



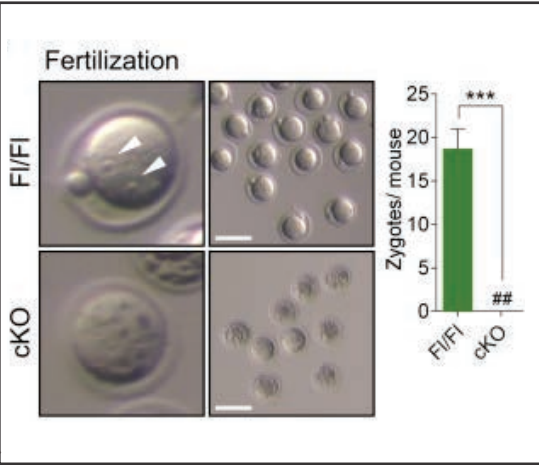
UC San Diego

GLOBAL LEADER
 REPRODUCTIVE SCIENTIST,
 SCHOLAR & VISIONARY
Kurt Benirschke
 (1924-2018)

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◆ Department Principle Investigators Cook-Anderson, Laurent and Wilkinson reveal how messages are regulated during the very, very, early stages of development. (See page 3)

New Milestone.
 The 8th printing of
**Maternal Fetal
 Medicine**
 Congratulations
 to
 Dr. Resnik
 (page 7)

Letter from the Chair



Dear Colleagues,

I am excited to share with you our first quarterly Department Newsletter, "Fimbria".

This name is a simple, beautiful sounding word that recognizes an organ that captures and communicates the reproductive process. We hope that our new quarterly will capture and communicate the events in the Department of Obstetrics, Gynecology, and Reproductive Sciences. I want to thank Dwayne Stupack who came up with this name and is immensely responsible for this new department communication. It will serve as our newsletter, and more. I would also like to thank Cynthia Peña for her collaboration and work on this project. If you have contributions or suggestions for future issues, contact Dwayne or Cynthia directly.

In this edition you will read about our tribute to Kurt Benirschke. Kurt was a founding member of our department and an internationally recognized leader across many disciplines in reproductive science. Kurt was among the first to understand the placenta and his work in all of animal reproduction has been groundbreaking.

We have had a good year in research. We are currently number six in NIH funding for obstetrics and gynecology departments, and this productivity is reflected in our prolific publication record over the last few months. In the *At the Frontier* section, we have listed some of our recent publications (from July 1st onwards). It becomes very clear that we are actively pushing back the "frontiers" of science. However, this list is not complete. The editors pass along their apologies if we missed one of your works, however, we encourage you to submit future work you would like featured in a coming edition of *Fimbria*.

Each edition will feature the outstanding work of our researchers. In this edition, you will learn about the work Heidi Cook- Andersen is doing in early oocyte development, and importantly, how it may explain some cases of infertility we see in the clinic. Published in *Developmental Cell* earlier this year, the work highlights two key characteristics of our department's research: collaboration and extremely high quality work. Supporting Heidi's group in this mission were the labs of Louise Laurent and Miles Wilkinson.

We also get to know two of our most recent faculty additions, Maureen Ries and Jorge Alvarado. Learn about them and their path to UCSD. Welcome and get to know our new fellows and residents, and also see where our graduated chief residents went.

Hope you enjoy this and find it informative. Please forward it on to colleagues if you do.

Charles Nager, MD

CHARLES NAGER
Distinguished Professor and Samuel Yen Chair
Department of Obstetrics, Gynecology
& Reproductive Sciences

DEPARTMENT OF OBSTETRICS, GYNECOLOGY
& REPRODUCTIVE SCIENCES DIVISION CHIEFS

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Contact us at: FIMBRIA@UCSD.EDU

News & New Arrivals

Congratulations to
Ramez N. Eskander, MD,
Yvette LaCoursiere, MD, &
Christine B. Miller, MD
 for being named
Top Docs
 in
San Diego Magazine's
 Annual "Physicians of Exceptional Excellence" Survey.

Department Highlights Funding Success:

The Research program in the department continues to prosper. We are doing great work at the forefront of science, and our level of funding reflects this. **We are currently ranked number 6 in NIH funding** among Gyn/Obs Departments, nationwide. Full ranking can be found at:

http://www.brimr.org/NIH_Awards/2017/NIH_Awards_2017.htm

Welcome to our new interns: **Selam Ghebrendrias, Sharon Heichman, Erica Magelky, Erin Mowers, Michelle Tang, and Ashten Waks.**



Selam Ghebrendrias Sharon Heichman Erica Magelky Erin Mowers Michelle Tang Ashten Waks

Follow Department News on Twitter
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Congratulations to Sarah Averbach

who was selected by the medical school search committee to be the Director of the **Global Health Academic Concentration**

Congratulations, also, to the new graduates of the UCSD Fellowship Programs:



Tatiana Catanzarite (FPMRS)



Victoria Fratto (MFM)



Tannaz Toloubeydokhti (REI)

Not Pictured: Kristin Anderson (Gynecologic Oncology)

In July we welcomed our new interns and fellows
 Our Newest Fellows are:

Jessica Jou (Gyn Onc), **Mary Rieger** (FPMRS), **Helen Swenson** (REI), **Sarah Tilford** (Family Planning), and **Kathy Zhang-Rutledge** (MFM).



Jessica Jou



Mary Rieger



Helen Swenson



Sarah Tilford



Kathy Zhang-Rutledge

In Other Funding news... Assistant Professor David Natale's collaborators at UT Southwestern just received an R01 award from the NIH for their collective studies of antiphospholipid syndrome. *Dr. Natale will receive a sub-contract to examine placental development in his transgenic mouse models.*

Bench & Bedside

Cook-Andersen Lab identifies Key Fertility Protein



For couples struggling with infertility, one of the most difficult things to hear is that the cause of their infertility is unknown. Unfortunately, this is the case for more than 15% of couples. Who could have guessed that a little known Zinc Finger Protein (ZFP) may be playing a key role in infertility?

Dr. Heidi Cook-Andersen's lab is interested understanding at the molecular level what is necessary for a "good egg", or oocyte, that can successfully become an embryo and develop normally over the course of a pregnancy. Cook-Andersen's lab discovered that a protein called "ZFP36L2" is critical for regulating the expression of genes in the oocyte," which regulates the expression of genes in the oocyte. ZFP36L2 turned out to be crucial for female fertility - at least in mice. Without this factor, the oocyte cannot be fertilized by a sperm.

In a recently published study¹, the Cook-Andersen group, in collaboration with Dr. Miles Wilkinson and Dr. Louise Laurent, discovered that ZFP36L2 is necessary for a process called oocyte global transcriptional silencing. It creates a critical pause in the message-making, or transcription, that come from the oocyte DNA. As it turns out, this brief holiday for the DNA is not only critical for fertility, it is a highly conserved developmental event across species, and we know that this happens in people as well.

This finding yields interesting insight into the process of early development. Remarkably, this means that each oocyte matures, is subsequently fertilized by sperm and then begins to develop as an early embryo in the absence of new mRNA production.

1. Dumdie et al., *Dev Cell*. 44:392-402, 2018

This translates to *no new instructions* from the nucleus.

Global transcriptional silencing itself is not new. It is a known phenomenon that is key for the transition from oocyte to embryo and essential for a successful pregnancy. Yet, the mechanisms controlling global transcriptional silencing have been poorly understood. ZFP36L2 activates a process called mRNA decay – a powerful mechanism that quickly degrades the RNAs in the cell, turning off the expression of those genes. This is like stopping the hard-drive in a computer, and it works a bit like removing bookmarks. The programs just can't find files.

In biological terms, the first authors on the paper, Jennifer Dumdie and Kyucheol Cho of the Cook-Andersen lab found that ZFP36L2 binds and degrades a large group of oocyte mRNAs that encode a class of proteins called histone demethylases. These critical enzymes remove epigenetic 'methyl marks' from histones, which are the proteins that bind to DNA and provide structure to chromosomes. They also serve as 'bookmarks' for transcriptional activity.

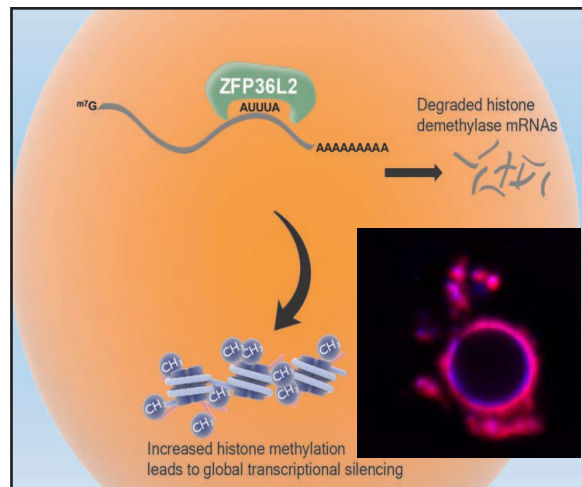


Figure 1. A Working Model depicting how ZFP36L2 drives global transcriptional silencing in the oocyte. (Inset) Immunofluorescent image of the oocyte nucleus showing the highly condensed ring of DNA (purple) and the histone methylation driven by ZFP36L2 (red) in association with global transcriptional silencing.

By turning off this group of histone demethylases, ZFP36L2 enables the widespread accumulation of histone methylation marks known to occur at the time of global transcriptional silencing.

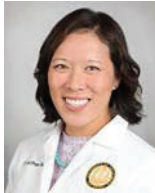
If this mechanism turns out to be conserved in human oocytes, it is possible that abnormal expression of ZFP36L2 or other factors regulating histone methylation in the oocyte might explain a subset of the currently unexplained cases of infertility in women. With the pathway now identified, we have a direction forward.

New Faculty

Maureen Ries & Jorge Alvarado

Fimbria Quarterly (FQ) recently caught up with two of the newest clinical faculty to join the division of Obstetrics and Gynecology, Dr. Jorge Alvarado and Dr. Maureen Ries.

FQ: Where did you grow up?



MR: I grew up in Southern California, not that far from San Diego, in the city of Claremont, at the edge of L.A. County.

JA: I was born and raised a little bit further away - in South Texas. I lived in a border town community that was predominantly comprised of Mexican or Mexican American families.

FQ: Where did you train on your path to San Diego?

MR: I went to Smith college in Massachusetts for undergraduate studies, and double majored in Anthropology and Biology. I went to medical school here at UCSD, and then did my residency at the Ohio State University.

After completing residency, I stayed on as faculty at Ohio State before living in Tanzania, east Africa as a Physician educator volunteer. I taught and worked in a rural hospital to build healthcare capacity through a program that partnered the Peace Corps and Seed Global Health. I'm currently the Director of Ob/Gyn for Seed and I still maintain a passion for sustainable global health.

FQ: Jorge, your path touched both coasts as well?

JA: I moved from Texas to Cambridge, MA to study Electrical Engineering at MIT. After finishing MIT, I had a major change of heart in respect to what I wanted to dedicate my life to. This meant that I needed to do a post-baccalaureate in the Boston area, and

ultimately I went to medical school at the University of Texas Southwestern Medical Center in Dallas, TX. I went on to do my residency at UCSF.

FQ: What attracted you here?



JA: For me, UCSD represented a place where I could foster my passion to care for the underserved and establish a practice that is both comprehensive and inclusive. I was attracted to UCSD because I wanted to be part of an academic institution where I could be intimately involved with the education of residents and medical students so as to train tomorrow's leaders in my specialty. I found all of this at UCSD, and am glad to have made the move here.

FQ: Maureen, you needed a two career solution?

MR: Yes. My husband works here at UCSD as an IM/Peds hospitalist. I always wanted to come back to San Diego. We have friends and family here. I am very happy to be back and hope to have a fulfilling career here providing excellent care to patients and being an engaging member of the department.

FQ: And the family is adjusting well?

MR: Great! We are enjoying the drastic improvement in our work commutes. Our two little boys (3 yr old and a 9 month old) are enjoying being closer to family and friends.

FQ: Jorge, looking forward, what do you hope to accomplish at UCSD?

JA: I would like to help my department and UCSD as a whole to increase it's ethnic, sexual, and intellectual diversity when it comes to it's providers, staff, and students. I am thrilled to be joining such an excellent group of providers, and look forward to working alongside you.

At the Frontier

Our Most Recent Publications

Since July, Department members have been very productive, including these 20 publications.

Lichtman A, Parker W, Goff B, Mehra N, Shoree E, Lefebvree G, Chiang A, Lenihan J, Schreuderg H. **A Randomized Multi-Center Study Assessing The Educational Impact of a Computerized Interactive Hysterectomy Trainer on Gynecology Residents.** J Minim Invasive Gynecol 2018;25:1035-1043.

Mody SK, Farala JP, Jimenez B, Nishikawa M, Ngo LL. **Paracervical Block for Intrauterine Device Placement Among Nulliparous Women: A Randomized Controlled Trial.** Obstet Gynecol. 2018 Sep;132(3):575-582. doi: 10.1097/AOG.0000000000002790. PMID: 30095776

Herrero T, Driebe A, Fratto V, Hamlin A, Lacoursiere DY. **Depression Scale: examining behavioral and pharmacological therapy on maternal and neonatal out-comes.** J Matern Fetal Neonatal Med. 2018 Jul 22:1-5.

Taylor KN, Schlaepfer DD. **Adaptive Resistance to Chemotherapy, A Multi-FAK-torial Linkage.** Mol Cancer Ther. 2018 Apr;17(4):719-723. doi: 10.1158/1535-7163.MCT-17-1177. PMID: 29610281

Anderson KM, Barback CV, Qin Z, Hall DJ, Hoh CK, Vera DR, McHale MT. **Molecular Imaging of endometrial sentinel lymph nodes utilizing fluorescent-labeled Tilmamcept during robotic-assisted surgery in a porcine model.** PLoS One. 2018 Jul 2;13(7):e0197842. doi: 10.1371/journal.pone.0197842. eCollection 2018. PMID: 29965996

Giraldez MD, Spengler RM, Etheridge A, Godoy PM, Barczak AJ, Srinivasan S, De Hoff PL, Tanriverdi K, Courtright A, Lu S, Khoory J, Rubio R, Baxter D, Driedonks TAP, Buermans HPJ, Nolte-'t Hoen ENM, Jiang H, Wang K, Ghiran I, Wang YE, Van Keuren-Jensen K, Freedman JE, Woodruff PG, Laurent LC, Erle DJ, Galas DJ, Tewari M. **Comprehensive multi-center assessment of small RNA-seq methods for quantitative miRNA profiling.** Nat Biotechnol. 2018 Sep;36(8):746-757. doi: 10.1038/nbt.4183. Epub 2018 Jul 16. PMID: 30010675

Alperin M, Burnett L, Lukacz E, Brubaker L. **The mysteries of menopause and urogynecologic health: clinical and scientific gaps.** Menopause. 2018 Oct 8. doi: 10.1097/GME.0000000000001209. [Epub ahead of print] PMID: 30300297

Thomas-White KJ, Gao X, Lin H, Fok CS, Ghanayem K, Mueller ER, Dong Q, Brubaker L, Wolfe AJ. **Urinary microbes and postoperative urinary tract infection risk in urogynecologic surgical patients.** Int Urogynecol J. 2018 Sep 28. doi: 10.1007/s00192-018-3767-3. PMID: 30267143

Brubaker L, Carberry C, Nardos R, Carter-Brooks C, Lowder JL. **American Urogynecologic Society Best-Practice Statement: Recurrent Urinary Tract Infection in Adult Women.** Female Pelvic Med Reconstr Surg. 2018 24(5):321-335. doi: 10.1097/SPV.0000000000000550. PMID: 29369839

Palmsten K, Nelson KK, Laurent LC, Park S, Chambers CD, Parast MM. **Subclinical and clinical chorioamnionitis, fetal vasculitis, and risk for preterm birth: A cohort study.** Placenta. 2018 Jul;67:54-60. doi: 10.1016/j.placenta.2018.06.001. Epub 2018 Jun 6. PMID: 2994117

Fok CS, Gao X, Lin H, Thomas-White KJ, Mueller ER, Wolfe AJ, Dong Q, Brubaker L. **Urinary symptoms are associated with certain urinary microbes in urogynecologic surgical patients.** Int Urogynecol J. 2018 Aug 16. doi: 10.1007/s00192-018-3732-1. PMID: 30116843

Rogers RG, Nolen TL, Weidner AC, Richter HE, Jelovsek JE, Shepherd JP, Harvie HS, Brubaker L, Menefee SA, Myers D, Hsu Y, Schaffer JI, Wallace D, Meikle SF; NICHD Pelvic Floor Disorders Network. **Open sacrocolpopexy and vaginal apical repair: retrospective comparison of success and serious complications.** Int Urogynecol J. 2018 Aug;29(8):1101-1110. doi: 10.1007/s00192-018-3666-7. Epub 2018 May 25. PMID: 29802413

Billquist EJ, Michelfelder A, Brincat C, Brubaker L, Fitzgerald CM, Mueller ER. **Pre-operative guided imagery in female pelvic medicine and reconstructive surgery: a randomized trial.** Int Urogynecol J. 2018 Aug;29(8):1117-1122. doi: 10.1007/s00192-17-3443-z. Epub 2017 Sep 7. PMID: 28884342

Jelovsek JE, Chagin K, Lukacz ES, Nolen TL, Shepherd JP, Barber MD, Sung V, Brubaker L, Norton PA, Rahn DD, Smith AL, Ballard A, Jeppson P, Meikle SF, Kattan MW; NICHD Pelvic Floor Disorders Network. **Models for Predicting Recurrence, Complications, and Health Status in Women After Pelvic Organ Prolapse Surgery.** Obstet Gynecol. 2018 Aug;132(2):298-309. doi: 10.1097/AOG.0000000000002750. PMID: 29995735

Delaney J, Stupack D.G. **"Genomic Copy Number Alterations in Serous Ovarian Cancer,"** in *Ovarian Cancer: From Pathogenesis to Treatment, pp111-133.* Devaja & Papadopoulos, eds. Intech Pub. DOI: 10.5772/intechopen.72695

Pandolfi EC, Hoffmann HM, Schoeller EL, Gorman MR, Mellon PL. **Haploinsufficiency of SIX3 Abolishes Male Reproductive Behavior Through Disrupted Olfactory Development, and Impairs Female Fertility Through Disrupted GnRH Neuron Migration.** Mol Neurobiol. 2018 Nov;55(11):8709-8727. doi: 10.1007/s12035-018-1013-0. PMID: 29589282

Hoffmann H, Pandolfi E, Larder R, Mellon P. **Haploinsufficiency of Homeodomain Proteins Six3, Vax1, and Otx2, Causes Subfertility in Mice Via Distinct Mechanisms.** Neuroendocrinology. 2018 Sep 27. doi: 10.1159/000494086. Epub ahead of print PMID: 30261489

Huang L, Shum EY, Jones SH, Lou CH, Dumdie J, Kim H, Roberts AJ, Jolly LA, Espinoza JL, Skarbrevik DM, Phan MH, Cook-Andersen H, Swerdlow NR, Gecz J, Wilkinson MF. **A Upf3b-mutant mouse model with behavioral and neurogenesis defects.** Mol Psychiatry. 2018 Aug;23(8):1773-1786. doi: 10.1038/mp.2017.173. Epub 2017 Sep 26. PMID: 28948974

Baah-Dwomoh A, Alperin M, Cook M, De Vita R. **Mechanical Analysis of the Uterosacral Ligament: Swine vs. Human.** Ann Biomed Eng. 2018 Jul 26. doi: 10.1007/s10439-018-2103-x. PMID: 30051246

Brady SS, Bavendam TG, Berry A, Fok CS, Gahagan S, Goode PS, Hardacker CT, Hebert-Beirne J, Lewis CE, Lewis JB, Kane Low L, Lowder JL, Palmer MH, Wyman JF, Lukacz ES; Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium. **The Prevention of Lower Urinary Tract Symptoms (PLUS) in girls and women: Developing a conceptual framework for a prevention research agenda.** NeuroUrol Urodyn. 2018 Nov;37(8):2951-2964. doi: 10.1002/nau.23787. Epub 2018 Aug 22. PMID: 30136299

Milestone

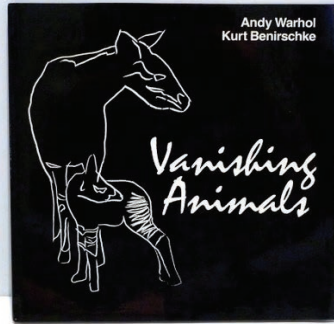
Benirschke Era

This fall, we lost one of the giants of reproductive medicine. Few, if any, can match his lifetime of achievements. He joined the faculty of University of California San Diego School of Medicine in 1970, shortly after the school opened. He served nearly a quarter of a century as a noted pathologist, geneticist and expert on the placenta and reproductive systems of humans and myriad mammalian species. He was internationally known for his efforts to create the world's first "frozen zoo."

He was born in the Glückstadt, a small town an hour north of Hamburg, Germany, in 1924. He received his medical degree from the University of Hamburg in 1948 and immigrated to the United States in 1949. He did his residency training in pathology at Harvard Medical School and, in 1955, became a pathologist at Boston Lying-in Hospital, now part of Brigham and Women's Hospital. One of the first dedicated maternity hospitals in the United States, it was there that he became particularly interested in the biology of the placenta and reproduction.

From 1960 to 1970, Benirschke served as chair of the Department of Pathology at Dartmouth Medical School, exploring placental pathology and comparative reproductive pathology. He investigated how viruses are passed from mother to fetus and did fundamental work on the phenomenon of chimerism, in which the different tissues of an individual possess different but complete sets of genetic material. His scholarly interests were vast. Why are mules sterile? How does twinning occur (in armadillos and in marmosets).

Benirschke did not see a dichotomy in his interests. He moved freely between human medicine and animal medicine, considering lessons learned to be universal. In 1970, Benirschke was invited to join the faculty of UC San Diego School of Medicine and moved his family to San Diego, quickly and naturally becoming involved with the San Diego Zoo. Almost immediately he became an influential voice and figure in the world of animal conservation.



At UCSD, Benirschke established a genetics laboratory, ran the autopsy service for the university hospital, and served as a conduit for technological advancement at the zoo. Benirschke lobbied for the creation of a novel "cell bank" to preserve the eggs, sperm and other tissues of endangered species.

"A number of mammals and other species are going to become extinct in the next decades, all efforts notwithstanding," Benirschke wrote to leaders at the San Diego Zoological Society.

"This is of very great concern to me and I hope that we can somehow proceed. I am going to summarize what I can contribute to the subject."

Benirschke believed the San Diego Zoo would be an ideal home for a so-called "frozen zoo." This visionary idea was to found a repository containing reproductive tissues from animals around the world, from rhinos and whales to apes and antelopes. At the time, there was no technology yet available to effectively thaw, study and revive frozen eggs and sperm, but Benirschke, quoting American historian Daniel Boorstin, said "You must collect things for reasons you don't yet understand."

His words would prove prophetic. Technologies subsequently emerged, advancing conservation science. In 1979, the Zoological Society established CRES, the Center for Research of Endangered Species, which Benirschke led until 1985, when he joined the Zoo's board of directors. Today, the renamed San Diego Zoo Institute for Conservation Research is the largest of its kind, with more than 10,000 living cell cultures, oocytes, sperm and embryos representing nearly 1,000 taxa, some extinct and many severely endangered. A 1984 tribute book to Benirschke, was written by 50 of his colleagues. The title was "One Medicine."

Kurt was the consummate scholar: teaching courses, conducting research, authoring and editing books, and lecturing around the world. From 1976 to 1978, Benirschke served as chair of the Department of Pathology at UC San Diego School of Medicine and played a key role in the creation and success of the Center for Academic Research and Training in Anthropogeny (CARTA). He formally retired as professor emeritus in 1994. Yet he remained active as a consultant to the autopsy service, and did fieldwork at a breeding facility in Paraguay for a newly discovered species of peccary. Of course, he continued to publish.

Continued on page 7

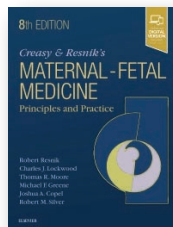
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Benirschke era, con't

Benirschke ultimately produced more than 500 scientific publications and more than 30 books. Among these, "Pathology of the Human Placenta," now in its sixth edition, continues to stand as the authoritative text in its field. He received numerous honors and awards, including the Virginia Apgar Award in 1998 from the American Academy of Pediatrics. He was a member of many scientific societies, including the American Academy of Arts and Sciences.

Since 1994, the department of Obstetrics, Gynecology & Reproductive Sciences, together with the department of Pediatrics, have collaborated to present the annual Kurt Benirschke Lecture, featuring international experts on topics relevant to reproductive biology and procreation. This past year's speaker was Dr. Oliver Ryder, Kleberg Endowed Director of Conservation Genetics at the San Diego Zoo Institute for Conservation Research. His lecture, "The Frozen Zoo: Evolution of a Unique Resource for Biodiversity Discovery, Conservation, and Genetic Rescue," provides a timely tribute to the lasting legacy to the father of comparative placentology.

Maternal-Fetal Medicine: Principles and Practice 8th edition



Creasy and Resnik's Maternal-Fetal Medicine hits a new landmark with the publication of its 8th edition (Elsevier). Long recognized as the authoritative leader in the field, this version encompasses more than 1400 pages of the latest evidence-based guidelines for obstetric and neonatal management. Special congratulations are due Robert Resnik, Professor and Chair Emeritus of the Department of Obstetrics, Gynecology, and Reproductive Sciences at UCSD, as well as Thomas Moore, Professor and past Chair-man of the Department of Obstetrics, Gynecology, and Reproductive Sciences at UCSD, two of the team of 6 renowned experts to contribute to the book. Other contributors include Charles Lockwood (OHSU), Michael Green (Harvard) Joshua Copel (Yale) and Robert Silver.

Fimbria
QUARTERLY

Upcoming Events

1st CMI International Microbiome Meeting

jointly held with

1st Urobiome Meeting

February 26-28, 2019

University of California, San Diego

On behalf of Linda Brubaker, MD, Clinical Professor in the UC San Diego Department of Obstetrics, Gynecology, and Reproductive Sciences, we announce the 1st annual Urobiome Meeting.

Researchers will present on the emerging science of the Urobiome and its recently discovered implications for human health, including common conditions such as urinary tract infection, urinary incontinence, and bladder overactivity.

website:

<http://cmi.ucsd.edu/event/2019>

Graduating Chiefs: At the end of June we celebrated the graduation of 5 chief residents. Our graduating chiefs and their next positions are listed:



Alaina Bennett
OHSU (Urogyn F/S)



Amy Driebe
Kaiser, San Diego



Anela Puljic
Woodglen Medical
Glendora, CA



Cat Uchino
Kaiser, Sacramento



Whitney Hendrickson-Cahill
Duke University (Urogyn F/S)

Fimbria is a publication of the UCSD Department of Obstetrics, Gynecology and Reproductive Sciences. Editors: DWAYNE STUPACK, CYNTHIA PEÑA fimbria@ucsd.edu