

Leadership Awards

Laurent and Lawson are recognized for their leadership on the local and national stage.

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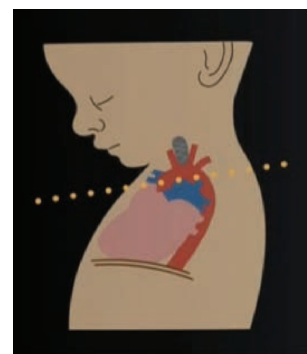
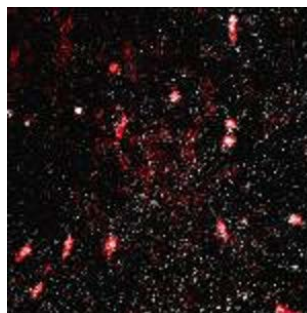
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◆ *It starts with a Kiss (-peptin.)*
Sasha Kauffman's lab studies the neural end of the REI axis.

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◆ *Tracy Anton, UCSD's Fetal Sonographer Extraordinaire*

Back Page:
WHRH Fellow
Slot Opens.

Letter from the Chair

Traditionally, spring is considered a time of rebirth or renewal, an optimistic sentiment as the promise of spring occurs annually. In our department, the yearly changes that signal rebirth are underway. This spring we assisted our medical students in securing residency positions, matched a new intern class, and prepared many of our third year residents for their fellowship applications. Our incoming interns, listed on page 2, come from as close as UC Irvine to as far as Columbia University. We are thrilled to welcome these new learners to our family.



As COVID restrictions relaxed, we resumed in-person society meetings nationally. Our faculty participated as speakers, moderators, organizers, and presenters for the Society for Reproductive Investigation (SRI), the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU), and the American Institute of Ultrasound in Medicine (AIUM) meetings. Our faculty were prominent in the Society for Gynecologic Oncology meeting, with numerous poster and oral presentations (photo, p2; story, p4). In May, we host the Annual Meeting of the American College of Obstetricians and Gynecologists (ACOG) here in lovely San Diego. Our department has a longstanding history of leadership roles in ACOG. Currently, Dr. Julia Cormano is the Chair of California Section 8, and Dr. Mai Hoang is the national Young Physician at Large, a position that allows her to represent young OBGYN physicians on the ACOG Board. In addition, our department's national leadership in addressing health disparities in obstetrics will be on display at the annual meeting as Dr. Audra Meadows, specialist in obstetrics and gynecology, presents the March of Dimes lecture on Obstetric Equity and later leads a call to action on health disparities.

This spring issue of the Fimbria features a sampling of the excellence I have come to know from our department. Dr. Mark Lawson, Professor and Director of the UC President's Postdoctoral Fellowship Program, was personally recognized for his 20 years of service to the NIDDK Network of Minority Health Research Investigators by Dr. Grif Rogers, who is the Director of the NIDDK. Dr. Louise Laurent, Professor and Vice Chair for Translational Research, was one of three women from the health system awarded the 2022 Health Sciences Women's Leadership Award, an honor given to women who have demonstrated extraordinary leadership within UC San Diego Health Sciences and beyond, especially during the COVID-19 pandemic.

CLICK: UC SAN DIEGO OBSTETRICS, GYNECOLOGY & REPRODUCTIVE SCIENCES DEPT. CURRICULUM VITAE

Several other honors are mentioned in this edition, and our 2021 department CV, celebrating the publications and accomplishments of our faculty, is now available in the link above. Our focus on advocacy has continued through this spring, with our Culture and Justice Quorum raising awareness of the US Black Maternal Health Crisis during Black Maternal Health Week. Led by chief resident, Dr. Ghebren-drias, and assisted by Drs. Lacoursiere, Brubaker, and Mr. Morales, the Quorum members will present their work at the SASGOG meeting in May. To support moving this effort forward, the department will appoint a Vice Chair for Culture and Justice.

Finally, I'd like to highlight some other newsletter content. We feature voluntary faculty member Tracy Anton. Her national lectures are well received, and she's taught numerous fellows and faculty over the past 20 years. Her story is found on page 3. We also feature the Kauffman Lab, established in 2009 and led by Dr. Alexander (Sasha) Kauffman. Their work on kisspeptin draws international acclaim. We plan to feature the work of our excellent basic science faculty in each edition moving forward. Thank you for taking the time to read this edition of Fimbria.

Thank you!

CYNTHIA GYAMFI-BANNERMAN, MD, MS
Professor and Chair
 Department of Obstetrics, Gynecology
 & Reproductive Sciences

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Newsbytes



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Funding News

Match Day

Congratulating all the new Interns that will be joining us this summer!

Sophia Angelides
UC Irvine

Kelsey Keverline
UNC Chapel Hill

Lillian Liao
Columbia University

Allison Rajan
University of Washington

Emma Roberts
University of Washington

Daniella Rogerson
Columbia University

Marni Jacobs PhD has received notification that the ACTRI Pilot grant has been funded. "Feasibility and utility of an ora/ fat tolerance test for prediction of preeclampsia".

Mandy Lewis PhD (MPI) and Warren Lewis PhD (Co-I) recieved a new R01 together with collaborators at the University of Louisville: "Long-Acting 3D Printed Scaffolds for Treatment of Bacterial Vaginosis" R01AI168475, 04/2022 – 03/2027

Karen J. Tonsfeldt, PhD received a Pathway to Independence K99/R00 Award from National Institutes of Health, 2022-2024. K99 NS119291-01, 4/1/22-3/31/24, "Functional Mapping of the Suprachiasmatic Nucleus"

Congratulations to

Kelly Breen-Church, PhD
on being selected as Symposium Chair,
*Neuroendocrine Interface of
Reproduction and Metabolism,
Endocrine Society Annual Meeting*

Louise Laurent, MD PhD
On Receiving the 2022
*Health Sciences Women
Leadership Award
from UC San Diego Health.*

Mark Lawson, PhD
was recognized for
*20 Years of Service
by the
NIDDK Network of
Minority Health Research Investigators*

UC San Diego Gynecologic Oncology, Past & Present

as assembled at the SGO meeting this past March in Phoenix (more on page 4).

Left to Right: Ramez Eskander MD, Pratibha Binder MD,
Allison Brodsky MD, Katherine Coakley MD,
Estefania (Nia) Fernandez MD, PhD., Marianne Hom-Tedla MD,
Allison Barrie MD, Lindsey Charo MD, Jessica Jou MD,
Michael McHale MD, Steven Plaxe, MD.



Spotlight

Professor Tracy Anton

You might not realize it if you just passed her in the hall, but Tracy Anton is a star. The sonography world knows it, and the department is fortunate to have this pioneer in the field of fetal ultrasound on our team. Through exceptional skills, a driving work ethic and a teacher's soul, she has become a recognized and lauded leader in the field.



Dr. Hull expanded on her talents "Tracy is gifted in her ability to interpret and explain complex three dimensional phenomenon as shown in a two dimensional image. She has an uncanny focus on detail."

This appreciation projects to social media. If you are intrested in fetal sonography and you don't follow her Twitter feed, you might consider it. For the record, her feed is ...

[@tracy_anton1](https://twitter.com/tracy_anton1).

When Tracy was awarded a faculty appointment in the department a few years ago, she became the first non-MD/non-PhD to receive this distinction at UC San Diego. It was one distinction among many. Tracy was awarded the 2018 Distinguished Sonographer Award by the American Institute of Ultrasound in Medicine, (AIUM) which honors an individual who has made outstanding contributions to the development of medical ultrasound.

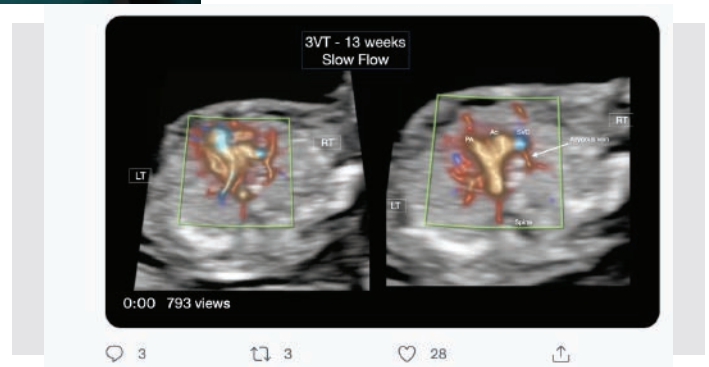
Having been at UC San Diego for two decades, she heads the Fetal Echocardiography program. In this role she performs ultrasound quality assurance, and is in the faculty rotation for UCSD's biweekly Fetal Medicine Conference. It has provided a critical service at our Sorrento Valley location, which would otherwise refer patients to Rady's.

Dr. Andrew Hull, MD, has known and worked alongside Tracy since she joined UC San Diego. "The ability to detect cardiac abonormalities as early as possible is critical for care providers and for patients," he noted. "Tracy is pushing the bounds of how early we can detect a range of different abnormalities, ranging from hypoplastic left heart to dysrhythmias to ductus arteriosus." He noted that the latter could, in some cases, be treated with IV prostaglandins.

As a midlevel provider, her day to day requires she interprets obstetric ultrasound studies, counsels patients, provides follow-up recommendations, and composes ultrasound reports. In a supervisory role, she checks sonographers' cases for quality and completeness, directing sonographers to get more images, obtaining images on difficult or complex cases, deeming the exam complete, writing preliminary reports, and discussing routine sonographic findings with patients.

Fimbria

QUARTERLY



Outside of UC San Diego, Tracy contributes to setting standards for the American Registry for Diagnostic Medical Sonography and serves on the registry's item writing and item development task forces. She is also currently on the Society for Maternal-Fetal Medicine/AIUM task force for development of a maternal-fetal medicine fellow ultrasound curriculum. With the AIUM, Tracy has participated as an Ultrasound Practice Accreditation Council member and reviewer, performed senior application reviews, presented webinars, and moderated and given lectures at numerous AIUM conventions. You might also find her participating in the UC Fetal Consortium, focusing on enhancing research opportunities, training, and clinical care among UC campuses.

Her most recent publication with collaborators at UCLA and UC San Diego focuses on guidelines for an increasing problem in fetal cardiac imaging: reduced acoustic window. The adaptations of the guidelines provides one more tool in addressing difficult case in MFM.

<https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/uog.24872>

How Ovarian Cancers Avoid Immunotherapy

Ovarian cancer is the fifth leading cause of cancer deaths among women. More than half of these cases are high-grade serous ovarian cancer (HGSOC) tumors, which claim the life of 6/10 women within 5 years.

HGSOC is lethal in part because it is either initially resistant to chemotherapy or acquires resistance upon recurrence. Immunotherapy, a therapeutic approach that uses a person's immune system to fight disease, has been promising in many cancers, but approaches to use immunotherapy have not yet shown success in HGSOC.

One approach to immunotherapy targets proteins called checkpoint receptors that act as brakes on immune system activation. Inhibitors of checkpoint receptors release this brake, allowing the immune system to attack cancer cells. However, for immunotherapy to work effectively against HGSOC, treatments need to also disable the protective environment created by the cancer cells.

A new study from the lab of David Schlaepfer, PhD, a professor in the Department of Obstetrics, Gynecology and Reproductive Sciences, provides insight into the molecular details of tumor and immune cell communication and resulting dysfunction in HGSOC.

"Ovarian cancer is one of oncology's greatest challenges," Schlaepfer said. "Tumors can develop without obvious symptoms. The most common sign of ovarian cancer is abdominal swelling when the disease is advanced, which is when most women are diagnosed."

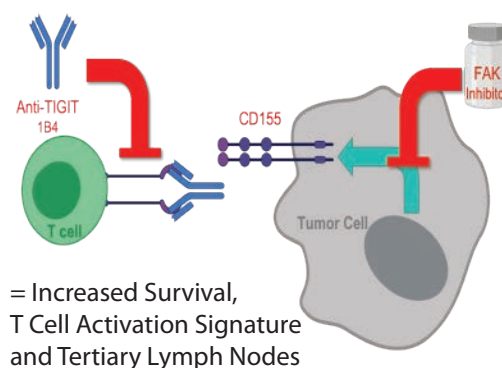
Duygu Ozmadenci, PhD, the lead author and a Sol and Anne Schreiber Ovarian Cancer Research Alliance Mentored Investigator, discovered that activation of a signaling protein within tumors called FAK (focal adhesion kinase) elevated the expression of checkpoint proteins that act to "calm" the immune system. In effect, the tumor cells were building a safe place to grow and evade immune detection.

The work joined two very different schools of thought. One focus for immunotherapy of cancer has been trying to target the an immune regulator called PD-L1. However, singular approaches targeting PD-L1 have not been successful in ovarian cancer. This work showed that FAK helped to maintain both PD-L1 and high levels of a second protein, CD155, as a shield against immune attack. FAK has been credited with roles in helping tumor cells invade tissue, but it is now becoming clear that it acts as a sensor to guide tumor responses to many different challenges.

In addition to data from patient tissues, focused studies were performed using a preclinical model of aggressive ovarian cancer developed in the Schlaepfer lab. The researchers found that an oral anti-FAK drug reduced checkpoint protein expression on the tumor cells. When the drug was used together with an immunotherapy blocking the T cell receptor for CD155 an elevated immune response was observed against the ovarian cancer cells. This, in turn resulted in smaller tumors and longer survival. Two mice survived the study. Importantly, the investigators linked this to an immune activation signature that included both cytokines and the formation of tertiary lymphoid structures proximal to tumors (or tumor remnants) in the omental tissue of the treated mice.

"Some companies are testing inhibitors to FAK; others have inhibitory antibodies to the TIGIT checkpoint receptor in clinical trials," said Schlaepfer. "In HGSOC tumors, high levels of CD155 and active FAK are common. Our results provide compelling support for targeting FAK and TIGIT as part of a new immune-boosting therapeutic strategy."

The studies were highly collaborative, involving investigators from the La Jolla Institute for Allergy and Immunology and from Harvard University department of immunology, as well as other labs in the Moores UC San Diego Comprehensive Cancer Center. The studies were published as part of the April 12th issue of the Proceedings of the National Academy of Sciences (USA).



Fimbria Focus On: Gynecologic Oncology

The Division of Gynecologic Oncology made a strong impact at the 2022 Meeting of the Society for Gynecologic Oncology last month in Phoenix, AZ. Multiple research initiatives were presented that highlighted the breadth of clinical research in the division.

Oral Presentations:

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Outcomes Across Three Academic Institutes Among Frail and Non-Frail Patients. Hari, A, Furey, K, Jou, J, Angelides, S, Arshad, F, Lucia, L, Sim, M, King, J, Tseng, J, Binder, P, and Cohen JG.

Using cancer immunity marker RNA expression level to compare immunogram across gynecologic cancers Jessica Jou, Shumei Kato, Ramez Eskander, Razelle Kurzrock.

MLH1 promoter hypermethylation among mismatch repair deficient, high-intermediate risk, endometrial cancer patients is associated with differences in prognostic factors Hom-Tedla MS, Coakley K, McHale M, Saenz C, Plaxe S, Binder P, Harrison T, Jacobs MB, Eskander R

Narcotic Waste in the Operating Room and Immediately Post-Operatively in Gynecologic Oncology Surgery A Brodsky, A Pemmaraju, O Mesina, C Saenz, R Eskander, M McHale, S Plaxe, P Binder.

Poster Presentations:

PARPi after PARPi: clarity from the Clarity real world experience. Jessica Jou, D. Zajchowski, R. Kurzrock, R Eskander.

Comparison of Rates of Vaginal Brachytherapy vs External Beam Radiation Post-Hysterectomy for Endometrial Cancer Patients in Rural vs Urban Settings. A Brodsky, M McHale, S Plaxe.

Comparing Loop Electrosurgical Procedure Pathology Results in the Inpatient and Outpatient Setting. A Brodsky, H Mathers, M Jacobs, O Fadare, R Eskander.

Lymph node evaluation in endometrial cancer patients after the FIRES trial. Hom-Tedla MS, Coakley K, Charo L, Jou J, Bondre I, McHale M, Eskander R, Binder P, Saenz C, Plaxe S

Higher US COVID-19 hospitalizations are associated with compromised endometrial cancer care; 20% fewer patients were treated surgically during the first year of the pandemic. Katie Coakley, Marianne Hom-Tedla, Cheryl Saenz, Pratibha Binder, Ramez Eskander, Michael McHale, Steve Plaxe

In addition to outstanding clinical (and basic) research, the division has a full portfolio of clinical trials in place.

160426 NRG-GY006 (Mell) A Randomized Phase II Trial of Radiation Therapy and Cisplatin Alone or in Combination with Intravenous Triapine in Women with Newly Diagnosed Bulky Stage IB2, Stage II, IIIB, or IVA Cancer of the Uterine Cervix or Stage II-IVA Vaginal Cancer

191020 Agenesis/GOG 3028 (McHale) A Randomized Phase II Trial of Radiation Therapy and Cisplatin Alone or in Combination with Intravenous Triapine in Women with Newly Diagnosed Bulky Stage IB2, Stage II, IIIB, or IVA Cancer of the Uterine Cervix or Stage II-IVA Vaginal Cancer

180480 Iovance/C-145-04 (McHale) A Phase 2, Multicenter study to Assess the Safety and Efficacy of Autologous Tumor Infiltrating Lymphocytes (Lifileucel, formerly LN-145) for Treatment of Patients with Metastatic Cervical Cancer.

200310 Astra Zeneca DUO-E (McHale) Durvalumab With or Without Olaparib as Maintenance Therapy After First-Line Treatment of Advanced and Recurrent Endometrial Cancer

210181 Merck Engot-EN11/Keynote-B21/GOG3053 (Eskander) Study of Pembrolizumab (MK-3475) in Combination With Adjuvant Chemotherapy With or Without Radiotherapy in Participants With Newly Diagnosed Endometrial Cancer After Surgery With Curative Intent

191379 NRG GY018 (Eskander) A phase III randomized, placebo -controlled study of pembrolizumab (MK-3475, NSC #776864) in addition to paclitaxel and carboplatin for measurable stage III or IVA, sgate IVB, or recurrent endometrial cancer.

201225 NRG GY020 (Binder) Testing the Addition of the Immunotherapy Drug, Pembrolizumab, to the Usual Radiation Treatment for Newly Diagnosed Early Stage High Intermediate Risk Endometrial Cancer

201297 Astra Zeneca Adagio (Eskander) A Study of Adavosertib as Treatment for Uterine Serous Carcinoma

201424 OncoQuest (Eskander) Oregovomab Plus Chemo in Newly Diagnosed Patients With Advanced Epithelial Ovarian Cancer Following Optimal Debulking Surgery (FLORA-5)

140912 Early Detection of Ovarian Cancer (Saenz)

170517 ROCKIF (McHale) ROCK-IF Trial: Re-sensitization of Carboplatin-resistant Ovarian Cancer with Kinase Inhibition of FAK, a Phase 1 clinical trial

190616 NRG GY014 (Eskander) A Phase II Study of Tazemetostat (EPZ-6438) (IND # 138671) in Recurrent or Persistent Endometrioid or Clear Cell Carcinoma of the Ovary, and Recurrent or Persistent Endometrioid Endometrial Adenocarcinoma

Additional trials for tissue collection, not listed here, are open for the molecular profiling of cancer. Though only modestly impacted by the pandemic, the clinical load continues to rise. Gyn/Onc has strongly contributed to the rising status of our department nationally, and is **the** place to go for academic medicine in San Diego.

Focus On: The Kauffman Laboratory

The Kauffman Lab at U.C. San Diego was established in 2009. Directed by Sasha Kauffman, the lab is a multifunctional group that uses a variety of molecular, cellular, physiological, and neuroanatomical platforms to study how the brain and hormones interact to control puberty and reproduction.



From left to right: Nathan Rizo, Jason Yang, Alexander Kauffman, Alexandra Hudson & Marcos Real.

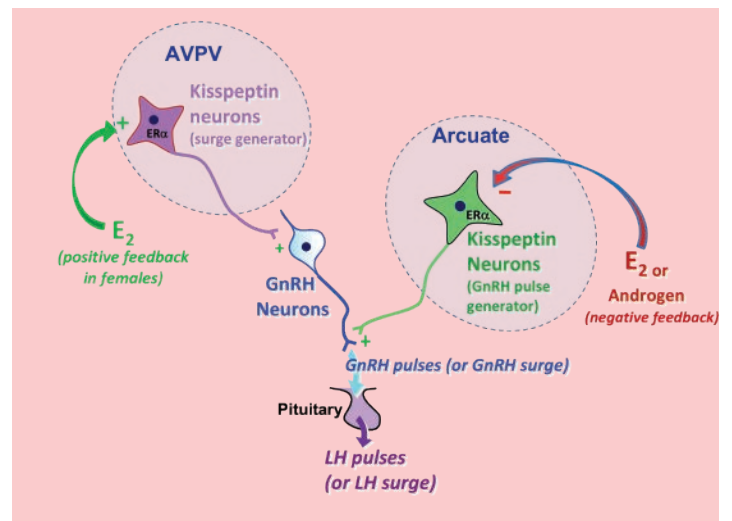
Not pictured: Adriana Ezparza and Andrew Kelton

More specifically, the Kauffman Lab assesses how the brain's neural circuits (such as those utilizing kisspeptin, NKB, dynorphin) stimulate or inhibit Gonadotropin-releasing hormone (GnRH) neurons, thereby regulating the neuroendocrine reproductive axis. Their studies use mouse models to examine the regulation of fertility in adulthood as well as the control of the reproductive axis during puberty. The lab's goal is to better understand the hormonal and neural mechanisms underlying reproduction in order to improve fertility treatments in humans, elucidate novel contraceptive methods, and enhance treatment of pubertal and developmental disorders.

Recent studies have been investigating how the brain controls the estradiol-induced preovulatory luteinizing hormone (LH) surge that triggers ovulation, the mechanisms of which remain poorly understood. In rodents, estrogen receptor α -expressing kisspeptin neurons in the hypothalamic anteroventral periventricular region (AVPV) are prime candidates to mediate estradiol positive feedback induction of LH surges.

Estradiol stimulates AVPV Kiss1 gene expression, but the full extent of estrogen effects in these kisspeptin neurons is unknown. Importantly, whether estradiol stimulates or inhibits other genes in AVPV kisspeptin neurons has been unclear and there is limited understanding of the overall molecular phenotype of AVPV kisspeptin neurons. To provide a more detailed profiling of co-expressed genes in AVPV kisspeptin neurons, including receptors and other signaling factors, and test how these genes respond to estradiol, the Kauffman lab selectively isolated actively-translated mRNAs from AVPV kisspeptin neurons of female mice and performed RNA sequencing (RNA-seq). This identified >13 000 mRNAs co-expressed in AVPV kisspeptin neurons, including multiple receptor and ligand transcripts positively or negatively regulated by estradiol. The lab also performed RNAscope to validate co-expression of several transcripts identified by RNA-seq, including Pdyn (prodynorphin), Penk (proenkephalin), and Cartpt (CART), in female AVPV kisspeptin neurons. Given the important role of AVPV kisspeptin neurons in estrogen positive feedback, estradiol effects on identified genes may relate to the LH surge mechanism.

Interestingly, androgen receptor (AR) was identified in the RNA-seq analysis as a key gene being highly expressed in female AVPV kisspeptin neurons. The Kauffman lab has therefore recently been studying how elevated androgens (testosterone, DHT) might regulate female kisspeptin neurons and downstream LH secretion. Their findings indicate that androgens potently block the LH surge from occurring, and inhibit AVPV kisspeptin neuron activation. This could have important implications for how elevated androgens alter the reproductive axis in transgender men or PCOS women.



UC San Diego
School of Medicine

**Department of Obstetrics, Gynecology,
& Reproductive Sciences**

Womens's Reproductive Health Research Fellow

The Department of Obstetrics, Gynecology and Reproductive Sciences at the University of California, San Diego (UCSD) (<http://obgyn.ucsd.edu>) has a Faculty Career Development Position available at the Assistant Professor level for MDs in MFM, REI, Gyn/Onc, Family Planning, Female Pelvic Medicine & Reconstructive Surgery, or General Ob/Gyn and is committed to academic excellence and diversity within the faculty, staff and student body.

Initial 2-5 years are supported by a Women's Reproductive Health Research Career Development Center grant from the NICHD. The objective of the career development program is to provide advanced training for outstanding physicians in basic, translational, and bedside research and thereby foster independent physician scientists in the field of Ob/Gyn.

The academic environment at UCSD is outstanding and includes well-funded programs in clinical, translational and basic research with studies at the cellular, molecular, and systems levels. The positions require 75% time for mentored and independent research, with 10-20% clinical and 5-10% teaching effort anticipated. Start date 7/1/2023.

Appointments will be at the Assistant Professor level in the Adjunct series. A link to full descriptions of each series is provided for your review: Adjunct Professor – see: http://ucop.edu/academic-personnel-programs/_files/apm/apm-280.pdf

Salary is commensurate with qualifications and based on University of California pay scales. Candidates must have a MD and must be board eligible or board certified in OB/GYN, and be eligible for a California medical license or equivalent certification/permit as determined by the Medical Board of California. Review of applications will begin on October 17, 2021 and continue until the positions are filled.

Appointments may require candidates to be self-funded. As a member of the Health Sciences Compensation Plan, the appointee should be aware that there are limitations on outside professional activities. Clinical moonlighting is expressly prohibited. Additional information can be found here:

https://www.ucop.edu/academic-personnel-programs/_files/apm/apm-671.pdf

The University of California, San Diego is an Equal Opportunity/Affirmative Action Employer advancing inclusive excellence. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability, age, covered veteran status, or other protected categories covered by the UC nondiscrimination policy.

As a condition of employment, you will be required to comply with the University of California SARS-CoV-2 (COVID-19) Vaccination Program Policy. All Covered Individuals under the policy must provide proof of Full Vaccination or, if applicable, submit a request for Exception (based on Medical Exemption, Disability, and/or Religious Objection) or Deferral (based on pregnancy) no later than the applicable deadline. For new University of California employees, the applicable deadline is eight weeks after their first date of employment. The University of California prohibits smoking and tobacco use at all University controlled properties. The UC San Diego Annual Security & Fire Safety Report is available online at: <https://www.police.ucsd.edu/docs/annualclery.pdf>. This report provides crime and fire statistics, as well as institutional policy statement & procedures.

MIRVIE STUDY

NOW OPEN TO ENROLLMENT!

Mirvie is a prospective observational study taking place at UC San Diego. The study collects biomarkers to predict preterm delivery, preeclampsia, and other pregnancy complications.

Eligibility Criteria:

- 18 to 45 years of age
- Singleton pregnancy in second trimester

QUESTIONS?

Contact Cynthia Gyamfi-Bannerman, MD, site PI.
cgyamfibannerman@health.ucsd.edu