COLUMBIA PRECISION MEDICINE INITIATIVE

PRECISION MEDICINE

ANNUAL NEWSLETTER 2019 - 2020

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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, conferences, published scholarship, and pilot awards, the Columbia Precision Medicine Initiative is moving forward. We are particularly pleased to welcome the new senior faculty members Dr. Simon John a leader in the genetics and biology of glaucoma (Department of Ophthalmology), and Kristin Baldwin a leader in stem cell biology (Department of Genetics & Development).

CPMI is also working closely with Dr. Ali Gharavi (Department of Medicine) in the establishment of the Center for Precision Medicine and Genomics in the Department of Medicine. The goal is to develop clinically oriented Precision Medicine programs in each subspecialty of Internal Medicine.

In 2019, three grant recipients were named in the Roy and Diana Vagelos Precision Medicine Pilot Awards program. We are currently accepting applications for the third year of pilot awards. We were excited to hold the inaugural CPMI Scholars Day, which featured the work of currently-funded Vagelos Precision Medicine scholars together with Irving Institute Precision Medicine Research Fellows and Pilot Award Recipients. The Initiative also supported 4 awards for Mouse Genome Editing to fund the generation of mouse models of human disease. A new call for Mouse Genome Editing awards will be issued later in the year.

The Precision Medicine and Society program, chaired by Paul Appelbaum, MD and Gil Eyal, PhD, sets Columbia apart from other precision medicine initiatives. One of the highlights of the previous year was our inaugural conference: Precision Medicine: It’s impact of patients, providers and public health.

Another highlight was our 3rd academic conference, Advances in Precision Medicine: Big Data, which saw a full day of high impact international speakers covering basic and applied science in this field of precision medicine. We look forward to hosting our fourth conference on April 24th, 2020, which will focus on the harmonization of clinical and genomic data in precision medicine.

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 in precision medicine research, and the infrastructure required to advance basic science. 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, one at the Zuckerman Institute and two on the medical school campus. This extraordinary infrastructure, Professor Joachim Frank's Nobel Prize- winning contributions to the establishment and application of CryoEM technology, and an exceptional Columbia-wide structural biology faculty, positions Columbia as an international leader in the application of this powerful new technology to basic and applied science. For example, the ability to rapidly determine atomic resolution protein structures is powerful tool in the development of new drugs - a key step in the realization of precision medicine.

A more detailed description of progress in the Precision Medicine Initiative during the past year and further details of the activities during the coming year is provided in this newsletter.

Tom

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Advances in Precision Medicine Conference: Big Data

Our third annual conference took place on April 8th, 2019, where we hosted 10 top international speakers, bringing together a broad focus spanning from high-throughput molecular profiling technologies and the increasing availability of clinical data for research and in electronic health records give major opportunities to accelerate precision medicine using a variety of computational methods. We learned about the latest research in machine learning, genomics, clinical research, electronic health records and data science.

We were honored to have these prestigious leaders in this field join us; **Jeannette Wing, PhD**, Columbia University; **Ewan Birney, PhD,** EMBL-EBI; **Goncalo Abecasis, PhD**, Regeneron; **Richard Durbin, PhD,** Wellcome Sanger Institute; **Rich Bonneau, PhD,** New York University; **Ron Shamir, MD,** Tel Aviv University; **Barbara Engelhardt, PhD,** Princeton University; **George Hripcsak, PhD,** Columbia University; **Mihaela van der Schaar, PhD,** University of Oxford, UK; **Jennifer Listgarten, PhD,** University of California, Berkeley

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

SAVE THE DATE

4th Annual Advances in Precision Medicine Conference:
Harmonizing Clinical and Genomic Data
Friday, April 24, 2020

Lectures in Precision Medicine Lectures

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.

MIHAELA van der SCHAAR

Learning Engines for Healthcare: Using Machine Learning to Transform Clinical Practice and Discovery

January 29, 2019

Professor van der Schaar is John Humphrey Plummer Professor of Machine Learning, Artificial Intelligence and Medicine at the University of Cambridge and a Turing Faculty Fellow at The Alan Turing Institute in London, where she leads the effort on data science and machine learning for personalized medicine. She has received the Oon Prize on Preventative Medicine from the University of Cambridge (2018). She has also been the recipient of an NSF Career Award, 3 IBM Faculty Awards, the IBM Exploratory Stream Analytics Innovation Award, the Philips Make a Difference Award and several best paper awards, including the IEEE Darlington Award. She holds 33 granted USA patents. Her current research focus is on data science and machine learning for medicine and education.

Precision Medicine Scholars Day

On October 11, 2019, the Columbia Precision Medicine Initiative along with Vagelos College of Physicians and Surgeons, and the Irving Institute for Clinical and Translational Research presented the Precision Medicine Scholars Day where Vagelos Precision Medicine Scholars and Irving Institute Precision Medicine Research Fellows and Pilot Award Recipients spent the day presenting their research.

Faculty Announcements

ANIL RUSTGI

Anil K. Rustgi, MD, a leading cancer researcher and physician whose career has focused on gastrointestinal tumors, has been named director of the Herbert Irving Comprehensive Cancer Center at Columbia University Irving Medical Center and NewYork-Presbyterian/Columbia University Irving Medical Center. Dr. Rustgi also serves as professor of medicine and associate dean of oncology in the Vagelos College of Physicians and Surgeons.

SIMON JOHN

Noted geneticist and glaucoma researcher Simon John, PhD, will join the Department of Ophthalmology at the Edward S. Harkness Eye Institute in the fall of 2019. A pioneer in the use of mice for glaucoma studies, Dr. John comes to Columbia from the Jackson Laboratory in Bar Harbor, Maine, where he has been Professor and Principal Investigator for the past twenty years.

KRISTIN BALDWIN

Professor Kristin Baldwin, a leading neuroscience researcher, will join Columbia's Department of Genetics and Development in early 2020. Dr. Baldwin's research focusses on pluripotent stem cells to model and study epigenetic changes occurring in the brain genome and the cardiovascular system. She completed post-doctoral work with Richard Axel, and she returns to Columbia from Doris Neuroscience Center, Scripps Research where she is currently a professor in the Department of Neuroscience.

Medical Campus Updates

Institute for Genomic Medicine

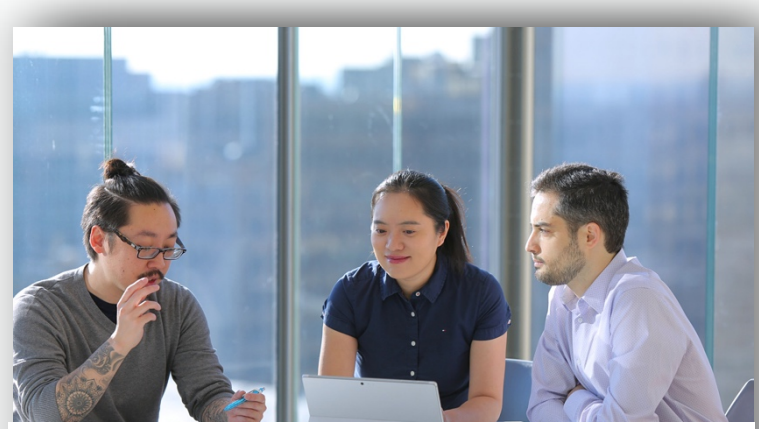
Over the past year, the Institute for Genomic Medicine (IGM), directed by Dr. David Goldstein; has continued to help make Precision Medicine a reality across the medical center. In partnership with several clinical departments, the IGM is breaking new ground to not only understand the clinical applications of genomics across the life span of an individual but to also determine how mutations can be studied in the laboratory to help develop personalized medicine to bring back to the clinic.

The IGM reached a milestone of over 100,000 samples sequenced to advance genomics at Columbia University. Partnerships with numerous departments in the Vagelos College of Physicians and Surgeons have been solidified through research, recruitments, and publications.

One clinical and research collaboration was published earlier this year in The *Lancet.* This study showed that whole exome sequencing—a technique that reads the smallest details of all protein-coding genes in the genome— can be used prenatally to improve obstetricians' ability to diagnose the underlying causes of fetal anomalies found during prenatal ultrasounds. But as with all new technologies, there are both benefits and limitations, and the results require expert interpretation from both geneticists and clinicians. Using whole exome sequencing, ten percent of the group was diagnosed with a known genetic disorder. The study was conducted in partnership with the Department of Obstetrics and Gynecology.

The IGM and the Department of Neurology successfully recruited Christopher Makinson, PhD, as an Assistant Professor in the Department of Neurology and in the IGM. His research focuses on how neural networks give rise to different brain states including sleep and arousal as well as disease states such as epilepsy. Chris is on a tenure track appointment and also appointed as a CTNI Scholar in the Columbia Translational Neuroscience Initiative. The Vagelos College of Physicians and Surgeons Precision Medicine Initiative will provide $1M of support to the development of Chris' research program.

Irving Institute for Clinical and Translational Research



Irving Institute's Precision Medicine Research Fellows James Chen, PhD (Dermatology), Yao Li, MD (Opthalmology), and Juan Arriaga, PhD (Pharmacology) (from left to right)

In the past year under the leadership of Wendy Chung, MD, PhD and co-directors Krzysztof Kiryluk, MD, Ronald Wapner, MD, David Goldstein, PhD, and Gary Miller, PhD, the Precision Medicine Resource team of the Irving Institute has established several new and exciting programs and continued building on the success of previous initiatives in this emerging domain of patient-centered healthcare. Three new interdisciplinary teams headed by investigators Vidhu Thaker, MD (Pediatrics/Molecular Genetics), Yuichi Shimada, MD (Medicine/Cardiology), and Howard Lieberman, PhD (Radiation Oncology), were selected to receive one-year Precision Medicine Pilot awards and will focus on tailoring medical care to the individual patient's needs in a wide range of pre-clinical and clinical domains. The Resource welcomed scholarly successes of Dean's Precision Medicine Research Fellows - Juan Arriaga, PhD, Suying Bao, PhD, and Ira Surolia, MD, - highlighted by the publication of their discoveries in several top biomedical journals (*Cell*, *Molecular Cell*, *Nature Cell Biology*, *Nature Communications*, among others). The one-semester Vagelos College of Physicians and Surgeons graduate course "Introduction to Precision Medicine", offered by the Resource for the third year consecutive year, allowed medical and other health sciences students and trainees to gain insights into such central to precision medicine topics as genomic medicine and its clinical implementation.
On October 11, 2019, research accomplishments of all award recipients were celebrated at the annual university-wide symposium "2019 Precision Medicine Scholars Day", hosted by the Resource jointly

with the Columbia Precision Medicine Initiative team. Now in its fifth year, a monthly seminar series "Advances in Precision Medicine" brought to campus such thought leaders in the field as Stephen Kingsmore, MD, DSc (RCHSD), Wylie Burke, MD, PhD (University of Washington), Joshua Denny, MD (Vanderbilt University), Diana Bianchi, MD (NICHHD), to name a few.

BRIDGE Biobank

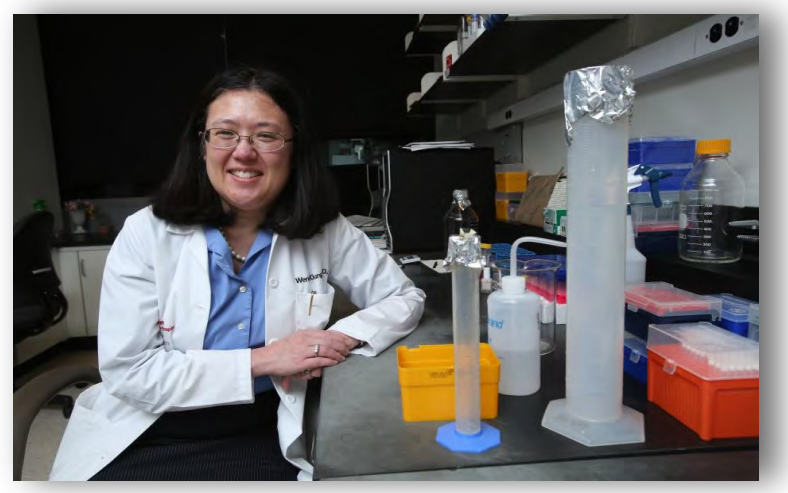
One of the biggest developments in the Irving Institute was the expansion of the Biobank Resource for Investigating Disease, Genes & Environment (BRIDGE) initiative. This effort now includes a recruitment team, a biorepository laboratory team, and a laboratory informatics team. A pilot initiative, Cardiometabolic Precision Medicine Program (executive leaders - Muredach Reilly, MBBCh, MSCE; Steven Marx, MD; Wendy Chung MD, PhD; program manager - Sheila M. O'Byrne, PhD), is underway in the Division of Cardiology/Department of Medicine, while the next phase of the expansion is planned to include the Departments of Pediatrics and Obstetrics/Gynecology under the guidance of Ronald Wapner, MD and Wendy Chung MD, PhD. The Resource is also collaborating and supporting the birepository efforts within the Institute of Genomic Medicine, led by David Goldstein, PhD. As part of the national *All Of Us* research program, several thousand biosamples from participants recruited by Columbia/Cornell/Harlem Healthcare Provider Organization were processed by the Irving Institute laboratory. Now that *All Of Us* recruitment is underway, the local BRIDGE bio`bank will expand markedly by synergizing with this initiative and expanding into additional departments.

Precision Medicine Publications

Led by Krzysztof Kiryluk, MD, the Resource team joined forces with a diverse group of Precision Medicine experts across the CUIMC to publish 9 articles in the Annals of Internal Medicine on various topics in Precision Medicine including a series of 8 case studies, each dealing with a common clinical issue regarding precision medicine.

Cases in Precision Medicine:
Precision Medicine in Internal Medicine: Overview of the series
The Role of Pharmacogenetics in Precision Prescribing.
When Patients Present With Direct-to-Consumer Genetic Test Results.
Should You Participate in a Study Involving Genomic Sequencing of Your Patients?
Genetic Assessment After a Sudden Cardiac Death in the Family.
The Role of Tumor and Germline Genetic Testing in Breast Cancer Management.
APOL1 and Genetic Testing in the Evaluation of Chronic Kidney Disease and Potential Transplant.
Concerns About Privacy and Discrimination After Genomic Sequencing.
A Personalized Approach to Stroke and Cardiovascular Risk Assessment in Women.

Targeted Research and Exploration Advancing Trial Models, Editing, and Next-generation Therapies (TREATMENT)



The Targeted Research and Exploration Advancing Trial Models, Editing, and Next-generation Therapies (TREATMENT) program was established by Dr. Wendy Chung to expand our capacity to care for patients with rare genetic diseases, understand the natural history and molecular mechanisms of genetic diseases, and develop new treatments for these conditions. The program was established to make Columbia a destination medical center for a growing international network of patients and families and serve as a nucleus of physicians and scientists in academia and industry working together toward cures for rare genetic diseases. We are developing novel molecular methods of treatment including the use of antisense oligonucleotides, gene edition, and gene therapy. We are currently participating in 5 clinical trials of new treatments for genetic disorders and have patients from around the United States participating in these trials. TREATMENT unites families, patients and families and provides them with hope for a brighter future.

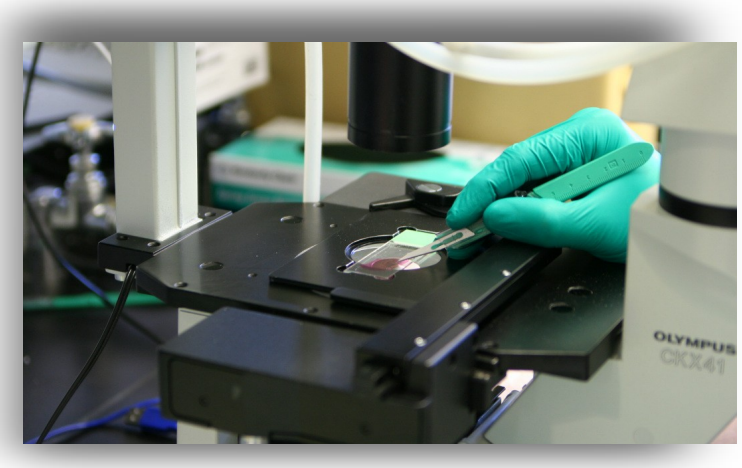
EpicTogether

EpicTogether, the operational managing team for New York Consortium Epic implementation, has established a Precision Medicine team with dedicated analysts to work on Epic's new Genomic module and other activities around genomic data. A collaborative group representing the 3 institutions (NYP, Columbia, Cornell) is developing the infrastructure to identify genomic lab tests, convert test results to genomic clinical indicators, and develop appropriate Best Practice Advisory alerts. The initial focus has been on Clinical Pharmacogenetics Implementation Consortium (CPIC) recommended guidelines for actionable pharmacogenetic results. Post go-live, the team will continue to champion, set goals and develop procedures for Precision Medicine data capture and alerting in Epic EHR.

Columbia has been a part of the NIH eMERGE (Electronic Medical Records and Genomics) network since 2011. Co-led by Drs. Chunhua Weng, Ali Gharavi, and George Hripcsak (project manager – Alexander Fedotov, PhD), CUIMC has significantly increased our genomic data for 2500 participants in eMERGE with integration of genomics into the EHR in eMERGE Phase 3. We have integrated the capacity to geocode all our patients to assist with determining environmental exposures.

As part of eMERGE, we developed the infrastructure to recruit a diverse group of participants, educate them about genomics, and return clinically actionable, valid, and reliable genetic results. As part of the eMERGE IMAGene study, we specifically studied strategies to recruit underserved communities, including our local Latina community and found that messaging that included the need to be represented and increase genomic knowledge about and for the Latina community to ensure access to advances in genomic health was effective and meaningful. We have a community advisory council available to provide feedback for genomic studies. Our CAC has helped to develop messaging and imagery in our communication materials to ensure that we use plain language and simple concept to explain complex genetic information. We developed clinical resources including templated language to include in results letter to participants and ACT sheets for the most common genomic findings to educate the participant and their family and providers about the medical and familial implications of the new genetic information.

Precision Genomics Laboratory (PGL)



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 of the PGL, which is housed in the Division of Laboratory Medicine, directed by Steven Spitalnik, MD.

The mission of the PGL is to apply advanced genomic science in a clinically actionable setting to improve the diagnosis and treatment of human disease. The PGL began clinical testing February 2018, and is CLIA/CLEP certified and accredited by the College of American Pathologists (CAP). Since its inception, the PGL's multidisciplinary clinician-scientist teams have worked to serve the needs of physicians and researchers at CUIMC by offering a range of services designed to enhance constitutional genomic diagnostics, research, and education.

The PGL currently offers clinical cystic fibrosis screening and Sanger sequencing of individual variants. The latter test is crucial to our local genomic sequencing initiatives because it ensures that high quality, clinical grade variant reports are transmitted to the electronic medical record, thereby translating laboratory-based precision medicine technologies into clinical decision-making tools. The PGL plans to begin offering whole exome sequencing, a genotyping array, and a 400 gene expanded carrier screening panel as clinical tests upon approval by the NYS Department of Health.

The PGL also employs a team of genetic counselors to act as liaison between clinical care providers and the laboratory in order to ensure that the genomic information generated by the PGL is used to inform and guide personalized, patient-focused healthcare for the CUIMC community and beyond.

Laboratory of Personalized Genomic Medicine (PGM)

The Laboratory of Personalized Genomic Medicine (PGM) in the Department of Pathology and Cell Biology is a state-of-the-art diagnostic laboratory that performs cutting-edge tests in the areas of genetics, neurogenetics, oncology, cytogenomics, and molecular microbiology. The CLIA-accredited laboratory, directed by Mahesh Mansukhani, MD, is accredited by the College of American Pathologists (CAP), and the Clinical Laboratory Evaluation Program of the New York State Department of Health (NYS-DOH). PGM offers multiple clinical molecular oncology and constitutional genomics assays, including single gene assays, small cancer panels, a large 467-gene cancer panel, as well as whole-exome and whole transcriptome sequencing. This past year, PGM received NYS DOH approval for Darwin OncoTarget/OncoTreat analysis of transcriptomes, a powerful and novel systems biology approach that assesses activity of potentially targetable master regulators (developed in collaboration with Dr. Andrea Califano in the Department of Systems Biology), which will further advance precision oncology efforts at CUIMC. In 2018, PGM performed over 52,000 clinical tests including nearly 9,000 constitutional genetics assays and over 5,000 oncology assays.

In recent years, the PGM has developed a national presence in the field of molecular oncology laboratory testing. In August 2018, PGM was selected to participate as a CLIA-certified laboratory for the NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) precision medicine trial. NCI-MATCH is the largest trial to date that seeks to determine whether therapies targeting specific gene mutations will be effective regardless of cancer type. Tumor gene testing by a designated lab is the only pathway for patients to enroll into the trial. In 2020, PGM will partner with the Herbert Irving Comprehensive Cancer Center and Department of Pediatrics in the upcoming ComboMATCH and NCI-COG Pediatric MATCH clinical trials, which employ combinations of precision medicine agents to treat a variety of cancers in the pediatric and adult patient populations.

PGM faculty and staff members participate in pediatric and adult molecular tumor boards at CUIMC and nationally in the American Society of Clinical Oncology's Targeted Agent and Profiling Utilization Registry (TAPUR) study molecular tumor board. Additionally, the PGM bioinformatics team has led CUIMC involvement in Project GENIE, an American Association for Cancer Research program for aggregation of cancer genomics and clinical outcome data in a HIPAA compliant registry with the goal of catalyzing clinical and translational cancer research. The Laboratory of Personalized Genomic Medicine is committed to supporting and enhancing clinical and research initiatives among the CUIMC precision oncology community.

Center for Precision Medicine and Genomics (CPMG)

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 Precision Medicine and Genomics (CPMG) 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 program 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.

Precision Oncology and Systems Biology (POSB) Program

Cancer is emerging as an increasingly complex and dynamic disease, requiring equally complex and multidisciplinary solutions, designed and implemented by transdisciplinary investigator teams. The Precision Oncology and Systems Biology (POSB) Program—one of four programs in the Columbia Herbert Irving Comprehensive Cancer Center (HICCC)—seeks to address this challenge by developing innovative, quantitative, multi-omics models and by leveraging molecular- and image-based biomarkers for their translation to the clinic. The POSB Program includes 41 Members from 12 departments, across three schools at Columbia University, and is co-led by Dr. Califano, Chair of the Systems Biology Department, and Dr. Carvajal, Professor of Medicine and Director of Phase 1 Experimental Therapeutics. POSB Members have developed and deployed quantitative methodologies for the effective prioritization of patient-specific treatments by seamlessly integrating both emergent cancer systems biology approaches and mainstream strategies. This is achieved by focusing on three Specific Aims including: (1) the assembly and interrogation of gene regulatory and signaling networks; (2) investigating tumor heterogeneity and plasticity, including at the single-cell level; and (3) developing and delivering a novel integrative precision oncology framework. For instance, POSB investigators have developed and translated innovative systems biology tests that have achieved NY State CLIA certification as well as a broad portfolio of mechanism-based, precision oncology clinical studies, including innovative N-of-1 basket trials.

The POSB Program has a strong portfolio of NCI and other cancer relevant funding. In 2019, members had a total of $10.6M in cancer-focused, peer-reviewed funding (direct costs). POSB Members authored 1,064 cancer-relevant publications, of which 164 (15%) were intra-programmatic and 268 (25%) were interprogrammatic. Strikingly, 20% appeared in high impact factor journals (IF ≥ 10), of which half were in journals with IF ≥ 20. The POSB Program has significant strength in leading both institutional and multicenter interventional trials. During the project period the POSB Program had 1,180 interventional enrollments of which 52% were to investigator-initiated trials. Under-represented minority and underserved patients' accrual to clinical trials is a particular strength of the POSB Program and is also 52%.

Precision Medicine Awards

Roy & Diana Vagelos Precision Medicine Pilot Awards

We are pleased to announce the winners of the 2nd Roy and Diana Vagelos Precision Medicine Pilot Awards. We were impressed with the response and with the broad range of proposals from Columbia faculty. The standard of the 34 applications we received was very high, and investigators came from all Columbia campuses. Thanks to all who submitted proposals and to those who participated in the review process.

The Roy and Diana Vagelos Awards are a cornerstone of the CPMI mission: to establish world class academic research centers of excellence to build precision medicine as a basic and applied

science at Columbia. Seeding basic research in precision medicine with these awards is an efficient way of converting this money to external research grants and we look forward to this return on investment in due course.

The three winning proposals reflect the high standard and the broad base of precision medicine basic science research being conducted and conceived at Columbia. They cover epilepsy research; neuro oncology research; and developing a synthetic cell communication tool for tissue engineering.

The winning proposals are:

Development of novel therapies for STXBP1 encephalopathy.
Michael Boland Ph.D. Dept of Neurology, Institute for Genomic Medicine; **Wayne Frankel** Ph.D. Dept of Genetics & Development

Molecular characterization of gliomas under immunotherapy.
Raul Rabadan PhD, Dept of Bioinformatics; Systems Biology; **Fabio Iwamoto** MD, Dept of Neurology (Neuro-oncology division)**; Junfei Zhao**, PhD.

Exploiting the basic mechanism of Notch activation to develop new diagnostic, therapeutic and tissue engineering tools for precision medicine.
Gary Struhl PhD; **Paul Langridge** PhD. Dept of Genetics and Development (in Neuroscience); Zuckerman Mind Brain Behavior Institute

2019 Irving Institute Precision Medicine Research Fellows and Pilot Award Recipients

Identification of Precision Diagnostic and Therapeutic Targets for Advanced Prostate Cancer Patients Based on Mechanistic RNA Landscape
Howard Lieberman, PhD, Radiation Oncology (Principal Investigator)
Israel Deutsch, MD, Radiation Oncology
Richard Friedman, PhD, Biomedical Informatics
Sven Wenske, MD, Urology

Application of Multi-omics Profiling to Predict Adverse Left Ventricular Remodeling and Cardiovascular Events in Hypertrophic Cardiomyopathy
Yuichi Shimada, MD, Medicine: Cardiology (Principal Investigator)
Matthew Maurer, MD, Medicine: Cardiology
Rajesh Soni, PhD, Medicine: Hematology and Oncology
Renu Nandakumar, PhD, Medicine: General Medicine
Kohei Hasegawa, MD, Medicine: Emergency Medicine

TBX3 as a novel regulator of POMC for therapeutic targeting
Vidhu Thaker, MD, Pediatrics: Molecular Genetics (Principal Investigator)
Claudia Doege, MD, Pathology and Cell Biology: Pathology

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 four proposals have been selected for funding.

Modeling HCN1 gene variants associated with human early infantile epileptic encephalopathy (EIEE) in mice. **Jonathan Barasch,** Professor of Medicine and Pathology and Cell Biology

A humanized mouse model to study the immunopathology of vitiligo. **Remi Creusot, PhD,** Assistant Professor in the Department of Medicine and principal investigator at the Columbia Center for Translational Immunology and the Naomi Berrie Diabetes Center

Molecular Genetics of FTO. **Rudolph Leibel**, Christopher J. Murphy Memorial Professor of Diabetes Research and Professor of Pediatrics and Medicine; Co-Director, Naomi Berrie Diabetes Center

Precision SNP Editing for Autosomal Dominant Retinitis. **Stephen Tsang, MD, PhD,** Associate Professor, Edward S. Harkness Eye Institute

Precision Medicine Professional Travel Family Fund

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 as part of Columbia's Precision Medicine and Society (PM&S) program within the University's overall Precision Medicine Initiative. The program 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 the 2018-19 academic year.

Precision Medicine: Ethics, Politics and Culture (PMEPC)

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 continued to organize a series of lectures and workshops on the theme of Precision Medicine: Ethics, Politics and Culture (PMEPC). Prof. Sabatello will be working with Prof. Eyal on the 2019-2020 series. You can find details of this year's lecture series here.

We have circulated a call for PMEPC Graduate Fellows at the beginning of the academic year and received 26 applications across departments and campuses. This high demand and impressive quality of applications led us to rethink the number of positions we can offer. We subsequently decided to increase the number of Graduate Fellows from 4 to 6 (with some additional support from PM&S). The selected Graduate Fellows are:

Sonia Mendoza-Grey (Mailman)
Larry Au (Sociology)
Diana Garofalo (Mailman)
Amy Weissenbach (Sociology)
Irina Kulichenkova (Narrative Medicine)
Sunny Jones (System biology)

All the Fellows will participate in our series of public talks and small group meetings. In addition, an innovative aspect of this year's Fellowship is that the 6 Graduate Fellows will develop a publishable research paper relating to PM&S.

This combination of public talks, working group discussion and publication will allow for an extensive engagement in PM&S issues among students in the upcoming year.

Precision Medicine & Economics

An important partnership between Columbia University, MIT, and the National Bureau of Economic Research resulted in the publication of an edited volume on precision medicine and economics, entitled Economic Dimensions of Personalized and Precision Medicine, based on a NBER-sponsored conference, co-led by Jack Rowe MD, Mailman School of Public Health; Frank Lichtenberg, a faculty member in the Business School, was a contributor to the volume. We have a number of copies available to distribute; anyone interested please contact us at precisionmedicine@columbia.edu.

Precision Medicine & Society Publications

The members of the PM&S Steering Committee collaborated on a paper published in Genetics in Medicine considering the likely impact of precision medicine on the physician-patient relationship. Members of the Steering Committee also published three papers aimed at educating primary care physicians on topics in precision medicine and society in the Annals of Internal Medicine, as well as articles on genomic literacy among adolescents, inclusion of people with disabilities in precision medicine research, and the psychosocial impact of genetic testing in major medical and bioethics journals. These publications can be found on our website here.

Precision Medicine & Society Events

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 16th - Gary Marchant, JD, College of Law, Arizona State University
January 13th - Josephine Johnston, LLB, MBHL, The Hastings Center
February 10th - Angela Bradbury, MD, Dept. of Medicine, UPenn
March 16th - Aaron Panofsky, PhD, Institute for Society and Genetics, UCLA
April 20th - Pamela Sankar, PhD, Dept. of Medical Ethics & Health Policy, UPenn
May 18th - Kathryn Tabb, PhD, Dept. of Philosophy, Bard College
June 22nd - Steven Hyman, MD, Broad Institute & Harvard University

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.

The PMEPC lecture series represents a broad-based exploration of questions that precision medicine raises in law, ethics, the social sciences, economics, and the humanities.

Dr. Shirley Sun (Nanyang Technological University) to give a talk on *"Should You Be Worried about Racialization of Precision Medicine? Insights from Asia and North America"*, on Wednesday, December 4th, 5pm-7pm, in the Seminar Room (IRWGS), 754 Schermerhorn Ext, 1200 Amsterdam Ave, New York, NY 10027.

Dr. Dan Navon (University of California, San Diego) to give a talk on *"Mobilizing Mutations: Remaking Illness in Genomic Medicine"*, on Wednesday, April 15th, 5pm-7pm, location TBD.

Dr. Barbara Prainsack (University of Vienna) to give a talk on *"The Value(s) of Precision Medicine: Societal, Political, and Ethical Aspects"*, on Wednesday, May 6th, 5pm-7pm, location TBD.

Inaugural Precision Medicine & Society Conference

In April, 2019, the PM&S program sponsored a well-attended, two-day symposium on Precision Medicine: Its Impact on Patients, Providers and Public Health, with physicians, social scientists, bioethicists, journalists, science policy leaders, economists and humanists speaking on a wide range of precision medicine topics, featuring Harold Varmus, MD and Paul Starr, PhD as keynote speakers. More about the inaugural conference can be found on our website here.

Planning is under way for another major conference at Columbia in the Spring of 2020 that will examine the global dimensions of precision medicine and its impact on healthcare and society.

Educational Initiatives

Genetic Counseling Graduate Program

Columbia's Genetic Counseling Graduate Program has launched with an inaugural class of 12 students, who kicked off their orientation with faculty and staff members on August 19 at a ribbon cutting ceremony on the medical campus. The 12 students enrolled in Columbia's inaugural Class of 2021 have a variety of educational backgrounds, including biology, psychology, philosophy, global and public health, bioethics, molecular and medical genetics, bioengineering, performing and media arts, music, and mathematics. They have collectively engaged in diverse human service initiatives such as serving in the Peace Corps, volunteering in food pantries, participating in global medical service trips, working with homeless and disadvantaged populations, and advocating for survivors of sexual assault and domestic violence.

The program is 21 months in length, culminating in a Master's degree in Genetic Counseling. During their time at Columbia, students will undertake coursework, fieldwork, and research that will allow them to develop the skills to help individuals, families, and communities navigate the increasingly complex maze of health-related genetic and genomic testing.

The program has partnered with the Jaharis Simulation Center in VP&S to break new ground in training the next generation of genetic counselors to provide client-centered, empathic care in the era of genomics and big data. This fall, the Class of 2021 is participating in a series of simulation workshops with standardized patients (SPs) to hone their skills in active listening and communication of complex topics to a wide array of audiences. Using SPs to portray various clients who might present for clinical genetic services, students develop early clinical skills prior to their interactions with live clients at the Columbia University Irving Medical Center. They are guided in the simulations by faculty from across Columbia (Genetics and Development, Pediatrics, Medicine, Obstetrics and Gynecology, and Neurology) with the goal of improved patient care.

Additionally, the Columbia program has a unique emphasis on advocating for the use of genetics and genomics to promote social justice in health care. Students in the inaugural class will be traveling with faculty to Puerto Rico during their winter intensive in January to engage in Spanish immersion and medical Spanish classes, as well as working with the local genetics community to establish genetic counseling outreach efforts that can be continued in the coming years. Puerto Rico currently has no genetic counselors, which means decreased access for residents to genetic testing and support for integrating genetic and genomic information into their healthcare.

One of the inaugural students, Denise Ma, was born in southern China and immigrated to New York City at age 10. She speaks three dialects of Chinese and is the first in her family to attend college. After graduating with a bachelor's degree in biology from Cornell University in 2017, she took a job as a research coordinator and genetic counseling assistant at the Center for Neurogenetics at Weill Cornell Medicine. "I was 12 the first time I met a genetic counselor and was accompanying a family member for an appointment," she says. "I remember the experience being pleasant and we communicated by using a phone interpreter. After that appointment, I wondered if there were any bilingual genetic counselors available. I did some online research and couldn't find any in my area. Ever since then, my interest in the field grew as I learned more by speaking to and shadowing genetic counselors. I hope to combine my multilingual skills with my passion for genetic counseling to expand care to non-English speaking families."

The program has launched a series of events for people interested in learning more about genetic counseling and the Columbia program, offering webinars and open houses throughout the year. As well, there is an experiential practicum program that allows prospective students the opportunity to observe client sessions with practicing genetic counselors at the Columbia University Irving Medical Center. More information about upcoming events can be found on the program website.

The program director is Amanda Bergner, MS, CGC, an Associate Professor of Genetic Counseling at Columbia University who was recruited to design, build, launch, and direct this innovative program. More information can be found at ps.columbia.edu/gc-program.