CARMEN J. WILLIAMS, M.D., PH.D. CURRICULUM VITAE

Work Address:

National Institute of Environmental Health Sciences 111 T. W. Alexander Drive Research Triangle Park, NC 27709 Phone: 919-541-2158 Fax: 919-541-0696 Email: williamsc5@niehs.nih.gov

Major Professional Interests:

Mammalian gametes and preimplantation embryos, human reproduction and infertility

Education and Professional Positions

Clinical Investigator, Tenure-track

Reproductive Medicine Group Laboratory of Reproductive and Developmental Toxicology National Institute of Environmental Health Sciences Research Triangle Park, NC September 2007 – present

Assistant Professor

Division of Reproductive Endocrinology & Infertility Department of Obstetrics & Gynecology University of Pennsylvania Philadelphia, PA July 2000 – September 2007

Research Associate

Department of Obstetrics & Gynecology University of Pennsylvania Health System Philadelphia, PA July 1992 – June 2000

Doctor of Philosophy

Cell and Molecular Biology Graduate Group School of Biomedical Graduate Studies University of Pennsylvania Philadelphia, PA September 1992 – August 1997

Fellow in Reproductive Endocrinology & Infertility

Department of Obstetrics & Gynecology Hospital of the University of Pennsylvania Philadelphia, PA July 1990 – June 1993

Resident in Obstetrics & Gynecology

Pennsylvania Hospital Department of Obstetrics & Gynecology Philadelphia, PA July 1986 – June 1990

Doctor of Medicine

Duke University School of Medicine Durham, NC August 1982 – May 1986

Engineer in Computer Graphics Design Division

International Business Machines, Inc. Poughkeepsie, NY June 1981 – August 1982

Bachelor of Science in Engineering

Department of Electrical Engineering Duke University Durham, NC September 1978 – May 1981

Awards and Honors

- 1982-1986 Charles B. Strickland Memorial Scholarship, Duke University School of Medicine
- 1986-1987 Outstanding Obstetric Resident in the Intensive Care Nursery, Pennsylvania Hospital
- 1989 Obstetrics & Gynecology Resident Teaching Award, University of Pennsylvania
- 1992 Physician Scientist Award, National Institutes of Health, NICHD
- 1997 Burroughs Wellcome Fund Career Award in the Biomedical Sciences
- 2002 Society for Reproductive Endocrinology and Infertility Fellowship Research Prize Paper Award, Society for Gynecological Investigation Annual Meeting

Certification/Licensure/Medical Appointments

Specialty Certification:

1994-present	American Board of Obstetrics & Gynecology

Medical Licensure:

1986-present	Pennsylvania (MD041090E)
1993-2007	New Jersey (MA059112)

Medical/Hospital Appointments:

1993-1994	Medical Staff, Dept. of Obstetrics & Gynecology, West Jersey
	Health System, Camden, NJ
1993-1994	Medical Staff, Summit Surgical Center, Voorhees, NJ
2000-2007	Attending Physician, Hospital of the University of Pennsylvania,
	Philadelphia, PA
2004-2007	Attending Physician, Hospital of the University of Pennsylvania
	Reproductive Surgery Facility, Philadelphia, PA

Publications

Peer Reviewed Papers:

- Lakoski, K., Williams, C., Saling, P: Proteins of the Acrosomal Region in Mouse Sperm: Immunological Probes Reveal Post-Testicular Modifications. Gamete Research 23(1): 21-37, May 1989.
- Williams, C.J., Schultz, R.M., Kopf, G.S.: Role of G Proteins in Mouse Egg Activation: Stimulatory Effects of Acetylcholine on the ZP2 to ZP2f Conversion and Pronuclear Formation in Eggs Expressing a Functional m1 Muscarinic Receptor. Dev. Biol. 151: 288-296, May 1992.
- 3. Williams, C.J., Schultz, R.M., Kopf, G.S.: G protein gene expression during mouse oocyte growth and maturation, and preimplantation development. Mol. Reprod. Dev. 44: 315-323, July 1996.
- Williams, C.J., Mehlmann, L.M., Jaffe, L.A., Kopf, G.S., Schultz, R.M: Evidence that Gq family G proteins do not function in mouse egg activation at fertilization. Dev. Biol. 198: 116-127, 1998.
- McAvey, B.A., Wortzman, G.B., Williams, C.J., Evans, J.P.: Involvement of calcium signaling and the actin cytoskeleton in the membrane block to polyspermy in mouse eggs. Biol. Reprod. 67: 1342-1352, October 2002.
- 6. Brown, R.L., Ord, T., Moss, S.B., **Williams, C.J.**: A-kinase anchor proteins as potential regulators of protein kinase A function in oocytes. Biol Reprod 67: 981-987, 2002.

- 7. Xu, Z., **Williams, C.J.**, Kopf, G.S., Schultz, R.M.: Maturation-associated increase in IP3 receptor type 1: Role in conferring increased IP3 sensitivity and Ca2+ oscillatory behavior in mouse eggs. Dev. Biol. 254(2): 163-171, February 2003.
- Deng, M., Kishikawa, H., Yanagimachi, R., Kopf, G.S., Schultz, R.M., Williams, C.J.: Chromatin-mediated cortical granule redistribution is responsible for the formation of the cortical granule-free domain in mouse eggs. Dev. Biol. 257: 166-176, May 2003.
- Brown, R.L., August, S.L., Williams, C.J.*, Moss, S.B.*: AKAP7 gamma is a nuclear RI-binding AKAP. Biochem. Biophys. Res. Comm. 306: 394-401, June 2003. *equal contribution
- 10. Dayal, M.D., Wheeler, J., **Williams, C.J.**, Barnhart, K.T.: Disruption of the upper female reproductive tract epithelium by nonoxynol-9 (N-9). Contraception 68(4): 273-279, October 2003.
- Ecker, D.J., Stein, P., Xu, Z., Williams, C.J., Kopf, G.S., Bilker, W.B., Abel, T., Schultz, R.M.: Long-term effects of culture of preimplantation mouse embryos on behavior. Proc. Nat. Acad. Sci. 101(6): 1595-1600, February 2004.
- 12. Tutuncu, L., Stein, P., Ord, T.S., Jorgez, C.J., **Williams, C.J.**: Calreticulin on the mouse egg surface mediates transmembrane signaling linked to cell cycle resumption. Dev. Biol. 270(1): 246-260, June 2004.
- Travis, AJ, Tutuncu, L, Jorgez, CJ, Ord, T, Jones, BH, Kopf, GS, Williams, C.J.: Requirements for Glucose Beyond Sperm Capacitation During In Vitro Fertilization in the Mouse. Biol. Reprod. 71(1): 139-145, July 2004.
- Deng, M., Williams, C.J.*, Schultz, R.M.*: Role of MAP kinase and myosin light chain kinase in chromosome-induced development of mouse egg polarity. Dev. Biol. 278(2): 358-366, February 2005. *equal contribution
- Duncan, F.E., Moss, S.B., Schultz, R.M.*, Williams, C.J.*: PAR-3 defines a central subdomain of the cortical actin cap in mouse eggs. Dev. Biol. 280: 38-47, March 2005.
 *equal contribution
- Michaut, M.A., Williams, C.J.*, Schultz, R.M.*: Phosphorylated MARCKS: A novel centrosome component that also defines a peripheral subdomain of the cortical actin cap in mouse eggs. Dev. Biol. 280: 26-37, March 2005. *equal contribution
- Knott, J.G., Kurokawa, M., Fissore, R.A., Schultz, R.M.*, Williams, C.J.*: Transgenic RNAi reveals role for mouse sperm phospholipase C zeta in triggering Ca2+ oscillations during fertilization. Biol. Reprod. 72(4): 992-996, April 2005. *equal contribution
- Nipper, R.W., Chennothukuzhi, V., Tutuncu, L., Williams, C.J., Gerton, G.L., Moss, S.B. : Differential RNA expression and polyribosome loading of alternative transcripts of the Akap4 gene in murine spermatids. Mol. Reprod. Devel. 70(4): 397-405, April 2005.

- Hess, K.C., Jones, B.H., Marquez, B., Chen, Y., Ord, T.S., Kamenetsky, M., Miyamoto, C., Kopf, G.S., Suarez, S.S., Levin, L.R.*, Williams, C.J.*, Buck, J.*, Moss, S.B.*: The 'soluble' adenylyl cyclase in sperm mediates multiple signaling events required for fertilization. Dev. Cell 9: 249-259, August 2005. *equal contribution
- Wadehra, M., Forbes, A., Pushkarna, N., Goodglick, L., Gordon, L.K., Williams, C.J., Braun, J.: Epithelial membrane protein-2 regulates surface expression of alpha v beta 3 integrin in the endometrium. Dev. Biol. 287: 336-345, October 2005.
- Wadehra, M., Dayal, M., Mainigi, M., Ord, T., Iyer, R., Braun, J., Williams, C.J.: Knockdown of the tetraspan protein epithelial membrane protein-2 inhibits implantation in the mouse. Dev. Biol. 292: 430-441, February 2006.
- 22. Wadehra, M., Natarajan, S., Seligson, D.J., **Williams, C.J.**, Braun, J., Soslow, R.A.: Expression of Epithelial Membrane Protein-2 is associated with endometrial adenocarcinoma of unfavorable outcome. Cancer 107(1): 90-98, July 2006.
- 23. Knott, J.G., Gardner, A.J., Madgwick, S., Jones, K.T., Williams, C.J.*, Schultz, R.M.*: Calmodulin-dependent protein kinase II triggers mouse egg activation and embryo development in the absence of Ca2+ oscillations. Dev. Biol. 296(2): 388-395, August 2006. *equal contribution
- 24. Duncan, F.E., Moss, S.B., **Williams, C.J.**: Knockdown of the cAMP-dependent protein kinase (PKA) type Iα regulatory subunit in mouse oocytes disrupts meiotic arrest and results in meiotic spindle defects. Dev. Dyn., 235(11):2961-2968, November 2006.
- Gardner, A.J., Williams, C.J., Evans, J.P.: Establishment of the mammalian membrane block to polyspermy: Evidence for calcium-dependent and -independent regulation. <u>Reproduction</u> 133(2):383-393, February 2007.
- 26. Alvarez, J.D., Hansen, A., Ord, T., **Williams, C.J.**, Moss, S.B. and Sehgal, A.: The circadian clock protein BMAL1 is necessary for fertility and proper testosterone production in mice. J. Biol. Rhythms, *in press*.

Editorials, Reviews, Chapters:

- 27. Schultz, R.M., Williams, C.J.: The Science of ART. Science 296(5576): 2188-2190, June 2002.
- 28. Williams, C.J.: Signalling mechanisms of mammalian oocyte activation. Hum Reprod Update 8(4): 313-321, Jul-Aug 2002.
- 29. Schultz, R.M., Williams, C.J.: Sperm-egg fusion unscrambled. Nature 434: 152-153, March 2005.
- 30. Thompson, J.R., **Williams, C.J.**: Genomic Imprinting and ART: Connections and potential risks. Seminars in Reproductive Medicine 23(3): 285-295, August 2005.

- Williams, C.J., Schultz, R.M.: Transgenic RNAi: A tool to study testis-specific genes. Mol. Cell. Endocrinol. 247: 1-3, March 2006.
- Strauss, III, J.F., Williams, C.J.: The Ovarian Life Cycle. Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management", 5th edition. Strauss, III, J.F., Barbieri, R.L. (eds.). W.B. Saunders, Philadelphia, 2004.

Invited Speaker

(last 5 years)

- Oct, 2002 "Spatial regulation of PKA by AKAP-RI interactions in mouse oocytes and embryos", Dept. of Biology, Univ. of Pennsylvania
- Oct, 2002 "Molecular Signaling at Fertilization.", Roundtable Luncheon presentation, American Society for Reproductive Medicine Annual Meeting, Seattle, WA
- Dec, 2002 "Spatial regulation of PKA by AKAP-RI interactions in mouse oocytes and embryos", Center for Research on Reproduction & Women's Health, Univ. of Pennsylvania
- May, 2003 "Spatial regulation of PKA by AKAP-RI interactions in mouse oocytes and embryos", Dept. of Cell Biology, Georgetown University Medical Center
- Jul, 2003 "AKAP7gamma is an embryonic RI-binding AKAP", Annual Meeting of the Society for the Study of Reproduction, Cincinnati, OH
- Jun, 2004 "Control of Implantation by Epithelial Membrane Protein-2 (EMP2)", Gordon Conference on Reproductive Tract Biology, New London, CT
- Nov, 2004 "Polarity and signaling at the initiation of mouse development", Cell & Molecular Biology Training Grant seminar, Univ. of Pennsylvania, Philadelphia, PA
- Nov, 2004 "Polarity and signaling at the initiation of mouse development", Dept. of Biochemistry & Molecular Biology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD
- Jan, 2005 "Polarity and signaling at the initiation of mouse development", Germ Cell Seminar series, University of Pennsylvania School of Veterinary Medicine, New Bolton Center, Kennett Square, PA
- Oct, 2005 "Developmental programming Use of genomic and proteomic tools to identify critical gene and signal pathways", in Postgraduate Course #5: Developmental Competence of Oocytes and Embryos: What We Know, What We Think We Know, and What We Fear, ASRM Annual Meeting, Montreal, Quebec
- Oct, 2005 "Epigenetic risks related to art: Impact of stimulation and lab culture", in Postgraduate Course #5: Developmental Competence of Oocytes and Embryos: What We Know, What We Think We Know, and What We Fear, ASRM Annual Meeting, Montreal, Quebec
- Oct, 2005 "Understanding the role of epigenetics in the oocyte and embryo", in Postgraduate Course #5: Developmental Competence of Oocytes and Embryos:

What We Know, What We Think We Know, and What We Fear, ASRM Annual Meeting, Montreal, Quebec

- Nov, 2005 "Control of Implantation by Epithelial Membrane Protein-2 (EMP2)", Tufts University School of Medicine, Boston, MA
- May, 2006 "Development of polarity during mouse oocyte maturation", Reproductive Biology and Medicine Branch, NICHD, NIH
- Jun, 2006 "Calcium signaling and embryo development: Importance of the sperm factor", Duke University, Durham, NC
- Jul, 2006 "In vitro fertilization at 25: The state of the ART (Assisted Reproductive Technologies)", The Penn Science Cafe, Philadelphia, PA
- Oct, 2006 "Introduction to epigenetics: Why does it matter?", Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA
- Feb, 2007 "Epithelial membrane protein-2 (EMP2) in endometrial function and dysfunction", NIEHS, Research Triangle Park, NC
- Jul, 2007 "Polarity (or asymmetry) of the mammalian egg and early embryo", Gordon Conference on Fertilization and the Activation of Development, Plymouth, NH

Organizing Roles in Scientific Meetings

- Jun, 2002 Chairperson, Mid-Atlantic Reproductive Biology meeting Center for Research on Reproduction & Women's Health, University of Pennsylvania, Philadelphia, PA
- Sep, 2004 Seminar Series Organizer, Center for Research on Reproduction & Women's Health University of Pennsylvania, Philadelphia, PA
- Oct, 2005 Moderator, "Clinical Female Infertility and Gynecology" oral abstract session at the Annual Meeting of the American Society for Reproductive Medicine, Montreal, Quebec, Canada
- Mar, 2006 Moderator, "Ovarian Biology/Neuroendocrinology" oral abstract session at the 53rd Annual Meeting of the Society for Gynecological Investigation, Toronto, Canada
- Oct, 2006 Moderator, "Prize Paper Candidates" oral abstract session, Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA
- Oct, 2006 Symposium chair, "Understanding Epigenetics and the Clinical Impact of IVF", Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA
- Mar, 2007 Moderator, "Gynecology" oral abstract session at the 54th Annual Meeting of the Society for Gynecological Investigation, Reno, Nevada
- Jul, 2007 Moderator, plenary session "Egg and embryo polarity", Gordon Conference on Fertilization and the Activation of Development, Plymouth, NH

Societies / Professional Organization Membership/Professional Activities

- Selection Committee, Reproductive Scientist Development Program
- Society for the Study of Reproduction
 - Clinical Outreach Committee (2001-2003)
 - Program Committee (2006-present)
- Endocrine Society
- American Society for Cell Biology
- Society for Gynecological Investigation
- American Society of Reproductive Medicine
- Fellow, American College of Obstetricians & Gynecologists
- Member, Developmental Systems Advisory Panel, National Science Foundation, Animal Development and Evolution of Development, October 2005
- Special Grants Review Committees, National Institute of Heath, Child Health and Human Development (RFA HD-02-012; RFA HD-02-029; RFA HD-01-011)
- Guest editor, Seminars in Reproductive Medicine 23(3), August 2005; special issue entitled "Frontiers in Gamete Biology".
- Ad Hoc referee for:
 - National Science Foundation (Grants)
 - United States Department of Agriculture; Reproductive Efficiency Section (Grants)
 - Israel Science Foundation (Grants)
 - Development
 - Developmental Biology
 - Biology of Reproduction
 - Journal of Biological Chemistry
 - Molecular Reproduction and Development
 - Cellular and Molecular Life Sciences
 - Human Reproduction
 - Reproduction
 - Reproductive Sciences
 - Fertility and Sterility

Academic and Institutional Committees

1998-2007	Member, Advisory/Admissions Committee for Combined Degree Program, University of Pennsylvania School of Medicine
2000-2007	Member, Admissions Committee for University of Pennsylvania School of Medicine
2005-2007	Member, Search Committee for tenure track Professor, Dept. of Ob/Gyn and Director, Center for Research on Reproduction & Women's Health

- 2006-2007 Member, Work Group on Translational Research, Dept. of Obstetrics & Gynecology, University of Pennsylvania
- 2006-2007 Member, Admissions Committee for Cell & Molecular Biology Graduate Group, Combined Degree Program, University of Pennsylvania School of Medicine

Teaching

- Medical School Curriculum 2000, Reproduction Block 2000-2007 Lecturer 2007 Facilitator for Reproductive Bioethics
- Medical School Curriculum 2000, Human Embryology 2006-2007 Lecturer
- Introductory Obstetrics & Gynecology clinical rotation (OG200) 2000-2007 Lecturer 2000-2007 Preceptor for small group
- Scientific Writing (CAMB 695) 2004-2007 Section leader
- Reproductive Endocrinology & Infertility Fellow weekly teaching conferences 2000-2007 Lecturer 2001-2004 Organizer
- Medical Resident Management Conferences
 2001
 Lecturer
- Bioethics Workshops, School of Biomedical Graduate Studies
 2002 Facilitator
 - 2005 Facilitator
- Laboratory course for Reproductive Endocrinology & Infertility Fellows "Introduction to Mouse In Vitro Fertilization & Micromanipulation" 2002-2004 Organizer, instructor

Training

Postdoctoral Fellows

Molina Dayal	Postdoctoral Fellow MD, MPH/1995/Johns Hopkins University Project: Role of EMP2 in mouse implantation Current Position: Assistant Professor, Dept. of Reproductive End Infertility, George Washington University, Washington, DC	Johns Hopkins University CMP2 in mouse implantation Assistant Professor, Dept. of Reproductive Endocrinology &	
Jason Knott	Postdoctoral Fellow PhD/2002/Univ. of Massachusetts, Amherst Project: Phospholipase C isoform functions during mouse egg ac Current Position: Staff Scientist, Serono Research Institute, Bost		

Marcela Michaut	Postdoctoral Fellow PhD/2001/National Univ. of San Luis, Argentina Project: PKC and phosphorylated MARCKS in mouse oocyte n Current Position: Investigador Asistente CONICET, Instituto de Embriologia, Facultad de Ciencias Medicas, Universidad Nacio Mendoza, Argentina	e Histologia y
Monica Mainigi	Postdoctoral Fellow MD/2000/New York Univ. School of Medicine Project: Role of EMP2 in mammalian implantation and endome Training Grant in Reproductive Biology (T32 HD007305), 2004 Current Position: Clinical Fellow, Division of Reproductive End Infertility, Dept. of Ob/Gyn, Univ. of Pennsylvania Health Syst Philadelphia, PA	4-2006 docrinology &
Scott Edwards	Postdoctoral Fellow MD/1991/Yale Univ. School of Medicine Project: Effect of extracellular ATP on sperm motility and in vir Current Position: Assistant Professor, Division of Reproductive Endocrinology & Infertility, Dept. of Ob/Gyn, Univ. of Pennsyl System, Philadelphia, PA	

Graduate Students

Rebecca Brown		9-2000
	BA/1996/University of Pennsylvania Howard Hughes Medical Student Fellowship, 1999-2000 Project: A kinase anchor proteins in mouse oocytes and embryos Current position: Assistant Professor, Division of Medical Endocrino	logy,
	Dept. of Medicine, University of Chicago Hospitals	
Katherine Masek	VMD/PhD Student Funding: Research Training Program Fellow, Summer 2000 Project: Soluble adenylate cyclase in mouse oocytes and embryos	2000
Francesca Duncan	Graduate Student, Cell & Molecular Biology Graduate Group 200 BS/2000/Haverford College National Science Foundation Predoctoral Fellowship, 2002-2004 Dissertation: <i>The role of PAR-3 (Partitioning-Defective Gene-3) in the</i> <i>development of asymmetry during mouse meiotic maturation</i> Current Position: Postdoctoral Fellow, Biology Dept., Univ. of Pennse	
Timothy Georoff	VMD/PhD Student Project: Identification of mouse oocyte AKAPs by SELDI-TOF mass spectrometry	2001
Jessica Bertout	VMD/PhD Student Funding: Research Training Program Fellow, Summer 2003 Project: Steroid hormone regulation of EMP2 expression in endometr	2003 rial cells

Jennifer Thompson Medical Student

Project: Screening an oocyte library for AKAPs Current position: Resident in Obstetrics & Gynecology, Jefferson University, Philadelphia, PA

Undergraduate Honors Students

Anna Azvolinsky	Undergraduate	BIO399	2002
Amanda Doherty	Undergraduate	BIO399/BIO499	2002 - 2003
Kathleen Sullivan	Undergraduate	BIO399	2004

Funding Record

Past—Funded

Source	P.I.	Title	Role on project	Dates	Direct Cost/Year
NIH/NICHD R01 HD044740	C. Williams	Spatial Regulation of PKA by AKAP-RI Interactions	P.I.	04/01/2004- 03/31/2009	\$180,000
NIH/NICHD R01 HD22732	R. Schultz	Mechanisms of Fertilization/Polyspermy Block	Co-Investigator	09/01/2002- 08/31/2007	\$262,676
NIH D43 TW000671	C. Williams	Reproductive Biology Research Training for Latin America	P.I.	5/1/2001- 4/30/2008 (no- cost extension)	\$225,000
Duska Therapeutics	S. Moss	Efficacy and safety of culture medium additive for in vitro fertilization	Co-Investigator	07/01/2005- 06/30/2006	\$195,000
CONRAD/ Mellon Foundation	C. Williams	Tetraspan Protein Function in Primate Implantation	P.I.	04/01/2003- 03/31/2004	\$88,000
NIH/NICHD R03 HD40376	C. Williams	Role of the Tetraspanin Emp2 in Early Reproduction	P.I.	04/01/2001- 03/31/2003	\$50,000
Andrew Mellon Contraceptive Centers Flexible Center Grant	C. Williams	Role of the Tetraspanin Emp2 in Early Reproduction	P.I.	07/01/2000- 12/31/2002	\$50,000
Burroughs Wellcome Fund Career Award in the Biomedical Sciences	C. Williams	Signal Transduction Mechanisms During Mouse Egg Activation	P.I.	09/01/1997- 08/31/2005	\$57,750
American Society for Reproductive Medicine/Serono Grant in Reproduction	C. Williams	Signal Transduction Mechanisms During Mouse Egg Activation	P.I.	07/01/1997- 06/30/1999	\$25,000
NIH/NICHD K11 HD00985	C. Williams	Signal Transduction Mechanisms in Mouse Egg Activation	P.I.	01/01/1992- 12/31/1997	\$135,840
Commonwealth of Pennsylvania	C. Williams	Developing Eggs from Stem Cells	P.I.	05/01/2004- 04/30/2006	\$100,000

b.