells, (iv) isolating stem cells once they became apparent, and (v) maintaining the isolated ES cells on feeder layers. Robertson 1983 at 649. Robertson 1983's ES cells were pluripotential, were maintained over a significant time period and retained a normal euploid karyotype. *Id.* at 647, 654 and 660 ("the B2B2 line has now been shown to retain normal XY karyotype after more than 45 passage generations").

A few years later, Robertson 1987 again taught the step-by-step process for isolating pluripotential mammalian ES cells, this time giving even further detail regarding each specific step. For example, Robertson 1987 gives highly technical instruction on preparing feeder

layers, collecting blastocyst stage embryos, transferring the embryos into culture, culturing the blastocysts, disaggregating the ICM, identifying ICM-derived colonies, expanding ES cells and culturing ES cells. Robertson 1987 at 76-94. Since Robertson 1983 and Robertson 1987 were penned by the same person and since Robertson 1987 expressly cites Robertson 1983, one of ordinary skill in the art would have been motivated to combine their teachings. Robertson 1987 at 112 (*citing* Robertson 1983).

The '913 patent contains only 3 claims, which read:

> 1. A replicating in vitro cell culture of human embryonic stem cells comprising cells which (i) are capable of proliferation in in vitro culture for over one year without the application of exogenous leukemia inhibitory factor, (ii) maintain a karyotype in which the chromosomes are euploid through prolonged culture, (iii) maintain the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) are inhibited from differentiation when cultured on a fibroblast feeder layer.
>
> 2. The preparation of claim 1, wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.
>
> 3. The preparation of claim 1 wherein the cells are negative for the SSEA-1 marker, positive for the SSEA-4 marker, and express alkaline phosphatase.

'913 patent, 21:21 – 22:27.

The only difference between Robertson 1983 and Robertson 1987 and the claims of the '913 patent is that Robertson 1983 and Robertson 1987 isolate mouse ES cells while the '913 patent claims human ES cells. However, Dr. Jeanne F. Loring, a leading research embryologist at the Burnham Institute in La Jolla, California, who was directing ES cell research and specifically focusing on derivation of novel ES cell lines at the time the earliest priority

application for the '913 patent was filed, states in the attached declaration that,

> [A]t the time the first application leading to the '913 patent was filed, it was obvious to one of ordinary skill in the art of ES cell derivation that the process taught by Robertson 1983 and Robertson 1987 for isolating mouse ES cells could be used to isolate ES cells of other mammals, including humans as claimed in the '913 patent, with a reasonable expectation of success.

Declaration of Dr. Jeanne F. Loring, p. 3.[3] In support of her opinion, Dr. Loring cites several conversations she had with other stem cell scientists prior to January 20, 1995, regarding how Robertson's method for deriving mouse ES cells could also be used to isolate human ES cells. *Id.* at 5-7. As such, Robertson 1983 and Robertson 1987 rendered each of the claims of the '913 patent invalid because they were no more than obvious implementations of Robertson's method.

With respect to those elements of the '913 patent's claims not found expressly in Robertson 1983 and Robertson 1987 – such as producing chronic gonadotropin when cultured to high density, being negative for the SSEA-1 marker and positive for the SSEA-4 marker and expressing alkaline phosphate – they are all attributes that the '913 patent concedes are inherent to human ES cells. '913 patent, 2:44-47 ("[c]horionic gonadotropin, expressed by the trophoblast, is ... in all primates, including humans"), 4:26-28 ("primate ES cell lines are preferably negative for the SSEA-1 marker ... and positive for the SSEA-4 marker"), 10:65-66 ("[a]lkaline phosphatase will also be present on all primate ES cells"), and 17:48-52 ("a series of cell surface markers (alkaline phosphatase, SSEA-3, SSEA-4, TRA-1-60, and TRA-1-81) ... are definitive markers for ... primate ES cells"). Therefore, those claim limitations provide no unobvious difference over Robertson 1983 and Robertson 1987.

3 The Declaration of Dr. Jeanne F. Loring, Ph.D. is attached hereto as Appendix C.

Although the '913 patent goes to great lengths to explain why human ES cells are more important and more beneficial for scientific research than mouse ES cells, it does not sufficiently address why a well known method for isolating mouse ES cells would not also work to isolate human ES cells. In fact, the method of isolating ES cells described in the '913 patent is the exact same process taught by Robertson 1983 and Robertson 1987 more than a decade earlier. '913 patent, 4:46-56. Thus, any argument that the process taught by Robertson 1983 and Robertson 1987 would not have been expected to work for humans is belied by the fact that the '913 patent – in fact – concedes that it did.

Further, there is no evidence of any (i) teaching away from using Robertson 1983's and Robertson 1987's method to isolate human ES cells or (ii) failure of others to isolate human ES cells using Robertson 1983's and Robertson 1987's method. To the contrary, other persons with ordinary skill in the art recognized that "[t]he development of mouse ES cells in 1981 provided the paradigm, and, much of the technology, for the development of human ES cells." U.S. Patent No. 6,875,607, 1:26-29. Thus, all of these secondary considerations further support the conclusion that the '913 patent was obvious in light of Robertson 1983 and Robertson 1987.

Piedrahita Alone Rendered the '913 Patent Obvious

Piedrahita taught a method of isolating murine (rodent), porcine (pig) and ovine (sheep) ES cells. Piedrahita at 882-883. The blastocysts were isolated and then the cells from the ICM were isolated. The ICM was then placed on an embryonic fibroblast feeder layer (Piedrahita taught the use of both STO and HEF feeder layers). After plating, the growing ICM was dissociated and replated onto fresh feeder layer. ES cells were then selected based on a large

nucleus and prominent nucleoli. These selected cells were then cultured on fresh feeder layer in order to prevent differentiation. Piedrahita's ES cells were pluripotential, were maintained over a significant time period and retained a normal euploid karyotype. *Id.* at 883-884 and 888 ("maintained for 42 passages with no sign of decreased growth rate or obvious morphological changes").

The only difference between Piedrahita and the claims of the '913 patent is that Piedrahita isolated murine, porcine and ovine ES cells while the '913 patent claims human ES cells. However, Dr. Loring states in the attached declaration that,

> [A]t the time the first application leading to the '913 patent was filed, it was obvious to one of ordinary skill in the art of ES cell derivation that the process taught by Piedrahita for isolating murine, porcine and ovine ES cells could be used to isolate ES cells of other mammals, including humans as claimed in the '913 patent, with a reasonable expectation of success.

Declaration of Dr. Jeanne F. Loring, p. 4. As such, Piedrahita rendered each of the claims of the '913 patent invalid because they were no more than obvious implementations of Piedrahita's method.

With respect to those elements of the '913 patent's claims not found expressly in Piedrahita – such as producing chronic gonadotropin when cultured to high density, being negative for the SSEA-1 marker and positive for the SSEA-4 marker and expressing alkaline phosphate – they are all attributes that the '913 patent concedes are inherent to human ES cells. '913 patent, 2:44-47 ("[c]horionic gonadotropin, expressed by the trophoblast, is ... in all primates, including humans"), 4:26-28 ("primate ES cell lines are preferably negative for the

SSEA-1 marker ... and positive for the SSEA-4 marker"), 10:65-66 ("[a]lkaline phosphatase will also be present on all primate ES cells"), and 17:48-52 ("a series of cell surface markers (alkaline phosphatase, SSEA-3, SSEA-4, TRA-1-60, and TRA-1-81) ... are definitive markers for ... primate ES cells"). Therefore, those claim limitations provide no unobvious difference over Piedrahita.

Although the '913 patent concedes that, "[p]luripotent cell lines have also been derived from preimplantation embryos of several domestic and laboratory animals species," it argues that "[w]hether or not these cell lines are true ES cells lines is a subject about which there may be some difference of opinion" and that "[s]trong evidence of these required properties have been published only for rodents ES cells." 3:50 – 4:13. However, the '913 patent fails to mention the "strong evidence" of Piedrahita that leaves no "difference of opinion" regarding its teaching of pluripotent ES cells of mammals other than rodents.

In fact, the method of isolating ES cells described in the '913 patent is the exact same process taught by Piedrahita several years earlier. '913 patent, 4:46-56. Thus, any argument that the process taught by Piedrahita would not have been expected to work for humans is belied by the fact that the '913 patent – in fact – concedes that it did. Further, there is no evidence of any (i) teaching away from using Piedrahita's method to isolate human ES cells or (ii) failure of others to isolate human ES cells using Piedrahita's method. Thus, these secondary considerations further support the conclusion that the '913 patent was obvious in light of Piedrahita.

It should be noted that during prosecution of one of the '913 patent's parent applications, U.S. Patent Application No. 08/376,327 ("the '327 application"), the Examiner applied Piedrahita in rejecting the then pending claims. *Office Action*, January 17, 1996, p. 5. In making the rejection, the Examiner stated,

> The only apparent difference between the method of Piedrahata [sic] et al. and that of the instant claims is that the claims isolate primate ES cells whereas Piedrahata [sic] et al. isolates murine, porcine and ovine ES cells. However, one of ordinary skill in the art would have a reasonable expectation of success in isolating primate ES using the same method taught by Piedrahata [sic] et al for isolating murine, porcine or ovine ES cells.

Id. at 6.[4]

The applicant responded to the Piedrahita rejection by arguing that "persons of high skill in the art still do not believe that they can predict whether methods worked out in one species will or will not work in another distantly-related species" and that "work from mice or sheep does not provide sufficient guidance, in this art, to demonstrate a reasonable expectation of success in primates." *Amendment*, July 23, 1996, pp. 6-7.[5] However, those conclusory arguments were completely unsupported with any evidence and correctly found unpersuasive by the Examiner, who responded to applicant's arguments by making the Piedrahita rejection final and stating that,

> ... the method of Piedrahata [sic] is identical to the claimed process with the exception of the source of the cells. The reference has applied the method to murine, porcine and ovine animals, three diverse categories of mammals and therefore the method could be applied to other mammals such as primates with a reasonable expectation of success.

4 A copy of the January 17, 1996, *Office Action* is attached hereto as Appendix D.

5 A copy of the July 23, 1996, *Amendment* is attached hereto as Appendix E.

Office Action, October 28, 1996, p. 4.[6]

In the face of the final rejection, the applicant abandoned the '327 application and shifted prosecution to a continuation-in-part application. The instant application leading to the '913 patent was a related application descending from a line of continuations and a divisional of the '327 application, but Piedrahita was never discussed during the prosecution of any of those other applications. In fact, Piedrahita was never cited or made of record by the applicant in the instant application leading to the '913 patent, despite the fact that the applicant obviously knew of its existence and that the Examiner of the initial '327 application found it to be highly material. Thus, the rejection made in the '327 application based on Piedrahita was never overcome by the applicant and remains a valid basis of rejection of the '913 patent's claims.

Robertson 1983, Robertson 1987 and Piedrahita Together Rendered the '913 Patent Obvious

The combined teachings of Robertson 1983, Robertson 1987 and Piedrahita further render the '913 patent obvious because they use virtually the same process to isolate ES cells of several different mammalian species. Dr. Loring states in the attached declaration that,

> [A]t the time the first application leading to the '913 patent was filed, it was obvious to one of ordinary skill in the art of ES cell derivation that the process taught by Robertson 1983, Robertson 1987 and Piedrahita for isolating mouse, murine, porcine and ovine ES cells could be used to isolate ES cells of other mammals, including humans as claimed in the '913 patent, with a reasonable expectation of success.

Declaration of Dr. Jeanne F. Loring, p. 5. Thus, since the same process was known, at the time the earliest claimed priority application for the '913 patent was filed, to work to isolate various

6 A copy of the October 28, 1996, *Office Action* is attached hereto as Appendix F.

types of mammalian ES cells, one of ordinary skill in the art would have expected the process to work for human ES cells as well because humans are yet another type of mammal and are no more different from mice, rats, pigs, and sheep than they are each from each other.

One of ordinary skill in the art would have been motivated to combine the teachings of Robertson 1983, Robertson 1987 and Piedrahita because they are directed to exactly the same field of scientific endeavor, namely the isolation of mammalian ES cells. In addition, Robertson 1987 was written by the same author as Robertson 1983 and Robertson 1987 and Piedrahita both expressly cited Robertson 1983, thus incorporating it by reference. Robertson 1987 at 112 (*citing* Robertson 1983); Piedrahita at 900 (*citing* Robertson 1983). As such, when viewed together, Robertson 1983, Robertson 1987 and Piedrahita render each of the claims of the '913 patent invalid because it would have been obvious that the method described in those references for isolating ES cells of several different mammalian species could be expected to work to isolate human ES cells as well.

[continued on next page]

CONCLUSION

For the reasons set forth above, each of the claims of the '913 patent are invalid for being obvious in light of Robertson 1983, Robertson 1987 and Piedrahita. As such, PUBPAT, on behalf of FTCR, respectfully requests that they be reexamined *inter partes* and ultimately canceled.

July 17, 2006
Date

Daniel B. Ravicher, Esq.
U.S.P.T.O. Reg. No. 47,015
PUBLIC PATENT FOUNDATION, INC.
1375 Broadway, Suite 600
New York, NY 10018
Tel: (212) 545-5337
Fax: (212) 591-6038
www.pubpat.org

Attorneys for the Foundation for Taxpayer and Consumer Rights

CERTIFICATE OF SERVICE

The undersigned certifies that a copy of this Request for *Inter Partes* Reexamination in its entirety, including all accompanying documents, is being deposited with the U.S. Postal Service as Priority Mail with Delivery Confirmation on the date of the signature below in an envelope addressed to the attorney of record for the assignee of U.S. Patent No. 7,029,913 as provided for in 37 C.F.R. § 1.33(c):

NICHOLAS J. SEAY
QUARLES & BRADY LLP
P. O. BOX 2113
MADISON, WI 53701-2113

July 17, 2006
Date

Daniel B. Ravicher, Esq.
U.S.P.T.O. Reg. No. 47,015
PUBLIC PATENT FOUNDATION, INC.
1375 Broadway, Suite 600
New York, NY 10018
Tel: (212) 796-0570
Fax: (212) 591-6038
www.pubpat.org

Attorneys for the Foundation for Taxpayer and Consumer Rights