VAGELOS COLLEGE OF PHYSICIANS & SURGEONS,
COLUMBIA PRECISION MEDICINE INITIATIVE,
IRVING INSTITUTE FOR CLINICAL AND
TRANSLATIONAL RESEARCH, AND THE
HERBERT IRVING COMPREHENSIVE CANCER CENTER

PRESENT

PRECISION MEDICINE SCHOLARS' DAY

Featuring Research Presentations by the Pilot Award Winners

NOVEMBER 5, 2021 10:00 AM–3:15 PM

VIRTUAL CONFERENCE

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Schedule

10:00 a.m.	**Opening Remarks: Tom Maniatis, PhD**
10:10 a.m.	**Michael Boland, PhD**
10:35 a.m.	**Richard Carvajal, MD; Grazia Ambrosini, PhD**
11:00 a.m.	**Raul Rabadan, PhD**
11:25 a.m.	**Brian Henick, MD**
11:35 a.m.	**Chaolin Zhang, PhD**
12:00 p.m.	**Yufeng Shen, PhD**
12:10 p.m.	**Keynote: Sam Sternberg, PhD**
1:00 p.m.	**LUNCH**
1:30 p.m.	**Remarks: Ronald J. Wapner, MD**
1:40 p.m.	**Xuebing Wu, PhD**
1:50 p.m.	**Lynn Petukhova, PhD**
2:15 p.m.	**Chi-Min Ho, PhD**
2:25 p.m.	**Srilaxmi Bearelly, MD, MHS**
2:35 p.m.	**Gary Struhl, PhD**
3:00 p.m.	**Closing Remarks: Muredach P. Reilly, MBBCh, MSCE**

This is a private meeting for Columbia researchers. By participating in this meeting, you agree to treat all information disclosed during the meeting as solely for Columbia internal use for academic purposes.

Tom Maniatis, PhD

Dr. Maniatis is the Isidore S. Edelman Professor of Biochemistry at Columbia University Irving Medical Center and the director of the Columbia University Precision Medicine Initiative. Dr. Maniatis also serves as the Evnin Family Scientific Director and chief executive officer of the New York Genome Center (NYGC), where he is one of the founders. At the NYGC, Dr. Maniatis leads research activities, including technology development and informatics, and directs the faculty and scientists in their individual and collaborative projects.

Dr. Maniatis is known for pioneering the development of gene cloning technology and its application to both basic research and biotechnology. He also coauthored the definitive laboratory manual on molecular cloning, which profoundly impacted the international dissemination of gene cloning technology. His research has led to fundamental advances in understanding the mechanisms of gene regulation and RNA splicing, the biochemistry of innate immunity signaling pathways, the function of single cell diversity in the nervous system, and neurodegenerative disease mechanisms. Dr. Maniatis's research has been recognized by many awards, including the Eli Lilly Award in Microbiology and Immunology, the Richard Lounsbery Award from the U.S. and French National Academies of Sciences, and the 2012 Lasker-Koshland Special Achievement Award in Medical Science. He is a member of the U.S. National Academy of Sciences and of the National Academy of Medicine and is a fellow the American Academy of Arts and Sciences. Dr. Maniatis cofounded the biotechnology companies Genetics Institute, ProScript, Acceleron, and Kallyope.

Michael Boland, PhD

Assistant Professor of Molecular Sciences (in Neurology and the Institute of Genomic Medicine), CUIMC; Director, Cellular Models of Disease, Institute for Genomic Medicine

Development of Novel Therapies for STXBP1 Encephalopathy

Dr. Boland and his group apply an integrated developmental and functional approach to model neurological disorders using human induced pluripotent stem cells (hiPSCs), with a primary focus on epilepsy and monogenic autism spectrum disorders. Disease-causing gene variants identified by human genetics studies conducted at the Institute for Genomic Medicine (IGM) serve as the basis for model development within his group. Their hiPSC models and differentiation schemes are tailored to the gene being studied. Dr. Boland and his group generate patient-derived hiPSC lines and use genomic editing via CRISPR/Cas9 to correct the mutation. Alternatively, a given pathogenic mutation will be edited into the genome of a validated, non-disease hiPSC line in order to match patient genotypes. Depending on the disease/mutation studied, his group uses monolayer and/or three-dimensional (organoid) neuronal differentiation of hiPSCs into clinically relevant cell types coupled with morphological studies, and transcriptomic and gene network analyses to identify and understand genotype-specific developmental phenotypes. Additionally, Dr. Boland's group has developed and advanced the use of patch clamp electrophysiology and multielectrode arrays combined with optogenetic and pharmacological network modulation to understand the functional etiology of these disorders.

In collaboration with other investigators at the IGM, Dr. Boland and his group study microcircuit and neural network behavior of cultured primary neurons and acute brain slices from genetic mouse models of epilepsy for preclinical drug design and development.

Richard Carvajal, MD

Assistant Professor of Medicine, CUIMC; Co-Leader, Precision Oncology and Systems Biology Program; Director, Experimental Therapeutics; Director, Melanoma Service

Biological and Therapeutic Relevance of Exosomes in Uveal Melanoma

As the director of Experimental Therapeutics and director of the Melanoma Service at Columbia University Irving Medical Center, Dr. Carvajal is focused on the development of novel therapies for patients with melanoma and other cancers, with the overall objective of controlling and curing these diseases.

To achieve this goal, he has used the increasing knowledge of the underlying biology of cancer to rapidly integrate this knowledge, novel therapeutic agents, and efficient trial design in order to improve the outcomes of cancer patients everywhere. Working closely with laboratory scientists, the group is using the techniques of molecular biology to identify specific proteins, genes, or other molecules that influence the growth of each person's cancer, with the goal of selecting the most promising therapies for individual patients.

Dr. Carvajal's melanoma research has included the study and treatment of uncommon clinical and molecular subsets of melanoma such as melanomas arising from the eye (uveal melanomas); from the mucosal surfaces of the body (mucosal melanomas); and from the palms of the hands, soles of the feet, or under the fingernails (acral melanomas). Although these tumors arise from pigment cells of the body just as do the more common melanomas that arise from the skin (cutaneous melanomas), they are clinically and biologically distinct from cutaneous disease. Once metastatic (that is, spread from where they originally began to other sites in the body), these diseases have proved to be difficult to treat.

In an advance that helped launch a new era of personalized medicine in melanoma therapy, Dr. Carvajal has led a clinical trial of imatinib (Gleevec) in patients with melanoma characterized by the presence of a mutation in a

gene called KIT. While this mutation is rare in cutaneous melanoma, it is found in about 20 percent of mucosal and acral melanomas. Based in part on the positive results of this trial, where long-lasting tumor responses were observed in patients with these diseases, the use of imatinib in melanomas harboring KIT mutations was added to the National Comprehensive Cancer Network guidelines for the treatment of melanoma. Uveal melanoma is characterized by mutations in genes called GNAQ and GNA11 that lead to activation of a growth pathway called the MAPK pathway. Before 2013, there were no effective treatments for metastatic disease; however, another trial that Dr. Carvajal has developed and conducted identified selumetinib, a medicine that blocks the MAPK pathway, as the first effective treatment for patients with advanced uveal melanoma.

Dr. Carvajal's research has been supported by the National Cancer Institute, the Food and Drug Administration, the Conquer Cancer Foundation, the Melanoma Research Alliance, the Melanoma Research Foundation, the Empire Clinical Research Investigator Program, and the generous philanthropy of patients and their families. He has authored or co-authored more than 150 peer-reviewed manuscripts, books, and book chapters. He has received several awards in recognition of his work, including the Louise and Allston Boyer Young Investigator Award and the Melanoma Research Foundation's CURE OM Vision of Hope Award.

In addition to Dr. Carvajal's work at Columbia University Irving Medical Center, he serves as the co-chair of the International Rare Cancer Initiative Uveal Melanoma working group, a joint initiative between the National Cancer Institute, the European Organization for Research and Treatment of Cancer, and the Cancer Research UK to enhance international collaboration in the conduct of clinical trials for uveal melanoma.

Grazia Ambrosini, PhD

Associate Research Scientist, Columbia University Irving Medical Center

As an associate research scientist in Dr. Gary K. Schwartz's laboratory, formerly at Memorial Sloan Kettering Cancer Center and presently at Columbia University Irving Medical Center, Dr. Ambrosini is involved in research programs focused on developing targeted therapies against rare cancers like uveal melanoma and sarcoma. More recently, she has become the leader of the Uveal Melanoma Program. The major focus of her research is studying the biology of this cancer of the eye, which is highly metastatic to the liver, and outlining targeted therapies against this deadly disease. She has further investigated the mechanisms of drug resistance with the overall objective of accelerating the development of more effective therapies for patients with uveal melanoma. These studies have been published in several peer-reviewed journals and have led to the development of clinical trials. Dr. Ambrosini has a broad background in biomedical research, ranging from molecular and cell biology to translational research. During her postdoctoral training at Yale University, she was the first to report the characterization of the gene *survivin,* in one of the most cited papers in the field of cell death modulation in cancer, that has been a target in numerous therapeutic approaches and clinical trials. She is confident that her contribution to translational research will continue to be productive and successful in the fight against cancer.

Raul Rabadan, PhD

Gerald and Janet Carrus Professor; Professor, Department of Systems Biology

Molecular Characterization of Gliomas under Immunotherapy

Raul Rabadan is the Gerald and Janet Carrus Professor in the Departments of Systems Biology, Biomedical Informatics, and Surgery at Columbia University. He is the director of the Program for Mathematical Genomics at Columbia University and the NCI Center for Topology of Cancer Evolution and Heterogeneity. From 2001 to 2003, Dr. Rabadan was a fellow at the Theoretical Physics Division at CERN, the European Organization for Nuclear Research, in Geneva, Switzerland. In 2003 he joined the Physics Group of the School of Natural Sciences at the Institute for Advanced Study in Princeton, New Jersey. Previously, Dr. Rabadan was the Martin A. and Helen Chooljian Member at The Simons Center for Systems Biology at the Institute for Advanced Study. He has been named one of *Popular Science*'s Brilliant 10 (2010) and a Stewart Trust Fellow (2013), and he received the Harold and Golden Lamport Award at Columbia University (2014) and the Diz Pintado Award (2018). Dr. Rabadan's current interest focuses on uncovering patterns of evolution in biological systems through the lens of genomics. His recent interests include the development of mathematical approaches to uncover the evolution of cancer and infectious diseases, including topological data analysis and Random Matrix Theory, among others.

Brian Henick, MD

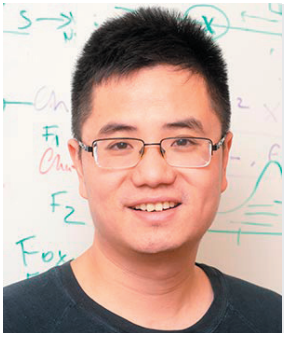
Assistant Professor of Medicine, CUIMC

Patient-Derived Organoids to Model and Manipulate Tumor Regulatory Dependencies in Esophageal Adenocarcinoma

Dr. Henick is a medical oncologist specializing in thoracic malignancies and experimental therapeutics. He studied economics and health care delivery as an undergraduate at the University of Pennsylvania and attended Rutgers New Jersey Medical School, where he was inducted into the Gold Humanism Honor Society. He completed his postgraduate training in internal medicine and hematology/medical oncology at Yale New Haven Hospital, where he studied the role of the innate immune system as a predictor of sensitivity or resistance to immunotherapy. He has presented his research, supported by Conquer Cancer Foundation/ASCO awards, at national conferences including ASCO. Dr. Henick's goal as a clinician and researcher is to improve upon existing treatment strategies, personalizing each patient's care through computational study of cancer immunobiology and being attuned to their values and needs alongside CUIMC's dedicated multidisciplinary team.

Chaolin Zhang, PhD

Assistant Professor of Systems Biology and Biochemistry and Molecular Biophysics (in the Motor Neuron Center)

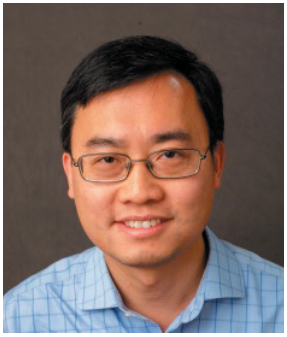


Unbiased Screen of Proximal and Distal Splicing Regulatory Elements toward Drug Discovery

Chaolin Zhang, PhD, is an assistant professor in the Department of Systems Biology, Department of Biochemistry and Molecular Biophysics, and Motor Neuron Center at Columbia University. His lab uses a combination of computational and experimental methods to study RNA regulatory networks in the nervous system. In particular, he is interested in characterizing the regulatory networks that specify neuronal cell types and in how these networks can be compromised in certain pathologic contexts, such as neurodevelopmental and neurodegenerative diseases.

Yufeng Shen, PhD

Associate Professor, Department of Systems Biology; Associate Director, Columbia Genome Center



Developing New Computational Methods to Predict Functional Impact of Missense Variants Based on Protein Structure Using Machine Learning

Yufeng Shen is an associate professor in the Columbia University Department of Systems Biology and Department of Biomedical Informatics. After completing his PhD in computational biology in 2007 at the Human Genome Sequencing Center at Baylor College of Medicine, he led the analysis of the first personal genome produced by next-generation sequencing (that of Dr. James D. Watson). In 2008 he joined Columbia University as a postdoctoral fellow, working in computational genomics and the genetics of drug adverse reactions, and then joined the faculty in July 2011. Dr. Shen is interested in developing and applying computational methods to study human genetics and diseases. The research in his group is at the interface of biology, statistics, and computer science. Specifically, his group is working in four areas, including genome sequencing and assembly, mapping of disease genes, the role of the major histocompatibility complex (MHC) in autoimmunity, and pharmacogenomics.

Sam Sternberg, PhD

Principal Investigator; Assistant Professor, Department of Biochemistry and Molecular Biophysics, Columbia University

Dr. Sternberg was born and raised in Lancaster, Pennsylvania. He earned his BA in biochemistry from Columbia University in 2007, where he trained with Professor Ruben Gonzalez, and his PhD in chemistry from the University of California, Berkeley, in 2014, under the mentorship of Professor Jennifer Doudna. He was awarded graduate student fellowships from the National Science Foundation and the Department of Defense, and he received the Scaringe Award from the RNA Society and the Harold Weintraub Graduate Student Award from the Fred Hutchinson Cancer Research Center. After a brief postdoc and book-writing stint, Dr. Sternberg spent a year working at Caribou Biosciences, a Bay Area biotech start-up focusing on genome engineering applications, as a scientist and group leader of technology development. He started his independent career in February 2018, in the Department of Biochemistry and Molecular Biophysics at Columbia, where he is a Sloan Research Fellow in Chemistry and Pew Scholar in the Biomedical Sciences. He is also the recent recipient of the NIH Director's New Innovator Award.

Dr. Sternberg's doctoral and postdoctoral research focused on the mechanism of nucleic acid targeting by RNA-guided bacterial immune systems (CRISPR–Cas) and on the development of these systems for genome engineering applications. His work has been published in the journals *Nature, Science,* and *Cell* and been covered in the *New York Times, Science News,* the *Scientist,* and various other news outlets. His lab employs a range of biochemical, biophysical, and structural techniques to investigate CRISPR–Cas biology, with an eye toward applying mechanistic knowledge for tool development.

Dr. Sternberg is committed to being a supportive mentor and effective lab manager and to nurturing a collaborative research environment. He has closely mentored over a dozen undergraduate and graduate students and has participated in numerous mentorship programs, including Student Mentoring and Research Teams (SMART) and Howard Hughes Medical Institute's Exceptional Research Opportunities Program (EXROP) at Berkeley. The desire to work with students in the lab was a major driver of Dr. Sternberg's decision to transition from industry back to academia.

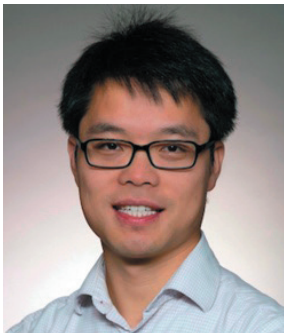
Ronald J. Wapner, MD

Professor of Obstetrics and Gynecology, CUIMC; Co-director, Precision Medicine Resource, Irving Institute for Clinical and Translational Research

Dr. Ronald Wapner is a professor of obstetrics and gynecology in the Division of Maternal-Fetal Medicine at the Department of Obstetrics and Gynecology and director of Reproductive Genetics for Columbia University Irving Medical Center. Prior to Columbia University, Dr. Wapner was a professor of obstetrics and gynecology at Drexel University College of Medicine and taught for 22 years at Thomas Jefferson University, where he also served as the director of Maternal Fetal Medicine. Dr. Wapner is an internationally known physician and researcher specializing in reproductive genetics. He pioneered the development of chorionic villus sampling (CVS) and multifetal reduction. He has authored or co-authored over 450 publications, and he has been an active investigator in the area of maternal-fetal medicine. The Society for Maternal-Fetal Medicine has honored Dr. Wapner with both a Lifetime Achievement Award (2015) and The Dru Carlson Memorial Award for Best Research in Ultrasound and Genetics (2012 and 2017). He has had a significant role in the development of multidisciplinary research studies and clinical research centers throughout his career.

Xuebing Wu, PhD

Assistant Professor of Medical Sciences (in Medicine and in Systems Biology)



A Special Ribosome in the Heart: Understanding How Mutations in Ribosomal Protein RPL3L Cause Neonatal Dilated Cardiomyopathy by Using Patient-Derived iPSCs and Genetically Engineered Mice

Xuebing Wu, PhD, joined Columbia University as an assistant professor in November 2018. Dr. Wu received his BS and MS in control science and engineering from Tsinghua University, Beijing. He pursued his PhD in computational and systems biology at MIT with Phillip Sharp and Christopher Burge. He worked as a Helen Hay Whitney Fellow in Dr. David Bartel's lab at Whitehead Institute/MIT prior to joining Columbia. The Wu lab integrates CRISPR, genomics, and machine learning to both decode and target RNA in human health and disease. The lab seeks to bridge the discovery of basic mechanisms of gene regulation with the development of novel therapeutics for human diseases, focusing on cancer and cardiometabolic diseases.

Lynn Petukhova, PhD

Assistant Professor of Dermatology and Epidemiology

Deciphering Monogenic and Polygenic Etiologies of a Longitudinal Multiethnic Hidradenitis Suppurativa Cohort

Dr. Lynn Petukhova is an assistant professor in the Department of Dermatology at NewYork-Presbyterian/Columbia University Irving Medical Center (CUIMC). Dr. Petukhova received her academic training at CUIMC in the Departments of Biostatistics and Epidemiology. As a genetic epidemiologist, she studies diseases that span the spectrum of etiological heterogeneity, deciphering single gene causes of rare disorders and resolving allelic contributions to diseases that are common in the population. Her research is primarily focused on gene discovery and the generation of medically relevant insight by translating genetic evidence to disease mechanisms.

Molecularly defined disease mechanisms provide the crucial link between patient and therapy in the emerging paradigm for precision medicine. Identifying disease subtypes among groups of patients who present with the same diagnosis, but whose disease arises from different physiological perturbations, allows physicians to develop effective and efficient treatment strategies. Identifying mechanistic links between diseases provides rationale for drug repurposing, which can have an immediate and substantial impact on unmet needs, as Dr. Petukhova has demonstrated with genetic studies in alopecia areata.

Dr. Petukhova works with genetic data from genome-wide genotyping assays, from targeted resequencing across linkage disequilibrium blocks identified in genome-wide association studies (GWAS), from exome sequencing in family cohorts and cohorts of unrelated people, and from public resources such as Online Mendelian Inheritance in Man (OMIM) and the Encyclopedia of DNA Elements (ENCODE). She also works with clinical data from electronic health records (EHR) and patient registries.

Chi-Min Ho, PhD

Assistant Professor, Department of Microbiology and Immunology

Direct Visualization of Malaria Parasite Invasion Using Cryoelectron Tomography

Dr. Chi-Min Ho was born and raised in Ames, Iowa, where she first discovered her love of protein structure and function as a summer research intern in the lab of Professor Gloria Culver at Iowa State University. After earning her BA in molecular and cell biology at the University of California, Berkeley, in 2004, she joined the lab of Professor Robert Stroud at the University of California, San Francisco, and worked on membrane protein structure determination. In 2011 she was recruited to the Infectious Diseases Division at the Novartis Institutes for Biomedical Research in Emeryville, California, where she worked for three years in small molecule drug discovery for infectious diseases before moving on to pursue a doctoral degree in 2014. She completed her PhD in biochemistry, biophysics, and structural biology at the University of California, Los Angeles, in 2019, under the mentorship of Professor Hong Zhou. She joined the faculty of the Department of Microbiology and Immunology at Columbia University in January 2020.

Dr. Ho's doctoral work focused on using single-particle cryoelectron microscopy to elucidate the structure and mechanism of an essential malarial membrane protein complex known as the Plasmodium Translocon of Exported Proteins (PTEX), which she purified directly from malaria parasites via an epitope tag inserted into the endogenous locus of a PTEX subunit using CRISPR/Cas9. Her lab uses biochemistry and the latest developments in cryoelectron microscopy to study the molecular basis of host-pathogen interactions.

Srilaxmi Bearelly, MD, MHS

Associate Professor of Ophthalmology, CUIMC

Retinal Imaging and Deep Learning to Identify Maternal Risk and Reduce Racial Disparities

Srilaxmi Bearelly, MD, MHS, is a retina specialist with expertise in the evaluation and treatment of age-related macular degeneration, diabetic retinopathy, retinal vascular occlusions, choroidal neovascularization, and macular disorders.

Her experience in the treatment of retinal diseases started with a seven-year tenure on the Vitreoretinal Service at Duke University Eye Center in North Carolina (2003 to 2010). Since then, she joined Columbia's faculty in 2010. She has treated thousands of patients and helped patients and their families through their treatments. She has also volunteered her medical expertise in underserviced areas, such as El Salvador and rural United States.

Dr. Bearelly received her undergraduate degree from Northwestern University, her MD from Northwestern University Medical School, and her master of health sciences from Duke University School of Medicine. Following her ophthalmology training at Northwestern University, she completed her fellowship training in diseases of the retina and vitreous at Duke University Eye Center.

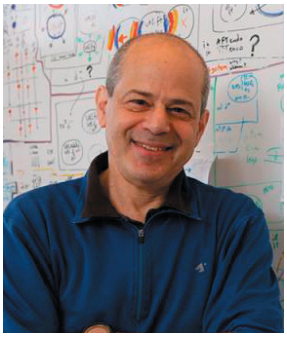
She has written 70 articles, chapters, and abstracts and frequently presents at scientific and professional conferences both nationally and abroad. Currently, Dr. Bearelly is a collaborator on a Columbia University clinical study of retinal changes in preeclamspia (a disease of pregnancy).

She is recognized as a Castle Connolly Top Doctor in Ophthalmology and with Castle Connolly's Exceptional Women in Medicine award. She has received several research awards, including an NIH/NEI K12 and K23 Mentored Research Career Award, and a Young Investigator Award by Retinal Degenerations Symposium at the International Congress of Eye Research Meeting in China.

Dr. Bearelly has been certified by the American Board of Ophthalmology (AAO). She is an active member of the AAO, the Association for Research in Vision and Ophthalmology (ARVO), and the American Society of Retina Specialists (ASRS).

Gary Struhl, PhD

Professor of Genetics and Development (in Neuroscience); Principal Investigator, Zuckerman Institute



Exploiting the Basic Mechanism of Notch Activation to Develop New Diagnostic, Therapeutic, and Tissue Engineering Tools for Precision Medicine

During development, cells are programmed to generate and interpret spatial information so that every cell within a population knows where it is and what to do as a consequence. Dr. Struhl's work uses genetical and molecular approaches in Drosophila to address these fundamental questions: (i) What is spatial information?; (ii) How is it generated?; and (iii) How is it interpreted? His work has led to discoveries about the nature and mode action of spatial determinants controlling cell and body patterns, tissue growth, and planar cell polarity. These include (i) the Polycomb and HOX "selectors" in specifying body segments; (ii) the transcription and translation factors Bicoid, Caudal, Hunchback, and Nanos in organizing global body pattern; (iii) secreted factors of the Hedgehog, Wnt, and BMP/TGFb superfamilies as the first, intercellular gradient morphogens; (iv) Delta/Notch signaling in cell-fate specification; and (v) the serpentine receptors Frizzled and Starry Night and the atypical cadherins Dachsous and Fat, in planar cell polarity.

Muredach P. Reilly, MBBCh, MSCE

Herbert and Florence Irving Professor of Medicine; Director, Irving Institute for Clinical and Translational Research; Director, Cardiometabolic Precision Medicine Program; Associate Dean for Clinical and Translational Research

Muredach P. Reilly serves as director of the Irving Institute for Clinical and Translational Research (Irving Institute), home to Columbia University's NIH/NCATS-funded Clinical and Translational Science Award Program hub. A cardiologist and the Herbert and Florence Irving Professor of Medicine, Dr. Reilly was recruited to Columbia in 2016 from the University of Pennsylvania to lead the Irving Institute into a new era of genomics and translational personalized healthcare. His research program is dedicated to precision medicine studies of cardiovascular disease and related metabolic disorders. This translational research emphasizes humans as the most ideal "model" to understand mechanisms of human disease and therapeutic opportunities for prevention. Dr. Reilly received his medical degree from University College Dublin, Ireland, and completed his residency and fellowship training in medicine and cardiovascular medicine at the University of Pennsylvania, where he also received an MS degree in clinical epidemiology. In 2010, Dr. Reilly was elected to the Royal College of Physicians in Ireland as well as to the American Society of Clinical Investigation. In addition, he has received numerous awards including the 2013 William Osler Patient Oriented Research Award; the American Heart Association's Mentor of Women Award in 2015; and, in 2018, the Jeffrey M. Hoeg Arteriosclerosis, Thrombosis, and Vascular Biology Award for Basic Science and Clinical Research.

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