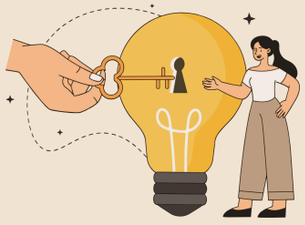
mprint newsletter

The Task Force on Research Specific to Pregnant Women and Lactating Women Implementation (PRGLAC) Working Group of Council Report on Implementation Progress has been finalized, shared with Congress, and released to the public.

PRGLAC task force

CLICK HERE

IMPAACT Early Career Investigator (ECI) Program



PROPOSAL DUE: 1 OCTOBER 2024

The application process is still open for the IMPAACT Early Career Investigator (ECI) program – do not delay!

The goal of the ECI program is to support early career investigators in the completion of a project using data or samples generated by IMPAACT Network studies. Through the program, early career investigators will build research skills and support IMPAACT's goal to improve health outcomes for infants, children, adolescents, and pregnant and postpartum people who are impacted by or living with HIV, tuberculosis, and other HIV-related conditions.
Approved applicants will receive funding for a period of two years, during which time they will be expected to submit a manuscript to a peer-reviewed journal and present findings at an IMPAACT Annual Meeting and at one or more other scientific meetings.
Full information about the IMPAACT ECI program, including the award notification, application, and budget-related documents are available on the IMPAACT website by clicking the button below.

CLICK HERE

The DMKRCC MPRINT Hub Opportunity Pool

The Opportunity Pool is designed to support projects that address emergent needs and leverage novel technologies in maternal and pediatric therapeutics. Examples of supported activities include, but are not limited to, expansion of existing or development of a new MPRINT Core and generation of new computational or experimental tools to enhance precision therapeutics in maternal and pediatric populations.

Clinical fellows / postdoctoral fellow awards are up to $25,000 and faculty awards up to $150,000 for a total award amount in the range of $500,000.

click here!

Previous Awardees

Faculty Opportunity Pool Awardee

Bernard de Bono MD, PhD
Hon. A/Prof of Bioengineering, University of Auckland
CEO Whitby et al, LLC, Indianapolis, USA

SUMMARY:
MPRINT's Modeling Support (MMS) will focus on enhancing the synergies between the MPRINT Hub Knowledgebase and the NIH Common Fund Data Ecosystem (CFDE). The key objective of the MMS effort is to build and populate a Modeling Knowledge Repository, which will centralize and extend MPRINT's knowledge resources on quantitative pharmacology models relevant to maternal and pediatric health. In addition, the project addresses the two-way interoperability between resources in MPRINT the CFDE data to enhance findability and access to biomedical data, such as tissue expression or biomarker data. Furthermore, the MMS effort will promote collaboration between MPRINT and CF communities through joint training workshops, knowledge dissemination, and the creation of a shared roadmap for training.

Stephani Stancil, PhD, APRN
Clinician Scientist
Divisions of Adolescent Medicine and Clinical Pharmacology at Children's Mercy
Assistant Professor in the Department of Pediatrics at the University of Missouri-Kansas City and University of Kansas Schools of Medicine.

Following her PhD in pharmacology and pharmaceutical science, she completed a NIH-funded T32 post-doctoral fellowship in pediatric clinical pharmacology. She is a practicing clinician in Adolescent Medicine and the GOLDILOKS Precision Therapeutics inpatient consult service at Children's Mercy. Her interdisciplinary, translational research focuses on developing precision therapeutics for adolescent mental health conditions by understanding variability in exposure and response.

SUMMARY:
Understanding drug disposition in the brain is critical to 1) uncovering the link between brain exposure and clinical response, tolerability, and safety, 2) enabling inquiry into mechanistic changes during dynamic periods of life such as childhood and pregnancy, and 3) improving pharmacometric precision. At present, brain disposition is generally inferred from experimentally derived drug distribution characteristics, such as lipophilicity and blood-brain barrier efflux. Positron emission topography (PET) imaging can be used to elucidate preclinical brain concentrations and the pharmacodynamic, target receptor binding properties of a drug, but does not directly measure brain concentrations following clinically-relevant dosing in humans. Further, due to radiation exposure, PET poses ethical challenges in children and pregnant people, who are traditionally not candidates for this higher risk method, despite their being end-users of the candidate medication. Alternative feasible and minimal risk strategies are needed to ensure all populations are included in research that promotes safe and effective use of medications.

19F-magnetic resonance spectroscopy (19F-MRS) is a non-invasive, non-radioactive MRI method that detects naturally-occurring, non-radioactive fluorine. Nearly 20% of FDA-approved medications include fluorine to improve solubility and cellular uptake, including many drugs targeting the central nervous system (CNS). We leverage the existing fluorine(s) in each drug molecule to detect their MRS signal in living human brain without ionizing radiation. The number of fluorines in the drug molecule impacts the signal strength, with stronger signal expected with 3 fluorines per molecule (e.g., fluoxetine, C17H18F3NO) compared with two (pantoprazole, C16H15F2N3O4S), for example. Our pilot work with fluoxetine successfully quantified brain concentrations in adolescents across a range of doses and demonstrated 3-fold variability in brain concentration at any given dose.

The goal of this project is to further develop 19F-MRS as safe, non-invasive, and highly sensitive tool to detect drug concentrations in the brain. We aim to 1) increase the sensitivity of 19F-MRS, 2) broaden the detectability of 19F-MRS to various fluorine-containing medicines, and 3) determine the feasibility of using 19F-MRS in youth of different ages and sizes. Our translational approach pairs in vitro experiments using phantom standards with in vivo optimization in humans. We will identify the most sensitive technique, comparing 3 distinct head coil designs (i.e., single loop, birdcage and helmet), then optimize and validate 19F-MRS parameters in youth taking fluoxetine. The enhanced 19F-MRS scan protocol will then be adapted for other drugs with varying fluorine signal strength (e.g., pantoprazole and lansoprazole). Successful completion of this work with demonstrate analytical validity and feasibility of 19F-MRS neuroimaging in pediatrics. The downstream applications of this technique are vast, including changing the landscape of drug development by generating data from a physiologic compartment not otherwise accessible (i.e., the brain), and enabling safer, more precise use of therapeutics.

Faculty Opportunity Pool Awardee

Sun Yang
Associate Professor
Department of Pharmacy Practice
Chapman University of Pharmacology

Dr. Yang completed an oncology translational research fellowship at the University of California, Irvine, and a PGY1 and PGY2 residency in Pediatric Pharmacy at CHOC Children's Hospital of Orange County. Dr. Yang is a Board-Certified Pediatric Pharmacy Specialist and an Advanced Practice Pharmacist.

Since joining the Chapman faculty in 2015, Dr. Yang has established a translational research laboratory focused on developing new cancer therapeutics and advancing pediatric patient care. Her research has been funded by the National Cancer Institute (NCI), the Kay Family Foundation, the Pediatric Pharmacy Association (PPA), Merck & Co., Inc., and Chapman University.

Faculty Opportunity Pool Awardee

Rishikesh Chavan, MD
Clinical Associate Professor, Department of Pediatrics at UCI School of Medicine
Medical Director of Stem Cell Transplant and Cellular Therapies, Hyundai Cancer Institute
Medical Director of Cell Therapy Lab and Cord Blood Bank,
Children's Hospital of Orange County (CHOC)

Dr. Chavan is a Clinical Associate Professor in the Department of Pediatrics at UCI School of Medicine, the Medical Director of Stem Cell Transplant and Cellular Therapies at the Hyundai Cancer Institute, and the Medical Director of the Cell Therapy Lab and Cord Blood Bank at Children's Hospital of Orange County (CHOC). He completed his general pediatric internship and residency at Tulane School of Medicine and clinical and research post-doctoral fellowship in pediatric hematology and oncology at Baylor College of Medicine. Dr. Chavan is board-certified in both general pediatrics and pediatric hematology-oncology through the American Board of Pediatrics. Since joining CHOC in 2019, his research has primarily focused on investigating the role of the host immune system and gut microbiome in treatment outcomes for patients receiving immunotherapies, chimeric antigen receptor (CAR) T cell therapies, and stem cell transplants. His work is supported by funding from St. Baldrick's Foundation, the Stanley Ekstrom Foundation, the Pediatric Subspecialty Foundation, and CHOC Hospital CSO grants.

SUMMARY:
Vitamin D and its metabolites are crucial in early life, including bone growth, metabolic regulation, and immune system development. Children with cancer may be particularly susceptible to fluctuating vitamin D levels because of their illness, younger age, extensive chemotherapy, reduced outdoor activities, and limited sun exposure. Consistent with other reports, our preliminary study demonstrated more than one-third of previously healthy children exhibited notable vitamin D deficiency upon diagnosis with cancer across diverse malignancies. However, health literacy on how vitamin D deficiency impacts pediatric oncology patients and their diseases is very limited. Immaturity of the gut microbiome has been shown to contribute to the development of childhood acute lymphoblastic leukemia (ALL), the most commonly diagnosed malignancy among children.

SUMMARY CONTINUED: (Yang & Chavan)

The gut microbiome diversity was much lower in patients with ALL compared to healthy children. Emerging research highlights the crucial role of vitamin D in promoting a healthy gut microbiome and regulating the immune response. Vitamin D supplementation significantly increased the gut microbial diversity and abundance of probiotic taxa. However, such studies have not been extensively explored in the pediatric population, particularly among patients with cancer receiving chemotherapy. There is a significant gap in our knowledge of vitamin D in regulating gut microbiome composition and function among this vulnerable population.
In the funded research project, we will: 1) recruit a cohort of pediatric patients newly diagnosed with ALL to determine if the gut microbiome is significantly different in vitamin D-deficient patients compared to vitamin D-normal ones; 2) characterize the impact of vitamin D supplementation on gut microbiome and metabolome among the patients receiving induction chemotherapy; 3) explore the modifications in vitamin D metabolism caused by changes in the microbiome either before or after induction chemotherapy. Together, these aims will provide mechanistic insights into the clinical benefits of monitoring vitamin D status and supplementation in pediatric oncology patients. A better understanding of the bidirectional interaction between vitamin D and the gut microbiome composition and function will lead to strategies for enhancing clinical care and optimizing treatment outcomes in pediatric patients with ALL.

Trainee/ Fellow Opportunity Pool Awardee

Marissa Berry, MD
Maternal-Fetal Medicine Fellow
The Ohio State University

Dr. Marissa Berry completed her medical training at University of Nebraska Medical Center and her residency in Obstetrics & Gynecology at University of Texas Medical Branch. She is currently a Maternal-Fetal Medicine fellow at The Ohio State University. Her research experience includes serving as principal investigator and publishing a randomized controlled trial on the timing of amniotomy during labor. She is currently leading a trial investigating the optimal prophylactic antibiotic regimen for use in pregnant individuals with preterm prelabor rupture of membranes. Her interests include clinical and translational approaches to infectious diseases in pregnancy.

SUMMARY:
Preterm prelabor rupture of membranes (PPROM) affects 1 in 3 individuals with spontaneous preterm birth. Expectant management is often recommended for PPROM diagnosed <34 weeks' gestation. A course of prophylactic antibiotics is given to decrease the risk of infection and prolong pregnancy. The currently recommended antibiotic regimen of ampicillin, amoxicillin, and erythromycin or azithromycin has remained largely unchanged in past decades. More research is needed regarding the optimal prophylactic antibiotic regimen to provide adequate coverage for common organisms implicated in infection, address changes in bacterial sensitivities over time, and provide adequate placental transfer and reduction of the fetal inflammatory response.

This is a randomized controlled trial comparing prophylactic antibiotics with the current standard regimen versus an expanded-spectrum regimen including ceftriaxone, metronidazole, and clarithromycin. This alternative regimen addresses limitations of the current standard regimen and has preliminary proof-of-concept data. We are assessing pregnancy latency, maternal and neonatal outcomes, and obtaining microbial samples for analysis.

Trainee/ Fellow Opportunity Pool Awardee

Mollie Walton, MD
Pediatric Cardiologist and Clinical Pharmacology Fellow
Children's Mercy Hospital at Kansas City, Missouri

Mollie Walton, MD is Pediatric Cardiologist and Clinical Pharmacology Fellow at Children's Mercy Hospital in Kansas City, Missouri. Her research goal is to determine how genetic variation and development impact pediatric cardiovascular pharmacotherapeutics, to determine factors that can predict cardiovascular drug response and individualize drug therapy. Her focus thus far has been the beta blocker drug class, specifically atenolol, which is a commonly used drug in the management of patients with Marfan syndrome.

SUMMARY:

Aortic root enlargement, a common manifestation of the connective tissue disorder, Marfan syndrome, is associated with life-threatening aortic root dissection. To mitigate this risk, initiation of prophylactic anti-hypertensive drug therapy is recommended. Atenolol, a beta blocker, is commonly utilized. Unfortunately, patients continue to have suboptimal response to drug therapy. The human organic cation uptake transporters (OCT) 1 and 2 are influx transporters involved in the uptake of atenolol. This objective of this study, Maximizing Atenolol Response through Functional Assessment iNvestigations (MARFAN), is to determine the role of genetic variants on the cellular uptake and clearance of atenolol, which may thereby affect drug disposition and clinical effect. This project will characterize the role of OCT1 and OCT2 on atenolol cellular uptake and test the hypothesis that OCT1 and OCT2 proteins with genetic polymorphisms, when expressed in vitro, will result in diminished cellular uptake of atenolol relative to the reference genotype. This approach will utilize transiently transfected OCT1 and OCT2 cell assays to perform time-dependent atenolol uptake experiments to generate kinetics parameters. The rationale for this study is to provide a mechanistic understanding of polymorphisms associated with OCT1 and OCT2 expression, and function as a means to individualize pharmacologic therapy for not only atenolol, but other OCT1 and OCT2-dependent drugs utilized in cardiovascular patients. Dr. Walton is supported by the mentorship of Jon Wagner, DO (Children's Mercy Hospital-Kansas City) and Bruno Hagenbuch, PhD (University of Kansas Medical Center).

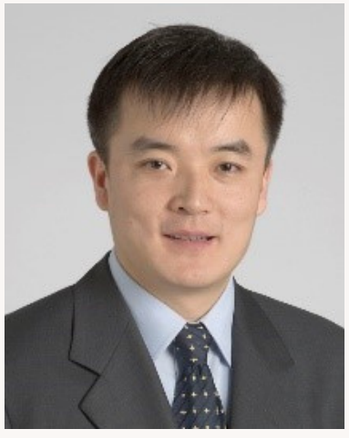
The VICE & UCSD MPRINT Hub Support Pool

The Support Pool is designed to fund innovative pilot or feasibility studies, or studies that address emerging needs or gaps in ongoing MPRINT projects. The goals of the study must align with the MPRINT mission, which is to foster and improve precision therapeutics in obstetrics, lactation, and pediatrics.

VICE Support Pool Awardee
Sudeep Sunthankar, MD, MSCI
Assistant Professor of Pediatric Cardiology, VUMC

Dr Sunthankar attended Medical University of South Carolina and completed his Residency in
Pediatrics at Vanderbilt University Medical Center, his Fellowship in Pediatric Cardiology and his M.S.C.I. at Vanderbilt University Medical Center.

Project: Genetic Implications for Transplant-Free Survival and Ventricular Function in Hypoplastic Right Heart Syndrome



VICE Support Pool Awardee
Yaomin Xu, PhD
Assistant Professor of Biostatistics and Biomedical Informatics, VUMC

Dr Xu received his PhD in Statistics at Case Western Reserve University, Cleveland, Ohio.
His research interests include translation bioinformatics, multivariate data analysis and visualization, unsupervised learning, cloud computing and big data analytics, biobanks and EHRs.

Project: Clonal Hematopoiesis of JAK2 Predisposes Pregnancy Complications in Pregnant Women

VICE Support Pool Awardee
Dr. Manaswitha Khare
Pediatric hospitalist, Rady Children's Hospital-San Diego
Associate physician at UC San Diego School of Medicine.

Dr. Khare completed her medical studies at Osmania Medical College in India. She then received clinical research certification at UC Irvine, where she served as a clinical research fellow, before completing her pediatric residency at the Icahn School of Medicine at Mount Sinai/Elmhurst Hospital. She then completed her pediatric hospital medicine fellowship at UC San Diego in the Division of Pediatric Hospital Medicine.

Project: The ability to assess and monitor airway inflammation in asthma can provide some insight on disease severity and inform variations in treatment response in ORCA

VICE Support Pool Awardee
Lauren Klein, MD
Pediatric Gastroenterology, Hepatology, and Nutrition, VUMC

Dr Klein attended the University of Virginia, Charlottesville, Virginia, and completed her Residency at Duke University, Durham, North Carolina. She completed Fellowships in Pediatric Gastroenterology, Hepatology, and Nutrition at Vanderbilt University Medical Center, Nashville, Tennessee and the Vanderbilt-Emory-Cornell Duke Fogarty Global Health Fellowship in Accra, Ghana, West Africa.

Project: Pilot Study to Predict Adverse Pregnancy Outcome in Pregnancies Complicated by Sickle Cell Disease

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VICE Support Pool Awardee
Thomas Reese, PharmD, PhD
Assistant Professor, Biomedical Informatics at VUMC

Dr Reese is a board-certified ambulatory care pharmacist and clinical informatician with a strong commitment to patient-oriented research. He was a fellow in the NCI's Multilevel Intervention Training Institute and trained on the National Library of Medicine T15 grant.

Project: Outcomes Associated with Receiving Prescription Stimulants During Buprenorphine Treatment in Pregnant Women

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UCSD Support Pool Awardee
Philip Gordts, M.S.c., PhD
Associate Professor
pgordts@health.ucsd.edu

Impact of Human Milk Oligosaccharides on Lipid Metabolism and Dyslipidemia

This project investigates the role of human milk oligosaccharides (HMOs), specifically 3'sialyllactose (3'SL), in lipid metabolism and the prevention of dyslipidemia, particularly hypertriglyceridemia, in infants and prospective mothers. Given that newborns and infants are regularly exposed to high-fat diets through breast milk, understanding how they avoid hypertriglyceridemia—a condition that poses risks of cardiovascular disease and pancreatitis in adults—becomes critical. Preliminary data indicate that 3'SL effectively reduces triglyceride-rich lipoproteins (TRLs) by enhancing their clearance from the liver. This project aims to explore two main objectives: (i) the role of 3'SL in facilitating TRL clearance via Syndecan-1 (SDC1) in the liver, and (ii) its potential to mitigate diet-induced intestinal inflammation and permeability, which may otherwise lead to increased liver SDC1 shedding.

The outcomes of this research could provide valuable insights into the mechanisms by which 3'SL modulates hyperlipidemia. Ultimately, the findings may support the development of 3'SL as a safe therapeutic option for managing hypertriglyceridemia, significantly benefiting the health of both infants and at-risk mothers.

UCSD Support Pool Awardee
Rashmi Dhital, MD
Instructor
Department of Medicine
Division of Rheumatology and Immunology
Vanderbilt University Medical
rashmi.dhital@vumc.org

Exploring the Impact of Autoimmune Rheumatic Diseases and Their Treatments on Human Milk Composition

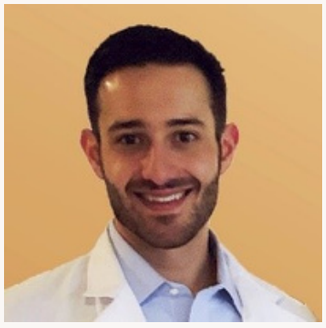
The World Health Organization recommends exclusive breastfeeding for the first six months, including for infants of mothers with autoimmune rheumatic diseases (ARDs). Milk constituents, including macronutrients (lipids, proteins, and carbohydrates), and micronutrients, serve essential roles such as nutrition, immune modulation, infection prevention, and reducing the risk of chronic diseases. Human milk oligosaccharides (HMOs) are complex carbohydrates that are unique to human milk and are non-nutritive but crucial for promoting protective bacterial species, blocking pathogen binding to the intestinal cell wall, protecting against gastroenteritis, and influencing infant physical and cognitive development, body composition, and the risks of allergies and asthma.

Systemic inflammation in ARDs may alter milk composition, similar to effects observed in other inflammatory conditions, partly due to alterations in the blood-milk barrier. Medications used to treat ARDs may also influence milk composition and potentially affect infant health. Given that ARD patients often exhibit deficiencies in serum Vitamin D and other micronutrients, it is possible that they also have lower levels of such micronutrients in breastmilk, indicating a need for targeted supplementation. However, data on these aspects are scarce to non-existent for the hundreds of thousands of women with ARDs who wish to breastfeed, underscoring the necessity and justification for investigating milk composition in lactating mothers with ARDs.

The primary objectives of the proposed project are to examine milk composition in individuals with ARDs, focusing on overall macronutrients (carbohydrates, lipids, proteins) and micronutrients, along with a comprehensive evaluation of HMOs among the milk carbohydrates. We aim to compare macronutrients in milk samples from breastfeeding women with ARDs (n=125) to milk samples from women without ARDs (n=125), matched on infant age and sex, and further examine variations in macronutrients in milk based on different ARD therapies. In the selected ARD subset with systemic lupus erythematosus (SLE) (n=15), we also aim to analyze HMOs and micronutrients, comparing them to samples from healthy control matched by infant age and sex.

This initiative will utilize the UCSD Milk Analytics Core and existing samples in the UCSD Human Milk Research Biorepository to address critical knowledge gaps relating to human milk composition in the ARD population. These efforts will collectively bridge knowledge gaps and inform clinical recommendations, potentially leading to personalized nutritional supplementation or modifications to maternal diet and infant feeding protocols to optimize nutrition and overall health for children born to mothers with ARDs.

The VICE Precision Therapeutics Academy 2024-2025



Mike Santarelli, MD
3rd Year Fellow, Pediatric Critical Care

Dr Santarelli attended Wake Forest School of Medicine and completed his Residency in Pediatrics at Vanderbilt University Medical Center. His academic interests include medical education, sepsis and septic shock and improving response to in-hospital clinical deterioration and resuscitation.

Megan Shuey, PhD
Research Assistant Professor, Clinical Pharmacology and Genetics
Dr Shuey earned her master's in Biological Sciences, Bacterial Genetics from Northern Arizona University, her PhD in Pharmacology from Vanderbilt, and completed a fellowship in Genetic Medicine at Vanderbilt. Her research focuses on identifying the genetic determinants of drug resistant hypertension.

Human Milk Institute Symposium 2025 - HMI'25

3rd Annual Kohlberg Johnson Family Human Milk Institute Symposium

Save the date

Monday March 4-Tuesday March 6, 2025
Scripps Seaside Forum, La Jolla, California

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Wei-Qi Wei, MD, PhD, FAMIA
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Vanderbilt University Medical Center

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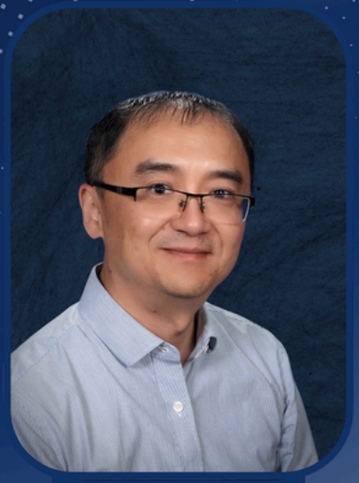

Professor
Center for Biomedical Informatics & Genomics
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Tulane University

Interpretable AI:
Data driven and mechanistic modeling for chemical toxicity and drug safety evaluations.

October 17, 2024
Thursday

2pm ET

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MARCH 19 – MARCH 21, 2025

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mprint2025
annual conference

may 14-16, 2025

nashville, tn

Open Proposal Submission

The 2024 MPRINT Annual Conference

DEADLINE
October 31, 2024

We are pleased to invite you to submit a proposal for the 4th Annual MPRINT Conference, taking place May 14-16, 2025, at the Homewood Suites Nashville Vanderbilt!

Hosted by the Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub, this conference serves as a platform for advancing research and collaborations in maternal and pediatric therapeutics. The MPRINT Hub invites proposals for workshops, panels, and research presentations.

Join us in shaping the future of maternal and pediatric precision therapeutics!

For more information visit: https://forms.office.com/r/eXEHjNrX7F