Letter from the Chair 1
News & New Arrivals  2 
Bench & Bedside: 3
  The Cook-Andersen Lab’s Key Finding
New Faculty 4
  Alvarado & Ries
At The Frontier 5
Milestone: Benirschke Era 6
The Back Page  7

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

Global Leader
Reproductive Scientist, Scholar & Visionary
Kurt Benirschke (1924-2018)

In this Issue:
LETTER FROM THE CHAIR 1
NEWS & NEW ARRIVALS  2
BENCH & BEDSIDE: 3
The Cook-Andersen Lab’s Key Finding
NEW FACULTY 4
Alvarado & Ries
AT THE FRONTIER 5
MILESTONE: Benirschke Era 6
THE BACK PAGE  7

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

Department again among top NIH-Funded in nation: Page 2
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 or 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, M.D.
Distinguished Professor and Samuel Yen Chair
Department of Obstetrics, Gynecology & Reproductive Sciences

Charles Nager
Distinguished Professor and Samuel Yen Chair
Department of Obstetrics, Gynecology & Reproductive Sciences

Department of Obstetrics, Gynecology & Reproductive Sciences Division Chiefs

Family Planning
Sheila Mody
Michael McHale
Maternal Fetal Medicine
Thomas Kelly
Obstetrics and Gynecology
Pamela Deak
Hospitalist
Gina Frugoni
Urogynecology
Emily Lukacz
Reproductive Endocrinology and Infertility
Antoni Duleba

Midwife Director
Karen Perdion

Contact us at: FMBRIA@UCSD.EDU
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.

Follow Department News on Twitter
@UCSD_ObGyn

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:

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

In Other Funding news... Assistant Professor David Natale’s collaborators at UT Southwestern just received an RO1 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. 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 study, 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.

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.

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.

1. Dumdie et al., Dev Cell. 44:392-402, 2018
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: 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: Where did you train on your path to San Diego?

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.
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 consumate 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
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.

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