

CURRICULUM VITAE

(with Bibliography and Summary of Research and Educational Accomplishments)

Name: Renee Ann Reijo Pera, PhD

Position(s): Director, Center for Human Embryo and Embryonic Stem Cell
Research and Education
Professor of Obstetrics and Gynecology
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EDUCATION

1979-1983	University of Wisconsin; Superior, WI	B.S. Magne Cum Laude, Biology
1984-1987	Kansas State University; Manhattan, KS	M.S. Biology
1988-1993	Cornell University; Ithaca, NY	PhD Molecular & Cell Biology
1993-1997	Whitehead Institute, MIT; Cambridge, MA	Fellow Human Genetics

PRINCIPAL POSITIONS HELD

2007-present	Director, Center for Human Embryo and Embryonic Stem Cell Research and Education Director, Reproductive and Stem Cell Biology Program Professor of Obstetrics and Gynecology Member, Institute for Stem Cell Biology and Regenerative Medicine Stanford University School of Medicine
2003-2007	Associate Professor (Tenured Ladder Rank) CoDirector, UCSF Human Embryonic Stem Cell Center (with SJ Fisher, CoDirector) Director, UCSF Training Program in Stem Cell Biology Associate Director, UCSF Center for Reproductive Sciences Department of Obstetrics, Gynecology and Reproductive Sciences

Department of Physiology
Department of Urology
Institute for Regeneration Medicine
Institute for Human Genetics
Program in Cancer Genetics Program
University of California at San Francisco

- 1997-2003 Assistant Professor
Department of Obstetrics, Gynecology and Reproductive Sciences
Departments of Physiology and Urology
Center for Human Genetics, Program in Cancer Genetics
Program in Developmental and Stem Cell Biology
University of California, San Francisco
- 1995 Instructor: Biology 734: Human Genetics
Dr. David Baltimore, Course Director
Massachusetts Institute of Technology
Department of Biology
- 1993-97 Damon-Runyan Fellow, Whitehead Institute for Biomedical Research
Laboratory of Dr. David C. Page

HONORS AND AWARDS

Lakehead Pipeline Association Scholarship (1982)
Magne Cum Laude Honors (1983)
Sigma Xi Research Excellence Award (1985)
Cornell Outstanding Teacher Award (1988)
Cornell Graduate Travel Award (1988)
DuPont Teaching Fellow (1989)
U.S. Army Biotechnology Graduate Fellowship (1991-1993)
Damon Runyon/Walter Winchell Postdoctoral Fellowship (1993-1996)
Searle Scholar (1998-2001)
Sandler Award in Basic Science (UCSF, 1999-2000)
Innovations in Basic Science Award (Chancellor's Office, UCSF, 1998-1999)
Member of the NIH Cellular, Molecular, & Integrative Reproduction (CMIR, 2002-2007)
Chair of the German American Frontiers of Science Program (National Academy of Sciences;
2000-2003)
American Stem Cell Research Foundation Award (2004)
Outstanding Faculty Mentor Award (UCSF Graduate Student Association; 2005)
UCSF:Coro Center for Leadership Training (January – May; 2006)
Newsweek; Twenty Influential Women Leaders in the USA (September 2006)
Distinguished Woman in Andrology Award; American Society of Andrology (ASA; April 2007)
American Society for Reproductive Medicine (ASRM) Bruce Stewart Lecture (October 2007)
Institute Senator for Stanford Medical School Faculty Senate (2008–2011)

Honorary Doctorate of Human Letters (2009); University of Wisconsin Superior

KEYWORDS/AREAS OF INTEREST

Human cell fate decisions, human germ cell development, human embryo development, human embryonic stem cells, teratoma, embryology, gametogenesis, oocytes, sperm, meiosis, germ line allocation (formation), germ line imprinting, human genetics, somatic cell nuclear transfer

PROFESSIONAL ORGANIZATIONS

Memberships

1999-present	American Society of Human Genetics
1999-present	American Association for the Advancement of Science
2004- present	International Society for Stem Cell Research
2004-present	Society for the Study of Reproduction
2004-present	American Society for Andrology

Service to Professional Organizations

2002	German American Frontiers of Science (GAFOS) Annual Meeting (National Academies of Science)	Organizing Committee Member
2002	GAFOS Stem Cell Biology Symposium	Chair, Organizing Committee
2003	GAFOS Annual Meeting	Chair, Organizing Committee
2004	NIH Symposium on Reproductive Genetics	Organizing Committee
2005	American Society for Human Genetics Annual Meeting	Symposium Chair
2005	NIH Frontiers in Human Embryonic Stem Cell Research Stanford School of Medicine; Stanford, CA	Co-Director
2005	Mid-Career Women Faculty Professionals Meeting	Participant

SERVICE TO PROFESSIONAL JOURNALS

2005-present Editorial Board, *Stem Cells*
2006-present Editorial Board, *Experimental Biology & Medicine*
2006-present Associate Editor, *Molecular Reproduction and Development*
2006-present Editorial Board, *Human Molecular Genetics*

1997-present

Adhoc Reviewer for the Following Journals

Development (5 papers in last 5 years)
Developmental Biology (10 papers in last 5 years)
Nature Genetics (5 papers in last 5 years)
American Journal of Human Genetics (5 papers in last 5 years)
Human Molecular Genetics (20 papers in last 5 years)
Proceedings of the National Academy of Sciences (5 papers in last 5 years)
Mechanisms of Development (3 papers in last 5 years)
American Journal of Medical Genetics (2 papers in last 5 years)

Biology of Reproduction (10 papers in last 5 years)
Fertility and Sterility (10 papers in last 5 years)
Human Reproduction (30 papers in last 5 years)
Journal of Urology (3 papers in last 5 years)
International Journal of Urology (1 paper in last 5 years)
Molecular Human Reproduction (20 papers in last 5 years)
Stem Cells (20 papers in last 5 years)
Science (3 papers in last 5 years)

Bibliograph (with publications only, in reverse chronological order)

- McElroy SL, Byrne JA, Chavez SL, Behr B, Hsueh AJ, Westphal LM, Reijo Pera RA.,
Parthenogenic blastocysts derived from cumulus-free in vitro matured human oocytes,
PLoS One. 2010; 5 (6): e10979 PMID: 20539753
- Tung JY, Rosen MP, Nelson LM, Turek PJ, Witte JS, Cramer DW, Cedars MI, Reijo-Pera
RA "Novel missense mutations of the Deleted-in-AZOOSPERMIA-LIKE (DAZL) gene in infertile
women and men." *Reprod Biol Endocrinol* 2006;(4):40 PMID: 16884537
- Haston, K.M., J.Y. Tung, and R.A. Reijo Pera, *Dazl functions in maintenance of pluripotency
and genetic and epigenetic programs of differentiation in mouse primordial germ cells in
vivo and in vitro*. PLoS One, 2009. **4**(5): p. e5654. PMID: 19468308
- Nicholas CR, Chavez SL, Baker VL, Reijo Pera RA. (2009) Instructing an embryonic stem cell-
derived oocyte fate: lessons from endogenous oogenesis. *Endocrine Reviews* 30, 264-83.
- Reijo Pera, R.A., C. DeJonge, N. Bossert, M. Yao, J.Y. Hwa Yang, N.B. Asadi, W. Wong, C.
Wong, and M.T. Firpo, *Gene expression profiles of human inner cell mass cells and
embryonic stem cells*. *Differentiation*, 2009. **78**(1): p. 18-23. PMID: 19398262.
- Nicholas CR, Banani SF, Xu EY, Hammer RE, Hamra FK, and Reijo Pera RA (in press)
Characterization of a *Dazl*-GFP germ cell specific reporter. *Genesis*.
- Shimono Y, Lao K, Cho RW, Liu H, Lobo N, Qian D, Diehn M, Somlo G, Panula S, Chiao E,
Reijo Pera RA, and Clarke MF (submitted) Down-regulation of 3 microRNA clusters links
normal and malignant breast stem cells. *Cell*.
- K Foygel, B Choi, S Jun, DE Leong, A Lee, CC Wong, E Zuo, M Eckart, RA **Reijo Pera**, WH
Wong, MWM Yao (2008) A novel and critical role for Oct4 as a regulator of the maternal-
embryonic transition. PLoS ONE 3(12): e4109 doi:10.1371/journal.pone.0004109.
- Kossack N, Meneses J, Shefi S, Nguyen H, Chavez S, Nicholas C, Gromoll J, Turek PJ, and
Reijo Pera (in press) Isolation and characterization of pluripotent human spermatogonial
stem cell-derived cells. *Stem Cells*. 2009. **27**(1): p. 138-49. PMID: 18927477
- Walsh TJ, **Reijo Pera RA**, and Turek PJ (2008) The genetics of male infertility. *Seminars in
Reproductive Medicine (in press)*.
- Scott CT and **Reijo Pera RA** (2008) The road to pluripotency: The research response to the
embryonic stem cell debate. *Human Molecular Genetics* 17, R3-9.

- Chavez SL, Meneses JJ, Nguyen HN, Kim S, and **Reijo Pera RA** (2008) Characteristics of six new human embryonic stem cell lines (HSF-7, -8, -9, -10, -12 and -13) derived with minimal animal product conditions. *Stem Cells and Development* 17, 535-546.
- Sunny H, Choi JB, Shahine L, Westphal LM, Behr B, **Reijo Pera RA**, Wong WH and Yao MW (2008) Defining human embryo phenotypes by cohort-specific prognostic factors. *PLoS One* 3, e2562. doi:10.1371/journal.pone.0002562.
- McElroy SL, Kee K, Tran N, Giudice LC, Meneses J and **Reijo Pera RA** (2008) Developmental competence of immature and abnormally-fertilized human oocytes in somatic cell nuclear transfer. *Reprod BioMed Online* 16, 684-693.
- Wong C, Gaspar-Maia A, Ramalho Santos M, and **Reijo Pera RA** (2008) High-efficiency stem cell fusion-mediated assay reveals Sall4 as an enhancer of reprogramming. *PLoS One* 3(4):e1955.
- Gallardo TD, John GB, Bradshaw K, Welt C, **Reijo Pera RA**, Vogt PH, Touraine P, Bione S, (2007) Toniolo D, Nelson LM, Zinn AR, Castrillon DH. Sequence variation at the human FOXO3 locus: a study of premature ovarian failure and primary amenorrhea. *Human Reproduction* 23:216-21.
- International Stem Cell Initiative (including **Reijo Pera RA**) (2007) Characteristics of human embryonic stem cell lines: Results from the International Stem Cell Initiative. *Nature Biotechnology* 25, 803-16.
- Angeles VT and **Reijo Pera RA** (2007) Differentiation of germ cells from embryonic stem cells. Chapter 7 in *Human Embryonic Stem Cells*. Edited by J Thomson, B Paulssen and J Masters; Springer-Verlag; New York, NY.
- Haston KM and **Reijo Pera RA** (2007) Germ line determinants and oogenesis. Chapter 8 in *Developmental Genetics*. Edited by S Moody; Elsevier Press; New York, NY.
- Fox MS, Clark AT, El Majdoubi M, Vigne JL, Urano J, Hostetler CE, Griswold MD, Weiner RI, and **Reijo Pera RA** (2007) Intermolecular interactions of homologs of germ plasm components in mammalian germ cells and embryonic stem cells. *Developmental Biology* 301, 417-431.
- Nicholas C, Gaur M, Leavitt AD and **Reijo Pera RA** (2007) Generation of genetically-stable, GFP-positive human embryonic stem cell lines for long term transplantation studies. *Stem Cells and Development* 16:109-17.
- Xu EY, Salmon NA, and **Reijo Pera RA** (2007) A gene trap mutation of a murine homolog of the *Drosophila* stem cell factor *Pumilio* results in smaller testes but does not affect litter size or fertility. *Molecular Reproduction and Development* 74, 912-921.
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- Tung J, Rosen M, Cramer D, and **Reijo Pera RA** (2006) Common variants in *Deleted in AZoospermia-Like (DAZL)* are correlated with reproductive parameters in men and women. *Human Genetics* 118, 730-740.
- Tung JY, Luetjens CM, Wistuba J, Xu EY, **Reijo Pera RA**, and Gromoll J (2006) Evolutionary comparison of the reproductive genes, *DAZL* and *BOULE*, in primates with and without *DAZ*. *Developmental Genes and Evolution* 216, 158-68.
- Tung JY, Rosen MR, Turek PJ, Witte JS, Nelson L, Cramer D, Cedars MI and **Reijo Pera RA** (2006) Novel missense mutations of the *Deleted-in-AZoospermia-Like (DAZL)* gene in infertile women and men. *Reproductive Biology and Endocrinology* 4, 40.

- Salmon NA, **Reijo Pera RA**, and Xu EY (2006) A gene trap knockout of the abundant sperm tail protein, outer dense fiber 2, results in preimplantation lethality. *Genesis* 44, 515-522.
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- Fox MS, **Reijo Pera RA** and Clark AT (2006) “Chapter 12 : The *DAZ* gene family and human germ cell development from embryonic stem cells” in *The Sperm Cell: Production, Maturation, Fertilization, Regeneration*; C DeJonge, editor; Cambridge University Press, Cambridge, UK.
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- Reijo Pera RA** (2005) “Chapter 5: Genetics and Infertility” in *Practical Pathways in Obstetrics and Gynecology – Infertility*; Marcelle I. Cedars, Editor; McGraw Hill Company, NY, NY.
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- Clark AT, Rodriguez R, Abeyta MJ, Firpo MT, **Reijo Pera RA** (2004) Human *STELLAR*, *NANOG*, and *GDF3* genes are expressed in pluripotent cells and map to chromosome 12p13, a hot-spot for teratocarcinoma. *Stem Cells* 22, 169-179.
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- Abeyta MJ, Clark AT, Rodriguez R, **Reijo Pera RA*** and Firpo MT (2004) Unique gene expression signatures of independently-derived human embryonic stem cell lines. *Human Molecular Genetics* 13, 601-608. *corresponding author
- Dobson AT, Raja R, Abeyta MJ, Taylor T, Shen S, Haqq C, **Reijo Pera RA** (2004) The unique transcriptome through day 3 of human preimplantation development. *Human Molecular Genetics* 13, 1461-1470.

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- Luetjens CM, Xu EY, **Reijo Pera RA**, Kamischke A, Nieschlag E, Gromoll J (2004) Association of meiotic arrest with lack of *BOULE* protein expression in infertile men. *Journal of Clinical Endocrinology and Metabolism* 89, 1926-1933.
- Fox MS, Ares VX, Turek PJ, Haqq C, **Reijo Pera RA** (2003) Feasibility of global gene expression analysis in testicular biopsies from infertile men. *Molecular Reproduction and Development* 66, 403-421.
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- Turek PJ and **Reijo Pera RA** (2001) "Fertility and Mutations" in *The Encyclopedia of Genetics*; Lee Silver, Editor; Academic Press, NY.
- Xu EY, Moore FL, **Reijo Pera RA** (2001) A gene family required for human germ cell development evolved from an ancient meiotic gene conserved in metazoans. *Proceedings of the National Academy of Sciences* 98, 7414-7419.
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- Cayan S, Lee DM, Black LD, **Reijo Pera RA**, Turek PJ (2001) Response to varicocelelectomy in oligospermic infertile men with and without coexisting genetic infertility. *Urology* 57, 530-535.
- Moore FL and **Reijo Pera RA** (2000) Male sperm motility dictated by Mother's mtDNA. *American Journal of Human Genetics* 67, 543-548.

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- Nudell D, Castillo M, Turek PJ, **Reijo Pera, RA**. (2000) Defective DNA repair in infertile men. *Human Reproduction* 15, 1289-1294.
- Moore FL and **Reijo Pera RA**. (2000) Male sperm motility dictated by Mother's mtDNA. *American Journal of Human Genetics* 67, 543-548.
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- Kostiner DR, PJ Turek, and **Reijo Pera RA** (1998) Male infertility: analysis of the markers and genes on the human Y chromosome. *Human Reproduction* 13, 3032-3038.
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- Reijo RA**, Seligman J, Dinulos MB, Jaffe T, Disteché CM, Page DC (1996). Mouse autosomal homolog of *DAZ*, a candidate male sterility gene in humans expressed in male germs cells before and after puberty. *Genomics* 35, 346-352.
- Reijo R**, Alagappan R, Patrizio P, Page DC (1996). Severe oligospermia resulting from deletions of the *Azoospermia Factor* gene on the Y chromosome. *Lancet* 347, 1290-1293.
- Saxena R, Brown LG, Hawkins T, Alagappan RK, Skaletsky H, Reeve MP, **Reijo RA**, Rozen S, Dinulos MB, Disteché CM, Page DC (1996) The *DAZ* gene cluster on the human Y chromosome arose from an autosomal gene that was transposed, repeatedly amplified and pruned. *Nature Genetics* 14, 292-299.
- Tsuchiya K, **Reijo RA**, Page DC, Disteché CM (1995) Gonadoblastoma: Molecular definition of the susceptibility region on the Y Chromosome. *American Journal of Human Genetics* 57, 1400-1407.
- Reijo R**, Lee TY, Salo P, Alagappan R, Brown LG, Rosenberg M, Rozen S, Jaffe T, Straus, D, Hovatta O, de la Chapelle A, Silber S, Page DC (1995) Diverse spermatogenic defects in humans caused by overlapping, *de novo* Y deletions encompassing a novel RNA-binding protein gene. *Nature Genetics* 10, 383-393.
- Reijo RA**, Cooper EM, Beagle GJ, Huffaker TC (1994) Systematic mutational analysis of the yeast beta-tubulin gene. *Molecular Biology of the Cell* 5, 29-43.
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SUMMARY of RESEARCH PROGRAM and ACCOMPLISHMENTS

Highlights of major research accomplishments include:

- 1) Identification of *Deleted in AZoospermia (DAZ)* genes as the most common molecularly-defined cause of human infertility.
- 2) Identification of interacting proteins that associate with DAZ and DAZL proteins in eggs and sperm.
- 3) Identification of novel genetic variants associated with age of onset of menopause and other reproductive parameters in women and men.
- 4) First complete transcriptome analysis of human oocyte to egg transition.
- 5) First differentiation of human embryonic stem cells (hESCs) to female and male primordial germ cells and meiotic cells.
- 6) Genetic modulation of germ cell genes to increase/decrease human germ cell formation *in vitro*.
- 7) Derivation of human spermatogonial stem cell lines (pluripotent hSSCs).

Current research efforts are focused on three areas of reproductive research as described below:

A. Human Reproductive Biology and Germ Cell Development

This is a unique time in scientific history: The last decade has seen astonishing advances that may now allow us to overcome two historically-significant limitations in human developmental genetic studies: namely, the inaccessibility of early human development to biological exploration and the genetic-intractability of the human genome during development. In the next five years, my laboratory will focus on using the powerful tools of hESC biology and human genetics to extend our findings in reproductive biology. Namely, we have identified a gene family required for germ cell formation/maintenance of initial populations, developed a testable model for germ cell formation, and differentiated germ cells from human embryonic stem cells in order to probe the genetics of germ cell formation and dependence on key genes that we have shown are deleted, mutated or variant in men and women with few or no germ cells. **A major focus of our laboratory is to address the hypotheses: 1) that multiple members of the *DAZ (Deleted in AZoospermia)* gene family are required for the formation and/or maintenance of nascent human germ cells and 2) that common genetic variants and unique mutations, highly enriched on chromosomes of infertile men and women, modulate early human germ cell development in both sexes, and 3) that differentiation of hESCs to the germ cell lineage provides an optimal system for screening new genes via siRNA and genome-wide peptide libraries.** This is a major scientific goal of my group and thus the specific aims are summarized in detail here:

Aim 1. Define the baseline molecular, temporal and genetic characteristics of differentiation of hESCs and mESCs to the germ cell lineage *in vitro* and *in vivo* in a transplant system. In order to develop a genetic system to specifically probe human gene function during germ cell development, we recently tested whether multiple, independently-derived human embryonic stem cell (hESC) lines could differentiate to germ cells *in vitro*. We demonstrated that hESCs can differentiate to nascent germ cells and subsequently showed that the formation of primordial germ cells (PGCs) is augmented in response to the addition of BMP4, BMP7 and BMP8 *in vitro*, as we would expect if human germ cell development *in vitro* recapitulates some of the functional elements of the pathways observed *in vivo* in mice. Building on these results, we developed a human *VASA* reporter system in order to isolate

nascent germ cells from the complex cell mixtures produced by *in vitro* differentiation of hESCs and mESCs; we demonstrated that VASA-positive germ cells constitute up to 8% of the population of differentiated cells, depending on BMP treatments. We will isolate differentiated human germ cells and track landmark events through time beginning with the birth of germ cells through post-translational assembly of homologs of germ plasm components and progressing through the sequential expression of germ cell specific mRNAs and proteins, erasure and re-establishment of sex-specific imprinting and entry into meiosis. We will then assay germ cell function *in vivo* via transplantation to mice, using mESC (mouse embryonic stem cell) and hESC-derived germ cells and ovarian and testicular xenotransplantation assays we recently developed. Note that although several studies of germ cell differentiation *in vitro* have been published, information regarding the baseline molecular, temporal and genetic requirements are lacking in mice and humans, with the exception of our studies on the role of BMPs. This aim addresses this deficit of knowledge.

Aim 2. Silence human DAZ, and human and mouse DAZL and BOL genes and assess germ cell development and examine functional significance of common variants and rare mutations in the human population. The human *DAZ* gene family was identified in a screen for genes on the Y chromosome that are deleted in men with few or no sperm; homologs in many organisms were subsequently shown to be required for germ cell development. Surprisingly, however, the structure of this gene family is unique to humans and closely-related primates. Whereas the human genome contains six members of the *DAZ* family, mice contain just single copies of the closely-related *DAZL* (*DAZ-Like*) and *BOULE* (*BOL*) genes but no Y chromosome *DAZ* genes, and invertebrates such as flies and worms have *BOL* genes but no *DAZ* or *DAZL* genes. Consequently, translation of experimental results directly from studies with model organisms to human infertility is difficult given the unique gene family structure in humans. Thus in this aim, we seek to delineate the function of each of the *DAZ* gene family members by genetic manipulation on a human genome background. Notably, to date there are no data demonstrating that germ cell development *in vitro* is dependent on genes known to function in this pathway *in vivo* (an observation that also extends to somatic development). Thus, we include mESC lines derived from male and female wildtype, *Dazl* +/-, and *Dazl* -/- mice in order to relate findings *in vitro* to phenotypic characterization of *Dazl* null mutants *in vivo*. Then, we use mouse genetics to model the functional significance of common variants and rare mutations we have identified in infertile women and men.

Aim 3. Screen for novel genes that are required for human germ cell development and characterize their function in humans and mouse models. As indicated above, we now possess the tools such as a *VASA* reporter to quantify human germ cell formation, differentiation and maintenance *in vitro*. In this aim, we will conduct genome-wide siRNA and secreted peptide screens to identify novel factors that are required for human germ cell development. We will then use human and mouse genetics to characterize the function of key genes.

B. Human Embryonic Stem Cells as the Preeminent Model for Human Developmental Genetics

The goal of these efforts is to establish the human embryonic stem cell system as the preeminent model for human developmental genetics studies. In the last decade, we have

witnessed the sequencing of the human genome, mapping of hundreds of simple Mendelian diseases/traits, writing of the catalog of millions of human sequence variants and the establishment of a haplotype map to identify genetic determinants of diseases that afflict a substantial portion of our population. Yet, as human genetic knowledge expands, the utility of simple systems to probe the basis of the diseased state has waned. In this void, human embryonic stem cell systems provide ideal models for studying the genetic bases of human diseases. Towards realization of the potential of human embryonic stem cells, we have: 1) established protocols to use SCNT to produce hESC lines from pedigrees with and without disease alleles; and 2) established a program to generate specific DNA variants on selected human embryonic stem cell backgrounds. We note, in particular, that our SCNT efforts build upon a component oocyte and embryo resource, human embryonic stem cell derivation core and a nuclear transfer core. Most notably and remarkably, we have established the ability to grow oocytes, that would normally be discarded, to blastocyst stage (approximately 40,000+ such oocytes are produced annually in the US). This will form the basis for a novel SCNT effort in conjunction with an oocyte donor program. The interest in SCNT extends beyond the usual generation of patient-specific line derivation to probing of the early molecular genetic events in human development. These basic science approaches will illuminate the fundamental genetic bases of diseases with phenotypes that replicate only in human cells and allow my own laboratory to further probe the developmental genetics of human germ cell function.

C. University-Wide Human Embryonic Stem Cell Center

In 2003, I proposed that UCSF should establish a formal human embryonic stem cell program. This program was aimed at taking advantage of the newly developed tools of human genetics and human embryonic stem cell biology in order to pursue human biology. I noted that human genetics has long suffered from the lack of a rigorous system to experimentally manipulate human genes of interest and likewise, that human stem cell biology suffers for lack of genetic rigor in its early stages. Thus, the overall goal of the Program in Human Embryonic Stem Cell Biology was to establish a combined program of human genetics and stem cell biology that allows the use of stem cells to address human genetic questions, and vice versa. Experiments in my own laboratory (as described above) have focused on characterization of fundamental properties of hESCs. These experiments use the same reagents that are already, or soon will be, required by other researchers: 1) multiple NIH-approved lines, 2) newly-derived human embryonic stem cell lines cultured on human feeder cells, 3) ability to silence, disrupt and overexpress genes specifically in human ES cells, and 4) ability to transplant labelled cells to an appropriate model *in vivo* (primates or rodents). Thus, the Program in Human Embryonic Stem Cell Biology fused the activities of generation of hESC lines and genetic modification and transplantation of undifferentiated and differentiated cell types. Note that the program was codirected by myself (Ob-Gyn & RS; UCSF School of Medicine) and Dr. Susan J Fisher (Tissue and Cell Biology; UCSF School of Dentistry). This program was expanded at Stanford University to include the activities described here and above in the section (B) entitled "Human Embryonic Stem Cells as the Preeminent Model for Human Developmental Genetics." It forms the basis for the Human Embryonic Stem Cell Research and Education program positioned within the Institute for Stem Cell Biology and Regenerative Medicine at Stanford.

SUMMARY of EDUCATIONAL ACCOMPLISHMENTS

I. Formal (Classroom) Teaching

Here I describe my educational activities, first at UCSF and then at Stanford University. Please note that I relocated, with my laboratory, to Stanford University in April of 2007.

At UCSF, I was an instructor in four courses and course director and instructor for a fifth course. I also directed the UCSF CIRM Stem Cell Training Program and was the principal investigator of an NIH-sponsored training and distribution program for human embryonic stem cells. More details regarding these activities are described below:

The courses in which I have instructed are: Medical Genetics (Pediatrics 100; 1998, 1999 and 2001), Genetics 200A (1999, 2000, 2001 and 2002), Advanced Human Genetics (1999), and Principles of Genetics (BMS255; 2003); I was course director and instructor in Biology of Human Tissues and Organ Systems (BMS 225A; 2004 – present), a course that I reorganized and renamed to “Developmental and Stem Cell Biology.”

The Medical Genetics course was attended by medical students, Genetics 200A was attended by first-year graduate students in the Program in Biological Sciences (PIBS) and BioMedical Sciences (BMS), and Advanced Human Genetics was attended by advanced graduate students and postdoctoral fellows. In each of these courses, I taught linkage analysis, imprinting, pedigree analysis, gene mapping, gene identification strategies in humans, the Human Genome Project, and sex determination.

As Course Director of BMS225A, I reorganized the course content from basic physiology to a focus on Reproductive, Developmental and Stem Cell Biology. The overall goal of this course was to teach the students the basics of human development with a focus on embryology, stem cell biology and differentiation, and the basic development and function of somatic systems such as the cardiovascular system. In parallel, I organized a series of discussion sections that focused on (i) the histology of the individual tissues and organs and (ii) the critical analysis of recent papers exploring human stem cell biology and animal transgenic models to illustrate the concepts put forth in the lectures. In addition, there was a set of basic laboratory experiments demonstrating mouse/chick embryo dissection, embryology and human embryonic stem cell growth, differentiation and genetic analysis. To my knowledge, this was the only graduate course in the United States, to teach human embryonic stem cell laboratory practices, and certainly was first to do so if others follow suit. Because of demand, the number of discussion groups and laboratories was increased, beginning with winter session (2005-2006). We included genetic modification and directed differentiation of human embryonic stem cells, as well.

As Director of the UCSF CIRM training program, we required scholars to attend Developmental and Stem Cell Biology (described above), a monthly course on ethical, legal and social issues related to stem cell biology, a translational biology course, and a two week course (which I designed to be offered 3 times annually) that includes a morning lecture and discussion and an afternoon of hands-on experience. I have since assumed co-Directorship with Dr Mike Longaker of the Stanford University CIRM Training Program and am serving on the Education committee of the Institute for Stem Cell Biology & Regenerative Medicine as we implement our full menu of courses in stem cell biology, development and translation to the clinic.

As Director of an NIH Training and Distribution Program grant, we have trained scientists from more than 20 laboratories, worldwide, in the culture, maintenance, differentiation and

analysis of human embryonic stem cells. In addition, my laboratory served as the resource center for the characterization and distribution of two NIH-registry human embryonic stem cell lines, UC01 and UC06. Finally, we constructed the necessary GFP-positive human embryonic stem cell lines (for transplantation experiments) on an H9 background for distribution through the National Stem Cell Bank (NSCB).

As Director of the Stanford University Center for Human Embryo and Embryonic Stem Cell Research and Education, I direct a curriculum that has three components. Our entry level course is scheduled for July 2007; advanced courses initiate in October 2007 (SCNT, derivation and reprogramming) and courses on systems approaches begin January 2008. The curriculum is as follows:

1. Basic hESC Biology: This course is the central component of education in the Stanford University Center for Human Embryo and Embryonic Stem Cell Research and Education. It will provide the essentials of hESC biology to individuals with little or no previous experience with hESCs with topics as described below. My anticipated outcome is that students will learn the basic techniques required to culture, differentiate and analyze hESCs. They will leave the laboratory with a detailed protocol book, appropriate frozen feeder cell preparations for several months of experiments, and established relationships for further assistance and troubleshooting as they begin their experiments in their own designated hESC laboratory space.

Day 1: Introduction to hESC biology and course overview; Descriptions of lines available for research (focused on lines from Stanford, UCSF, Harvard and the Karolinska Institute); Practical considerations in culturing NIH registry and non-registry lines; Equipment requirements; Discussion of supplies, media, and other materials; Sterile technique; Preparation of mouse feeders from E14 (embryonic day 14) embryos; Inactivation of feeders via gamma irradiation and mitomycin C; Plating of mouse feeders

Day 2: Examination of mouse feeders from Day 1 and assessment of morphology and quality; Discussion of human feeders used in different laboratories; Preparation of human feeders (from ATCC; human foreskin feeder cells); Inactivation of feeders via gamma irradiation and mitomycin C; Preparation of hESC media; Thawing and plating of hESCs; Examination of numerous cultures of hESCs for assessment of quality, differentiation and cell death

Day 3: Discussion of differentiation of hESCs via embryoid body (EB) formation, hanging drop and suspension cultures; Preparation of hESC differentiation media; Passaging of hESCs under self-renewal conditions; Transfer of hESCs to differentiation media; Immunofluorescence analysis of hESC cell surface markers (SSEA3/4, Tra1-81, and Tra1-60); Immunohistochemical analysis of OCT4 and Nanog; Differentiation assays (quantitative RT-PCR and immunohistochemistry)

Day 4: Discussion of genetic markers of differentiation to endoderm, mesoderm; ectoderm, the germ cell and extra-embryonic cell lineages; Quantitative RT-PCR of undifferentiated and differentiated hESCs; Preparation of hESCs and analysis via karyotype for assessment of genetic stability; Fluorescence-activated cell sorting (FACS) of undifferentiated and differentiated hESCs

Day 5: Discussion of practical problems commonly encountered and potential solutions; Freezing of hESCs; Teratoma and other transplantation assays (demonstration); Ethical, legal and social implications of hESC research

2. Individualized Training in Advanced or Specialized Stem Cell Techniques: Building on our experience at UCSF, we decided to provide individuals or small groups with tailored instruction on a case-by-case basis in the Stanford University Center for Human Embryo and Embryonic Stem Cell Research and Education core facility. In particular, after the end of each Basic hESC Biology course, we offer specialized advanced techniques of interest to the community, including the derivation of hESCs, somatic cell nuclear transfer, and clinical aspects of human embryology, as well as other subjects such as genetic or genomic screens, directed differentiation and isolation of differentiated cell types, advanced microscopy and bioengineering applications as demand merits. These sessions will accommodate the needs of individuals or small groups of scientists with common interests and will generally cover four or more days of instruction in the Shared Research Laboratory and Teaching Facility at Stanford University ISCBRM. We expect to offer three courses each year to follow the hESC Biology courses. The first two courses are outlined below. My anticipated outcome for these classes is that participants will become familiar with basic and clinical aspects of human embryo growth, practices followed for procurement of embryo and oocyte samples, optimal methods of derivation of lines from normal embryos and those that carry disease alleles, and common techniques required for successful SCNT in model systems and the human. They will form collaborations and interactions to augment the research in their own laboratories.

Advanced Individualized Course 1: Reprogramming, SCNT and Derivation of hESC Lines. This course focuses on reprogramming, via generation of induced pluripotent stem cells (iPSCs) and SCNT for studies of human reprogramming and derivation of hESC lines.

Day 1: Introduction to human embryology; Clinical aspects of human oocyte retrieval; Oocyte staging and developmental competence; Somatic cell nuclear transfer (SCNT) discussion of ethical issues and practical concerns (equipment, supplies and strategies); Oocyte enucleation (use of mouse oocytes on Day 1); Preparation of donor somatic cells; Transfer techniques (injection and fusion); Oocyte activation; Culture conditions for growth to blastocyst stage; Plating of mouse SCNT embryos

Day 2: Introduction to derivation of hESC lines; Assessment of embryo quality and potential; Preparation of feeders for derivation; Preparation of media for derivation; Strategies for removal of trophoblast cells; Plating of human embryos for derivation; Preparation of virus for induced pluripotent stem cells,

Day 3: Examination of products of mouse SCNT; Introduction to human SCNT via oocytes that would be discarded; SCNT protocols with human oocytes; SCNT and plating of NT products; infection of fibroblasts with “Yamanaka factors” for reprogramming

Day 4: Analysis of derivation and SCNT products (morphology, transfer protocols, cleavage, and genetic analysis of embryo-specific genes); Discussion, questions and follow-up

Day 5: Examination of colonies (from previous platings prior to class onset) to explore products of iPSC technology, description of assays and confounding factors. Class dismissal with invitation to feed cells, monitor and return for three weeks.

Advanced Individualized Course 2: Stem Cell Applications in Neuroscience. This advanced applications course to be offered in the Stanford University Center for Human Embryo and Embryonic Stem Cell Research and Education focuses on the evolving concepts in neural development, injury and disease as they relate to hESC culture methods and transplantation. It

is anticipated that students will gain additional hands-on experience with the differentiation of neural derivatives, their function and analysis. Course preparation and structure will allow participants to gain experience in key steps of the differentiation protocols that typically span 1-2 months thus accelerate research in their own laboratories where the special emphasis is on applications to neuroscience and neurological disease or injury.

Day 1: Basic concepts in hESC culture and differentiation – Culture and neural induction methods: EB formation, co-culture, or direct induction.

Day 2: Concepts in neural development – Lineages, stages of differentiation and role of growth-factor induced transient amplification. Neurosphere intermediates vs. continuous induction strategies

Day 3: Neural subtype specification - Review of established protocols for generating dopamine neurons, motor neurons, GABAergic interneurons, Glutamatergic projection neurons.

Day 4: Concepts in transplantation – disease models, immunology, teratoma formation. Cell purity, cell harvesting, preparation for injection, animal care and hESC-specific issues in breeding and acquisition of human traits

Day 5: Staining and microscopy methods: Antibodies, microscopy, stereology - Fixation and staining methods, appropriate controls and methods to validate specificity

3. Systems Biology (BME (Biomolecular Engineering) 211). Given strong common interests in this area by a diverse group of scientists across several campuses, I also proposed to share a course in systems biology between the Stanford University Center for Human Embryo and Embryonic Stem Cell Research and Education and faculty at UCSC. This course will be taught at UCSC with relay to the Shared Research Laboratory and Teaching Facility at Stanford University ISCBRM. The course is lecture-based, teaching students with programming experience machine-learning methods relevant for analysis of high-throughput molecular biology experiments. Enrollment is limited to graduate students and postdoctoral fellows at the UCSC campus and participants at the Human Embryonic Stem Cell Facility at Stanford University. Participants may come from a broad background of graduate, postdoctoral, clinical fellows and faculty. We will provide facilities and host discussion and practical sessions for computer-based modules to translate course knowledge to applications in hESC biology. It is anticipated that students will gain insights into basic systems biology concepts and practices and will apply those insights specifically to informatics and computational biology in human embryonic stem cell research. They will form collaborations and interactions to augment the research in their own laboratories with special emphasis on consideration of hESCs as a model system uniquely amenable to the tools provided by computation and network theory. The core topics to be covered over a 10-week course are as follows:

- 1) Manipulating large-scale datasets; 2) Introduction to functional genomics databases; 3) Navigating and visualizing large-scale datasets; 4) Identifying discriminating marker genes with feature selection; 5) Unsupervised analysis of large datasets; 6) Supervised and semi-supervised analysis of large datasets; 7) Graph-theoretic approaches; 8) Data mining practices: search engines, identifying recurrence; 9) Understanding basics of Probabilistic Graphical Models (PGMs); 11) Making inferences with PGMs; 12) Learning PGM parameters from data; 13) Learning PGM structure from data; 14) Causal reasoning with PGMs; 15) Using randomization to simulate random data

Other Teaching

Graduate Students: I currently have six doctoral graduate students; six students previously graduated from my laboratory. Kelly Haston, Cory Nicholas and Vanessa Angeles are members of the Biomedical Sciences (BMS) program at UCSF and relocated with me to Stanford University. In addition, Henrike Siemen, is an exchange student with the Neurobiology Institute in Bonn, Germany. Three other students also have joined my group: Blake Byers, is a bioengineering student, Antonia Dominquez is a Genetics student and Kevin Loewke is a Mechanical Engineering student, all at Stanford University, joining our group in 2008 (note K Loewke has conducted research in human embryology but is officially-based in Engineering). Each of these students has centered their thesis projects on human reproduction, embryonic stem cell biology, induced pluripotent stem cells and/or genetic analysis.

Undergraduates: We often train undergraduate students in my laboratory, primarily from San Francisco State University and the University of California at Berkeley. We have trained the following: Samar Lightfoot (SFSU), Leslie Woo (Cornell University), Douglas Lee (UC-Berkeley), Antonio Casanova (University of Puerto Rico), Lysandra Castro (University of Puerto Rico), Nicole Morison (UC-Berkeley), Janet Lo (UC-Berkeley), Salman Banani (UC-Berkeley), Julianne Moore (UW-Superior) and Dan Culy (UW-Supeior).

Postdoctoral Fellows: I have six postdoctoral fellows: Dr. Connie Wong from Stanford University, Dr. So Hyun Lee from Seoul National University, Dr. Shawn Chavez from Yale University, Dr. Kehkooi Kee from Cornell University, Dr. James Byrne from Cambridge University, and Dr. Sonya Schueh Huerta from the University of Washington. To date, my fellows have succeeded in both academic and private venues with Dr. Rajiv Raja currently serving as the Director of Molecular Biology at Molecular Devices Corporation, Dr. Eugene Xu appointed as an assistant professor at Northwestern University and Dr. Amander Clark as an assistant professor at the University of California at Los Angeles (see attached table).

Medical Fellows/Residents/Mentorships: I have trained or am currently training many Medical fellows in my laboratory: Dr. Dana Kostiner (Clinical Genetics (Pediatrics)), Dr. David Nudell (Urology), Dr. Anthony Dobson (Obstetrics and Gynecology), Dr. Amy Sehnert (Pediatric Cardiology), Dr. Renius Owen (Clinical Genetics (Pediatrics)), Dr. Mitchell Rosen (Obstetrics and Gynecology), Dr. Uche Ezeh (Obstetrics and Gynecology), Dr. Shai Shefi (Urology) and Dr. Katherine Bianco (Genetics), and Dr Raul Clavijo (Urology).

CIRM Trainees: I served as Director of the UCSF CIRM training program (a new training program that has just begun in 2006). I directed the coordination of formal education, consulted on laboratory research, and arranged seminars and other educational venues for scholars. I currently am Co-Director of the Stanford CIRM training program which combines reproductive sciences (embryology), embryonic stem cells, bioengineering and developmental biology into a coherent curriculum and research training plan.

High School Students: I have hosted several high school students from the San Francisco public school system in the High School Summer Internship Program through SEP (Science and Health Education Partnership). These students worked with graduate students in my laboratory but met with me in joint meetings with the graduate students for 30 minutes/week.

Other: Staff Research Associates in my laboratory during 1998 - 2007 were Michael Castillo, Carthon Johnson, Brenda Marsh, Matthew Bensley, Michael Abeyta, Frederick Moore, Juanito Meneses, Sarita Panula, Martha Flores, Ha Nam Nyugen, and Cynthia Klein. I also have sponsored two visiting scientists, Dr. Jadwiga Jaruzelska, of the Institute of Human

Genetics, Polish Academy of Sciences, Poznan, Poland and Dr. Jorg Gromoll of the Institute for Reproductive Medicine in Muenster, Germany. In a similar manner, I co-mentored Dr. Jingly Fung-Weier in conducting her research on preimplantation genetic diagnosis (PGD) (2001-2006). I have also sponsored the initial training phase for Debradenise Brooks, a student in the adult OnRamp program (2003-2004). Finally, I have mentored three junior faculty: Paolo Rinaudo, MD (Ob-Gyn & RS), Miguel Santos-Ramalho, PhD (Medicine) and Robert Blelloch, MD, PhD (Urology) assisting with lab set-up, grant-writing and manuscript preparation.

Summary of Past Trainees

Past Trainees of Reijo Pera Laboratory

Past Trainees	Pre or Post	Training Period	Prior Academic Deg	Yr	Institution	Title of Research Project	Current Position
Ares, Ximena	Post	98-01	PhD	98	University of Buenos Aires	Global Gene Expression in Testicular Biopsies of Infertile Men	Technology Specialist, UCSF Office of Technology Management
Raja, Rejiv	Post	98-01	PhD	97	Oklahoma State University	Microarray analysis of oocytes and embryos	Director of Molecular Biology, Molecular Devices Corporation
Nudell, David	Post	99-02	MD	94	Stanford University	DNA repair and meiotic errors in infertile men	Infertility Associates San Jose, CA
Jaruzelska, Jarwiga	Post	99-01	PhD	unknown	Inst. of Human Genetics; Poznan, Poland	The human NOS1 gene and germ cell development	Scientist, Inst. of Hum. Genet., Poznan, Poland
Shearin, Jennifer	Pre	99-01	BS	98	North Carolina State University	Proteins that interact with human BOULE.	PhD Student, U. North Carolina
Dobson, Anthony	Post	99-03	MD, PhD	93	University of California at Los Angeles	Transcript modulation during human embryo development	Assistant Professor, UCSF
Moore, Frederick	Pre	98-02	BS	97	University of California at Berkeley	Identification and characterization of proteins that interact with the human DAZ and DAZL proteins	Author; Independent Consultant
Xu, Eugene	Post	99-02	PhD	96	University of Chicago	The human BOULE gene and male and female infertility	Assistant Professor, Northwestern University
Clark, Amander	Post	02-03	PhD	99	University of Melbourne	Differentiation of germ cells from human ES cells	Assistant Professor, UCLA
Owen, Renius	Post	02-04	PhD	01	University of Florida	Use of comparative genome hybridization (CGH)	Assistant Professor, Clinical Genetics, Oregon Health Sciences University
Urano, Jun	Post	02-04	PhD	99	University of California at Los Angeles	Characterization of RNAs to which DAZL proteins bind	Postdoctoral Fellow, UCLA
Tung, Joyce	Pre	00-05	BS	99	Stanford University	The human DAZL gene and age at menopause.	Postdoctoral Fellow, Stanford University
Rosen, Mitchell	Post	02-05	MD	94	University of California at San Diego	Premature ovarian failure and DAZL polymorphisms	Assistant Professor, UCSF
Gonsalves, Joanna	Pre	01-05	BS	01	Long Beach State University	Defective meiosis in human infertility	Analyst, Worldwide Market Research, San Mateo, CA

RESEARCH SUPPORT

Ongoing Research Support (in reverse chronological order)

1. (Renee A. Reijo Pera, Principle Investigator) 07/01/07 to 06/30/11

- **California Institute for Regenerative Medicine**
- **RC1-00137-1 Comprehensive Grant**
- **Human Oocyte Development and Reprogramming**

The major goal of this project is to differentiate multiple non-federal hESC lines to oocytes and to use SCNT on differentiated oocytes, and those from the clinic, to characterize the developmental program of human reprogramming, as it is executed by oocytes.

2. (Renee A. Reijo Pera, Principle Investigator) 07/01/07 to 06/30/10

- **California Institute for Regenerative Medicine**
- **CL1-00518-1 Shared Facilities and Stem Cell Courses Grant**
- **Stanford University Center for Human Embryonic Stem Cell Research and Education**

The major goal of this project is to establish a premiere center for human embryo development and stem cell research and education in the state of California. The project establishes shared resources for stem cell research and courses in basic, advanced and systems approaches to human embryo and embryonic stem cell biology.

3. (Renee A. Reijo Pera, Co-Director) 06/01/07 to 5/31/09

- **California Institute for Regenerative Medicine**
- **T1-00001 Training Grant**
- **Stanford CIRM Training Program**

The major goal of this project is to establish a CIRM training program at Stanford to support the training of 6 predoctoral, 6 postdoctoral and 4 clinical fellows in stem cell research from bench to bedside.

4. (Renee A. Reijo Pera, Project I, Principle Investigator) 03/01/07 to 2/28/12

- **National Institute of Child Health and Human Development U54HD055764**
- **Differentiation of Germ Cells from Human Embryonic Stem Cells**

The major goal of this project is to examine the hypothesis that common deletions and polymorphisms in humans impact germ cell development.

5. (Renee A. Reijo Pera, Principle Investigator) 7/01/05 to 6/30/10

- **National Institute of Child Health and Human Development NIH R01 HD047721-01**
- **Genetic Analysis of Human Germ Cell Formation**

The major aims of this grant are to: 1) Characterize the ability of male germ cells to differentiate from human ES cells, 2) Silence Y chromosome genes implicated in male germ cell development and assess development *in vitro* and 3) Silence Y chromosome genes implicated in male germ cell development and assess development *in vivo* in a primate transplant system.

6. (Renee A. Reijo Pera, Co- Investigator: Marcelle I. Cedars, PI) 01/01/05 to 12/31/09

- **National Institute of Aging NIH 1 RO1 44876**
- **Genetic Epidemiology of Ovarian Aging**

The major goal of this project is to explore the hypothesis that ovarian aging, as reflected by antral follicle count (a reflection of oocyte number), is largely determined by genetic polymorphisms (in genes such as *DAZL* and *Interacting Genes*) that impact initial oocyte endowment and rate of oocyte loss over time.

7. (Renee A. Reijo Pera, Principle Investigator) 06/01/06 to 05/31/09

- **March of Dimes FY06-326**
- **Molecular Genetic Analysis of Human Imprinting and Assisted Reproduction**

The major goal of this program is to examine imprinting in cultured human embryos.

8. (Renee A. Reijo Pera, Principle Investigator) 6/01/05 to 05/31/08

- **Tobacco Related Disease Research Program (California) 14RT-0159**
- **Human Oocyte Development and PAH Exposure**

The major goal of this program is to differentiate human oocytes from hESCs in the presence and absence of PAH (polycyclic aromatic hydrocarbons) to assess effects of exposure to chemicals commonly found in secondhand smoke.

9. (Renee A. Reijo Pera, Principle Investigator) 10/01/08 to 09/30/11

- **California Institute for Regenerative Medicine RL1-00670**
- **Derivation and comparative analysis of human pluripotent hESCs, iPSCs and hSSCs: Convergence to an embryonic phenotype**

The major goal of this project is to derive and characterize isogenic human pluripotent spermatogonial stem cell and induced pluripotent stem cell lines, and compare key characteristics with human embryonic stem cells, with the goal of defining optimal cells for novel developmental genetic and potential cell-based preclinical and clinical applications.

Support for Research Personnel

Graduate Students

Vanessa T. Angeles

Cory R. Nicholas

Kelly R. Haston

Nina Kossack
Henrike Siemen

Postdoctoral Fellows

Kehkooi Kee

So Hyun Lee

Source of External Research Support

National Institutes of General Medical Sciences
Predoctoral Award

California Tobacco Related Disease Research
Program Predoctoral Award

Canadian Institute for Health Research
Predoctoral Award

Daimler Chrysler Predoctoral Award

Stiftung der Deutschen Wirtschaft Predoctoral Award

California Tobacco Related Disease Research
Program Postdoctoral Award

Lalor Foundation

Shawn Chavez (Postdoc)

NIH/NICHD F32 Award

Past Research Support (Projects Completed)

1. (Renee A. Reijo Pera, Principle Investigator) 07/01/99 to 6/30/05
 - **NIH R01HD37095**
 - **The *DAZ* genes and early germ cell development in humans**

The major goal of this project is to determine how the *DAZ* gene family functions in allocation (formation) of germ line stem cells in men and women.

2. 1. (Renee A. Reijo Pera, Principle Investigator) 07/01/99 to 6/30/05
 - **NIH R01HD37095 – S1**
 - **The *DAZ* genes and early germ cell development in humans – Supplement for human ES cell research**

The major goal of this project is to determine how the *DAZ* gene family functions in allocation of germ stem cells in men and women, using the human ES cell system.

3. (Renee A. Reijo, P.I.) 7/1/98 to 6/30/01
 - **Searle Scholar**
 - **Genetic and molecular strategies for identification of factors required for allocation and totipotency of human germ cell lineage**

The goals of this research included identification of proteins and RNAs that interact with the *DAZ* gene family, identification of other genes necessary for germ cell allocation to occur and to determine what phenotypes are associated with mutations in the *DAZ* gene family.

4. (Renee A. Reijo, P.I., Andrew Wyrobek, CoInvestigator) 10/1/98 to 12/31/00
 - **University of California Campus-Laboratory Collaboration**
 - **Use of cDNA microarrays to identify and characterize quantitative and qualitative defects in expression of fertility genes in infertile men**

The goals of this project included the identification of genes that map to autosomes or sex chromosomes that are necessary for men to make sperm, exploring the function of each gene by using cDNA microarrays and to determine the order of function of each gene and mutations which disrupt their function.

5. (Renee A. Reijo, P.I.) 11/1/98 to 10/31/99
 - **UCSF Chancellor's Award in Basic Science**
 - **Meiotic arrest and defects in the recombination and DNA repair pathways in infertile men**

The goal of this project was to compare sperm from infertile men with meiotic arrest with that of fertile men in two ways: the percent of recombination and the fidelity of DNA repair in each group of men

6. (Renee A. Reijo, Principal Investigator) 10/1/01 to 9/30/02
 - **RO1 ES 08750**

- **Cellular and Molecular Response to DNA Repair Deficiency**

- This project was transferred to Dr. Reijo by Dr. Pedersen in order to allow completion of research begun by Roger A. Pedersen, Ph.D. The goal of this project was to understand the role of the XRCC1 in modulating damaging effects of various mutagens, particularly DNA damage induced by exposure to radiation or radio-mimetic chemicals, in the germ cells and embryo.

7. (Renee A. Reijo, P.I.)

05/01/02 - 04/30/03

- **Sandler Family Foundation**

- **Genetic Analysis Of Pluripotency In Human Embryonic Stem Cells**

This was seed funding from the UCSF School of Medicine intended to establish the fundamentals of a human embryonic stem cell program including growth, differentiation and genetic modification of hESCs.

8. (Renee A. Reijo and Paul J. Turek, CoInvestigators)

7/01/01 to 6/30/02

- **California Urology Association**

- Gene Expression Patterns in Laser-Captured Germ Cell Populations

The overall goal of the proposed research is to elucidate gene expression in particular germ cell populations, especially the germ stem cells.

9. (Renee A. Reijo Pera, Principle Investigator)

9/01/03 to 8/31/04

- **UCSF Developmental and Stem Cell Biology Award**

- Molecular Exploration of New Candidate Pluripotency Factors, *GDF3*, *STELLA* and *NSTEM* in Humans and Mice

The major goals of this project were to characterize genes, *GDF3*, *STELLA* and *NANOG* by overexpressing and silencing the genes in human embryonic stem cells.

10. (Renee A. Reijo Pera, Principle Investigator)

4/01/01 to 3/31/07

- **NIH 1 RO1 HD38987**

- Genetic Analysis of Meiosis in Men and Risks Associated with ICSI

The major goals of this project are to determine if defects in DNA repair and recombination cause infertility in men, to identify and characterize genes that cause meiotic arrest in men, and to assess genetic risks in children conceived via intracytoplasmic sperm injection from sperm obtained from men with meiotic arrest.

11. (Renee A. Reijo Pera, Principle Investigator)

6/01/04 to 4/30/06

- **NIH 1 RO1 HD38987-S1**

- Genetic Analysis of Meiosis in Men and Risks Associated with ICSI – Supplement for Human ES Cell Research.

The major goals of this project are to use the human ES cell system to characterize the effect of defective DNA repair and recombination on meiotic progression.

12. (Renee A. Reijo Pera, Principle Investigator)

04/01/04 to 8/31/06

- **American Cell Therapy Research Foundation**

- Imprinting and human ES Cell-Derived Germ Cells

The major goals of this project are to: 1) Optimize differentiation of human germ cells of each sex *in vitro* and 2) examine sex-specific imprinting in differentiated germ cells.

13. (Renee A. Reijo Pera, Principle Investigator) 01/01/05 to 12/31/08

- **UCSF School of Medicine**

- Establishment of the UCSF Program in Human Embryonic Stem Cell Biology

The major goal of this project is to establish the UCSF Human Embryonic Stem Cell Research Center that possesses the personnel and scientific tools to derive, characterize and genetically manipulate hESCs and their somatic and germ line fates.

14. (Renee A. Reijo Pera, Principle Investigator) 07/01/05 to 6/30/07

- **National Center for Research Resources NIH 2 R24 RR017498**

- **Federally Registered Human Embryonic Stem Cell Center**

The major goals of this project are to: 1) Distribute human embryonic stem cell lines, HSF-6 and HSF-1 and 2) establish a training program in human embryonic stem cell culture.

PATENTS

Patent Issued: No. WHI94-07: *DAZ*: A Gene Associated with Azoospermia (DC Page and RA Reijo Pera)

Patent Pending Stanford Review: Generation of human spermatogonial stem cell lines for basic and clinical use. (N Kossack, P Turek and RA Reijo Pera)

STUDY PROTOCOLS (Listed below are study protocols that required significant effort to develop and are available to researchers in the community as a resource)

PI	Number	Title
Reijo Pera	04024640	Regulation of gene expression during preimplantation human embryo development
Reijo Pera	AN075720	Growth, characterization and distribution of human ES cell lines (animal use protocol)
Reijo Pera development	H9618-24116	Human embryonic stem cells as a model for
Reijo Pera	H9618-27490	Growth, characterization and distribution of human ES cell lines UC01 and UC06
Reijo Pera	H9618-28386	Somatic cell nuclear transfer with human oocytes
Reijo Pera	H9618-29595	Use of embryonic cells for somatic cell nuclear transfer with human oocytes
Dobson Reijo Pera, Co-PI	H10470-16550	The genetics of abnormal oocytes and preimplantation embryos

Select Invited Presentations

International (Selected presentations)

Medical Research Council (MRC); Edinburgh, Scotland; September 1998
American Society of Reproductive Medicine (ASRM); Toronto, Ontario; September 1999
International Andrology Society; L' Aquila, Italy; March 2000
South American Infertility and Sterility Conference; Santiago, Chile; November 2000
European Society for Human Reproduction and Embryology, Vienna; June 2002
American Society of Reproductive Medicine (ASRM); San Antonio, TX; October 2003
3rd European Congress of Andrology, Munster, Germany, September 2004
Swedish American Stem Cell Meeting: April 2005
International Society for Stem Cell Research: June 2005
UCSF and IMSUT (Institute of Medical Sciences, University of Tokyo) Joint Meeting; July 2005; Tokyo, Japan
Seoul National University; October 2005
Valencia International Stem Cell Conference; March 2006
University of Finland, Tampere; Tissue Engineering Conference; May 2006
CIRM (California Institute for Regenerative Medicine):United Kingdom Stem Cell Workshop; November 2006
International Society for Stem Cell Research (ISSCR); June 2007; Germ Cell Development Chataqua Institute Address; July 2007; Human Embryo Development and Embryonic Stem Cells
Hinxtion Assembly; March 2008; Guidelines on Differentiation of Germ Cells from Human Pluripotent Stem Cells
University of Newcastle (UK); November 2008
5th International Stem Cell Meeting; Westphalia, Germany; March 2009

National (Selected presentations)

American Society of Andrology; Louisville, Kentucky; April 1999
Searle Scholars Meeting; April 1998; April 1999
Gordon Research Conference On Reproductive Tract Biology; Connecticut College; July 2000
Woods Hole Marine Laboratory; "Reproductive Biology Course;" June 2000
American Society of Andrology – Testis Workshop; Seattle, WA; April 2002
Jackson Laboratory - Mouse Initiative IV: Complex Human Disease and Mouse Models; July 2002
Cold Spring Harbor Symposium, "Germ Cells;" October 2002
Endocrinology Division Grand Rounds, National Institutes of Health, January 2003.
NIH Celebration of the 50th Anniversary of the NICHD, June 2003
American Society of Andrology – Baltimore, MD; April 2004
Keynote Address: Pacific Coast Reproductive Society, May 2004
Cold Spring Harbor Symposium, "Germ Cells;" October 2004
NIH Conference: "Crossing Over;" October 2004
US Senate Appropriations Committee Staff Meeting; Derivation and propagation of human ES cells. February 2005
Keynote Address: NIH U54 Centers for Infertility Research; April 2005

NSF AGEP Colloquim for Minority Students: Human Embryonic Stem Cells: April 2005
Endocrinology Society: June 2005
Genes of the Y chromosome; NIH conference at Asilomar; September 2005
Human Genetics and Stem Cell Biology: American Society for Human Genetics; October 2005
American Society for Cell Biology: November 2005
Keynote Address: Western Association of Physicians (WAP) Annual Conference; February 2006
New York State Stem Cell Foundation: Symposium on Human Embryonic Stems and Somatic Cell Nuclear Transfer
National Academies of Sciences symposium on Emerging Issues in Human Embryonic Stem Cell Research; November 2006 (Alternative methods for deriving “embryonic stem cells: Germ Cells)
National Academies of Sciences symposium on Reprogramming; October 2007 (Beckman Center, CA)
American Society for Reproductive Sciences (ASRM) Keynote Speaker; October 2007
Lasker Seminar Series; Stanford University; November 2007
Stanford Graduate School of Business Alumni Association - Bay Area Chapter *Forum on Stem Cell-Based Opportunities in the Healthcare Industry*; June 2008
World Science Festival Panelist (New York, NY); June 2008
Children’s Hospital of Oakland Research Institute (Oakland, CA); June 2008
BioScience Forum (San Francisco, CA); July 2008
National Institute of Standards and Technologies “Keys to Innovation” Meeting; October 2008
National Institute of Standards and Technologies “Human Embryonic Stem Cells”; April 2009

Universities (Selected presentations)

University of Washington at Seattle; Department of Genetics; October 1998
University of Wisconsin at Madison; Department of Genetics; February 1999
University of California at Irvine; Minority Students Program; November 1999
Dean's Research Seminar Series; UCSF; February 1999
Panelist for UCSF Foundation Wellness Day (Palace Hotel; SF; May 1999)
Grand Rounds for Obstetrics, Gynecology & Reproductive Sciences; Pediatrics; Urology; Medicine and Lab Medicine (2 to 3 times each in last 5 years)
University of Virginia; Center for Reproductive Sciences, Department of Obstetrics, Gynecology and Reproductive Sciences; March 2001
Georgetown University; Department of Cell Biology; October 2001
Cornell University, Department of Genetics and Molecular Biology; Ithaca, NY; March 2002
Whitehead Institute for Biomedical Research at MIT, Cambridge, MA; May 2002
University of Arizona in Tucson; Program for Minority Student Scientists; January 2003
Georgetown University; Department of Cell Biology; February 2003
University of Pittsburgh; Human Embryonic Stem Cell Growth; Pittsburgh Development Center, May 2003
UT-Southwestern, Green Center for Reproductive Sciences; October 2003
Diversity Day Presentation; October 2004
UCSF Foundation Presentation; October 2004
Nobel Stem Cell Symposium; October 2005

Keynote Address: Stanford University Genetics Retreat; October 2005
Stanford University; Reproductive Research Day; January 2000, 2001, 2002, 2003, 2004, 2005,
2006
Morehouse University, Student-Invited Speaker; February 2006
University of Connecticut; September 2006
Harvard University Stem Cell Institute; November 2006
Human Genetics Institute; Bringing Stem Cells and Genetics together; January 2006
William Bowes Symposium on Human ES Cell Biology; May 2006
Andy Grove Panel on Parkinson's Disease; July 2006
Bay Area Entrepreneurs (WPO); Stem Cell Medical Research Panel; September 2006
25th Anniversary of Stem Cell Research at UCSF; October 2006
Northwestern University School of Medicine; Department of Medicine; September 2007
UCLA Stem Cell Symposium on Stem Cell Advances; February 2008
Keynote Address: University of Southern California (USC) Stem Cell Retreat; September 2008
San Francisco State University; April 2009
University of Illinois – Champagne/Urbana; April 2009

UNIVERSITY SERVICE

Chancellor's Advisory Committee on the Status of Women (CACSW)
Admission Committee for Graduate Students in the Program in Biological Sciences (UCSF)
Admissions Committee for Medical Genetics Fellows (1997-1998)
Panelist for UCSF Foundation Wellness Day (Palace Hotel; SF; May 1999)
Member UCSF Human Genetics Course Planning Committee (Jane Gitscher, chair, 1999)
Member UCSF BioMedical Sciences Genetics Course Committee (Joe Gray, chair, 2001-2002)
Steering Committee - Center for Reproductive Sciences (1999 – present)
Member of the Academic Senate Committee on Research (COR; 2001-present)
Member of the Steering Committee for UCSF Developmental and Stem Cell Biology Program
(2002-present)
Represented UCSF for Minority Graduate Program Recruitment by Presentations (UC-Irvine,
November 1999; UCSF Faculty Host, December 2001; UCSF Faculty Research Speaker,
February 2002)
Panelist for UCSF Foundation Presentation, October 2002, "Stem Cells" (Home of John and
Francis Bowes)
Steering Committee; Developmental and Stem Cell Biology Program (2002 – present)
Planning Committee; Proposition 71 Human Embryonic Stem Cell Application (2004 – present)
Core Member; UCSF Center for Human Genetics (2004 – present)
Panelist; UCSF Diabetes Research Program (Stem Cells and Diabetes; May 2005)
Co-Organizer; UCSF BioMedical Sciences (BMS) Retreat (with Kevin Shannon, MD; 2005)
Presentation of Stem Cell Research Opportunities (Dr. Kessler (Dean of School of Medicine)
hosted Minister of Health, India (Dr. Anbumani Ramadoss)); June 2005
Member; UCSF Oocyte, Embryo, and Stem Cell Research (OESCR) Committee; June 2005 –
present
Teacher/Coordinator; "Human Embryonic Stem Cells;" Mini-Medical School Curriculum; June
2005

Teacher/Coordinator; “Human Embryonic Stem Cells;” Mini-Medical School Curriculum; June 2006
Director; Stanford University Center for Human Embryonic Stem Cell Biology; April 2007 to present
Stanford SCRO (Stem Cell Research Oversight) Committee; Stanford University; April 2007 to present
Steering Committee; Stanford PRM (Program in Regenerative Medicine); April 2007 to present
Steering Committee; Stanford University Institute for Stem Cell Biology & Regenerative Medicine; April 2007 to present
Education Committee; Stanford University Institute for Stem Cell Biology & Regenerative Medicine; April 2007 to present
Division Chief; Reproductive Biology and Stem Cell Program; Stanford Department of Obstetrics and Gynecology
Disease Planning Team; Cardiovascular Institute (2008; R Robbins, Group Leader)
Disease Planning Team; Craniofacial Defects and Repair (2008; M Longaker, Group Leader)
Disease Planning Team; Muscular Dystrophy and Stem Cells (2008; T Rando; Group Leader)
Co-Author of CIRM Large Facilities Application (2008; \$43.8M for SIM1)
Organizer; Stanford University Reproductive and Stem Cell Biology Retreat; January 30, 2009
Faculty representative – Institute for Stem Cell Biology & Regenerative Medicine; Dean’s Retreat (February 2009)
Faculty presenter; National Advisory Council Meeting for the Dean of the School of Medicine (March 2009)
Freshman – Sophomore College Speaker; Stanford University Living Group; April 2009

PUBLIC SERVICE

Women’s 98 Forum (Betty Ford Center; Palm Springs, CA), 1998
Consultant for International Quality Control Assessment Programme for Y-Chromosomal Microdeletions (Institute for Reproductive Medicine Munster Germany), 1999-2000
Ad Hoc Member of the Reproductive Biology Study Section (NICHD, NIH), 2001-2002
Ad Hoc Member of the U54 Contraceptive Study Section (RFA; NICHD, NIH), 2002
Ad Hoc Member of the Mammalian Genetics Study Section on Mouse Phenotyping (RFA; NIGM, NIH; 2002)
Scientific Reviewer for the Italian Funding Agency - Fondazione Telethon; Milano, Italy; June 2002 - 2004
Continuing Medical Education Instructor; Clinical Infertility and Reproductive Endocrinology (San Francisco, CA; April, 2002)
Member of the *Faculty of 1000*, a group of faculty providing reviews of relevant literature in area of expertise (www.facultyof1000.com)
Permanent Member of the CMIR (Cellular, Molecular and Integrative Reproduction) Study Section (NICHD, NIH – June, 2004 to 2008)
Coalition Member to Promote Proposition 71 – Women’s Advocacy Groups; Medical and Scientific Community Leaders (2004-present)
Scientific Reviewer for the Research Funding and Policy Division of the Health Research Board in Ireland (2005)

Scientific Reviewer for the Research Funding for Embryo Research in Animals (NSERC of Canada; 2005)
CoDirector; Frontiers in Human Embryonic Stem Cells Course (Stanford University, School of Medicine; June 2005)
Scientific Education on Derivation and Propagation of hESCs; US Senate Appropriations Committee Staff Meeting (February 2005)
Scientific Reviewer for the Programming Committee for the International Embryo Transfer Society; Annual Meeting, Orlando, FL (January 2006)
Scientific Reviewer for the Illinois Regenerative Medicine Institute (April 2006)
External Advisory Committee Member; Oregon Health Sciences University (September 2006 - present)
Organizer; Cold Spring Harbor Laboratory (CSHL) Meeting "Germ Cell Development" in 2008
College of Reviewers for the Canada Research Chairs Program; 2006
Loreal Women in Science Program Moderator (February 2007)
Reviewer; German Funding Initiative for Stem Cell Research (DFS) (November 2007)
Americans for Cures; State of Stem Cell Advocacy Conference Speaker (April 2008)
CIRM Town Hall Forum for public awareness of stem cell research (March 2009)
Science Day Speaker; Los Altos High School (March 2009)
Keynote address at St Francis Middle School (Los Gatos, CA) Science Symposium – Inspiration and Innovation (March 2009)
NIH Review Panel "Fertility Preservation" (March 2009)
Invited Attendee to Whitehouse Stem Cell (hESC) Presidential Order Signing (March 2009)

POPULAR PRESS (Selected)

Good Morning America; "Update on infertility;" January 5, 1998
The San Francisco Chronicle; "UCSF study finds new clue to male infertility;" June 5, 2000
The Economist; "Infertility treatments;" December, 2000
The Scientist; "California steaming;" June, 2001
Forbes; "Help for male infertility;" February 18, 2002
ScienceDaily News; "From flies to humans -- male infertility;" January 15, 2003
San Jose Mercury News; "Seeking clues on fertility's window; Making choices: tests would predict childbearing prime, helping women plan;" April 13, 2004
Contra Costa Times; "The stem cell initiative;" November 3, 2004
Inside Bay Area; "Who gets stem cell funding is the \$3 billion question;" November 10, 2004
Los Angeles Times; "Stem cells carry mouse antigens;" January 15, 2005
Oakland Tribune; "Who gets stem cell funding is the \$3 billion question: Bay Area scientists studying Alzheimer's, sickle cell anemia among those seeking cash;" April 10, 2005
Sacramento Bee; "Stem cell guidelines get mixed reception;" April 27, 2005
Center for Genetics and Society (Newsletter); "Stem cell guidelines get mixed reception: Critics say voluntary rules are too lax;" April 27, 2005
Numerous daily newspapers; "UCSF stem cell experts discuss research aims;" June, 2005
The Scientist; Feature Article: "Stem cells.....an emerging portrait" July 4, 2005
Nature; "Stem-cell 'heroes' celebrate a series of breakthroughs;" July 7, 2005
San Francisco Chronicle; Medical schools get stem cell grants: UCSF, Stanford set for \$3.7 million each; September 10, 2005

Science; News and Views: "Seeking immortality in a petri dish;" September 23, 2005
Milwaukee Journal Sentinel; "Wisconsin to house US stem cell bank;" October 1, 2005
Nature; News and Views: "The hands that guide: Good mentors deserve wider recognition;"
November 9, 2005
Medical News Today; "Activity of several embryonic stem cell genes is elevated in testicular
and breast cancers;" December 1, 2005
USA Today; Cloning race begins; January 18, 2006
National Geographic News; Mouse testicles yield promising stem cells; March 24, 2006
Wall Street Journal; "Embryo stem-cell research spreads despite curbs;" April 4, 2006
The New Atlantis; "Stem cell spin;" Spring 2006
Technology Review; "Stem cells reborn;"
May/June, 2006
New York Times; "Two new efforts to develop stem cell lines for study;" June 7, 2006
International Herald Tribune; "Scientists to develop stem cells from patients;" June 7, 2006
National Public Radio; "Harvard goes private for stem cell research;" June 7, 2006
USA Today; "Embryonic stem cell research before, after 'Dolly';" June 7, 2006
Technology Review (MIT Press); Stem cells reborn (therapeutic cloning); May/June 2006
Science; Stem cell research: Cloners get OK to proceed with caution; June 2006
Los Angeles Times; "New stem cell ethics issue emerges;" September 13, 2006
Newsweek; "Twenty women leaders;" September 25, 2006
NewScientist; "Reproduction revolution: The egg and sperm race;" October 11, 2006
PBS; Wired Science; "Stem cell explorer;" January 5, 2007
San Francisco Chronicle; "California: More stem cell research grants are on the way;" March
17, 2007
Los Angeles Times; "Embryonic stem cell research gets surprise support;" March 20, 2007
Stanford Report; "Stanford opens embryonic stem cell lab: Director Reijo Pera hails a new era
of exploration: "the search within." September/October, 2007
ABC7 News; "Stem cell research grants given to universities: Stanford gets the biggest chunk;"
June 06, 2007
Science (2008) "A Seismic Shift for Stem Cell Research: The development of pluripotent cells
from individual skin cells has opened up a new world of research, but scientists say they still
need to work with embryonic stem cells
Nature (2008) "Monkey stem cells cloned: Advance could renew enthusiasm for the field"
Forbes (2009) "What the stem cell ban reversal means for you"
Science News (2009) "Testes stem cell can change into other body tissues"
San Francisco Chronicle (2009) "Testes found to yield versatile stem cells"
San Jose Mercury News (2009) "Scientists identify new kind of stem cell found in testes"
San Jose Mercury News (2009) "Proposed NIH stem cell guidelines dismay leading Stanford"