



Mount Sinai

Department of Obstetrics, Gynecology and Reproductive Science

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New Institute Focuses on Science and Care in Women's Health

The Blavatnik Family Women's Health Research Institute was established in 2018 by the Icahn School of Medicine at Mount Sinai, with a unique mission to advance science in ovarian and endometrial cancers, postpartum depression, pregnancy-related deaths, and severe maternal complications—health conditions affecting one out of every three to four women in the United States.

The Institute, supported by a \$10 million gift from the Blavatnik Family Foundation, aims to bring together many disciplines to build translational research programs that will make Mount Sinai a thought leader in women's and reproductive medicine. Its founding Director is a nationally recognized physician-scientist, Elizabeth A. Howell, MD, MPP, Vice Chair of Research in Obstetrics and Gynecology, Mount Sinai Health System, and Professor of Obstetrics, Gynecology and Reproductive Science, and Population Health Science and Policy, Icahn School of Medicine.

"This is a critical time for women's health research," Dr. Howell says. "While a number of clinical centers exist for women's health, few centers



Elizabeth A. Howell, MD, MPP, center, with Teresa Janevic, PhD, MPH, left, and Tracy Layne, PhD, both Assistant Professors of Population Health and Policy, and Obstetrics, Gynecology and Reproductive Science.

are aimed at advancing science in women's health. We will aim to find solutions to common women's health problems, close gaps in quality of care that exist for underserved populations, and improve the health and well-being of women in New York City and beyond."

Two Centers of Excellence will provide the initial platform for achieving the Institute's goals: The Center for Outcomes and Quality Research in Women's Health will build upon Mount Sinai's strong research

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Advancing Genetic Testing for Prospective Parents

The application of genetics to reproductive medicine now starts in the pre-conception period, says Alan B. Copperman, MD, Director of Reproductive Endocrinology and Infertility, Mount Sinai Health System. With tools like Expanded Carrier Screening, pioneered by the Icahn Institute for Genomics and Multiscale Biology at the Icahn School of Medicine at Mount Sinai, physicians now routinely perform pan-ethnic testing for hundreds of diseases on prospective parents rather than trying to pinpoint based on self-reported ethnicity which specific genes should be looked at.

Among the options available to prospective parents, Expanded Carrier Screening is offered through Sema4, a patient-centered predictive

health company and a venture of Mount Sinai. The panel includes a wide range of testing for more than 280 conditions, including cystic fibrosis, fragile X syndrome, Smith-Lemli-Opitz syndrome, and spinal muscular atrophy. The screen also has a high rate of detection for genes traditionally difficult to sequence, including CYP21A2 (in which mutations cause growth and development problems related to adrenal disorders) and GBA (in which mutations cause Gaucher disease, which can result in liver disorders, bone pain, and anemia). If both parents carry a mutation in the same gene, they are offered options including in vitro fertilization (IVF) with embryo biopsy and next generation sequencing of DNA to identify the embryo most likely to result in a healthy child.

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Michael Brodman, MD



I have seen the practice of women's health care change dramatically during nearly 40 years as an obstetrician and gynecologist at the Icahn School of Medicine at Mount Sinai. In 1980, when I was a resident, the specialty was limited mostly to pregnancy and childbirth. Today, we recognize that a woman's health care needs change over the lifespan. Our physicians are trained to treat women of all ages and at all stages of life. The Mount Sinai Hospital is proud to have

been nationally ranked in gynecology by *U.S. News & World Report*, and in this Specialty Report, we highlight a year of achievement in multiple disciplines:

The Blavatnik Family Women's Health Research Institute was created with a unique mission to advance science in women's health. Led by a renowned physician-scientist, Elizabeth A. Howell, MD, the Institute aims to bring together many disciplines to build translational research

programs, find solutions to common women's health problems, and close gaps in quality of care.

Genetic testing for prospective parents offers increasingly sophisticated screens for hundreds of diseases and mutations. These analytics—some pioneered by the Mount Sinai venture Sema4—help parents maximize the chance of a healthy pregnancy. In a complex case, Stephanie V. Blank, MD, managed the treatment of a patient with endometrial cancer who was seeking to conceive. That difficult journey resulted in a healthy baby and no evidence of disease. A groundbreaking drug for endometriosis was approved by the U.S. Food and Drug Administration, based on foundational research by Stuart C. Sealfon, MD. And the Division of Global Women's Health and Department of Surgery were awarded a grant that helped continue our efforts to rebuild obstetrics, gynecology, and surgical specialties in Liberia.

These examples of Mount Sinai's educational, scientific, and clinical initiatives are advancing women's health and developing our legacy as a leader in the field.

Michael Brodman, MD, Ellen and Howard C. Katz Chairman's Chair in Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai.



> NEW INSTITUTE TO FOCUS ON SCIENCE AND CARE *continued from page 1*

portfolio on quality of care and outcomes, with a focus on developing and evaluating interventions to improve women's health and wellness. In addition, the Center for Early Translational Research in Women's Health will draw on the expertise of multiple departments, institutes, and programs to develop tools and core resources for translational research in genetics and immunology and build new diagnostic and treatment techniques for gynecologic cancers and other conditions in women's health.

The Institute is also expanding on Dr. Howell's work. Supported by grants from the National Institutes of Health, she leads research concerning maternal depression, outcomes for very low-birth-weight

babies, and the effect of hospital quality on severe complications and death in childbirth, which are persistently higher for black women and other ethnic minorities. Among other influential efforts, Dr. Howell was the lead author of an article published in May 2018 in *Obstetrics and Gynecology* that gave health care providers and health systems insights into racial and ethnic disparities in maternal outcomes.

"I am very interested in quality of care—particularly in maternal and child health—how we measure it, and how we improve it," Dr. Howell says. "The physicians and scientists at The Blavatnik Institute are all passionate about improving the health and wellness of women, and we aim for the Icahn School of Medicine at Mount Sinai to lead this charge."

> ADVANCING GENETIC TESTING *continued from page 1*



Alan B. Copperman, MD

Even when a couple does not carry a risk for known diseases, molecular techniques can be used to improve success rates in patients undergoing IVF. In a procedure known as preimplantation genetic testing for aneuploidy (PGT-A), a test routinely used by the Mount Sinai fertility specialists at Reproductive Medicine Associates of New York, eggs are fertilized by sperm and grown to the blastocyst stage, at which point they are biopsied and vitrified or cryopreserved. Using sequencing techniques, nearly one million data points can be derived from each

embryo, and the chromosomally normal embryos can be identified. Combined with morphological and morphokinetic information observed under the microscope, sequencing data helps determine the single best embryo for transfer.

"Today's analytics are so sophisticated that we can even tell if small pieces of DNA are duplicated or deleted," says Dr. Copperman, who is also Chief Medical Officer of Sema4. "Ultimately, this strategy will maximize the chance of a healthy singleton pregnancy and minimize the possibility of a failed cycle, a miscarriage, a chromosomally abnormal pregnancy, or a multiple gestation that puts mom and baby at significant risk." Addressing the ethics accompanying these advances remains of paramount importance, Dr. Copperman says, adding, "As always, the patients must be fully informed and their interests put first."

Rebuilding Obstetrics and Gynecology in Liberia

The Division of Global Women's Health and the Department of Surgery at the Icahn School of Medicine at Mount Sinai are working to improve obstetrics, gynecology, and surgical specialties in Liberia in an effort supported by a \$2.1 million grant from the World Bank's Health Workforce Program. The team, led by Ann Marie Beddoe, MD, Assistant Professor, Obstetrics, Gynecology and Reproductive Science, is helping train Liberian faculty who will eventually take over for foreign physicians. The goals are to improve patient outcomes and overall health care and to help Liberia recover and rebuild from years of civil war and the Ebola epidemic that ravaged the country in 2014.

"This program is crucial to training the future health care leaders in Liberia," says Dr. Beddoe, who has been working in Liberia since 2008. "From my first trip here, I have seen a definite increase in the number of physicians, particularly specialists, who are working in Liberia. We view Mount Sinai's contribution to the surgical services of Liberia as being very effective in preparing Liberian physicians to take over leadership roles."

The Ebola crisis led to the scaling down of training of residents and interrupted medical school training, disrupting the pipeline of future



At the John F. Kennedy Medical Center in Monrovia, Liberia, physicians, from left, Ehigha Enabudoso, MD, Edwin Olorok, MD, Etedafe Gharoro, MD, and Ayyuba Rabi, MD, are among staff members funded by the World Bank Workforce grant.

physicians. Led by Dr. Beddoe, the Division is overseeing the selection and deployment of faculty to Liberia and is responsible for educational programs and activities. Since receiving the grant in 2017, Mount Sinai has sent 15 faculty members to Liberia, on deployments lasting up to a year, including the Obstetrics and Gynecology and Surgery Department chairs; four obstetricians; two urogynecologists; one specialist in maternal fetal medicine; two general surgeons; an anesthesiologist; and teams of radiologists, in conjunction with the nonprofit group Rad-Aid International.

David Alele, MD, was deployed by Mount Sinai in January 2018 and is to remain until May 2019, becoming the first full-time pathologist to join the John F. Kennedy

Medical Center in the capital, Monrovia, since the end of the war in 2003. Dr. Alele, the only pathologist in Monrovia, has completed more than 400 fine-needle aspiration biopsies, helping to establish the nation's cancer burden in conjunction with the Liberian Cancer Registry. In August 2018, the Surgery Department at the Medical Center received accreditation from the West African College of Surgeons, and five obstetrics and gynecology residents completed the required clerkship program and passed Liberia College of Physicians and Surgeons exit exams.

New Treatment for Endometriosis Stems From Discovery

A groundbreaking drug that received approval in July 2018 from the U.S. Food and Drug Administration for the treatment of pain associated with endometriosis had its genesis two decades ago in the laboratory of Stuart C. Sealfon, MD, at the Icahn School of Medicine at Mount Sinai. The drug, Orilissa™, is the first oral regimen that specifically helps to ease the moderate to severe pain that accompanies endometriosis as tissue that forms in the lining of the uterus also grows outside the uterus.

"Orilissa is a drug that resulted from the basic research we conducted at Mount Sinai, and it will help millions of women," says Dr. Sealfon, the Sarah B. and Seth M. Glickenhau Professor and Chair Emeritus of the Department of Neurology. "At Mount Sinai, we discovered how to clone the drug target that was needed to develop this new drug."

More than two decades ago, Dr. Sealfon led the Mount Sinai team that cloned the gonadotropin-releasing hormone receptor (GnRHR) and genetically engineered host cells that express GnRHR. Gonadotropin-releasing hormone (GnRH), which is secreted by the hypothalamus, plays a key role in controlling reproduction and acts via its receptor GnRHR. In 1992, Dr. Sealfon authored a paper describing the cloning procedure of the receptor in the journal *Molecular Endocrinology*,

and the next year, his paper on the receptor's primary structure was published in *Molecular and Cellular Endocrinology*. This research provided a better understanding of the interplay of hypothalamic, pituitary, and gonadal hormones, which underlie pharmacotherapy and the reproductive system. Two U.S. patents, in 1998 and 1999, assigned these inventions to Mount Sinai.



Stuart C. Sealfon, MD

Orilissa—also known by its generic name, elagolix—is an oral pill taken daily in doses of either 150 mg or 400 mg. It enables women to dial down the reproductive system, suppressing the luteinizing hormone and the follicle-stimulating hormone, which leads to decreased blood concentrations of estradiol and progesterone. The drug was released by the global pharmaceutical company AbbVie, in cooperation with Neurocrine Biosciences, Inc. In two phase 3 clinical trials, Orilissa has also been shown to be helpful in the treatment of uterine fibroids.

Battling Endometrial Cancer While Seeking to Conceive

A young businesswoman experienced “the highest highs and the lowest lows” as she pursued two goals: to beat endometrial cancer and to have a baby. She is thankful that she had the guidance of Stephanie V. Blank, MD, Director of Gynecologic Oncology for the Mount Sinai Health System, and Professor of Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai.

At the start of her medical journey, Andrea was 31 years old and ready to start a family. After she and her husband tried to conceive for a few months, she asked her physician to test her fertility.

Dilation and curettage showed that Andrea had a grade 1 endometrial cancer, and she was referred to Dr. Blank, a renowned physician-scientist specializing in gynecologic oncology. Dr. Blank also ordered genetic tests, which showed that Andrea had an MUYTH mutation, predisposing her to endometrial cancer.

Endometrial cancer, with its defining imbalance of progesterone and estrogen, typically affects women over 50, and the standard of care is removal of the uterus, ovaries, and fallopian tubes. Considering Andrea’s age and goals, Dr. Blank prescribed megestrol acetate, which can realign the hormonal balance by increasing progesterone. Side effects left Andrea exhausted and 60 pounds heavier, but the treatment succeeded, with a repeat D&C showing complete pathologic response, no evidence of disease. Determined to conceive, Andrea tried in vitro fertilization (IVF) with follicle-stimulating hormonal injections. She produced more than 20 eggs, but none resulted in viable embryos, and a follow-up with Dr. Blank showed that the cancer had recurred, as the follicle-stimulating treatments altered the balance of her hormones.

After extensive counseling and discussion, Andrea went through



Stephanie V. Blank, MD, with Andrea and her son, Joaquin

another round of megestrol acetate, which was successful, and then IVF, again producing dozens of eggs and no viable embryos. D&C showed that endometrial cancer had also recurred. This time a hysterectomy appeared more likely, but Dr. Blank and Andrea tried another solution. Andrea continued her cancer treatment via an IUD that releases the progestin levonorgestrel, and at the same time she underwent IVF with lower doses of follicle-stimulating drugs, producing only three to five eggs but also reducing the chance her cancer would recur.

This course of treatment resulted in one viable embryo. In a “rollercoaster” of events, the IUD was removed for possible implantation of the embryo, then Andrea became pregnant naturally but miscarried at nine weeks. “It was very tough; we were very sad,” she says. By then Andrea was 37, and she planned to have the embryo implanted right away, but work obligations caused a delay. Instead, after nine cycles of IVF over six years, she tried a basic option one more time—undergoing intrauterine insemination—and her journey came to a joyful end: “I got pregnant, and now we have a son,” Andrea says. “We have our baby boy.”

Dr. Blank struck a complex balance of accommodating Andrea’s goals while monitoring closely to make sure the cancer had not progressed or spread. “As much as we wanted Andrea to have a baby, we did not want to allow her curable cancer to become incurable,” she says. Andrea, who has been free of cancer since 2016, is grateful that Dr. Blank was willing to work with her and her other doctors to pursue conservative treatments that also preserved her fertility. “I ran into Dr. Blank when I was pregnant and touring the maternity facilities at The Mount Sinai Hospital,” Andrea says. “I told her, ‘I’m here because of you.’”

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