

Division Details

Division Data Summary

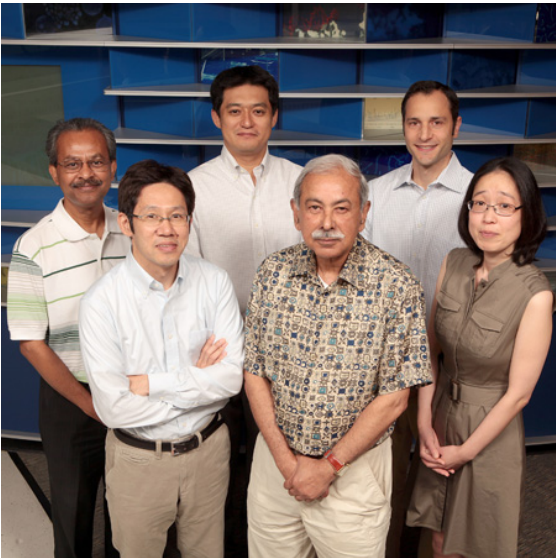
Research and Training Details

Number of Faculty	7
Number of Research Fellows	11
Number of Research Students	1
Number of Support Personnel	7
Direct Annual Grant Support	\$1,526,399
Peer Reviewed Publications	13

Clinical Activities and Training

Number of Clinical Staff	0
Number of Clinical Fellows	1

Division Photo



Row 1: Y Ogawa, SK Dey, T Daikoku
Row 2: S Das, S Namekawa, T De Falco

Significant Accomplishments

Fetal Programming and Environmental Exposures

S.K. Dey, PhD, Jeff Whitsett, PhD, and Susan Fisher, PhD, University of California San Francisco, organized “Fetal Programming and Environmental Exposures: Implications for Prenatal Care and Pre-Term Birth, ” a meeting jointly sponsored by the New York Academy of Science and Cincinnati Children’s. Held in New York City, the meeting drew 140 researchers and clinicians to discuss factors affecting prenatal development and how to better deal with those factors.

Funding and Research

All five of our division’s full-time faculty members are funded by at least one external grant, and three of the five have more than one external grant. Three out of five are also funded by one internal grant. Overall, the division is supported by five NIH, five private, and two internal grants.

Although preterm birth and prematurity are worldwide problems, the underlying mechanisms are still unknown. Uterine decidual senescence via the mammalian target of rapamycin complex 1 (mTORC1) signaling is a novel approach to understanding the cause of preterm birth. We found that decidual senescence could be reversed by administering either a very low dose of rapamycin (an inhibitor of mTORC1 signaling) or Celebrex, a COX-2 inhibitor (an anti-inflammatory). This work was highlighted by the American Association for the Advancement of Science (AAAS) in *Cell Signaling*, *Biology of Reproduction*, and *Cell Cycle*.

Report on our Adjunct Professors Abroad

Report on our Adjunct Professors Abroad

The Division of Reproductive Sciences has two adjunct professors stationed at universities abroad. Yasushi Hirota, MD, PhD, is based at the National Institute of Genetics of Japan in Shizuoka, Japan. He published two papers in FY12, along with members of Dey's lab, in the *Proceedings of the National Academy of Science USA* and *Developmental Cell*. He also received a research award from the Japan Society of Reproductive Medicine and an outstanding presentation award from the 64th Annual Congress of the Japan Society of Obstetrics & Gynecology.

Hirota also received three new grants in FY12: a grants-in-aid for scientific research (KAKENHI) from the Japan Society for the Promotion of Science; a research grant from the Mochida Memorial Foundation for Medical and Pharmaceutical Research; and a research grant from the Kanae Foundation for the Promotion of Medical Science. This year, Hirota was named to the editorial board of the journal *Molecular Human Reproduction*.

Hyunjung (Jade) Lim, PhD, is based at Konkuk University in Seoul, South Korea. She published three papers in FY12: two in *Molecular Human Reproduction* and one in *Molecular Biology Reports*. She was awarded a center grant on Fertility Preservation Network as principal investigator of Project 4, which will run for five years and look into the development of molecular cell biological markers for oocyte and ovarian tissue cryopreservation.

Division Highlights

SK Dey, PhD

Keynote Speaker at the ICRS 2011 Symposium in St. Charles, IL. His talk was titled, "**Annual Kang Tsou Memorial Lecture.**" (July 6-10, 2011)

SK Dey, PhD

Invited session leader at the Nature Medicine Herrenhausen Symposium on Reproductive Biology in Seeon, Germany. He led the Funding and Training session. (October 4-7, 2011)

SK Dey, PhD

Keynote Speaker at the 2nd International Symposium on Reproductive Medicine in Seoul, Korea. His talk was titled, "**Endocannabinoid signaling in early pregnancy: Lessons from mouse models.**" (October 28, 2011)

SK Dey, PhD

Participated in the NIH-sponsored 6th Collaborative Team Meeting on Interdisciplinary Research on Blastocyst Implantation held in Rockville, MD. (February 21 and 22, 2012)

SK Dey, PhD

Gave an invited talk at the 2012 Annual Society for Gynecologic Investigation (SGI) Meeting in San Diego, CA (March 20-24). His talk was titled, "**Premature Decidual Senescence Provokes Preterm Birth.**"

SK Dey, PhD

Invited to give an endowment lecture at the Magee-Womens Research Institute in Pittsburgh, PA, for their annual Research Day in Reproductive Biology and Women's Health (May 25, 2012). His lecture was titled, "**Premature Decidual Senescence Provokes Preterm Birth.**"

Takiko Daikoku, PhD

Invited to Northwestern University in Chicago, IL to give a lecture titled, “**PTEN, mTORC1, COX-2 and Endometrial Cancer.**” (April 5, 2012)

Jeeyeon Cha, Graduate Student MD/PhD

Selected to give an oral presentation at the Society of Gynecologic Investigation 59th Annual Scientific Meeting in San Diego, CA. Title: “Increased mammalian target of rapamycin complex-1 (mTORC1) signaling is a major contributor to preterm birth.” (March 21-24, 2012)

Hosu Sin, PhD

Awarded the Japan Society for Reproductive Medicine/MSD Scientific Award for her paper entitled, “**Features of constitutive gr/gr deletion in a Japanese population.**”(December 8, 2011)

Satoshi Namekawa, PhD

Selected to give a talk at The Institute of Cancer Research in Sutton, UK, titled, “**A link between DNA damage response pathway and epigenetic programming.**” (July 19, 2011)

Satoshi Namekawa, PhD

Selected to give a talk at the EMBO Conference on 50 Years of X-inactivation Research in Cambridge, UK titled, “**Sex Chromosome Inactivation in Male.**” (July 20-24, 2011)

Satoshi Namekawa, PhD

Selected to give a talk at the Gordon Research Conference on Mammalian Gametogenesis and Embryogenesis in Waterville Valley, NH, titled “**Meiotic Sex Chromosome Inactivation: Mechanism and Evolution.**” (August 21-26, 2011)

Satoshi Namekawa, PhD

Invited to give a talk at the Cold Spring Harbor Asia: Developmental Control of Sex, Growth and Cellular Fate conference in Suzhou, China, titled, “**Sex chromosome inactivation in male germ cells-Mechanism and evolution.**” (October 11-15, 2011)

Satoshi Namekawa, PhD

Invited to give a talk at the MDB seminar at Cincinnati Children's Hospital Medical Center in Cincinnati, OH titled, “**Journey of the sex chromosomes through reproduction and evolution.**” (February 1, 2012)

Satoshi Namekawa, PhD

Invited to give a talk at The second SKLRB Symposia on Frontiers in Reproductive Biology in Beijing, China titled, “**Regulatory Mechanism of Sex Chromosome in Germ Cells: Chromosome-wide Inactivation and Activation.**” (May 6-11, 2012)

Satoshi Namekawa, PhD

Selected to give a talk at the 14th Annual Midwest DNA Repair Symposium in Cincinnati, OH titled, “**DNA Damage Response on the Sex Chromosomes in Germ Cells: Chromosome-wide Inactivation and Activation.**” He was also a session chair. (May 19-20, 2012)

Satoshi Namekawa, PhD

Invited to give a talk at the Gordon Research Conference on Meiosis in New London, NH titled, "**A novel role of the DNA damage response pathway in meiosis: Chromosome-wide gene activation of inactive sex chromosomes.**" (June 3-8, 2012)

Satoshi Namekawa, PhD

Invited to give a talk at the University of Cincinnati in Cincinnati, OH for a Physiology seminar titled, "**Journey of the sex chromosomes through reproduction and evolution.**" (June 12, 2012)

New Hires

September - Sandi Newman, Grant Specialist

March - Macarena Vargas Vargas, PhD, as a Postdoctoral Fellow in S.K. Dey's lab

March - Monica Cappelletti, PhD, as a Postdoctoral Fellow in Reproductive Sciences
and Immunology (joint between S.K. Dey, PhD, and Senad Divanovic, PhD).

April - Kazuteru Hasegawa, PhD, as a Postdoctoral Fellow in Satoshi Namekawa's lab

May - Tyler Broering, Research Assistant II for Satoshi Namekawa's lab

June - Dustin Sams, Research Assistant II for S.K. Dey's lab

June - Jake Burlew, SURF Student, for S.K. Dey's lab

June - Kris Alavattam, SURF Student, for Satoshi Namekawa's lab

Promotions

Takiko Daikoku, PhD, to Research Associate Professor

Sandi Newman to Financial Analyst I

Division Publications

1. Cha J, Hirota Y, Dey SK. **Sensing senescence in preterm birth.** *Cell Cycle*. 2012; 11:205-6.
2. Chung D, Das SK. **Mouse primary uterine cell coculture system revisited: ovarian hormones mimic the aspects of in vivo uterine cell proliferation.** *Endocrinology*. 2011; 152:3246-58.
3. Chung D, Gao F, Ostmann A, Hou X, Das SK. **Nucleolar Sik-similar protein (Sik-SP) is required for the maintenance of uterine estrogen signaling mechanism via ERalpha.** *Mol Endocrinol*. 2012; 26:385-98.
4. Daikoku T, Cha J, Sun X, Tranguch S, Xie H, Fujita T, Hirota Y, Lydon J, DeMayo F, Maxson R, Dey SK. **Conditional deletion of Msx homeobox genes in the uterus inhibits blastocyst implantation by altering uterine receptivity.** *Dev Cell*. 2011; 21:1014-25.
5. Daikoku T, Jackson L, Besnard V, Whitsett J, Ellenson LH, Dey SK. **Cell-specific conditional deletion of Pten in the uterus results in differential phenotypes.** *Gynecol Oncol*. 2011; 122:424-9.
6. Himaki T, Masui Y, Chono K, Daikoku T, Takemoto M, Haixia B, Okuda T, Suzuki H, Shiraki K. **Efficacy of ASP2151, a helicase-primase inhibitor, against thymidine kinase-deficient herpes simplex virus type 2 infection in vitro and in vivo.** *Antiviral Res*. 2012; 93:301-4.
7. Hirota Y, Burnum KE, Acar N, Rabinovich GA, Daikoku T, Dey SK. **Galectin-1 markedly reduces the**

- incidence of resorptions in mice missing immunophilin FKBP52.** *Endocrinology*. 2012; 153:2486-93.
8. Hirota Y, Cha J, Yoshie M, Daikoku T, Dey SK. **Heightened uterine mammalian target of rapamycin complex 1 (mTORC1) signaling provokes preterm birth in mice.** *Proc Natl Acad Sci U S A*. 2011; 108:18073-8.
 9. Ma X, Gao F, Rusie A, Hemingway J, Ostmann AB, Sroga JM, Jegga AG, Das SK. **Decidual cell polyploidization necessitates mitochondrial activity.** *PLoS One*. 2011; 6:e26774.
 10. Sin HS, Ichijima Y, Koh E, Namiki M, Namekawa SH. **Human postmeiotic sex chromatin and its impact on sex chromosome evolution.** *Genome Res*. 2012; 22:827-36.
 11. Sroga JM, Ma X, Das SK. **Developmental regulation of decidual cell polyploidy at the site of implantation.** *Front Biosci (Schol Ed)*. 2012; 4:1475-86.
 12. Sun X, Dey SK. **Endocannabinoid signaling in female reproduction.** *ACS Chemical Neuroscience*. 2012; 3:349-355.
 13. Sun X, Zhang L, Xie H, Wan H, Magella B, Whitsett JA, Dey SK. **Kruppel-like factor 5 (KLF5) is critical for conferring uterine receptivity to implantation.** *Proc Natl Acad Sci U S A*. 2012; 109:1145-50.

Faculty, Staff, and Trainees

Faculty Members

Sudhansu K. Dey, PhD, Professor

Leadership Division Director; Lova Rieker Chair

Research Interests Pregnancy and implantation; reproductive cancers

Takiko Daikoku, PhD, Associate Professor

Research Interests Reproductive cancers; blastocyst implantation

Sanjoy Das, PhD, Professor

Research Interests Uterine decidualization; environmental estrogens

Satoshi Namekawa, PhD, Assistant Professor

Research Interests Epigenetics of germ cells; X chromosome inactivation

Yuya Ogawa, PhD, Assistant Professor

Research Interests Molecular mechanisms of X chromosome inactivation

Yasushi Hirota, MD, PhD, Adjunct

Research Interests Human reproduction; endometrial biology; implantation (Home Institution: National Institute of Genetics of Japan)

Hyunjung "Jade" Lim, PhD, Adjunct

Research Interests Embryo Implantation (Home Institution: Konkuk University, Korea)

Trainees

- **Jeeyeon Cha, BS**, University of Cincinnati, Medical School
- **Daesuk Chung, PhD**, University of Colorado
- **Fei Gao, PhD**, Vanderbilt University
- **Kazuteru Hasegawa, PhD**, National Institute of Genetics
- **Yosuke Ichijima, PhD**, Harvard University
- **Xinghong Ma, PhD**, Mayo Clinic, Minneapolis, MN
- **Ho-Su Sin, PhD**, Kanazawa University, Japan

- **Julie Sroga, MD**, University of Cincinnati
- **Xiaofei Sun, PhD**, Vanderbilt University
- **Macarena Vargas Vargas, PhD**, Pontificia Universidad Católica de Chile
- **Huirong Xie, PhD**, Vanderbilt University
- **Norishige Yamada, PhD**, RIKEN Center for Developmental Biology, Kobe, Japan
- **Mikihiro Yoshie, PhD**, Tokyo University of Pharmacy and Life Sciences

Division Collaboration

Division of Biomedical Informatics » Anil Jegga, PhD

Title: Bioinformatics Approach to Preimplantation Embryo Development with Respect to Endocannabinoid Signaling

Collaboration with: SK Dey

Division of Developmental Biology » Steve Potter, PhD

Title: Hox Genes in Female Reproduction

Collaboration with: SK Dey

Division of Endocrinology » Stuart Handwerger, PhD

Title: Role of Endocannabinoid in Uterine Decidualization

Collaboration with: SK Dey

Division of Molecular Immunology » Senad Divanovic, PhD

Title: Role of Endocannabinoid in Preterm Birth

Collaboration with: SK Dey

Division of Neonatology and Pulmonary Biology » Jeff Whitsett, PhD

Title: Role of KLF5 in Uterine Biology and Implantation

Collaboration with: SK Dey

Division of Biomedical Informatics » Anil Jegga, PhD

Title: Molecular signaling analysis of decidual cell polyploidy development

Collaboration with: Sanjoy Das

Division of Endocrinology » Stuart Handwerger, PhD

Title: Analysis of molecular signaling axis for Hoxa-10 and H19 during uterine decidualization in human

Collaboration with: Sanjoy Das

Division of Experimental Hematology & Cancer Biology » Paul R. Andreassen

Title: Role of DNA damage response pathways in spermatogenesis

Collaboration with: Satoshi Namekawa

Division of Developmental Biology » Rashmi S. Hegde , Richard A. Lang, PhD, and Visual Systems Group

Title: Role of tyrosine phosphatases in spermatogenesis

Collaboration with: Satoshi Namekawa

Division of Allergy and Immunology » Artem Barski, PhD

Title: Analysis of germline epigenome

Collaboration with: Satoshi Namekawa

Division of Pulmonary Biology » Machiko Ikegami, MD, PhD

Title: DNA methylation analysis of lung cancer suppressor genes

Collaboration with: Yuya Ogawa, PhD

Grants, Contracts, and Industry Agreements

Grant and Contract Awards	Annual Direct
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CHA, J

Premature Uterine Aging and Preterm Delivery

National Institutes of Health

F30 AG 040858	09/16/11-09/15/15	\$46,800
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DAS, S

Environmental Toxins and Uterine Gene Expression

National Institutes of Health

R01 ES 007814	09/15/08-05/31/13	\$220,523
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DEY, S

Endocannabinoid Signaling During Early Pregnancy

National Institutes of Health

R37 DA 006668	08/01/08-12/31/12	\$300,289
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Endocannabinoid Signaling Via CB2 Protects Against Preterm Birth by Modulating Immune Responses

March of Dimes

03/01/12-02/28/15	\$160,240
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Molecular Signaling in Uterine Receptivity to Implantation

National Institutes of Health

R01 HD 068524	09/26/11-06/30/16	\$212,500
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Pten-COX2-mTOR Signaling in Endometrial Cancer

National Institutes of Health(The University of Texas)

P01 CA 077839	06/01/12-05/31/17	\$185,422
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NAMEKAWA, S

DNA Damage Response Pathways in Meiotic Sex Chromosome Inactivation

National Institutes of Health

R01 GM 098605	08/01/11-07/31/16	\$182,200
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Regulation of Sex Chromosome Inactivation by the FANC/BRCA Pathway

March of Dimes

02/01/11-01/31/13	\$68,182
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OGAWA, Y

Regulation of Escape Genes on the Inactive X-Chromosome

March of Dimes

	06/01/12-05/31/15	\$74,243
SIN, H		
Controlling Mechanism of Sex-Linked Genes Required for Sperm Function		
Lalor Foundation		
	06/01/12-05/31/13	\$38,000
SUN, X		
Zinc Finger-Containing Transcription Factor, KLF5, is Critical to the Uterine Receptivity		
Lalor Foundation		
	06/01/12-05/31/13	\$38,000
	Current Year Direct	\$1,526,399
	Total	\$1,526,399