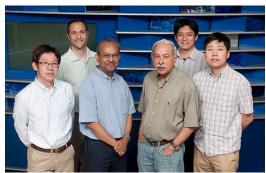


# **Reproductive Sciences**

## **Division Details**

#### RESEARCH AND TRAINING DETAILS

| Faculty                          | 8           |
|----------------------------------|-------------|
| Joint Appointment Faculty        | 1           |
| Research Fellows and Post Docs   | 8           |
| Total Annual Grant Award Dollars | \$1,658,003 |
| Total Publications               | 21          |



Row 1: Y Ogawa, S Das, SK Dey, X Sun

Row 2: T De Falco, S Namekawa

## Research Highlights

## SK Dey, PhD

- Invited Speaker: Molecular and Cellular Biology Seminar Series, Balor College of Medicine, September 30, 2015, Houston, Texas.
- NIH Reviewer: CMIR Study Section Regular Member, October 22-24, 2015 and June 22-24, 2016.
- Invited Speaker: 10th Meeting of the Interdisciplinary Collaborative Team on Blastocyst Implantation Research, NIH, November 12-13, 2015, Bethesda, Maryland.

#### Sanjoy Das, PhD

NIH Reviewer: RAG Study Section Regular Member, October 16, 2015; February 26, 2016 and June 24, 2016

NURSA Reviewer: Nuclear Receptor Signaling Atlas (NURSA) Data Source Projects (NDSP), July 29, 2015

### Satoshi Namekawa, PhD

New Investigator Award: Recipient of the 2015 Study for the Society of Reproduction (SSR) New Investigator Award

Invited Speaker: "Programmed Gene Silencing During Meiosis: Mechanism and Function." Gordon Research Conference—Molecular Mechanisms, Regulation and Integration of the Meiotic Program. June 26-July 1, 2016. New London, New Hampshire

#### Tony De Falco, PhD

- Featured Publication: Macrophages Contribute to the Spermatogonial Niche in the Adult Testis (PMID 26257171): Publication featured on the cover of the August 18th issue of *Cell Reports*, highlighted as a "Preview" in *Cell Reports*, highlighted in "World of Reproductive Biology" in *Biology of Reproduction*.
- Invited Speaker: "Macrophages: diverse players in testis biology." American Society of Andrology 41st Annual Conference, April 2016, New Orleans, Louisiana.
- Award: Recipient of the 2016 Cincinnati Children's Achievement Award

# Significant Publications

Sin HS, Kartashov AV, Hasegawa K, Barski A, Namekawa SH. Poised chromatin and bivalent domains facilitate the mitosis-to-meiosis transition in the male germline. *BMC Biol.* 2015 Jul 22;13:53.

This study reveals the essential mechanisms underlying the global epigenome in male germ cells. Investigators identified the epigenomic signature of male germ cells, which potentially supports the recovery of totipotency after fertilization.

Sun X, Deng W, Li Y, Tang S, Leishman E, Bradshaw HB, Dey SK. Sustained Endocannabinoid Signaling Compromises Decidual Function and Promotes Inflammation-induced Preterm Birth. *J Biol Chem.* 2016 Apr 8;291(15):8231-40.

FAAH mutant females with sustained excessive cannabinoid levels are more vulnerable to preterm birth upon lipopolysaccharide. Elevated endocannabinoids targeting on CB1 activate p38 signaling pathway, which further causes premature decidual senescence. The publication not only demonstrated the association of marijuana exposure with parturition, but also revealed an mTOR independent pathway increasing decidual senescence.

Yamada N, Hasegawa Y, Yue M, Hamada T, Nakagawa S, Ogawa Y. Xist exon 7 contributes to the stable localization of Xist RNA on the inactive X-chromosome. *PLOS Genet*. 2015 Aug 5;11(8):e1005430.

In this study, investigators demonstrated that exon 7 of Xist RNA plays an important role for stable Xist RNA localization and silencing of the X-linked genes on the Xi, possibly acting through an interaction with hnRNP U.

Gao F, Bian F, Ma X, Kalinichenko VV, Das SK. Control of regional decidualization in implantation: Role of FoxM1 downstream of Hoxa10 and cyclin D3. *Sci Rep.* 2015 Sep 9;5:13863.

Investigators provided evidence supporting the hypothesis that proper development of mesometrial (a presumptive site for placentation) and antimesometrial decidualization in implantation requires FoxM1, a Forkhead box transcription factor, signaling downstream of Hoxa10 and cyclin D3, two well-known markers of decidualization.

Blaisdell A, Crequer A, Columbus D, Daikoku T, Mittal K, **Dey SK**, Erlebacher A. **Neutrophils Oppose Uterine Epithelial Carcinogenesis via Debridement of Hypoxic Tumor Cells**. *Cancer Cell*. 2015 Dec 14;28(6):785-99.

Investigators studied the role of Polymorphonuclear neutrophils (PMNs) in epithelial carcinogenesis using a mouse model of PTENdeficient uterine cancer. PMNs surprisingly inhibited early-stage tumor growth in the model and slowed malignant progression. These findings provide insight into tumor-associated PMNs and reveal a context-specific capacity for PMNs to directly combat tumorigenesis.

### **Division Publications**

- 1. Bian F, Gao F, Kartashov AV, Jegga AG, Barski A, Das SK. Polycomb Repressive Complex 1 Controls Uterine Decidualization. *Sci Rep.* 2016; 6:26061.
- 2. Blaisdell A, Crequer A, Columbus D, Daikoku T, Mittal K, Dey SK, Erlebacher A. Neutrophils Oppose Uterine Epithelial Carcinogenesis Via Debridement of Hypoxic Tumor Cells. Cancer Cell. 2015; 28:785-99.
- 3. Broering TJ, Wang YL, Pandey RN, Hegde RS, Wang SC, Namekawa SH. **Baz1b** Is **Dispensable for H2ax Phosphorylation on Tyrosine 142 During Spermatogenesis**. *Biol Open*. 2015; 4:873-84.
- 4. DeFalco T, Potter SJ, Williams AV, Waller B, Kan MJ, Capel B. Macrophages Contribute to the Spermatogonial Niche in the Adult Testis. *Cell Rep.* 2015; 12:1107-19.
- 5. Du W, Amarachintha S, Erden O, Wilson A, Meetei AR, Andreassen PR, Namekawa SH, Pang Q. Fancb Deficiency Impairs Hematopoietic Stem Cell Function. *Sci Rep.* 2015; 5:18127.

- 6. Gao F, Bian F, Ma X, Kalinichenko VV, Das SK. Control of Regional Decidualization in Implantation: Role of Foxm1 Downstream of Hoxa10 and Cyclin D3. Sci Rep. 2015; 5:13863.
- 7. Huang EL, Piehowski PD, Orton DJ, Moore RJ, Qian WJ, Casey CP, Sun X, Dey SK, Burnum-Johnson KE, Smith RD. **Snapp:**Simplified Nanoproteomics Platform for Reproducible Global Proteomic Analysis of Nanogram Protein Quantities.

  Endocrinology. 2016; 157:1307-14.
- 8. Kato Y, Alavattam KG, Sin HS, Meetei AR, Pang Q, Andreassen PR, Namekawa SH. Fancb Is Essential in the Male Germline and Regulates H3k9 Methylation on the Sex Chromosomes During Meiosis. *Hum Mol Genet*. 2015; 24:5234-49.
- 9. Kyle JE, Zhang X, Weitz KK, Monroe ME, Ibrahim YM, Moore RJ, Cha J, Sun X, Lovelace ES, Wagoner J, Polyak SJ, Metz TO, Dey SK, Smith RD, Burnum-Johnson KE, Baker ES. **Uncovering Biologically Significant Lipid Isomers with Liquid Chromatography, Ion Mobility Spectrometry and Mass Spectrometry.** *Analyst.* 2016; 141:1649-59.
- 10. Potter SJ, DeFalco T. **Using Ex Vivo Upright Droplet Cultures of Whole Fetal Organs to Study Developmental Processes During Mouse Organogenesis.** *J Vis Exp.* 2015:e53262.
- 11. Potter SJ, Kumar DL, DeFalco T. **Origin and Differentiation of Androgen-Producing Cells in the Gonads.** *Results Probl Cell Differ*. 2016; 58:101-34.
- 12. Richard JL, Ogawa Y. Understanding the Complex Circuitry of Lncrnas at the X-Inactivation Center and Its Implications in Disease Conditions. *Curr Top Microbiol Immunol.* 2016; 394:1-27.
- 13. Robertshaw I, Bian F, Das SK. Mechanisms of Uterine Estrogen Signaling During Early Pregnancy in Mice: An Update. *J Mol Endocrinol*. 2016; 56:R127-38.
- 14. Sin HS, Kartashov AV, Hasegawa K, Barski A, Namekawa SH. Poised Chromatin and Bivalent Domains Facilitate the Mitosis-to-Meiosis Transition in the Male Germline. *BMC Biol.* 2015; 13:53.
- 15. Sun S, Payer B, Namekawa S, An JY, Press W, Catalan-Dibene J, Sunwoo H, Lee JT. **Xist Imprinting Is Promoted by the Hemizygous (Unpaired) State in the Male Germ Line.** *Proc Natl Acad Sci USA*. 2015; 112:14415-22.
- 16. Sun X, Deng W, Li Y, Tang S, Leishman E, Bradshaw HB, Dey SK. **Sustained Endocannabinoid Signaling Compromises Decidual Function and Promotes Inflammation-Induced Preterm Birth.** *J Biol Chem.* 2016; 291:8231-40.
- 17. Sun X, Park CB, Deng W, Potter SS, Dey SK. Uterine Inactivation of Muscle Segment Homeobox (Msx) Genes Alters Epithelial Cell Junction Proteins During Embryo Implantation. FASEB J. 2016; 30:1425-35.
- 18. Yamada N, Hasegawa Y, Yue M, Hamada T, Nakagawa S, Ogawa Y. **Xist Exon 7 Contributes to the Stable Localization of Xist Rna on the Inactive X-Chromosome.** *PLoS Genet.* 2015; 11:e1005430.
- 19. Yamada N, Ogawa Y. **Mechanisms of Long Noncoding Xist Rna- Mediated Chromosome-Wide Gene Silencing in X- Chromosome Inactivation**. In: R Kurokawa, ed. *Long Noncoding Rnas Structures and Functions*. New York: Springer; 2015:151-71.
- Yue M, Charles Richard JL, Ogawa Y. Dynamic Interplay and Function of Multiple Noncoding Genes Governing X Chromosome Inactivation. Biochim Biophys Acta. 2016; 1859:112-20.
- 21. Zhang T, Wilson AF, Mahmood Ali A, Namekawa SH, Andreassen PR, Ruhikanta Meetei A, Pang Q. Loss of Faap20 Causes Hematopoietic Stem and Progenitor Cell Depletion in Mice under Genotoxic Stress. Stem Cells. 2015; 33:2320-30.

# Grants, Contracts, and Industry Agreements

#### **Annual Grant Award Dollars**

Investigator Title Sponsor ID Dates Amount

| Sudhansu K Dey, PHD     | Molecular Signaling in Uterine<br>Receptivity to Implantation                                   | National Institutes of Health               | R01<br>HD068524 | 9/26/2011<br>-<br>6/30/2017 | \$316,996 |
|-------------------------|---|---|-----------------|-----------------------------|-----------|
| Sudhansu K Dey, PHD     | The Role of Bioactive Lipids in Inflammation and Cancer   | National Institutes of Health (Mayo Clinic) | P01<br>CA077839 | 12/1/2012<br>-<br>5/31/2017 | \$237,916 |
| Sudhansu K Dey, PHD     | Endocannabinoid Signaling during Early Pregnancy  | National Institutes of Health               | R01<br>DA006668 | 4/1/2015 -<br>3/31/2020     | \$423,221 |
| Satoshi H Namekawa, PHD | Regulatory Mechanism of Active<br>Epigenetic Modifications and its<br>Transgenerational Effects | March of Dimes                              | #1-FY13-<br>510 | 6/1/2013 -<br>5/31/2017     | \$100,000 |
| Satoshi H Namekawa, PHD | DNA Damage Response Pathways in Mieotic Sex Chromosome Inactivation                             | National Institutes of Health               | R01<br>GM098605 | 8/1/2011 -<br>7/31/2017     | \$289,170 |
| Yuya Ogawa, PHD         | Organization of the Inactive X-chromosome   | National Institutes of Health               | R01<br>GM102184 | 9/1/2012 -<br>8/31/2017     | \$290,700 |

\$1,658,003

**Total Annual Grant Award Dollars**