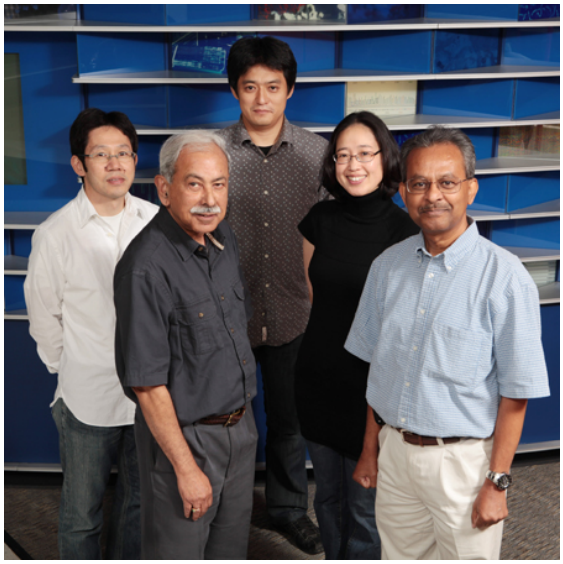
Reproductive Sciences

Division Data Summary

Research and Training Details

Number of Faculty	**5**
Number of Joint Appointment Faculty	**1**
Number of Research Fellows	**9**
Number of Research Students	**2**
Number of Support Personnel	**8**
Direct Annual Grant Support	**$1,173,798**
Peer Reviewed Publications	**6**

Division Photo



Row 1: SK Dey, S Das
Row 2: Y Ogawa, T Daikoku
Row 3: S Namekawa

Significant Publications

Hirota Y, Acar N, Tranguch S. Burnum KE, Xie H, Kodama A, Osuga Y, Ustunel I, Friedman DB, Caprioli RM, Daikoku T, Dey SK. **Uterine FK506-binding protein 52 (FKBP53)-peroxiredoxin-6 (PRDX6) signaling protects pregnancy from overt oxidative stress**. *Proc Natl Acad Sci USA*. 107, 15577-15582. 2010.

This paper showed that immunophilin FKBP52, a co-chaperone for progesterone receptor activity, provides critical regulation of oxidative stress (via the antioxidant PRDX6) in the uterus during pregnancy. Oxidative stress is a significant risk factor for preterm birth in humans.

Gao F, Ma X, Ostmann AB, Das SK. **GPR30 activation opposes estrogen-dependent uterine growth via inhibition of stromal ERK1/2 andestrogen receptor alpha (ER□)phosphorylation signals**. *Endocrinology*. 152:1434-1447. 2011.

This paper uncovered a novel role for GPR30 in the regulation of uterine decidualization by E2. This may have implications for the understanding of both normal and pathological instances of uterine decidualization. This work was highlighted in the "Endocrine News" April 2011 issue.

Hirota Y, Daikoku T, Tranguch S, Xie H, Bradshaw HB, Dey SK. **Uterine-specific p53 deficiency confers premature uterine senescence and promotes preterm birth in mice**. *J Clin Invest*. 120(3):803-815, 2010.

Using mouse models conditionally-deleted of p53, we showed that p53 deficiency confers premature senescence of uterine decidual cells via activation of the prostaglandin pathway. This senescence provokes preterm birth in mice, and was successfully rescrued with the adminsitration of the Cox-2 inhibito celecoxib. This paper was rated as "excellent" by the Faculty of 1000 Biology and the Faculty of 1000 Medicine, and was highlighted in Nature Medicine.

Sun X, Xie H, Yang J, Wang H, Bradshaw HB, Dey SK. **Endocannabinoid signaling directs differentiation of trophoblast cell lineages and placentation**. *Proc Natl Acad Sci USA*. 107(39):16887-16892. Epub Sept 13, 2010.

Using trophoblast stem cells, this paper conclusively showed that trophoblast cell fate is mediated by cannabinoid receptor 1 signaling. This is significant in that proper trophoblast differentiation is critical for proper placental development and pregnancy success.

Lee JE, Oh HA, Song H, Jun JH, Roh CR, Xie H, Dey SK, Lim HJ. **Autophagy regulates embryonic survival during delayed implantation**. Endocrinology. 152(5):2067-2075. 2011.

This paper provides the first evidence that autophagy maintains embryo dormancy during diapause. This paper was highlighted in an Endocrinology Special Report.

Division Collaboration

Endocrinology; Reproductive Sciences; Reproductive Sciences; Reproductive Sciences » Dr. Stuart Handwerger; Sanjoy Das; Dr. S. K. Dey; Dr. Takiko Daikoku

Epigenetic regulation of uterine receptivity for embryo implantation and 2) Analysis of molecular signaling axis for Hoxa-10 and H19 during uterine decidualization in human

Biomedical Informatics; Reproductive Sciences » Anil Jegga; Sanjoy Das

Molecular signaling analysis of decidual cell polyploidy development

Experimental Hematology & Cancer Biology; Reproductive Sciences » Paul R. Andreassen; Satoshi Namekawa

Role of DNA damage response pathways in spermatogenesis

Division of Developmental Biology; Visual Systems Group; Reproductive Sciences » Rashmi S. Hegde; Richard A. Lang; Satoshi Namekawa

Role of tyrosine phosphatases in spermatogenesis

Neonatology and Pulmonary Biology; Reproductive Sciences; » Jeffrey Whitsett; SK Dey

Examining KLR5 and associated female reproductive phenotypes

Developmental Biology; Reproductive Sciences » Steve Potter; SK Dey

Examining Hoxa genes and associated female reproductive phenotypes

Molecular Immunology; Molecular Immunology; Reproductive Sciences » Christopher Karp; Senad Divanovic; SK Dey

CB2 signaling and immunity in pregnancy

Faculty Members

Sudhansu K. Dey, PhD, Professor

Division Director
Lova Riekert Chair

Research Interests Pregnancy and implantation; reproductive cancers

Takiko Daikoku, PhD, Assistant 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

Joint Appointment Faculty Members

Jade Lim, PhD, Adjunct

Konkuk University, Korea

Research Interests Embryo Implantation

Trainees

- Jeeyeon Cha, BS, University of Cincinnati, Medical School
- Poornima Chandran, MS, Osmania University, Hyderabad, India - Fulbright Fellow
- Daesuk Chung, PhD, University of Colorado
- Norishige Yamada, PhD, RIKEN Center for Developmental Biology, Kobe, Japan
- Mikihiro Yoshie, PhD, Tokyo University of Pharmacy and Life Sciences
- Fei Gao, PhD, Vanderbilt University
- Ho-Su Sin, PhD, Kanazawa University, Japan
- Xiaofei Sun, BS, Vanderbilt University
- Huirong Xie, PhD, Vanderbilt University
- Yosuke Ichijima, PhD, Harvard University
- Xinghong Ma, PhD, Mayo Clinic, Minneapolis, MN
- Tarita Pakrashi, MD, University of Cincinnati
- Julie Sroga, MD, University of Cincinnati

Significant Accomplishments

Division Members Receive Grant Funding

Several faculty members received new grant awards in FY11.

- Takiko Daikoku, PhD, received the $50,000 Perinatal Institute Pilot and Feasibility Funding grant from Cincinnati Children's Perinatal Institute for her project, "In pursuit of Lgr5 regulation and function in the uterus."
- Satoshi Namekawa, PhD, received the March of Dimes Basil O'Connor Starter Scholar Research Award of $150,000 for a two-year period for his project, "Regulation of sex chromosome inactivation by the FANC/BRCA Pathway."
- S.K. Dey, PhD, received the Bill and Melinda Gates Foundation Grand Challenges Round 5 grant of $100,000 for 18 months for his project, "Targeting mTOR signaling to prevent preterm birth." This pilot funding allows for the opportunity to compete for additional research funds.
- Yuya Ogawa, PhD, received a Cincinnati Children's Trustee Grant of $60,000 a year for two years for his project, "The mechanism of escape genes on the inactive X-chromosome."
- Sanjoy Das, PhD, had his National Institute of Environmental Health Sciences R01 grant, "Environmental Toxins and Uterine Gene Expression," funded at $330,000 a year.

Training of Students and Postdoctoral Fellows

The Division of Reproductive Sciences continued to demonstrate its commitment to training the next

generation of reproductive sciences researchers. Xiaofei Sun (in the Dey lab) successfully defended his dissertation and received his PhD from Vanderbilt University in July 2010. He has chosen to stay with the Dey lab to continue his postdoctoral work. Sun is a recent recipient of a Lalor Foundation postdoctoral fellowship. Poornima Chandran, a Fulbright fellow from Osmania University in Hyderabad, India, trained with the division for 10 months. Her research will contribute to her PhD requirements. Mikihiro Yoshie, PhD, joined the division as a visiting research fellow. Yoshie is supported by the Tokyo University of Pharmacy and Life Sciences. In addition, the division has continued to train many postdoctoral fellows and graduate students from other institutions in specific laboratory techniques, in the hopes that these skills will be used to expand the field of reproductive research.

Division Publications

1. Gao F, Ma X, Ostmann AB, Das SK. **GPR30 activation opposes estrogen-dependent uterine growth via inhibition of stromal ERK1/2 and estrogen receptor alpha (ERalpha) phosphorylation signals**. *Endocrinology*. 2011; 152:1434-47.
2. Hirota Y, Acar N, Tranguch S, Burnum KE, Xie H, Kodama A, Osuga Y, Ustunel I, Friedman DB, Caprioli RM, Daikoku T, Dey SK. **Uterine FK506-binding protein 52 (FKBP52)-peroxiredoxin-6 (PRDX6) signaling protects pregnancy from overt oxidative stress**. *Proc Natl Acad Sci U S A*. 2010; 107:15577-82.
3. Hirota Y, Daikoku T, Tranguch S, Xie H, Bradshaw HB, Dey SK. **Uterine-specific p53 deficiency confers premature uterine senescence and promotes preterm birth in mice**. *J Clin Invest*. 2010; 120:803-15.
4. Ichijima Y, Ichijima M, Lou Z, Nussenzweig A, Camerini-Otero RD, Chen J, Andreassen PR, Namekawa SH. **MDC1 directs chromosome-wide silencing of the sex chromosomes in male germ cells**. *Genes Dev*. 2011; 25:959-71.
5. Lee JE, Oh HA, Song H, Jun JH, Roh CR, Xie H, Dey SK, Lim HJ. **Autophagy regulates embryonic survival during delayed implantation**. *Endocrinology*. 2011; 152:2067-75.
6. Sun X, Xie H, Yang J, Wang H, Bradshaw HB, Dey SK. **Endocannabinoid signaling directs differentiation of trophoblast cell lineages and placentation**. *Proc Natl Acad Sci U S A*. 2010; 107:16887-92.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct / Project Period Direct
DAIKOKU, T		
Pten-Akt-Cox2 Signaling Axis in Endometrial Cancer		
Ohio Cancer Research		
	01/01/10-06/30/11	$30,000
DAS, S		
Environmental Toxins and Uterine Gene Expression		
National Institutes of Health		
R01 ES 07814	06/01/11-05/31/12	$220,523
Molecular Signaling in Decidualization		
National Institutes of Health		
R01 HL 056044	08/15/09-07/31/11	$346,442
DEY, S		
Aspects of Blastocysts		

National Institutes of Health
R37 HD 012304 08/01/10-07/31/11 $71,275

Targeting mTOR Signaling to Prevent Preterm Birth
Bill & Melinda Gates Foundation
11/01/10-04/30/12 $100,000

Endocannabinoid Signaling During Early Pregnancy
National Institutes of Health
R37 DA 006668 01/01/11-12/31/11 $302,376

NAMEKA, S

Regulation of Sex Chromosome Inactivation by the FANC/BRCA Pathway
March of Dimes
02/01/11-01/31/13 $68,182

SUN, X

Kruppel-Like Factor 5 is Critical to the Establishment oof Receptive Uteri for Successful Implantation
Lalor Foundation
05/01/11-04/30/12 $35,000

Current Year Direct $1,173,798

Total $1,173,798