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| BIOGRAPHICAL SKETCH Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person.  **DO NOT EXCEED FOUR PAGES.** | | | | |
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| NAME  **Cooke, Paul S.** | | POSITION TITLE  Professor and Department Chair | | |
| eRA COMMONS USER NAME (credential, e.g., agency login)  P-COOKE | |
| EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)* | | | | |
| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | | MM/YY | FIELD OF STUDY |
| Westminster College, Fulton, MO | B.A. | | 1978 | Biology |
| University of California-Berkeley | Ph.D. | | 1983 | Physiology |
| University of California-San Francisco | Postdoc | | 1984-1987 | Reproductive Biology |

A. Personal Statement

The overall goal of the proposed project is to gain a better understanding of spermatogonial stem cells (SSCs) in the human. Specifically, we plan to definitively identify the human SSC, determine whether adult human SSCs retain developmental plasticity and can be transdifferentiated into a variety of other epithelia, and to identify critical signaling pathways important in human SSC proliferation and differentiation. My specific role in this project as co-PI will be to perform experiments to test whether adult human SSCs can be differentiated into other epithelial tissues. This work will also establish whether this differentiation involves an intermediate step where the SSCs express ES-like characteristics (e.g., expression of pluripotency genes) prior to differentiating into the epithelium specified by the mesenchyme. I have over 25 years of research experience using the tissue recombination technique that is at the heart of this work, and this technique is used regularly in my lab. Furthermore, I have also worked for over 20 years in testicular biology, and for the last 4 years my main focus in this area has been the factors regulating SSCs. Therefore, my lab is well prepared to take on the proposed project. In addition, we have performed and published the critical mouse studies suggesting that SSCs can be directly induced to form a variety of epithelia, and it is these studies that underlie the proposed work with human SSCs. Therefore, my lab is experienced in all facets of the proposed studies. Dr. Martin Dym, the PI of this application, has extensive expertise in testicular biology, and in addition has been one of the pioneers in identifying and establishing the properties of human SSCs. His expertise in these areas, in conjunction with my lab’s expertise in SSCs and our previous tissue recombination studies, have prepared us well to successfully conduct the proposed studies. In summary, I have a demonstrated record of research accomplishment in SSC biology and the tissue recombination methodology that is key for this application, and I can contribute effectively to the successful completion of the experiments that Dr. Dym has proposed.

**Positions and Employment**

## 1984-1987 University of California-San Francisco, NIH Postdoctoral Fellow

1987-1993 University of Illinois at Urbana-Champaign, Assistant Professor

1993-1998 University of Illinois at Urbana-Champaign, Associate Professor

1998-2011 University of Illinois at Urbana-Champaign, Professor

2004-2011 Billie A. Field Endowed Chair in Reproductive Biology, University of Illinois

2011- present University of Florida, Professor and Department Chair, Dept. of Physiological Sciences

Other Experience and Professional Memberships

***Associate Editor***: Biology of Reproduction (2009- present)

***Editorial Boards*:** *J. of Andrology* (1995-1997); *J. Endocrinol. Reprod.* (1997-2000*);* *Endocrinology* (1998-2001); *Dom. Animal Endocrinol.* (2000-2003); *J. Endocrinol.* (2001-2010*); Biol. Reprod. (2006-2008); Toxicol. Appl. Pharmacol.* (2008-2013)

***Study Section member, NIH, Other***: Reproductive Biology, 2001; Integrative NIEHS Superfund Basic Research Program Review. Panel Member, 2004, 2005; Clinical Endocrinology & Reproduction, 2005, 2006; Panel Member, Nat’l Tox. Program Review of Genistein, Res. Triangle Park, NC, 2006; Development 1, 2007; Cellular Aspects of Diabetes and Obesity (CADO), 2008;Reproduction, Andrology and Gynecology**,** 2007,2008; Special Emphasis Panel On BPA, 2009; K applications Review for NIEHS, 2010, Xenobiotic and Nutrient Disposition and Action (XNDA), 2010

Honors

2004-2011 Billie A. Field Endowed Chair in Reproductive Biology, University of Illinois

2004 Krueger All-Around Excellence Award, College of Veterinary Medicine, Univ. of Illinois

2001 Pfizer Animal Health Award for Research Excellence, College of Veterinary Medicine, University of Illinois

2000 Research Excellence Award, University of Illinois

1997–2000 University Scholar, University of Illinois

1996 Young Andrologist Award, American Society of Andrology

1993 The Levine Award for Research, University of Illinois

1988, 1989, 1991, Incomplete List of Teachers Ranked Excellent, Univ. of Illinois

1995, 1999–2002,

2006, 2007, 2009, 2010

**C. Selected Peer-reviewed Publications** (selected from 145 total)

**Most relevant to the current application**

1. Simon L, Ekman GC, Tyagi G, Hess RA,Murphy KM, **Cooke PS** **(2007)** Common and distinct factors regulate expression of ERM and GDNF, Sertoli cell proteins essential for spermatogonial stem cell maintenance. Exp Cell Res 313:3090-3099. PMID: 17574550
2. Simon L, Ekman GC, Kostereva N, Zhang Z, Hess RA, Hofmann MC, **Cooke PS** (2009) Direct transdifferentiation of spermatogonial stem cells into reproductive and non-reproductive tissues of all germ layers. Stem Cells 27:1666-1675. PMID: 19544441
3. Schlesser HN, Simon L, Hofmann MC, Murphy KM, Hess RA,**Cooke PS** (2008) Effects of ets variant gene 5 (ERM) on testis and body growth, time course of spermatogonial stem cell loss and fertility in mice. Biol Reprod 78:483-489. PMID: 18032421
4. Simon L, Hess RA, **Cooke PS** (2010) Spermatogonial stem cells, in vivo transdifferentiation and human regenerative medicine. Expert Opinion Biological Therapy 10:519-530. PMID: 20146635
5. Simon L, Ekman GC, Carnes K, Zhang Z, Murphy T, Murphy KM, Hess RA, **Cooke PS,** Hofmann MC. (2010) ETV5 regulates Sertoli cell chemokines involved in stem/progenitor spermatogonia maintenance. Stem Cells Stem Cells 28:1882-1892. PMID: 20799334

**Additional publications of importance to the field (in chronological order)**

1. **Cooke PS**, Hess RA, Porcelli J, Meisami E (1991) Increased sperm production in adult rats after transient neonatal hypothyroidism. Endocrinology 129:244-248. PMID: 2055187
2. **Cooke PS**, Porcelli J, Hess RA (1992) Induction of increased testis growth and sperm production in the adult rat by neonatal administration of the goitrogen propylthiouracil (PTU): the critical period. Biol Reprod 46:146-152.
3. Kirby JD, Jetton AE, **Cooke PS**, Hess RA, Bunick D, Ackland J, Turek FW, Schwartz NB (1992) Developmental hormonal profiles accompanying the neonatal hypothyroidism induced increases in adult testis size and sperm production in the rat. Endocrinology 131:559-565. PMID: 1639007
4. Bunick D, Kirby JD, Hess RA, **Cooke PS**  (1994) Developmental expression of testis mRNAs in the rat following propylthiouracil-induced neonatal hypothyroidism. Biol Reprod 51:706-713. PMID: 7819453
5. **Cooke PS**, Zhao Y-D, Bunick D (1994) Triiodothyronine inhibits proliferation and stimulates differentiation of cultured neonatal Sertoli cells: possible mechanism for increased adult testis weight and sperm production induced by neonatal goitrogen treatment. Biol Reprod 51:1000-1005. PMID: 7531505
6. Arambepola NK, Bunick D, **Cooke PS** (1998) Thyroid hormone effects on androgen receptor (AR) messenger RNA expression in rat Sertoli and peritubular cells. J Endocrinol 156:43-50. PMID: 9496232
7. Arambepola N, Bunick D, **Cooke PS** (1998) Thyroid hormone and follicle-stimulating hormone regulate Mullerian-inhibiting substance messenger ribonucleic acid expression in cultured neonatal rat Sertoli cells. Endocrinology 139:4489-4495. PMID: 9794457
8. Holsberger DR, Jirawatnotai S, Kiyokawa H, **Cooke PS** (2003) Thyroid hormone regulates the cell cycle inhibitor p27Kip1 in postnatal murine Sertoli cells. Endocrinology 144:3732-3738. PMID: 12933641
9. Sridharan S, SimonL, MelingDD, CyrDG, GutsteinDE, Fishman GI,Guillou F, **Cooke PS** (2007) Proliferation of adult Sertoli cells following conditional knock out of the gap junctional protein GJA1 (Connexin 43) Biol Reprod 76:804-812. PMID: 17229929
10. Tyagi G, Carnes K, Morrow C, KosterevaNV, Ekman GC, Meling DD, Hostetler C, Griswold M, Murphy KM, Hess RA, Hofmann MC, **Cooke PS** (2009) Loss of Etv5 decreases proliferation and RET levels in neonatal testicular germ cells and causes an abnormal first wave of spermatogenesis. Biol Reprod 81:258-266. PMID: 19369650

D. Current Research Support

**Ongoing Research Support**

Source: NIH (R01 HD059961)

P. Cooke, PI

Title: Cell fate determination in fetal testes Period: 09/01/10-08/31/12Description: Factors regulating establishment of fetal and adult Leydig cell lineages will be determined.

Source: Morris Animal Foundation

P. Cooke, PI

Title: Use of neonatal progestin treatment as a permanent, non-surgical contraceptive methodology in dogs

Period: 8/01/10-7/31/11

Description: Neonatal progestin treatment will be used to inhibit uterine gland development and induce infertility in dogs.

**Funded, Activation Awaited**

Source: NIH (R01 DK58105)

P. Cooke, co-investigator and subcontractor (L. Baskin, University of California-San Francisco, PI)

Title: Hypospadias, differentiation and endocrine disruptors

Period: 7/01/10-06/30/15

Description: A new paradigm suggesting that estrogen may have a role in development of the female and male external genitalia will be tested.

**Completed Research Support**

Source: NIH (P01 Program Project; AG24387)

P. Cooke, PI of one component of P01 (W. Helferich, Univ. of Illinois, PI of overall P01)

Title: Phytoestrogens and aging: Dose, timing and target tissue

Period: 07/01/04-06/30/10

Description: This P01 Program Project analyzed phytoestrogen effects on aging.

Source: NIH ES01332

P. Cooke, PI (subcontract in a larger NIH MERIT grant; R. Peterson, University of Wisconsin, PI)

Title: Reproductive and developmental toxicity of dioxin

Period: 09/01/00-07/31/10Description: Rodent model systems will be used to examine the mechanism by which 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) inhibits prostatic development.