

COLUMBIA PRECISION MEDICINE INITIATIVE

2018 - 2019 NEWSLETTER

COLUMBIA PRECISION MEDICINE

Dear Colleagues,

Over the past year, The Columbia Precision Medicine Initiative (CPMI) has continued to grow and take shape with the engagement and collaboration of faculty and leadership throughout the University. With more critical recruitments, our flagship lecture series, and new awards, the Columbia Precision Medicine Initiative is moving forward. We are particularly pleased to welcome senior faculty and leaders Drs. Jeannette Wing, Simon Tavaré, and Kevin Gardner.

In 2018, the inaugural Roy and Diana Vagelos Precision Medicine Pilot Awards made 3 awards. We are currently evaluating the applications for the second year of pilot awards. The Initiative also supported 5 awards for Mouse Genome Editing for the generation of mouse models of human disease. A new call for Mouse Genome Editing awards will be issued later this year.

We also launched a Precision Medicine Childcare Subsidy program to help junior faculty and post-docs pay for child care costs during a conference. One of Columbia University's core values is to expand scholarship, while increasing inclusion and success of highly qualified candidates. This program aims to expose future leaders in precision medicine to current leaders in the field.

Our Precision Medicine and Society program sets Columbia apart from other precision medicine initiatives. The program is chaired by Paul Appelbaum and Gil Eyal, and we thank outgoing chair Alondra Nelson for her leadership, and continued input. A number of pilot grants were awarded last year; and a conference is planned for April 24th and 25th 2019. Following the partnership with National Bureau of Economics Research, a book will be published soon containing the jointly commissioned scholarship.

A new initiative we are excited to launch is The Center for Medical Genetics and Genomics in the Department of Medicine. The goal is to develop clinically oriented Precision Medicine programs in each subspecialty of Internal Medicine.

One of the highlights of the previous year was our 2nd academic conference, Advances in Precision Medicine: Cancer, which saw a full day of high impact international speakers covering basic and applied science in cancer precision medicine. We look forward to hosting our third conference on April 8th, 2019, which will focus on the impact and importance of Big Data in precision medicine.

Over the last year, we also had the pleasure of hosting Professors Cori Bargmann, Doug Wallace, Richard Scheller and Alondra Nelson for the Distinguished Lecture in Precision Medicine series.

I would like to take this opportunity to thank Dr. Roy Vagelos for his continuing scientific and medical leadership in precision medicine, and his generous gift to the Precision Medicine Initiative. The gift is being used to fund a number of critical recruitments supporting precision medicine research and the infrastructure required to make Columbia a leader in this field. In particular, Roy's contribution to Cryoelectron microscopy in conjunction with an earlier gift from Lynn Shostack made it possible purchase and install 3 new state of the art microscopes. This extraordinary infrastructure, Professor Joachim Frank's Nobel Prizewinning contributions to the establishment and application of CryoEM technology, and an exceptional Columbia-wide structural biology faculty, positions Columbia as an international leader in this powerful new technology. The ability to rapidly determine atomic resolution protein structures is an essential tool in the development of new drugs - a key step in the realization of precision medicine.

The precision medicine leadership is grateful to the Columbia faculty and staff for participating in this initiative. Please read on for a recap of Columbia's recent accomplishments in Precision Medicine and further details of the activities during the coming year.

Tom

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Advances in Precision Medicine Conference: Cancer Genomics

Following the success of the inaugural conference in 2017, our second annual conference, which took place on April 9th, 2018, where we hosted 10 top international speakers, bringing together a broad focus spanning from research insights to clinical applications of cancer genomics.

We were honored to have these prestigious leaders in this field join us; Arul Chinnaiyan, MD, PhD, Michigan Center for Translational Pathology; Luis A. Diaz, MD, Memorial Sloan Kettering Cancer Center; William C. Hahn, MD, PhD, Dana-Farber Cancer Institute; Arnold J. Levine, PhD, Institute for Advanced Study; Serena Nik-Zainal, MD, PhD, University of Cambridge; Raul Rabadan, PhD, Columbia University; Nitzan Rosenfeld, PhD, University of Cambridge; Charles L. Sawyers, MD, Memorial Sloan Kettering Cancer Center; David Tuveson, PhD, Cold Spring Harbor Laboratory; Catherine J. Wu, MD, Dana-Farber Cancer Institute



See more from the 2nd annual conference on our website here.

SAVE THE DATE: MONDAY, APRIL 8, 2019 3rd Annual CPMI Conference ADVANCES IN PRECISION MEDICINE: BIG DATA The Forum at Columbia University, Manhattanville 8:30am–5:00pm

Distinguished Lectures

CORI BARGMANN, PhD

The Chan Zuckerberg Initiative: Accelerating Science through Tools and Collaborations

January 8, 2017

Cori Bargmann, President of Chan Zuckerberg Science, is an internationally recognized neurobiologist and geneticist, leads the Chan Zuckerberg Initiatives science work. Dr. Bargmann provided an overview of the exciting Chan Zuckerberg initiative, which she heads.





DOUGLAS C. WALLACE, PhD

A Mitochondrion Etiology of the Common "Complex" Diseases January 24, 2018

Douglas C. Wallace; Director, Center for Mitochondrial and Epigenomic Medicine (CMEM) at The Children's Hospital of Philadelphia Research Institute; Professor, Department of Pathology and Laboratory Medicine at the Hospital of the University of Pennsylvania. Doug Wallace focused on his lifetime of contributions to the understanding of the genetics and physiology of mitochondria in health and disease.

JEANNETTE WING, PhD

Data for Good: Data Science at Columbia At the Intersection of Health and Data

April 24, 2018

Jeannette M. Wing is Avanessians Director of the Data Science Institute and Professor of Computer Science at Columbia University. As the new director of Columbia's Data Science Institute, she has woven ethics and social impact into the Institute's mission. Her vision comes amid a backlash over the tech industry's use and misuse of consumer data and a broader



shift.



RICHARD SCHELLER, PhD

March 15, 2018

Richard Scheller is the Chief Science Officer and head of the newly formed therapeutics group. Richard Scheller presented the efforts of "23&me" to provide genetic information on a massive scale, and to connect this data to healthcare information as a means of identifying new drug targets.

ALONDRA NELSON, PhD

Even a Moon Shot Needs a Flight Plan: Genetics and Ethics in the Obama Administration October 4, 2018

Alondra Nelson is president of the Social Science Research Council. She is also professor of sociology at Columbia University, where she served as the inaugural Dean of Social Science and director of the Institute for Research on Women and Gender. Alondra discussed the importance of establishing efforts to address ethical considerations as part of major initiatives such as the human genome project and the national precision medicine initiative (All of Us).





ARIS BARAS, MD, MBA

Rewriting the Rules in Drug Discovery and Development: The Power of Genomics and Precision Medicine October 24, 2018

Dr. Baras serves as Vice President, Regeneron Pharmaceuticals and Head of the Regeneron Genetics Center (RGC), one of the largest human genetics programs in the world, spanning large-scale sequencing, informatics, and translational sciences using human genetics to advance and guide the development of Regeneron's pipeline of important new medicines.

Faculty Announcements



KEVIN GARDNER

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SIMON TAVARE





Herbert and Florence Irving Institute of Cancer Dynamics. Professor Tavaré is a pioneering statistician and internationally recognized cancer researcher with a principal focus on cancer genomics. His appointments at Columbia are in the departments of Statistics and Biological Sciences, and he also will be a member of the Herbert Irving Comprehensive Cancer Center.



JEANNETTE WING

Professor Jeannette M. Wing is Avanessians Director of the Data Science Institute and Professor of Computer Science at Columbia University. She came to Columbia in July 2017 from Microsoft, where she served as Corporate Vice President of Microsoft Research, overseeing a global network of research labs. She is widely recognized for her intellectual leadership in computer science, particularly in trustworthy computing.

Medical Campus Updates

Institute for Genomic Medicine



Over the past year, the Institute for Genomic Medicine (IGM) has made significant progress in advancing clinical practice and research for precision medicine at Columbia. The IGM's precision medicine initiatives have continued to flourish, with recruitment and enrollment of CUMC/NYP patients across a large range of specialties including epilepsy, ALS, liver and kidney disease, undiagnosed pediatric disease, ophthalmology, neuropsychiatric disease and neurodegenerative disease. These initiatives allow for the sequencing of enrolled patients, providing important diagnostic and research data for disease gene discovery and targeted treatments.

Additionally, enrollment in the national "All of Us" Precision Medicine Initiative has begun, including local community outreach and engagement activities.

Other exciting developments include the recruitment of two new IGM faculty members; Jennifer Gelinas MD, PhD and Yueqing Peng, PhD, who bring exceptional research programs in functional disease modeling in rodents, in epilepsy and sleep, respectively. Finally, the IGM has expanded its broad research portfolio to form a strategic alliance with AstraZeneca's Centre for Genomic Research. This partnership will utilize large genomic data sets, paired with cutting-edge statistical genetic and computational approaches pioneered at the IGM to uncover disease mechanisms and develop novel precision medicine based therapeutics.

Irving Institute for Clinical and Translational Research

The past year has seen many exciting developments in the programs and initiatives supported by the Precision Medicine Resource team of the Irving Institute, led by Wendy Chung, MD, PhD and co-directors Krzysztof Kiryluk, MD, Ronald Wapner, MD, and David Goldstein, PhD. Five new interdisciplinary teams headed by investigators Kristen Cleary, MD, Adi Cohen, MD, Rosemary Sampogna, MD, Bryan Winn, MD, and Kevin Wong, PhD were selected to receive Precision Medicine Pilot awards and will focus on tailoring medical care to the individual patient's needs in a wide range of clinical domains. The Resource welcomed two new postdoctoral fellows - Juan Arriaga, PhD and Suying Bao, PhD - into its prestigious two-year Dean's Precision Medicine Research Fellowship program. Remarkable success of both fellows who completed their training in the past year - James Chen, PhD and Matthew Lewis, MD - was highlighted by publication of their discoveries in a top biomedical journal (Cell Systems, Dr. Chen is the lead author), and NIH career development award (K23, to Dr. Lewis). Addition of new faculty experts to the line-up of guest speakers for the two-semester graduate course "Introduction to Precision Medicine", offered by the Resource for the second year, allowed students to gain insights into such central to precision medicine topics as digital health and ethical challenges of genomic medicine.

In June 2018, research accomplishments of all award recipients were celebrated at the Annual Symposium "2018 Precision Medicine Updates", hosted by the Resource for the third time. Now in its fourth year, a monthly seminar series, "Advances in Precision Medicine", brought to campus such thought leaders in the field as Leslie Biesecker, MD (NHGRI), Joel Hirschhorn, MD, PhD (Harvard University), and Matthew State, MD, PhD (UCSF).

One of the biggest developments in the Institute was the launch of a pilot phase of the Biobank Resource for Investigating Disease, Genes & Environment (BRIDGE) initiative. To accommodate this initiative, Irving Institute renovated ~400 square feet of laboratory space for the purpose of collecting and storing genomic DNA, plasma/serum, cells (including those from which to make iPSC), and tissues, collaborated and supported the Institute of Genomic Medicine biorepository efforts, and engaged with local Washington Heights/Inwood and Harlem communities to ensure representation of their members in the biobank.

DISCOVER Program

The <u>DISCOVER program</u>, led by Wendy Chung, MD, PhD, provides coordinated clinical services to patients with undiagnosed disorders and provides consultations and diagnostic testing for children and adults with Columbia's best diagnosticians. The program has made diagnoses in about one quarter of the patients, including genetic, infectious, and autoimmune conditions and has discovered 10 new genes for disease and connected patients to other families with the same genetic condition around the world. The DISCOVER program has supported the



development of family groups for 7 genetic diseases and held family meetings to educate families about the condition and support research on these new disorders. For referrals call 212-342-4622.



Precision Genomics Laboratory

In the summer of 2017, the Institute for Genomic Medicine (IGM) and the Department of Pathology and Cell Biology announced the creation of the Precision Genomics Laboratory (PGL), led by David Goldstein, PhD, Director of the IGM and Kevin Roth, MD, PhD, Chair of Pathology and Cell Biology. Vimla Aggarwal, MBBS, FACMG is the Medical Director overseeing this CLIA-certified, clinical laboratory in the Division of Laboratory Medicine, directed by Steven Spitalnik, MD. Since its inception, the PGL's

multidisciplinary clinician-scientist teams have worked to serve the needs of physicians and researchers in the CUIMC community and beyond, by offering a range of services designed to enhance constitutional genomic diagnostics, research, and education.

The Center for Medical Genetics and Genomics in the Department of Medicine

The success of the CPMI requires a transformation of our clinical and translational paradigms and infrastructures, and extensive education of our faculty. A collaboration between the Department of Medicine (DoM) and the Institute of Genomic Medicine (IGM), the newly created center for Medical Genetics and Genomics in the Department of Medicine will bring together physicians, scientists and other health professionals to implement Precision Medicine for adult constitutional disorders. Led by Dr. Ali Gharavi, MD, the center will build on the existing collaborations between the DoM, the IGM and virtually every clinical and basic science departments at CUIMC. The short-term goal of the center is to develop a clinically oriented Precision Medicine programs in each subspecialty of Internal Medicine. The long-term vision is to become a national model for the application of genomic medicine to medical practice. In addition to a strong clinical sequencing component, the Center also envisions education, research and recruitment programs that will enhance our capacity for Precision Medicine across the entire campus.

Vagelos Precision Medicine Mouse Genome Editing Subsidy

Proposals will be requested shortly to generate new mouse models of disease, discovered by human sequencing, primarily in constitutional genetics. Fore more details, follow the instructions at the Columbia Precision Medicine Initiative web page https://precision medicine.columbia.edu/content/funding-opportunities

Cross Campus Initiatives

Roy & Diana Vagelos Precision Medicine Pilot Awards

The inaugural Roy and Diana Vagelos Precision Medicine Pilot Awards received 56 applications from across all Columbia campuses. The 3 winning proposals, reflect the high standard, the broad base, and the collaborative nature of precision medicine basic science research being conducted and conceived at Columbia:

1. Programmable probiotics for personalized cancer immunotherapy. Nicholas Arpaia, PhD, Assistant Professor, Dept. of Microbiology and Immunology; Tal Danino, PhD, Assistant Professor, Dept. of Biomedical Engineering

 Elucidating the tissue-specific molecular mechanisms underlying disease associations through integrative analysis of genetic variation and molecular network data.
Tuuli Lappalainen, PhD, Assistant Professor, Dept. of Systems Biology;
Harmen J Bussemaker, PhD, Professor, Dept. of Biological sciences; Dept. of Systems Biology

3. Notch2 polymorphisms as predictors of low -cell mass and increased type 2-diabetes risk. Utpal Pajvani, MD, PhD, Assistant Professor, Dept. of Medicine, Endocrinology; Dieter Egli, PhD, Maimonides Assistant Professor of Developmental Cell Biology, Pediatrics; Domenico Accili, MD, Russell Berrie Foundation Professor of Diabetes

Mouse Genome Editing Awards

Awards funds to subsidize the creation of mouse models of human disease, using molecular tool, CRISPR/Cas9. Review process is complete and five proposals have been selected for funding.

1. Modeling HCN1 gene variants associated with human early infantile epileptic encephalopathy (EIEE) in mice. Steven A. Siegelbaum, Professor and Chair, Department of Neuroscience

2. The role of Wdfy3 in CNS development and disease. Ai amamoto, Ph.D., Department of Neurology

3. The Parkinson's disease associated GBA variant, E326K, as a therapeutic target. Lorraine N. Clark, Ph.D., Associate Professor and Assistant Medical Director, PCB, LPGM and Taub Institute for research on Alzheimer's disease and the aging brain

4. Mouse models of intellectual disability with novel lissencephaly associated with CRADD mutations. Carol M. Troy, MD, PhD, Professor of Pathology & Cell Biology

5. De novo truncating mutations in TRIM8 define a novel syndrome characterized by childhood epilepsy,

focal segmental glomerulosclerosis (FSGS), and vesicoureteral reflux (VUR). Simone Sanna-Cherchi, Florence Irving Assistant Professor of Medicine Paul Marks Scholar, Division of Nephrology -Columbia University College of Physicians and Surgeons

Precision Medicine Travel Award for Child Care

This program assists scholars to attend conferences in the field of Precision Medicine by subsidizing child care and travel costs. One of Columbia University's core values is to expand scholarship, while increasing inclusion and success of highly qualified candidates. This program aims to expose future leaders in precision medicine to current leaders in the field. This program has a rolling deadline and applications may be submitted here.

Precision Medicine and Society

In the past year, Columbia faculty have continued to explore the impact of precision medicine on diverse fields, including economics, law, the humanities, and sociology.

The Precision Medicine and Society (PM&S) program at Columbia is directed by a Steering Committee of faculty now chaired by Paul Appelbaum, MD and Gil Eyal, PhD; Alondra Nelson, PhD, one of the founding chairs, stepped down from that role at the end of last year, although she remains involved as a member of the committee.

The PM&S program has funded a number of pilot projects in sociology, the clinical use of genomic technologies, and ethics. Maya Sabatello, JD, PhD and Rachel Adams, PhD continue to organize a series of lectures and workshops on the theme of Precision Medicine: Ethics, Politics and Culture. You can find details of this year's lecture series here.

An important partnership between Columbia University, MIT, and the National Bureau of Economic Research has resulted in the publication of an edited volume on precision medicine and economics, based on an NBER-sponsored conference, co-led by Jack Rowe MD, Mailman School of Public Health; a faculty member in the Business School is a contributor to the volume. The Steering Committee also collaborated on a paper published in Genetics in Medicine considering the likely impact of precision medicine on the physician-patient relationship.

Planning is also under way for a major conference at Columbia in the Spring of 2019 which will examine the impact of PM&S on healthcare and society, including the potential implications for medicine as a social institution embedded in political, legal and economic structures.

SAVE THE DATE: APRIL 24th and 25th

INAUGURAL PRECISION MEDICINE & SOCIETY CONFERENCE

Precision Medicine and Society: Pilot Awards

We are delighted to announce the awardees of the inaugural Precision Medicine and Society Pilot Grants. The Precision Medicine and Society Program (part of Columbia's Precision Medicine Initiative) Pilot Grants are designed to support work on issues relating to the social, legal, economic, humanistic

and ethical impact on society of the introduction of precision medicine and new genomic technologies.

Comparing Precision Medicines Boundaries and Identities in China and the United States LARRY AU (SOCIOLOGY) AND DR. GIL EYAL (SOCIOLOGY)

Compare the emergence of precision medicine in the United States and China using interviews and ethnographic observation of scientists and doctors in the two countries.

Comparing Inclusion/Exclusion in Precision Medicine Trials and Clinical Trials ADAM OBENG (SOCIOLOGY), MORAN LEVY (SOCIOLOGY), AND DR. GIL EYAL (SOCIOLOGY)

An examination of how the rise of precision medicine affects inclusion of patients from diverse social groups in cancer clinical trials.

Precision Medicine and Society: Pilot Awards (cont'd)

Establishing meaningful informed consent for whole-genome/exome sequencing in pediatric oncology: A web-based educational intervention

DR. JENNIFER OBERG (CUMC-PEDIATRICS), DR. JENNIFER LEVINE (CUMC-PEDIATRICS), AND DR. JULIA BENDER (CUMC-PEDIATRICS)

Pilot test a web-based educational intervention to facilitate informed consent for whole genome/exome sequencing in pediatric oncology and improve parent understanding of the risks and benefits of genomic testing.

Intervening in Digital Grief with Artificial Intelligence DR. DESMOND UPTON PATTON (SCHOOL OF SOCIAL WORK)

A social media-based intervention development study that will identify and analyze the sequence of traumatic and threatening content on Twitter that inform the adaption of an emotionally intelligent chatbot that disseminates resources and supports to youth of color who express grieving and aggressive related content on Twitter.

What Do Teenagers Think about Precision Psychiatry? DR. MAYA SABATELLO (CUMC-PSYCHIATRY), DR. JEHANNINE AUSTIN (MEDICAL GENETICS, UNIVERSITY OF BRITISH COLUMBIA), AND DR. PAUL APPELBAUM (CUMC-PSYCHIATRY) A study of teenagers' perspectives about precision medicine in psychiatry.

Upcoming Events:

The Precision Medicine: Ethics, Politics, and Culture Project; Cosponsored by Precision Medicine & Society and the Center for the Study of Social Difference.

February 19th – Dr. Kim Tallbear, University of Alberta, 4:30 - 6:30pm

April 25th – Ronit Ovadia Mazzoni, Santa Clara Valley Medical Center, San Jose, CA

Seminar on Ethical, Legal and Social Implications of Genetics; Center for Research on Ethical/ Legal/Social Implications of Psychiatric, Neurologic & Behavioral Genetics; Department of Psychiatry; Columbia University Medical Center

All talks will take place in Rm. 10-405A&B, Irving Institute for Clinical and Translational Research, 10th Floor, Presbyterian Hospital (PH) Building, 622 W. 168th Street; 12:00 - 1:00pm

December 17th – Eric Juengst, PhD, Dept. of Social Medicine, and Center for Bioethics, University of North Carolina – Note location change to PH 10-204

January 14th – Michelle Meyer, PhD, JD, Center for Translational Bioethics and Health Care Policy, Geisinger Health System

February 11th – Steven Joffe, MD, MPH, Division of Medical Ethics, and Department of Pediatrics, University of Pennsylvania

For further information or to convey suggestions about future speakers, contact Paul S. Appelbaum, MD, Department of Psychiatry, at 646-774-8630 or psa21@columbia.edu.



Educational Initiatives

The Columbia University Genetic Counseling Graduate Program has officially launched. The program has been approved by the Vagelos College of Physicians and Surgeons, Columbia University, and the New York State Education Department. Applications opened in September and approval from the Accreditation Council for Genetic Counseling is anticipated by early winter. The inaugural class of 12 students will begin the 21-month program in Fall 2019. Through coursework, fieldwork, and research across both the uptown and downtown campuses, students develop a strong foundation not only in the genetic and genomic sciences and their application to health in the era of precision medicine but also in the social implications of these advancing technologies. The program director is Amanda Bergner, MS, CGC, an Associate Professor of Genetic Counseling at Columbia University who was recruited to design, build, and launch this innovative program. More information can be found at https://www.ps.columbia.edu/gc-program.

We continue establishing exposure to the fundamentals of precision medicine for medical students, incorporating exposure to top scientists in relevant fields, as well as at the undergraduate and graduate levels in multiple disciplines. We are also particularly pleased to be working closely with the Irving Institute for Clinical and Translational Science, led by Muredach Reilly, MD, PhD, in collaborating and promoting the Precision Medicine monthly lecture series and other activities.

CPMI has written a detailed background paper for physicians regarding the principle of PM. The lead author of the paper, which will soon appear in Annals of Internal Medicine, is Dr Krzysztof Kiryluk. Dr Kiryluk has also led the effort to develop a series of clinical case studies of PM which are also slated to appear in the Annals. These publications are a result of the collaboration between CPMI and the American College of Physicians, which publishes Annals, one of the most widely read medical journals in the world.

New research is constantly reflected in Columbia's faculty-led education programs. The Columbia Precision Medicine Initiative will continue that trend, and expand offerings to comprehensively train academics and professionals needed for delivery of precision medicine.

