



**Mount
Sinai**

inside

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Surprising New Evidence of How Cancer Cells Spread

New research from the Icahn School of Medicine at Mount Sinai has found that cancer cells can spread without the benefit of a primary tumor and remain dormant for months or even years before triggering aggressive, deadly breast cancer metastases. This surprising new model of early cell dissemination and metastasis appeared in the December 14, 2016, issue of *Nature*. It upsets the long-held scientific belief that tumors only spread from a pathologically defined and highly mutated invasive tumor. In fact, the findings revealed that a primary tumor may never develop.

“As a biologist who has been measuring tumors since I was 20 years old, this was, indeed, a very surprising finding,” says lead author Julio Aguirre-Ghiso, PhD, Professor of Medicine (Hematology and Medical Oncology) at the Icahn School of Medicine at Mount Sinai. “It provides an alternative scenario for how metastases develop, and that could have a profound effect on our work going forward.”



Julio Aguirre-Ghiso, PhD

Dr. Aguirre-Ghiso’s preclinical research, which focused on very early-stage breast cancer in animal models, was published with a companion paper authored by a team led by Christoph A. Klein, MD,

at the University of Regensburg in Germany. The companion paper supported Mount Sinai’s findings with evidence of the same occurrence in human cancer cells and tumors.

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Pioneering, and Teaching, New Thyroidectomy Technique



Surgeons in the Mount Sinai Endocrine Surgery Thyroid Program, who have become national leaders in performing a new minimally invasive technique for thyroidectomy, hosted a workshop in February to train other physicians, a two-day event that drew an audience of clinicians from around the world.

The procedure, known as a transoral endoscopic thyroidectomy (TOETVA), involves the removal of the thyroid gland through small hidden incisions inside the lower lip, an approach that can be used in select cases when traditional thyroidectomy, typically performed through the front of

From left: Aída Taye-Bellistri, MD, Assistant Professor of Surgery, Icahn School of Medicine at Mount Sinai; Timo Hakkarainen, MD, Endocrine Surgery Fellow; William B. Inabnet III, MD; Angkoon Anuwong, MD; and Jennifer Barnes, Certified Surgical Technologist, perform the new thyroidectomy procedure for workshop participants.

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Angela Diaz, MD, PhD, MPH, is Elected to Leadership Role in the National Academy of Medicine

Angela Diaz, MD, PhD, MPH, a leader in adolescent medicine, has been elected to the governing Council of the National Academy of Medicine. Membership in the Academy reflects major contributions to the medical sciences, health care, and public health. The group's Council members, who serve three-year terms, are elected by their peers.

A member since 2008 of the Academy and its predecessor, the Institute of Medicine of the National Academies, Dr. Diaz is the Jean C. and James W. Crystal Professor in Adolescent Health; Professor of Pediatrics, and Environmental Medicine and Public Health, at the Icahn School of Medicine at Mount Sinai; and Director of the Mount Sinai Adolescent Health Center. Under the leadership of Dr. Diaz, the Center has become one of the nation's largest adolescent health centers, known for outstanding research and training, and for serving more than 10,000 vulnerable youths each year with care that is free of judgment, free of charge, and completely confidential.

Dr. Diaz is a national and international leader in her field, says a longtime mentor, Kurt Hirschhorn, MD, Professor Emeritus of Pediatrics, Genetics, and Medicine, and Chairman Emeritus of Pediatrics, Icahn School of Medicine at Mount Sinai. "She was so

impressive that I recruited her to our high school program for teenagers interested in careers in medicine and health science. When she finished medical school, I recruited her as a resident in Pediatrics and later as a fellow in adolescent medicine. The rest is history. She is a member of the highest organization in medicine, and is now becoming one of its leaders."



Angela Diaz, MD, PhD, MPH

Dr. Diaz, who will join about 20 Council members governing the National Academy of Medicine, says, "I'm honored to have been elected to serve on the Council of such an esteemed organization that is a trusted resource for the nation."

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The studies' new findings offer insights into several questions that have long puzzled scientists. First, why do as many as 10 percent of cancer patients worldwide have cancer metastases but no original tumor? Equally important, why is it so difficult to treat



This image captures early disseminating cancer cells in mouse models (cyan) moving toward blood vessels (red).

cancer that has spread? To that point, a key finding was that most early-spread cells remain dormant while most chemotherapeutic and targeted treatments are aimed at cells that are proliferative.

"Those cells that leave early can spend a long time without growing, or they can grow so slowly that any antiproliferative therapy will ignore them," Dr. Aguirre-Ghiso says.

In women, the spread of early breast cancer cells is an extension of the normal process of creating a branching tree of breast milk ducts. Two major pathways are altered in the process: p38, a tumor suppressor, and HER2, an oncogene. As a mammary tree develops, p38 and HER2 are alternatively turned off and on, allowing cells to move through the mammary gland.

In their experiments with mouse models, the researchers found that if

"Those cells that leave early can spend a long time without growing, or they can grow so slowly that any antiproliferative therapy will ignore them."

– Julio Aguirre-Ghiso, PhD

HER2 is over-activated or switched on, and p38 is permanently turned off, cells are able to enter the bloodstream and travel to organs such as the lungs and bone marrow, where a growth switch can later activate the metastases.

With the help of a team of researchers from Albert Einstein College of Medicine, the Mount Sinai scientists were able to monitor the movement of oncogene cells that had been tagged with a fluorescent protein as they moved from the mammary tree to surrounding tissue and into the blood stream. "It was quite amazing," says Dr. Aguirre-Ghiso.

Developing full-scale biomarkers and mechanisms that can identify early-spread cells is a logical next step for Dr. Aguirre-Ghiso and his team. "If we had tests or imaging tools that could tell us in a minimally invasive way exactly where these cells are and if they're evolving or growing, then we could take steps to eradicate them or keep them dormant," he explains. "That kind of approach could truly be transformative."

A Collaboration Between Mount Sinai and CityMD Aims to Enhance Quality and Access to Care

The Mount Sinai Health System and CityMD have launched a joint collaboration to enhance and expand urgent care services throughout New York City, a partnership that will combine Mount Sinai's vast network of providers and CityMD's urgent and clinical care management expertise to create a unique model of timely access to health care.

Significantly, the relationship allows CityMD patients access to Mount Sinai providers, when needed, for prompt follow-up care with a primary care physician or a specialist for further treatment or management of chronic conditions. Provider access includes all Health System hospitals, faculty at the Icahn School of Medicine at Mount Sinai, and other Mount Sinai-associated physicians.

Says Arthur Klein, President of the Mount Sinai Health Network: "This

collaboration will establish a more comprehensive model that meets the full spectrum of health care needs of patients throughout the city. We look forward to achieving significant milestones with CityMD."

The partnership also provides an added benefit to Health System staff enrolled in a Mount Sinai health plan. As a member of the Health System network, CityMD is now a "top tier" provider in the employee health plan. Enrolled employees will have zero or lower copays, depending on their plan, as well as no deductibles, when receiving care from a CityMD practice. Founded in 2010, CityMD now has more than 50 practice locations in the tri-state area.

Under the collaboration, both parties will also share electronic medical records and establish quality metrics to further improve patient outcomes and reduce health care costs.

➤ Pioneering, and Teaching, New Thyroidectomy Technique *(continued from page 1)*

the neck, is not the best course of action. TOETVA is best suited for cases involving smaller nodules and early-stage papillary thyroid cancer.

The workshop was led by William B. Inabnet III, MD, Chair, Department of Surgery, Mount Sinai Beth Israel, and Professor of Surgery, Icahn School of Medicine at Mount Sinai, who performed the first TOETVA in New York State—and only the second in the United States—in September 2016. Teams from Duke University Medical Center, Cleveland Clinic, Rush Medical College, and Weill Cornell, as well as from an institute in Mexico City and a hospital in Madrid, attended the workshop in person or via video conference. The event was organized to welcome Angkoon Anuwong, MD, Department of Surgery, Police General Hospital, in Bangkok, Thailand, who developed the technique and last year trained Dr. Inabnet and Gustavo Fernandez-Ranvier, MD, Assistant Professor of Surgery, Icahn School of Medicine at Mount Sinai.

The TOETVA approach is the latest of three remote access, or "hidden-scar," endoscopic thyroidectomy techniques to be pioneered by Mount Sinai physicians. The robotic bilateral axillo-breast (BABA) approach was performed for the first time in the United States in 2015 at Mount Sinai Beth Israel, by Hyunsuk Suh, MD, Assistant Professor



William B. Inabnet III, MD, and Angkoon Anuwong, MD, front row left, and center, respectively, with some of the workshop attendees.

of Surgery. It involves four small incisions to the breasts and axilla (underarms) and is an option for larger thyroid glands and select cases of thyroid cancer. (Dr. Suh also performed the first BABA lymph node dissection for thyroid cancer in January 2017.) In the transaxillary approach, one incision is made in the underarm, which allows the thyroid gland to be reached from the side. Mount Sinai is the only institution in the United States, and one of only a few in the world, to offer all three types of hidden-scar thyroid procedures.

"The addition of the transoral route with the

introduction of TOETVA is a natural evolution of our growing program and our interest in these minimally invasive approaches," says Dr. Inabnet.

While workshop attendees received an overview on the BABA and transaxillary techniques, TOETVA was the focal point of instruction, which included a live surgery demonstration of two TOETVA cases. The Mount Sinai Endocrine Surgery Thyroid Program plans

to host three additional workshops in March, June, and July.

"Mount Sinai's reputable standing in the field of minimally invasive surgery is a result of the work being done across multiple divisions within the Health System," says Michael L. Marin, MD, the Dr. Julius H. Jacobson II Chair in Vascular Surgery and Surgeon-in-Chief at the Mount Sinai Health System. "We are proud to bring TOETVA to the American population and further establish the Health System's commitment to providing care that is consistently on the forefront of surgical innovation."

Around the Health System

Celebrating the Legacy of Tauba Pasik, MD, and Pedro Pasik, MD

Suzanne N. Haber, PhD, Professor of Pharmacology, and Physiology, University of Rochester Medical Center, presented the inaugural Tauba Pasik, MD and Pedro Pasik, MD Lecture in Neurology at the Hess Center for Science and Medicine on Friday, February 17. The lecture, established by Dr. Pedro Pasik after the passing of his wife, Tauba, in 2015—and now named for both—recognizes notable women in neurology and neuroscience. Dr. Pedro Pasik, who passed away in 2016, and Dr. Tauba Pasik were Mount Sinai luminaries in the fields of neurology, neuroscience, and academic medicine for more than six decades. Together, they helped create the Laboratory of Experimental Neurology at Mount Sinai, and translated and edited the three-volume annotated version of *Texture of the Nervous System of Man and the Vertebrates* by renowned neuroscientist Santiago Ramón y Cajal. Following the lecture, Department of Neurology faculty gathered with members of the Pasik family, where Barbara G. Vickrey, MD, MPH, the Henry P. and Georgette Goldschmidt Professor of Neurology and Chair of Neurology for the Mount Sinai Health System, presented the Pasik family with a plaque commemorating the annual event.



From left: Barbara G. Vickrey, MD, MPH, with Pasik family members: granddaughter and first-year Icahn School of Medicine at Mount Sinai student Sara Diana Pasik; daughters Deborah Pasik, MD, and Lilia Pasik Gendler, PhD; and daughter-in-law Agata Stancato Pasik, MD.

Students Meet Mount Sinai Staff Who Have Walked the Same Path



America Needs You fellows with Mount Sinai panelists, back row, from right: Jose Sepulveda, JD; Berthe Erisnor, MBA; and Lisa Eiland, MD.

A group of first-generation college students—with questions about health care careers and academic life—recently received advice from Mount Sinai officials who were also among the first in their families to attend college. The young people were fellows of America Needs You, a mentoring program, invited by the Mount Sinai Health System's Office for Diversity and Inclusion. In the Black History Month event, on Friday, February 10, at Mount Sinai West, the fellows met Lisa Eiland, MD, Assistant Professor, Pediatrics, and Director of Newborn Medicine at Mount Sinai West; Berthe Erisnor, MBA, Vice President, Ambulatory Care, Mount Sinai St. Luke's; and Jose Sepulveda, JD, Manager, Compliance, New York Eye and Ear Infirmary of Mount Sinai. Dr. Eiland advised the students to build inner strength for the days “when people try to say, ‘you can’t,’ and categorize you.” She said it was equally important to cultivate a support system of friends and mentors: “Find people who will put themselves out there to help you succeed.”

A Nurse Shares Her Affinity for Art

Mary Patricia Fretz, RN, has shared her love for art—and for the stately giraffe—by donating ceramic-tile collages that now hang at Mount Sinai West (shown at right) and the Pediatric Emergency Department at Mount Sinai St. Luke's. Ms. Fretz, a postpartum nurse at Mount Sinai West, has long been fascinated by giraffes: “When I was 3, I wanted one; I remember planning where the hole would be in the ceiling for its head.” She has been creating pottery for more than 30 years, producing tiles, vases, and sculptures that led fellow potters to nickname her “the Giraffe Lady.” Usually she bases her work on photos taken at the Bronx Zoo, but in February, she traveled to Tanzania to see giraffes in their natural habitat for the first time. “It was beyond belief,” says Ms. Fretz, who is already planning new projects based on her new memories.



Previously Unknown Microbes in Humans May Provide Extra Immune Protection

The discovery of a novel type of microbe found in laboratory mice at the Icahn School of Medicine at Mount Sinai has shed new light on the existence of similar organisms in humans, which may help boost the immune system and protect against food-borne toxins, such as salmonella.

Scientists led by Miriam Merad, MD, PhD, Director of the Immunology Institute at the Icahn School of Medicine, described the discovery of the mouse microbe—called *Tritrichomonas musculus* (*T. mu*)—in the October 6, 2016, issue of *Cell*. Their findings suggest that a previously unknown set of single-cell organisms, or protists, which belong to a different biological classification than bacteria, live in the guts of mice and influence their immune system.

The significance of the Mount Sinai study was featured in a subsequent blog by Francis S. Collins, MD, PhD, Director of the National Institutes of Health, who commented: “Recently, we humans have started to pay a lot more attention to the legions of bacteria that live on and in our bodies because of research that’s shown us the many important roles they play in everything, from how we efficiently metabolize food to how well we fend off disease. As it turns out, bacteria may not be the only interior bugs with the power to influence our biology positively.”

Prior to the new findings, scientists

considered protists similar to *T. mu* to be disease-carrying parasites. In fact, *T. mu* seemed to increase the number of tumors in mice with a genetic susceptibility for colon cancer and it increased weight loss and tissue damage in mice with pre-existing inflammatory disease. But, the inflammation caused by a rapid increase in immune cells—dendritic and T cells—brought about by *T. mu*, led to beneficial results for mice, overall.

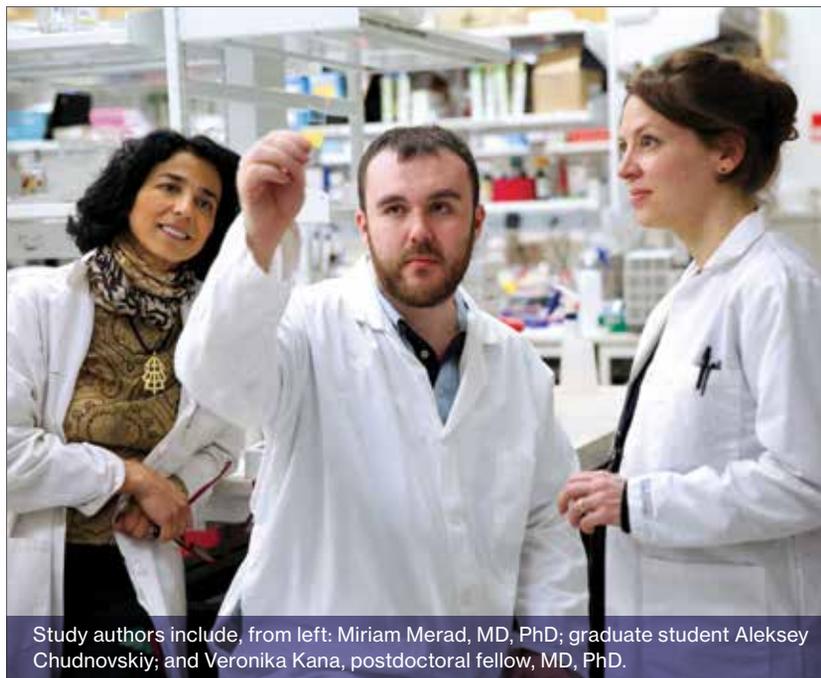
Mount Sinai’s scientific team also included investigators from the National Institute of Allergy and Infectious Diseases, and Universidad del Rosario, Bogotá, Colombia. The study found that humans from around the world harbor a related microbe, *Dientamoeba fragilis* (*D. fragilis*). This protist—taken from the fecal samples from people in South America, Africa, Europe, and Asia—has been associated with irritable bowel

syndrome, but its effects are not completely clear. The scientists theorized that the absence of this microbe could also explain why some people are more susceptible to certain infections than others.

In recent years, advances in DNA sequencing technologies have enabled scientists to identify and study previously unknown microbes that could not be studied in traditional laboratories for various reasons. This new field of study of the human microbiome aims to characterize these microbes and understand their role in supporting health and triggering disease.

“The most important result in this study is the finding that a non-bacterial bug in our flora could potentially protect from severe intestinal infections,”

says Dr. Merad. “This illustrates the need to study non-bacterial species of the microbiome, including protists, which remain very prominent in the developing world.” Further study, she adds, will likely identify novel “crosstalks” or interactions between the microbiome and immune cells that impact health and disease.



Study authors include, from left: Miriam Merad, MD, PhD; graduate student Aleksey Chudnovskiy; and Veronika Kana, postdoctoral fellow, MD, PhD.

“The most important result in this study is the finding that a non-bacterial bug in our flora could potentially protect from severe intestinal infections.”

– Miriam Merad, MD, PhD

“Protists probably aren’t all bad when it comes to our health,” according to Dr. Collins. “As in the laboratory mice, they may afford us with extra immune protection, which could be especially beneficial for those living in parts of the world where infectious disease is an ever-present threat.”

Celebrate Brain Awareness Week March 13 – 19!

This national effort, organized by the Dana Alliance for Brain Initiatives and the Society for Neuroscience, raises awareness of the progress and the benefits of brain research. Join The Friedman Brain Institute, along with Mentoring in Neuroscience Discovery at Sinai (MiNDS) and the Center for Excellence in Youth Education at the Icahn School of Medicine at Mount Sinai, at the following events:

5th Annual Brain Awareness Fair

Interact with Mount Sinai scientists and physicians who study and treat the brain; play brain games; and stop by a large inflatable model of the brain to learn about brain structures.

Tuesday, March 14

11 am – 3 pm

Program for invited New York City students

3 – 5 pm

Open to the public

Art of the Brain Exhibition

The Friedman Brain Institute presents an art exhibition of photographs, medical illustrations, and sculptures celebrating the beauty of the brain as seen through the eyes of Mount Sinai researchers. For more information, email veronica.szarejko@mssm.edu.

Exhibition

Monday, March 13 – Thursday, March 30

Grady Alexis Gallery

215 East 99th Street

Opening Reception

Monday, March 13

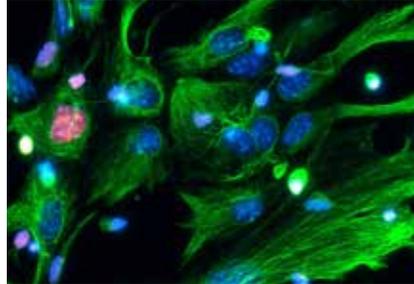
6 – 8 pm

PS 171 Visit

Friday, March 17

11:45 am – 1:45 pm

PS 171 students get a private tour and participate in interactive activities with Mount Sinai scientists.



Mouse Neural Stem Cells This image, created by Nicolas Daviaud, PhD, postdoctoral fellow, Neuroscience, will be featured at the Exhibition.

Studying the Brain: An Evening of Science Storytelling

Five Mount Sinai neuroscientists explore the deeply human side of brain research through true, personal stories of science told live onstage. To register for free tickets, email casey.lardner@icahn.mssm.edu. *Sponsored by The Friedman Brain Institute.*

Tuesday, March 14

8 – 10 pm

El Barrio's Artspace PS 109

215 East 99th Street

A Commitment to Patient Safety

Each year, The Mount Sinai Hospital promotes National Patient Safety Awareness Week. This year's program—Every Day is Patient Safety Day—aims to increase awareness about patient safety, recognize outstanding faculty and staff, offer new ideas on creating safer systems, and encourage collaboration among providers and with patients. Activities include games, prizes, demonstrations, and daily lectures by patient safety leaders, including Marc Napp, MD; Michael Leitman, MD; and Amanda Rhee, MD. All faculty, staff, and visitors are encouraged to stop by and learn more about patient safety. For additional information, email: patientsafety@mountsinai.org or michele.bennett@mountsinai.org.



Patient Safety Wednesday

Monday, March 13, Tuesday, March 14, and Thursday, March 16

10 am – 2 pm

**Games, prizes, demonstrations, and more
Guggenheim Pavilion**

Monday, March 13 – Friday, March 17

**Daily lectures by patient safety
leaders**

Hatch Auditorium

Mount Sinai Transformation Update

For the most recent updates on Mount Sinai's downtown transformation, please go to: <http://www.mountsinaihealth.org/locations/downtown>

Corporate Compliance (ACS) Update: Conflicts of Interest

The Mount Sinai Health System is committed to ensuring that staff and faculty are free from conflicts of interest. In accordance with the Mount Sinai Business Conflicts of Interest policy (ACS.C5), the Annual Report of Relationships with Outside Entities Disclosure form is required to be completed by all faculty, select staff (Director-level and above) and others who have decision-making authority and/or can influence purchasing decisions. The form is available now at <https://sinaicentral.mssm.edu/>. For any questions, please contact: kenneth.brower@mssm.edu (for faculty conflicts of interest); and alma.azua-cassady@mountsinai.org or nwerner@chpnet.org (for staff conflicts of interest).

22nd Annual Medical Student Research Day

Medical students present the results of basic and clinical research projects. Student oral presentations will be given by Robyn Jordan, Aakash Keswani, Michela Leone, Jessica Rizzuto, and Hrishi Srinagesh. *Hosted by the Medical Student Research Office.*

Thursday, March 16

12:30 - 2 pm

**Introduction and student oral
presentations
Stern Auditorium**

2 - 4 pm

**Poster presentations and lunch
Guggenheim Pavilion Atrium**

The Mount Sinai Health System complies with applicable Federal civil rights laws and does not discriminate, exclude, or treat people differently on the basis of race, color, national origin, age, religion, disability, sex, sexual orientation, gender identity, or gender expression.