

JOHNS HOPKINS Gynecology & Obstetrics

WINTER 2019



NEWS FROM THE JOHNS HOPKINS
DEPARTMENT OF GYNECOLOGY AND OBSTETRICS

BENCH TO BEDSIDE

Uniting Basic and Applied Science for Ovarian Cancer

New Johns Hopkins-led SPORE helps speed translation from the lab to the clinic.



DESPITE MANY RESEARCH EFFORTS, OVARIAN CANCER SURVIVAL HAS improved only slightly over the past half-century. However, a federally funded research model combining basic and clinical work could help speed discoveries that lead to earlier detection and more effective interventions to fight ovarian cancer.

Johns Hopkins, in collaboration with the University of Pennsylvania, has recently become one of four Specialized Programs of Research Excellence (SPOREs) in the nation for this disease, joining the Mayo Clinic, Roswell Park Cancer Institute, and University of Texas/MD Anderson.

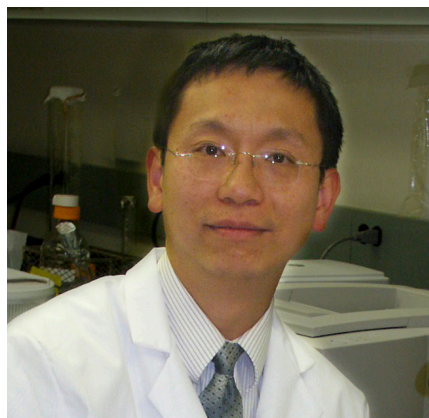
Each project funded by the SPORE, which provides \$12.5 million over five years, is uniquely headed by both basic and applied scientists. The program requires that each of these projects produces a human end point within the five-year funding period.

Johns Hopkins physician-scientist **le-Ming Shih**, the principal investigator of the new SPORE, explains that late detection and a lack of effective treatments for late-stage disease are the two biggest hurdles to improving survival.

“To accelerate the discoveries and to deliver tools and new therapy critical for our patients, we need to integrate basic and clinical scientists together,” says Shih.

Shih and colleagues are partnering to translate recent discoveries in ovarian high-grade serous cancer (HGSC) into clinical tools for early detection and more effective interventions through four projects. The specific aims of each project include:

1. Apply PapGene test for early ovarian cancer detection, using routinely collected liquid based cervical cytology specimens.
2. Modulate the ovarian tumor microenvironment with listeria-based vaccination.
3. Introduce epigenetic therapy to augment immune signaling and sensitize ovarian cancer to immune checkpoint inhibitors.
4. Explore the potential of SYK inhibitors to sensitize ovarian cancer to the anti-tumor effects of paclitaxel.



IE-MING SHIH WORKS TO TRANSLATE DISCOVERIES IN HGSC INTO TOOLS FOR EARLY DETECTION AND EFFECTIVE INTERVENTIONS.

Amanda Fader, a clinical researcher leading the first SPORE project, is applying a specialized Pap smear test to detect ovarian cancer in its earliest stages, when it can be treated more easily. This test, when combined with an accompanying blood test, could help identify the presence of tumor DNA. “The work coming out of this SPORE has the potential for immediate or near-term impacts on patient care and patient outcomes,” says Fader.

The three other projects listed above, says Shih, are aimed at overcoming ovarian cancer’s ability to evade treatment or become resistant to chemotherapies. One of these aims to exploit a vulnerability in ovarian cancer cells by combining therapeutics; another seeks to overcome resistance to platinum chemotherapies through a different class of drugs known as BET inhibitors; the third seeks to make ovarian cancer cells more sensitive to paclitaxel by inhibiting a cancer protein called spleen tyrosine kinase.

To accomplish the goals of each of these four projects, the new SPORE will have three cores (Administration, Biorepository/Pathology, Biostatistics) and two programs for Developmental Research and Career Enhancement, mechanisms that can bring new ideas and new investigators into ovarian cancer research. ■



The Johns Hopkins Department of Gynecology and Obstetrics has a long history of outstanding patient care and teaching. Recently, we have made tremendous strides in expanding the research side of Johns Hopkins' tripartite mission.

As few as two years ago, our annual extramural funding totaled a little over \$2 million. This year, we are projecting nearly \$10 million.

These funds will be supporting a variety of projects. They include the Specialized Program of Research Excellence (SPOR) focused on ovarian cancer that will begin this fall (featured on page 1). The SPOR programs, funded by the National Cancer Institute, pair basic and applied scientists to speed translational research from the lab to the clinic.

Maternal-fetal medicine specialist **Angie Jelin** (featured in a story on page 3), recently received an award from the National Institute of Child Health and Human Development to look at the impact of novel genes on fetal anomalies. In addition, three members of our faculty—**A. Jason Vaught, Anna Powell, and Anna Beavis**—became prestigious Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Scholars (featured on the back).

In the meantime, we have not rested when it comes to patient care and teaching. We are expanding our Women's Health Center at Greenspring Station, one of our ambulatory care centers, to include contiguous space for all our divisions and moving most cases of gynecologic surgery to minimally invasive and robotic platforms. Our new director of the Division of Reproductive Endocrinology and Infertility, **Valerie Baker**, will join us in early 2019 (featured at right). We have also rolled out two new fellowships: one in minimally invasive surgery, and the other in global women's health.

It has been an extraordinary year for our department in each area of our mission. Department faculty continue national and international leadership within our specialty and subspecialties.

This year I began a four-year term as President of the American Board of Obstetrics and Gynecology. We are very proud of our tradition, but we are not sitting on our laurels.

Andrew J. Satin, M.D.
Director
Johns Hopkins Department of
Gynecology and Obstetrics

LEADERSHIP

Taking the Lead in Reproductive Endocrinology and Infertility

Valerie Baker will become the division's new director in 2019.

IN 1981, THE COUNTRY'S FIRST IVF BABY WAS born after Howard and Georgeanna Jones—doctors who trained and held leadership positions at Johns Hopkins—brought this procedure to the U.S. Throughout the years since, the department team has continued making advancements in fertility care through research and advancements in technology. Next year, the Johns Hopkins Division of Reproductive Endocrinology and Infertility will start a new chapter linking this strong legacy in the field to the present. **Valerie Baker**, who currently serves as medical director and chief of the Division of Reproductive Endocrinology and Infertility at Stanford, will become the division director of Reproductive Endocrinology and Infertility and the inaugural TeLinde-Wallach Professor of Gynecology and Obstetrics at Johns Hopkins in 2019, a position endowed by Howard Jones.

"I feel so grateful to be able to lead the division I've been learning about since I was a medical student," Baker says. "It's an incredible opportunity to join this team during such an exciting period of growth."

Baker, who received her medical degree from Harvard Medical School and residency and fellowship training at the University of California, San Francisco Medical Center, will lead the division as their ambulatory clinical space expands dramatically. The division is currently in the planning phases, she says, to move the majority of its services and academic offices into a consolidated space.

Rather than sending patients elsewhere for procedures such as sperm retrieval, hysteroscopy, or dilation and curettage, these procedures will eventually be performed onsite, Baker explains. The assisted reproductive technology laboratory will also move to the same space and will continue to expand its services, offering more access to preimplantation genetic testing of embryos, ovarian tissue cryopreservation, egg freezing, and others.

Baker says that she also hopes to streamline workflows in ways that improve patient experience—for example, she says, making it easier for patients to coordinate care with other specialists at Johns Hopkins, such as rheumatologists or maternal-fetal medicine specialists, or to finance their treatments and work with insurance companies.



Valerie Baker has been named director of the Division of Reproductive Endocrinology and Infertility and the inaugural TeLinde-Wallach Professor of Gynecology and Obstetrics. Baker says she aims to integrate services and streamline workflows to improve the patient experience.

Each of these changes will be key to helping the division care for an increased number of patients, says **Mindy Christianson**, an assistant professor of gynecology and obstetrics in the Division of Reproductive Endocrinology. "In the past five years, the number of patients who come here for just IVF has doubled," Christianson says. "Dr. Baker's leadership will help us better serve patients as our volume continues to grow."

Baker says that she's also excited to join the division during a time of rapid research discoveries, such as the outcomes and fertility preservation work by Christianson; research on nutritional contributors to uterine fibroids by **Chantel Cross**; and studies on uterine fibroids, polycystic ovarian syndrome, and genetic causes of fertility by **James Segars**. She adds that she hopes to increase the number of outstanding physician-scientists within the division and mentor those early in their career to help them achieve their goals.

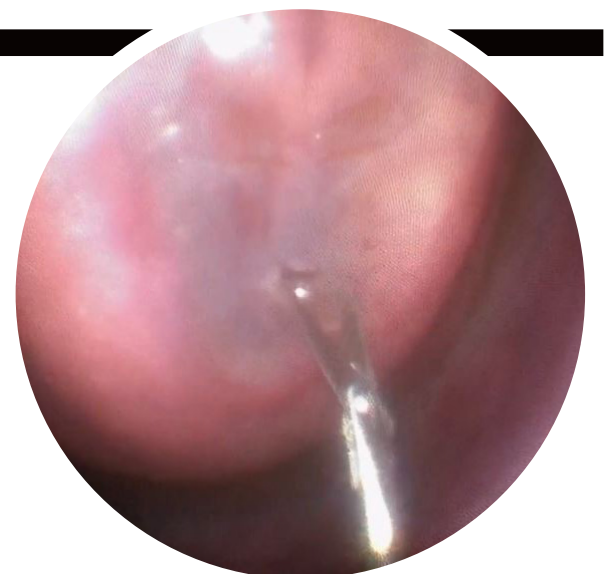
"Johns Hopkins has a strong legacy in this field and a group of clinician-scientists who will continue to advance patient care and research discoveries into the future," Baker says. ■

VIDEO SPOTLIGHT

Fetoscopic Spina Bifida Repair Procedure

Watch as **Ahmet Baschat**, director of the Johns Hopkins Center for Fetal Therapy, and Ob/Gyn **Jena Miller** narrate surgical footage of a fetoscopic spina bifida repair procedure and discuss the benefits of the approach, recovery for mother and fetus, and ideal candidates for the operation.

Visit bit.ly/FSBR_Hopkins or contact 1-844-JH-FETAL (1-844-543-3825)



From Fetal Imaging to Beyond: A Multidisciplinary Approach

Experts from different specialties come together to make a definitive diagnosis and care plan for patients with fetal anomalies.



Maternal-fetal medicine specialist Angie Jelin and colleagues meet once a week to discuss complex cases, looping in other experts from fetal therapy, NICU and PICU physicians and nurses, and other pediatric subspecialties, depending on the case. Image shows artistic rendering of fetus at 9 months.

WHEN PATIENTS RECEIVE NEWS that there may be something wrong with the fetus they are carrying, maternal-fetal medicine specialist

Angie Jelin and her colleagues have a comprehensive and multidisciplinary system in place to help patients and their families know more about their baby's condition and what to expect through pregnancy, birth and beyond. The first step, she says, is getting a better look at the fetus in utero to make a more conclusive diagnosis.

Using ultrasound and occasionally MRI, a skilled team of technologists perform imaging not just of the abnormality in question, but of the entire fetus to identify any additional anomalies that might be affected by global syndromes. Once they've identified any issues affecting the fetus, the patient is offered a consult with genetic counseling, if necessary, so they can better understand the diagnosis.

Once the diagnosis is clear, the multidisciplinary team springs into action. Jelin and her colleagues meet once a week to discuss all their complex cases, looping in other experts from fetal-maternal medicine, fetal therapy, NICU and PICU physicians



“WHEN PATIENTS COME TO THE PERINATAL ULTRASOUND UNIT, WE PROVIDE THEM WITH SPECIFICS ABOUT HOW THINGS ARE GOING TO HAPPEN, HOW THEIR BABY'S CONDITION WILL BE MANAGED, AND WHO THEY'LL WORK WITH.”

—ANGIE JELIN

and nurses, and other pediatric subspecialties, depending on the issues being discussed. These might include cardiology, neurology, neurosurgery, or experts from Johns Hopkins' Greenberg Center for Skeletal Dysplasia. Social workers and chaplains also often attend these meetings as well, Jelin notes.

After this multidisciplinary team develops a plan, patients and their families are invited to meet with each of the members involved in their care. As often as possible, Jelin says, these appointments occur in conjunction, sparing patients multiple appointments on different days. A new fetal program nurse coordinator, who started in August 2018, works with patients and members of the care team to schedule these joint appointments, help them navigate the

medical system, and stay well informed throughout this process.

The team then follows patients throughout their pregnancies, deliveries, and postnatal/neonatal period, making sure that they and their babies receive the most comprehensive care possible. Such close follow-up during this stressful time can help ease patients' anxieties at each step, Jelin says.

“The unknown is a cause of stress for patients,” she adds. “When they come to the perinatal ultrasound unit, we provide them with specifics about how things are going to happen, how their baby's condition will be managed, and who they'll work with. This knowledge can help empower them, and takes away the stress of the unknown.” ■

Clinical Trial: Fetoscopic Repair for Myelomeningocele

The gold standard for spina bifida has long been surgery within two days after birth to close the defect over the spinal cord with the baby's muscle tissue and skin and correct spinal deformities. However, research within the past decade has shown that surgically repairing the defect in utero, between about 20 to 26 weeks gestation, leads to better outcomes—significantly more children who can walk independently and have better motor function, and significantly fewer who require a shunt for hydrocephalus.

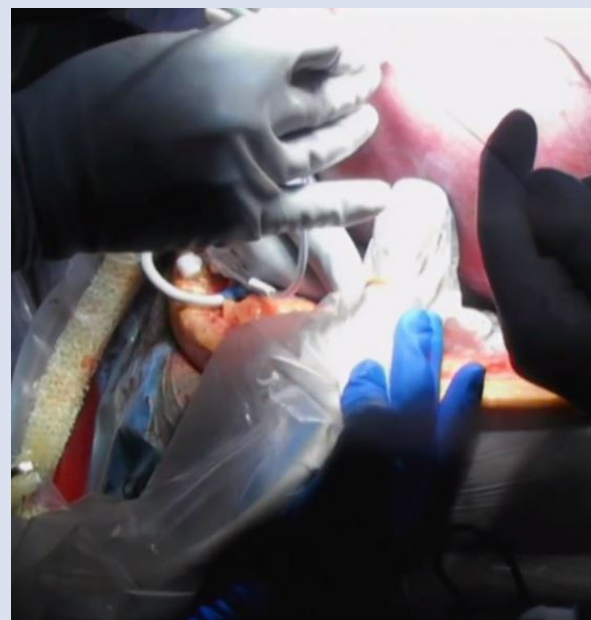
But the benefits of repair before birth are overshadowed by the risks of this procedure, which apply mainly to the mother, says Johns Hopkins fetal therapy specialist **Jena Miller**. Because this procedure is typically performed in an open fashion, requiring a substantial incision in the uterus, there's a high risk from the surgery itself and of the scar opening during the current and future pregnancies. Cesarean birth is always required afterward, and babies are typically delivered preterm.

To avoid these problems, Miller and her colleagues are

currently investigating repairing myelomeningocele with minimally invasive fetoscopy. She's leading a clinical trial at Johns Hopkins that will enroll at least 15 mothers whose fetuses have this condition. The researchers are recording extensive details from each operative case and following the babies' health during the rest of gestation, birth, and up to 30 months afterward. They're particularly interested in whether the surgery reduces the need for shunts and allows these babies to retain motor skills, particularly movement in their lower limbs.

Thus far, nine of the babies enrolled in the study have been born, with the first patient just recently turning a year old. Outcomes look promising, Miller says, with results in line with other published data using a similar technique at Baylor College of Medicine.

“If the data holds up and the outcomes are durable,” she says, “we hope that this procedure will become an acceptable alternative for myelomeningocele that's better for moms and better for babies.”



HONORS AND AWARDS

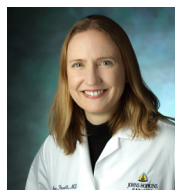
Building Interdisciplinary Research Careers in Women's Health Awards

This year, three members of the Department of Gynecology and Obstetrics faculty received prestigious Building Interdisciplinary Research Careers in Women's Health (BIRCWH) awards.



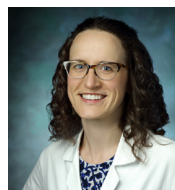
Arthur Jason Vaught is an assistant professor in the Division of Maternal-Fetal Medicine. His BIRCWH project

focuses on HELLP syndrome and possible therapies of complement inhibition and cardiovascular outcomes of women diagnosed with preeclampsia.



Anna Powell, an assistant professor based on the Johns Hopkins Bayview Medical Center campus, is board-certified in obstetrics

and gynecology, with advanced training in infectious disease. Her BIRCWH project focuses on how markers of microbial translocation, vitamin D and progesterone correlate with preterm birth among pregnant women living with HIV.



Anna Beavis is an assistant professor in the Division of Gynecologic Oncology. Her BIRCWH project addresses the lack of screening

techniques for endometrial cancer, which is largely driven by obesity. She aims to assess obese women's knowledge and attitudes towards endometrial cancer screening. ■

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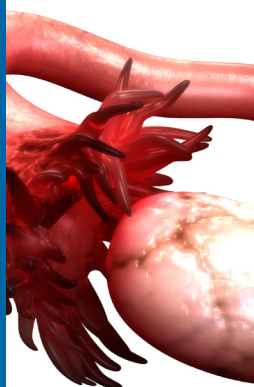
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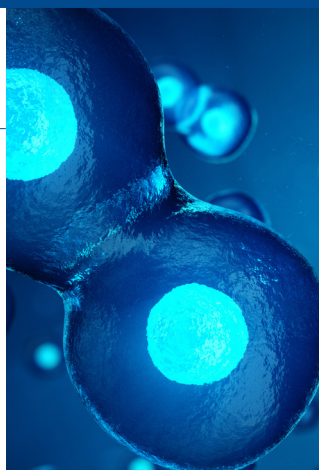
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