



**Mount
Sinai**

inside

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Novel Tool Finds Genetic Variations That Predict Disease

Sequencing-based genetic tests are making personalized medicine a reality for patients who carry certain mutations for serious diseases, including breast and prostate cancer. Armed with information about the pathogenicity of such variants in their genome, these patients can now make proactive decisions about their health care early enough to increase the odds of success in preventing or treating disease.

But for each step forward in this new frontier of personalized medicine, physicians and scientists are stymied by their lack of knowledge about thousands of other rare variants in a patient's genome that could also portend disease. For this reason, two researchers at the Icahn School of Medicine at Mount Sinai developed REVEL, a novel tool designed to make sense of these variants of unknown importance in order to help guide patient care and risk management and to facilitate research.

Developed by Weiva Sieh, MD, PhD, Associate Professor of Population Health Science and Policy, and Genetics and Genomic Sciences; and Joseph Rothstein, MS, an Instructor of Genetics and Genomic Sciences, and Population Health Science and Policy, REVEL is an acronym for Rare Exome Variant Ensemble Learner. The tool predicts the likelihood of whether a particular coding variant in a person's genome is disease-causing or benign.

"REVEL is timely and significant because the number of rare variants



REVEL developers Weiva Sieh, MD, PhD, left, and Joseph Rothstein, MS

discovered by sequencing studies is vast and growing and little is known regarding their function," says Dr. Sieh. "Yet few pathogenicity prediction tools have targeted rare missense variants, leaving researchers and clinicians to struggle with their interpretation."

The ability to distinguish among the approximately 10,000 missense variants in each person's genome that result in protein changes that

continued on page 4 >

Mount Sinai Students Meet the Future at Match Day 2017



Sarah Utz was matched with SUNY Stony Brook at Mather Hospital and Wayne State University (dermatology); and Olufolarin Oke with the Stanford University School of Medicine (internal medicine).

The countdown went a bit awry at the 2017 Match Day, on Friday, March 17, when graduating students at the Icahn School of Medicine at Mount Sinai learned which residency programs they would be attending. At the count of "three, two, one" in the packed Annenberg West lobby, the students were to open the envelopes containing their assignments all at once. But around the "two" mark, some students peeked at their news, and as their whoops and cheers erupted, the rest gave in to the excitement—countdown forgotten.

"This might be the most exciting day of the year," said David Muller, MD, Dean for Medical Education and the Marietta and Charles C. Morchand Chair in Medical Education at the Icahn School of Medicine. "This is the day everyone finds out how all of their hard work has paid off—all the research they did, all the work they've done in the community in East Harlem, the patients they've taken care of—this is the day it all comes together."

continued on page 4 >

Seven Mount Sinai Luminaries Receive 2017 Jacobi Medallion



Sandra Masur, PhD, at the podium, congratulated the Jacobi Award recipients, from left: Louis R. DePalo, MD; Celia M. Divino, MD; Ian R. Holzman, MD; Leslie Dubin Kerr, MD; Alice C. Levine, MD; Eric J. Nestler, MD, PhD; and Jonathan S. Stamler, MD.

Seven physicians who have distinguished themselves in medicine or biomedicine, or extraordinary service to The Mount Sinai Hospital, the Icahn School of Medicine at Mount Sinai, or its alumni, were honored with the 2017 Jacobi Medallion—one of Mount Sinai’s highest awards—on Thursday, March 16, at a special event held at The Plaza. Donald Bergman, MD, MSH ’77, President of the Mount Sinai Alumni Association, opened the evening’s events, and Sandra Masur, PhD, Chair of the Jacobi Medallion Award Committee, introduced the recipients.

Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean, Icahn School of Medicine at Mount Sinai, and President for Academic Affairs, Mount Sinai Health System, addressed nearly 325 alumni, donors, faculty, and staff at the award ceremony, including Kenneth

L. Davis, MD, President and Chief Executive Officer, Mount Sinai Health System, an alumnus of the medical school class of 1973.

“We have invested in the development of intellectual property, patents, and novel partnerships with industry,” Dr. Charney told the audience. “Exciting discoveries have poured forth, including a new understanding of the role of the microbiome in Crohn’s and colitis diseases. We’ve identified genetic risk factors for Alzheimer’s, Parkinson’s, autism, and other mental illnesses, and developed new therapies for multiple myeloma, melanoma, depression, and avian flu, to name just a few.” These advances, he said, were a tribute to the generosity and support of Mount Sinai’s alumni and to the dedicated educators who carry out “Mount Sinai’s longstanding tradition of excellence.”

THE HONOREES ARE:

Louis R. DePalo, MD, MSH ’85, Sarah and Eric Lane Professor of Pulmonary Medicine, Clinical Director, Mount Sinai-National Jewish Health Respiratory Institute

Dr. DePalo is an expert in pulmonary, critical care, and sleep medicine. His research interests include the study of human airway smooth muscle cell function, sarcoidosis, and advanced lung diseases. He has published important articles in peer-reviewed journals and has received numerous grants, American Lung Association research awards, and a National Institutes of Health career development award. Dr. DePalo is highly experienced in implementing new technology for use in medical education, patient care, and the distribution of information throughout the medical community.

Celia M. Divino, MD, MSH ’97, Stanley Edelman, MD Professor of Surgery, Chief, Division of

General Surgery, Vice Chair for Education and Quality, Program Director, General Surgery Training Program

A surgical educator, leader, and innovator, Dr. Divino has extensive experience in advanced minimally invasive techniques. She established Mount Sinai’s Surgical Simulator Center to help residents hone their technical skills in both minimally invasive and traditional procedures. Dr. Divino has been listed among the “Best Doctors in America” and has been included in *New York* magazine’s Top Doctors list since 2014. Within the Mount Sinai Health System, Dr. Divino maintains oversight of the Quality Assurance, Surgical Education, and Performance Improvement Committees, and the American College of Surgeons National Surgical Quality Improvement Program.

Ian R. Holzman, MD, Professor of Pediatrics, Division of Newborn Medicine, Jack and Lucy Clark Department of Pediatrics, Professor,

Department of Obstetrics, Gynecology and Reproductive Science

Under Dr. Holzman’s leadership, the Jo Carole and Ronald S. Lauder Newborn Intensive Care Unit in The Mount Sinai Hospital opened in the spring of 2016, following a complete renovation and expansion. Dr. Holzman, who serves as the Pediatric Vice Chair for Hospital Operations and Faculty Affairs, has also been Chair of the Hospital’s ethics committee for more than 20 years. The author of more than 120 scientific articles and 36 book chapters, Dr. Holzman’s research has included studies of fetal intestinal oxygen consumption and the physiological responses to hypoxemia and anemia in both fetal and neonatal lambs. He has lectured nationally and internationally, most recently on various topics in bioethics. Dr. Holzman has received the Dean’s Award for Excellence in Clinical Medicine, the Alexander Richman Award for Humanism in Medicine, and multiple attending physician and teaching awards from both physicians and nurses. ➤

New Health Center Attuned to the Performing Arts

Mount Sinai Doctors and The Actors Fund recently opened The Samuel J. Friedman Health Center for the Performing Arts, a medical facility in a very “Broadway” location—upstairs from the Actors Fund headquarters at 729 Seventh Avenue and up the street from the Times Square TKTS booths.

The Center is open to the general public, but its services and flexible hours are targeted to people in entertainment and the performing arts. Staffed by Mount Sinai physicians, it offers primary care services, including wellness checkups, urgent sick visits, and health screenings, and is planning to add specialty services in fields like orthopedics and otolaryngology later this year. “This really is a collaboration; it’s like putting on a show,” the actor Brian Stokes Mitchell, Chairman of the Board of Trustees of the Actors Fund, said at the ribbon-cutting ceremony on Thursday, March 2.

Partly funded by a \$1 million donation from the Gerald J. and Dorothy R. Friedman New York Foundation for Medical Research, the Center is a project special to the Friedman family, which has deep ties to both medicine and the arts. It

is named for the late Samuel J. Friedman, a publicist who worked with performers Bette Davis and Gypsy Rose Lee—and who was the brother of the late Gerald J. Friedman, MD, founder of the Diabetes Institute at Mount Sinai Beth Israel that bears his name.

“Mount Sinai has a long history of providing primary and specialty care for the performing arts community, and we are proud to continue that legacy in our partnership with The Actors Fund,” says Evan L. Flatow, MD, President of Mount Sinai West.



From left: Barbara Davis, Chief Operating Officer of The Actors Fund; Brian Stokes Mitchell; and Lisa Mazie, Chief Administrative Officer of Mount Sinai West.

Leslie Dubin Kerr, MD, MSH '85, Professor of Medicine, and Geriatrics, Division of Rheumatology

Dr. Kerr leads clinical and educational programs in rheumatology for the departments of Medicine and Geriatrics. For 18 years, she served as Assistant Director and then Program Director of the Rheumatology Program Fellowship. After perceiving there was an unmet need in the rheumatologic care of the elderly, Dr. Kerr developed the geriatric rheumatology practice for the multidisciplinary Phyllis and Lee Coffey Geriatrics Practice at the Martha Stewart Center for Living. Upon completing her internship and residency at Mount Sinai, Dr. Kerr received the Association of the Attending Staff/Bella Trachtenberg Award for House Staff Excellence. She completed her rheumatology fellowship at Mount Sinai under the mentorship of Harry Spiera, MD.

Alice C. Levine, MD, MSH '86, Professor of Medicine, Division of Endocrinology, Diabetes, and Bone Disease, Professor, Department of Oncological Sciences

Cited as one of *America's Top Doctors*® by Castle Connolly and by *Super Doctors*® in New York, Dr. Levine focuses on patients with diseases of the adrenal, pituitary, and reproductive glands. She is co-director of a translational prostate cancer research lab, which has received grants from the U.S.

Department of Defense, the T.J. Martell Foundation, the Prostate Cancer Foundation, and Prostate Action, Inc. In addition, Dr. Levine has published extensively in peer-reviewed journals and is a highly sought-after speaker in the field of prostatic and adrenal diseases. As one of Mount Sinai's most respected teachers, Dr. Levine in 2011 received an Excellence in Teaching Award from the Icahn School of Medicine at Mount Sinai's Institute for Medical Education. She has also received the Cullman Family Award for Excellence in Physician Communication.

Eric J. Nestler, MD, PhD, Nash Family Professor of Neuroscience, Director, The Friedman Brain Institute, Dean for Academic and Scientific Affairs

The goal of Dr. Nestler's research is to better understand the molecular mechanisms of addiction and depression based on work in animal models, and to use this information to develop improved treatments for these disorders. A prolific investigator, Dr. Nestler has published more than 450 peer-reviewed studies and book chapters, and is active in numerous research projects that are funded by the National Institute on Drug Abuse and the National Institute of Mental Health. Dr. Nestler is a member of the National Academy of Medicine (formerly Institute of Medicine) and a Fellow of the American Academy of Arts and Sciences. He is a past President of the American College

of Neuropsychopharmacology and current President of the Society for Neuroscience.

Jonathan S. Stamler, MD, MSSM '85, President, Harrington Discovery Institute, Robert S. and Sylvia K. Reitman Family Foundation Distinguished Chair in Cardiovascular Innovation, Professor of Medicine and of Biochemistry, Director, Institute for Transformative Molecular Medicine, Case Western Reserve University, University Hospitals Cleveland Medical Center

A Mount Sinai alumnus, Dr. Stamler is recognized for broadly influencing the biological sciences by discovering protein S-nitrosylation, a fundamental mechanism for controlling protein function, and for advancing the understanding of cellular signaling by small gaseous messengers. He has published more than 300 scientific papers and chapters, edited two books, authored more than 125 patents and patent applications, and cofounded multiple companies. After receiving his medical degree at Mount Sinai, Dr. Stamler completed his internship, residency, and fellowships in both Cardiovascular and Pulmonary Medicine at Harvard Medical School and Brigham and Women's Hospital. Before joining Case Western Reserve School of Medicine, he held faculty positions at Harvard Medical School, Duke University School of Medicine, and the Howard Hughes Medical Institute.

› Novel Tool Finds Genetic Variations That Predict Disease *(continued from page 1)*

could potentially be harmful also helps researchers set priorities for the variants they may wish to study further as new disease-causing genes. Identifying more of these variants would enable personalized medicine to realize its potential in helping more patients benefit from prevention and treatment regimens tailored to their individual disease risks.

Other tools that use different predictive features do exist, but they often do not agree with each other on the likelihood of pathogenicity. Dr. Sieh and Mr. Rothstein created REVEL as an ensemble method that uses machine learning to combine information from many of these other tools in order to generate a consensus score. REVEL incorporates 18 pathogenicity prediction scores from 13 tools, and it specializes in prioritizing the most clinically or functionally relevant variants among the sea of rare variants that are being discovered through next-generation sequencing.

To make REVEL easily accessible to researchers and clinicians, the tool provides precomputed scores for all 80 million possible protein-altering variants in the human genome. These scores are available online via open access to the worldwide medical and scientific community, along with estimates of their sensitivity and specificity.

In a study that appeared in the October 6, 2016, issue of *The American Journal of Human Genetics*, the researchers showed that REVEL outperformed seven other existing ensemble methods in distinguishing disease variants from rare neutral variants.

“As sequencing-based genetic tests become more widely available and these studies expand in scale, it is our hope that REVEL will be used to interpret variants of unknown significance for a broad range of clinical conditions,” says Dr. Sieh.

› Mount Sinai Students Meet the Future at Match Day 2017 *(continued from page 1)*



Efe Chantal Ghanney, right, (urology at UCLA Medical Center) celebrated with Maureen Byrne, who is seeking an MD-MSCR degree.



Kamini Doobay (emergency medicine at Bellevue Hospital-NYU School of Medicine) with her mother, Alya Doobay.



Sameer Khan (internal medicine at Yale-New Haven) with Saif Khan, and Valerie Parkas, MD, Senior Associate Dean for Admissions.

The graduating students were matched to residency programs throughout the country, including highly competitive ones at Brigham and Women's Hospital; the University of California, San Francisco Medical Center; the Hospital of the University of Pennsylvania; Duke University Medical Center; and Columbia University Medical Center. Forty students will remain within the Mount Sinai Health System to continue all or part of their graduate training.

Efe Chantal Ghanney was very happy to be matched with the UCLA Medical Center. Raised in Ghana, she found the West Coast institution a perfect fit. “I did a clinical rotation there last year, and I completely fell in love with the people, the way of life, the weather. I also found mentors who I believe are genuinely invested in my success.” Ms. Ghanney, an inductee into the Gold Humanism Honor Society for

compassionate patient care, will specialize in urology because it combines her interests in surgery, palliative care, and geriatrics.

The 132 Icahn School of Medicine students were among 18,539 who participated in the annual Match Day event, which is managed by the National Resident Matching Program, a private, nonprofit organization that matches students with residencies in U.S. teaching hospitals. The results are generated by an algorithm that aligns the preferences of applicants with those of residency programs. In all, 43 percent of Mount Sinai's graduating class will receive residency training in primary care; 24 percent will enter programs in surgical specialties; and 33 percent will pursue training in other specialties that include emergency medicine, anesthesiology, and psychiatry.

Sameer Khan was thrilled with his match, internal medicine at Yale-New Haven

Hospital. He said the program emphasized one of his clinical interests, mental health, and its intellectual caliber and sense of community reminded him of Mount Sinai. His father, Saif Khan, was thankful for an additional reason: “Yale is the closest” to the family's home in Hell's Kitchen.

Anne Hart said she was ecstatic to be staying at Mount Sinai. “It's my top choice. I love the Psychiatry department, and I'm so excited to be staying with a lot of my friends.” Kamini Doobay also got her wish, a residency in emergency medicine at Bellevue Hospital-NYU School of Medicine. Ms. Doobay, who helped found the multiagency NYC Coalition to Dismantle Racism in the Health System, has a strong sense of social justice. She said her residency will help fulfill her goal to “serve the underserved.” Her mother, Alya Doobay, looked on with pride: “She has always been a good child, now she is going to be a good doctor.”

Around the Health System

Celebrating the “Art of the Brain”

To commemorate Brain Awareness Week—a global endeavor showcasing the progress and benefits of brain research—The Friedman Brain Institute sponsored its fourth annual “Art of the Brain” exhibition. Featuring photographs, medical illustrations, and sculptures that celebrate the beauty of the brain as seen through the eyes of Icahn School of Medicine at Mount Sinai scientists, the exhibition took place at the Grady Alexis Gallery in East Harlem.

The opening reception, held Monday, March 13, was attended by many of the researchers who displayed their work, which they created by using the latest technological advances in imaging and 3D printing to help them gain a deeper understanding of the brain. During the 18-day run, the exhibition drew Mount Sinai faculty and staff, and the public.



Nicolas Daviaud, PhD, postdoctoral fellow, neuroscience, explained his work to visitor Shauntay Williams.

The gallery also hosted PS 171 middle school students for several hours of immersive, interactive brain-related activities, in an event organized by The Friedman Brain Institute in collaboration with the Icahn School of Medicine’s Center for Excellence in Youth Education (CEYE) and Mentoring in Neuroscience Discovery at Sinai (MiNDS). Among the students’ scientific adventures—which they and CEYE staff detailed using Snapchat—was a guided tour of the exhibition by MiNDS volunteers Xin-an Liu, PhD, postdoctoral fellow in neuroscience; Denise Croote, a first-year PhD student in the neuroscience program; and Eric Rath, a former traumatic brain injury (TBI) patient at Mount Sinai, who is now a TBI and addictions counselor. Additionally, CEYE teaching assistants helped students view their own brain waves through the NeuroSky® MindWave—educational software that uses an electroencephalogram sensor to detect brain activity. Meanwhile, medical illustrators Christopher M. Smith, MA, and Jill K. Gregory, MFA, brought additional pieces of their work and spoke with students about the rewards and challenges of creating beautiful, yet functional, images to accurately illustrate a scientific topic.



PS 171 middle school students participated in brain-related activities.

Two at Mount Sinai Win “Courage to Teach” Award

Two physicians at the Icahn School of Medicine at Mount Sinai have received the 2017 Parker J. Palmer Courage to Teach Award for fostering innovation in their residency programs. Vicki Lynn Shanker, MD, Assistant Professor of Neurology, and Director of the Mount Sinai Beth Israel Neurology residency program, cultivated a program committed to supporting residents in research and subspecialty care. Adam I. Levine, MD, Professor of Anesthesiology (Perioperative and Pain Medicine), and Director of The Mount Sinai Hospital Anesthesiology residency program, developed a program that allows residents to refine their clinical and teaching skills with simulation. Dr. Shanker and Dr. Levine were among 10 clinical educators receiving the award on Friday, March 10, at the Accreditation Council for Graduate Medical Education (ACGME) annual conference in Chicago. “We are very proud,” says I. Michael Leitman, MD, FACS, Senior Associate Dean for Graduate Medical Education, Icahn School of Medicine. “Their programs have become pioneers in the field.”



From left: Saadia Akhtar, MD, Associate Dean for Graduate Medical Education, Mount Sinai Beth Israel; Vicki Lynn Shanker, MD; Adam I. Levine, MD; and Thomas J. Nasca, MD, MACP, Chief Executive Officer, Accreditation Council for Graduate Medical Education.

>>> MARCH FOR SCIENCE

The March for Science—a nonpartisan celebration of the value of scientific research—will take place on **Saturday, April 22, in Washington, D.C.** Numerous satellite events will occur throughout the United States and around the world, including in New York City. The Icahn School of Medicine at Mount Sinai supports the principles of the March.

The March offers an opportunity to advocate for why the sustained robust support for biomedical science must be a top national priority. The past several decades have seen transformative discoveries in the treatment of illnesses, including cancer, heart disease, immunological disorders, and infectious diseases. In the next decade, similar advances in the treatment of brain disorders—made possible by rapidly emerging tools and technologies in the neurosciences—will be within reach.

The March has received the support of most major scientific organizations in the United States, including the American Association for the Advancement of Science, Research!America, and The New York Academy of Sciences. For more information, visit marchforscience.com.

New York Eye and Ear Infirmary of Mount Sinai Visiting Professor Lecture Series

Oscar A. Cruz, MD, Anwar Shah Endowed Chair of Ophthalmology, Professor, Ophthalmology, Saint Louis University Eye Institute, presents “Pediatric Resident Case Presentations and Discussion.”

Thursday, April 13

5 – 6 pm

Third Floor Conference Room

Suite 314 North Building

Dr. Cruz also presents “Strabismus Surgery in Thyroid Eye Disease.”

Friday, April 14

7:30 – 8:30 am

(Same location as above)

Clinical Research Education Program Online Information Sessions

The Icahn School of Medicine at Mount Sinai’s Clinical Research Education Program is accepting applications for the PhD, MS, and Certificate programs for Fall 2017. Those interested can attend an interactive online information session to learn more about the program, curriculum, and admission criteria. This session will also help participants learn how an advanced degree in Clinical Research will prepare them for leadership roles in translational science and medicine, and how to better compete for academic and professional opportunities. To RSVP or for more information, call a program representative at 212-824-7014 or email clred@mssm.edu.

Wednesdays, April 5, April 26

Noon – 1 pm

Mount Sinai Transformation **update**

For the most recent updates on Mount Sinai’s downtown transformation, please go to:

<http://www.mountsinaihealth.org/locations/downtown>

April is Autism Awareness Month

To commemorate Autism Awareness Month, the Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai will host weekly information tables at The Mount Sinai Hospital campus throughout April. Stop by and talk to members of the research team—comprised of specialists in genetics, molecular biology, model systems, neuroimaging, and experimental therapeutics—who are dedicated to understanding the biological causes of autism spectrum disorder and developing groundbreaking diagnostic tools and treatments. For more information about autism and research, visit www.seaverautismcenter.org.

Thursdays, April 6, 13, 20, 27
11 am – 2 pm

Guggenheim Pavilion
Outside the Plaza Café



INSIDE MOUNT SINAI

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