



March of Dimes Research Newsletter

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Dr. Emre Seli
Chief Scientific Officer
March of Dimes

From the desk of our Chief Scientific Officer

March of Dimes is entering a new phase of research and our programs will address the multi-faceted challenges in the U.S. maternal and infant health crisis. Diversified funding allows us to focus deeper on translational projects and take discoveries from the laboratory to clinical settings faster to provide lifesaving diagnostics and treatments to moms and babies.

Earlier this month, we announced the launch of the inaugural March of Dimes Research Center for Advancing Maternal Health Equity. The new Center, based at the University of Pennsylvania, will address poor health outcomes and longstanding racial disparities that make the U.S. among the most dangerous developed nations for childbirth. The Center will work collaboratively with researchers from March of Dimes Prematurity Research Centers, as well as experts from Historically Black Colleges and Universities, Tribal Colleges and Universities and Hispanic-Serving Institutions. It will launch under the leadership of Dr. Elizabeth A. Howell, Chair of the Department of Obstetrics and Gynecology at the University of Pennsylvania, and Chair of the Scientific Advisory Committee and Principal Investigator for the new Center. We look forward to providing updates on the Center's work in future newsletters.

In this newsletter, learn more about:

- **New Prematurity Research Center at the University of California San Francisco** will focus on data sharing, computational drug discovery and electronic medical record research to reduce rates of preterm birth.
- Global leader in maternal, infant nutrition receives **Agnes Higgins Award**: A look into the research of Dr. Nancy Krebs.
- **Researchers from the Imperial University** use lateral flow test (LFT) to detect cell-free microRNAs to predict preterm birth.
- **Giving back.** Learn why one of our generous donors supports March of Dimes research.

Thank you for helping to make this important research possible.

New Prematurity Research Center at the University of California San Francisco

Data sharing, computational drug discovery and electronic medical record research is the focus of March of Dimes new Prematurity Research Center (PRC) at the University of California San Francisco (UCSF). This new PRC launched in June 2022 and is part of an organizational shift to speed the pace of discovery to reduce rates of preterm birth in the U.S.

The UCSF PRC is under the direction of Dr. Marina Sirota, an associate professor in the Bakar Computational Health Sciences Institute and the department of Pediatrics at UCSF, and Dr. Tomiko Oskotsky, a senior research scientist in the Sirota Lab.

Dr. Sirota is a celebrated women's health computational scientist who also created a program to train minority high school students in the fields of AI and big data and has been part of the March of Dimes Stanford University Prematurity Research Center since 2014. She's been integral in using advanced computational techniques to glean new insights from various types of molecular data and beginning work on a data-sharing repository for preterm birth research.

"I'm honored to be a part of the March of Dimes prematurity research network, which has been making tremendous progress to uncover the root causes of prematurity through countless research projects over the years," said Dr. Sirota, who leads the center. "The resulting data from these inquiries, when looked at together through the lens of computational analytics, has the potential to lead to scientific discoveries that could one day drastically alter prematurity clinical care in this country and around the world."

The UCSF PRC will focus on three goals:

- 1. Expand data sharing:** March of Dimes Database for Preterm Birth Research, co-directed by Dr. Marina Sirota, an associate professor in the Bakar Computational Health Sciences Institute and the department of Pediatrics at UCSF, and Dr. Tomiko Oskotsky, a senior research scientist in the Sirota Lab, launched in 2020 to collect, organize and make public molecular data from all of the PRCs. The greater computational community is encouraged to use the data to make new discoveries that can address some of the toughest challenges in preterm birth research.
- 2. Computational drug repurposing:** Applying this groundbreaking technique that seeks to match existing, market-approved medications with previously unassociated medical conditions using publicly available data to moms at risk of delivering preterm, a first in the medical field.
- 3. Leveraging electronic medical records (EMR):** Across the University of California medical system, UCSF will apply advanced machine learning techniques to make new hypothesis about links between preterm birth and other maternal clinical features. The work will be expanded across the country and beyond to identify women at risk of future preterm birth and to develop appropriate interventions.

The UCSF PRC is part of the March of Dimes global network, with other locations at Imperial College, London; University of Pennsylvania; Stanford University; and the Ohio Collaborative (Cincinnati Children's Hospital Medical Center, Case Western Reserve and Vanderbilt University). Each of these centers channels its own expertise to investigate different assigned research themes.

Global leader in maternal, infant nutrition receives Agnes Higgins Award



Dr. Nancy Krebs

With more than 20 years of experience and 350 research and scholarly publications, Dr. Nancy Krebs from the University of Colorado School of Medicine, was awarded the Agnes Higgins Award at the Pediatrics Academics Society (PAS) Annual Meeting on April 21, 2022 in Denver, Colorado for her pioneering research on maternal and infant nutrition. The award was presented by Jonathan Cherry, March of Dimes' Senior Director of Research.

A prodigious researcher, Dr. Krebs' body of work has covered components of the entire 1,000 days, with focus on the impact of nutrition and feeding on impaired growth of breastfed infants and young children in the U.S. and international settings. She has conducted extensive research applying stable isotope methodologies to characterize zinc and iron homeostasis and requirements in vulnerable populations in austere settings consuming supplements, micronutrient powders, and biofortified foods.

"I am profoundly honored and humbled to join the esteemed group of Agnes Higgins award winners, many of whom I have looked up to throughout my career. This award affirms the value of rigorous research in expanding and refining the evidence base to impact the well-being of

women, children and infants," said Dr. Krebs. "My career in academic medicine has offered me incredible opportunities to be an inquirer, learner and teacher, and I hope more young people are inspired to continue to pursue their passions for equity and sustainability in nutrition, diet and health."

Dr. Krebs currently serves as the Head of the Division of Nutrition and Associate Vice Chair of Academic Affairs in the Department of Pediatrics at the University of Colorado School of Medicine. She received her Doctor of Medicine from the University of Colorado, and is board certified in General Pediatrics, Clinical Nutrition and Pediatric Gastroenterology. Her research has ranged from detailed metabolic studies of trace mineral metabolism across the life cycle to large scale nutrition randomized control trials. The intention of these studies has been to define dietary zinc requirements and to characterize homeostasis, including metabolic regulation and adaptation to different physiologic states in the average infant, specifically those who are breastfed, as well as pregnant and lactating women.

Along with being one of our country's preeminent nutrition thought leaders, Dr. Krebs' impact is also felt internationally. Her recent international research investigates the impact of a pre-conception maternal nutrition Intervention to improve fetal and infant growth in low resource settings in four countries.

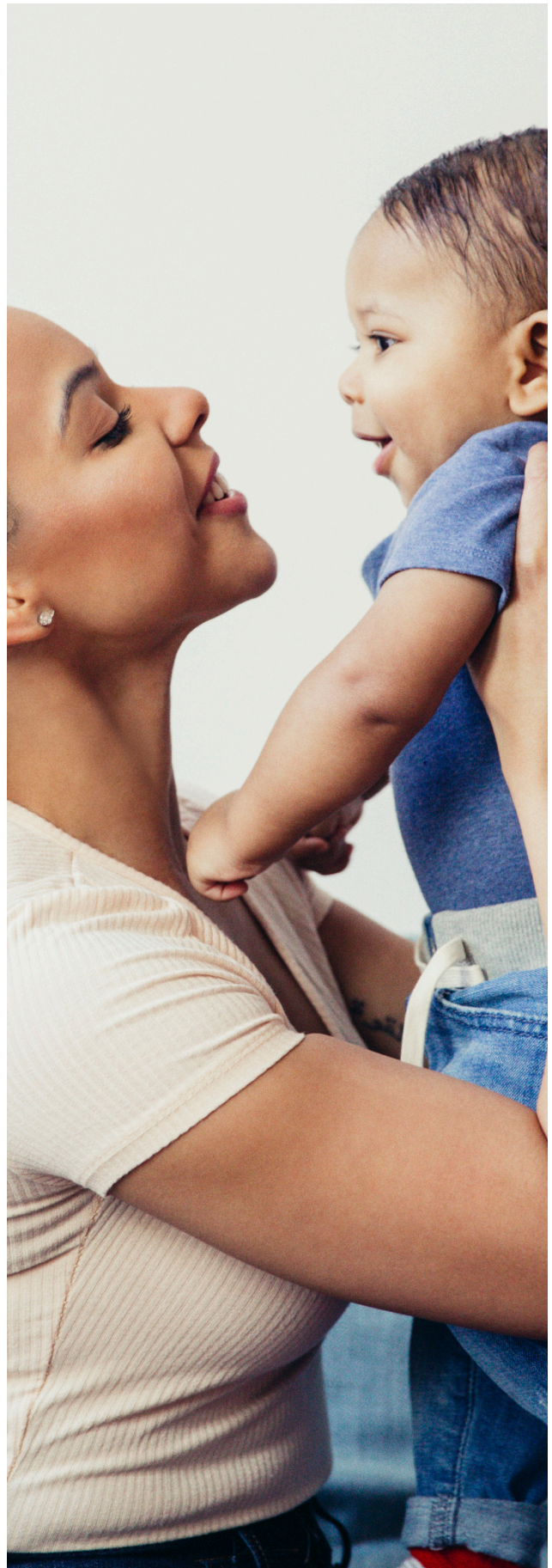
Considering how critical micronutrient nutrition is for fetal and postnatal immune and brain health, Dr. Krebs's work in micronutrient nutrition has influenced organizations such as the World Health Organization (WHO), American Academy of Pediatrics (AAP), and the National Institutes of Health, who funds her work. She has also advised the World Health Organization, the Bill and Melinda Gates Foundation and UNICEF.

Her work has also addressed populations with low breastfeeding rates and supported breastfeeding initiation and continuation, and she

has conducted extensive research applying zinc and iron requirements in vulnerable populations consuming supplements, micronutrient powders and biofortified foods. Most recently, she conducted international research investigating the impact of pre-conception maternal nutrition intervention to improve fetal and infant growth in low resource settings.

Dr. Krebs is not only a world-class researcher, but a phenomenal mentor and teacher. Her nomination noted that her students now populate major universities around the world as faculty members, both as teachers and researchers, as well as governmental and non-governmental agencies as policy makers. She has created a pipeline of research, advocacy, and teaching to influence generations going forward.

“As a research scientist, teacher, and subject matter expert, Dr. Krebs has dedicated her life’s work to advancing the field of maternal-infant nutrition and improving the health of our nation’s moms and babies,” said Dr. Emre Seli, Chief Scientific Officer at March of Dimes. “She exemplifies what the Agnes Higgins prize is all about and we’re grateful to her for her many contributions, including advancing our understanding of micronutrient nutrition in fetal and postnatal immune and brain health.”



March of Dimes awards two scientists the Basil O'Connor Research Grant for advancing maternal and infant health



Dr. Antonina Frolova



Dr. Isaac Marin-Valencia

Two early career scientists were selected as recipients of the 2022 Basil O'Connor Starter Scholar Research Awards: Dr. Antonina Frolova, MD, PhD from Washington University, St. Louis and Dr. Isaac Marin-Valencia, MD, MS from Icahn School of Medicine at Mount Sinai. These annual awards support outstanding investigators embarking on independent research careers who are committed to advancing the health of moms and babies. Named for the first March of Dimes chairman and president and now in its 27th year, the Basil O'Connor Starter Scholar Research Awards carry a \$150,000 grant.

The awards are part of March of Dimes' research strategy to address the multi-faceted nature of the maternal and infant health crisis with funding that supports discovery, translational and social science research, and data collection and analysis.

"We are proud to recognize these excellent investigators with this year's Basil O'Connor Starter Scholar Research Awards. This research will help bring critical discoveries from laboratories to patient bedsides and advance our understanding of medical conditions that impact moms and babies," said Dr. Emre Seli, Chief Scientific Officer at March of Dimes. "March of Dimes works to help every mom have a healthy pregnancy and give every baby the best possible start and research like this helps us get one step closer to the development of lifesaving diagnostics and treatments for all moms and babies."

Each investigator's research represents an important public health and research topic:

- Dr. Antonina Frolova's research focuses on the role of sphingosine-1-phosphate in preterm birth and addresses the prevention of preterm birth by exploring hormonal control of uterine contractions. This research award will examine a key element in the cascade of signals that transforms the uterine muscles from relaxed to laboring state. Dr. Frolova is an Assistant Professor at Washington University, St. Louis.
- Dr. Isaac Marin-Valencia's research aims to identify new therapies for neurodevelopmental mitochondrial diseases. The research will lay the foundation for significant improvements in the lives of infants born with pyruvate dehydrogenase deficiency (PDHD) by identifying both critical pathways of, and potential drugs to support one of the more common human mitochondrial diseases. Dr. Marin-Valencia is an Assistant Professor at the Icahn School of Medicine at Mount Sinai.

Improving sample preprocessing for earlier prediction of preterm birth

A practical and important development toward earlier bedside prediction of preterm birth (PTB) is presented by the March of Dimes Prematurity Research Center (PRC) at Imperial College London. In a new research article in *Advanced NanoBiomed Research*, studies conducted by Dr. Sylvain Ladame's group discovered and developed a way to incorporate the tricky and time-intensive preprocessing of a sample onto the test chip. This critical improvement reduces the risk of sample mishandling, contamination, and more importantly, drops the time from sample collection to risk-assessment. This means that healthcare providers will be able to shorten the time to providing care for at-risk moms and babies. These bedside tests build upon work from our PRCs to deliver point-of-care (POC) testing, analysis, and assessment of PTB risk as close to the patient and provider as possible. Beyond this specific test, the findings of the PRC will also improve other POC tests using similar biomarkers and sample materials. This discovery will help more than moms and babies, and truly unlocks the potential for better health for all of us.

Reach out to the March of Dimes Research Department for more information.



Research in action: On-site visits to our PRCs

By Jonathan Cherry, March of Dimes Senior Director Research Operations

Each year the research team travels to several Prematurity Research Centers (PRCs) for their annual site visits. These events involve external, non-March of Dimes reviewers, March of Dimes staff, and investigators from each PRC. During our visits, we learn about current progress, obstacles, and future plans for solving the complex issue of preterm birth. This also gives us a chance to have conversations about how those future plans align with the goals of March of Dimes over the next few years.

Over the past few months, we've had the incredible opportunity to visit Stanford University, University of Pennsylvania, and our newest PRC, University of California San Francisco (UCSF). In our next installment, we'll be on-site at Imperial College London and our Ohio collaborative, which includes University of Cincinnati Children's Hospital, Case Western Reserve University, and Vanderbilt University.

This season's visits highlighted several new discoveries.

The PRC at Stanford is digging into understanding and creating a new taxonomy for how we understand preterm birth and the impacts of our environment on birth outcomes. Dr. Aghaeepour's group identified several pro-inflammatory signaling pathways that are associated with preterm birth (PTB) through an integrated look at transcriptomics, metabolomics, and proteomics. This multi-omics approach is beginning to uncover how each factor contributes in different ways to PTB. The biology of pregnancy is incredibly complex—a fine balance of gene expression, silencing of proteins, and movement of metabolic products in and out of the cells can be the difference between a healthy term birth and a complicated and painful loss of pregnancy.

We're learning how psychosocial and stress-related factors affect pregnancy outcomes, including sleep quality and quantity, and further, how we can monitor and identify some of those signals earlier in the pregnancy journey to provide the proper health care.



Jonathan Cherry

Through machine learning models and new algorithms developed at the Stanford PRC, we're finding strong connections that we didn't know about between environment and PTB.

At the UCSF PRC, we heard how Dr. Sirota and team are gathering, organizing, and making sense of the mass quantities of data from our PRCs and other research groups through the **March of Dimes prematurity database**. This is a central repository for multiple data types (transcriptomics, genomics, microbiome, proteome, CYTOF, methylation, metabolize, etc). This allows us to probe for new scientific questions, enhance collaboration, pave the way for coordination among PRCs and external partners, and overall accelerate the pace of discovery.

This group has leveraged crowdsourcing to answer complex questions about how we can predict and identify those at a higher risk of PTB. This has led to new hypotheses concerning microbial diversity and specific strains of bacterial types that are associated with PTB. Additional work in computational drug discovery by the UCSF group has uncovered new opportunities

for re-purposing existing FDA approved drugs to reduce PTB. This approach uses incredible quantities of data to sift and sort through the vast pharmacopeia of options. The results are promising, with testing of a safe, available, and inexpensive treatment for reducing the impact of inflammation on pregnancy loss. More to come from this group!

Our most recent visit to the University of Pennsylvania PRC showcased this groups progress on the research themes of bioenergetics, extracellular vesicle signaling, and placental dysfunction. It also highlighted their commitment to research into the understanding of, and finding solutions to the issues of inequities in healthcare and adverse pregnancy outcomes. We learned about new discoveries that may use mitochondrial DNA, extracellular vesicle signatures, and other biomarkers as signals for early detection of PTB and some promising potential therapeutics for the same.

An addition to the PRC's presentation was an innovative approach to improving maternal outcomes. These approaches combine partnerships with community-based organizations and new technology options for remote monitoring of physiological signals of both mom and baby. Additionally, layered data from social determinants and environmental exposures is being used to enhance and improve the ability of healthcare providers to rapidly find patients who are most at risk and help them sooner.

A thread through all of our PRC site visits has been the close collaboration among PRCs and common goal of ending preventable preterm birth. Our investment in these research groups has been showing significant tangible outcomes by way of newly identified markers, in-development bedside tests, and critical identification of previously invisible factors impacting the health of moms and babies.

I couldn't be prouder to be a part of this organization.



Donor Feature



Fred and Emma Goltz

Fred and Emma Goltz began volunteering with March of Dimes following the birth of their twins, William and Kate. Emma went into unexplained preterm labor with the twins in 2004 and delivered them at 30 weeks. During their NICU stay, William was struggling with respiratory distress and was given surfactant—it saved his life. Fifteen months later, Emma went into preterm labor once again and delivered their daughter, Elsbeth, at 35 weeks.

The Goltzs were living in California's Bay Area at the time. Fred spent endless hours researching what went wrong with their pregnancies. When the twins were about six months old, Fred was walking through an airport and saw a sign connecting March of Dimes to prematurity. They credit March of Dimes with saving their son's life due to March of Dimes research that led to surfactant therapy.

Fred and Emma have been steadfast volunteers and donors as a way to show their gratitude. "We wanted no other family to go through what we had. Having gone through preterm labor

and having preterm infants, we were incredibly frustrated with the lack of answers for 90% of what we encountered on our journey," they said. "We don't know why women go into labor early, there are no drugs for them. March of Dimes is a very research driven organization and has ambitious goals for programs and advocacy for moms and babies."

The Goltz family has served in multiple local roles and significant national roles. Initially, they became involved through California's Bay Area March for Babies and quickly took on leadership roles at the local level such as chairing March For Babies and Signature Chef events, serving as an ambassador family, as well as Bay Area Board members.

Nationally, the Goltzs have made a major impact serving on the National Campaign To End Premature Birth Committee. In 2010, the Goltzs chaired the \$20M Prematurity Research Center Capital Campaign for Stanford. They connected March of Dimes to the right resources that led to a major gifts infrastructure being stood up within the organization. After moving to London, they continue to volunteer.

"We have volunteered for a long time and have gone on a journey with March of Dimes. The same way our children were infants in the NICU and are now freshman in college, March of Dimes has evolved during our time together. One of the most pivotal moments for us was the establishment of the Prematurity Research Center at Stanford. That similarly progressed to a conversation around major gift philanthropy and a different approach to medical research."

The Goltzs have helped transform the organization. Over the last three years, they provided their professional expertise, countless hours building strategy, invaluable guidance and significant funding to start the March of Dimes Innovation Fund.

The Innovation Fund is a venture philanthropy initiative to solve the world's most pressing maternal and infant health challenges by

developing therapeutics and diagnostics. The Fund is focused on our three goals of ending preventable preterm birth, ending preventable maternal mortality and ending the health equity gap. By investing in startup companies, we will accelerate our impact for maternal and infant health. Emma and Fred provided the leadership gift to launch the Innovation Fund and have volunteered hundreds of hours to build the vision, strategy, governance, processes and communications of the Fund from the ground up. Fred has an extensive background in private equity and business deals and Emma has a banking background and expertise in philanthropy that make them the perfect candidates to lead this effort. They have met with many donor prospects to share their vision for the Fund, which has resulted in new volunteers and additional revenue. They have applied all of their knowledge and skills in building out the Fund.

According to the Goltzs, “Philanthropy is changing and people are focused on impact. If you can use your philanthropy to further an organization’s mission while also making it stronger by taking it to the next level that feels like a win-win. If we invest in innovations that directly impact mission and also generate revenue to contribute to underwriting research, the fund is successful. One of the critical success factors in the Innovation Fund is March of Dimes’ credentials within the scientific community that comes from decades of supporting their work. This will allow us to continue our commitment to research well into the future.”

For close to two decades, the Goltzs have given March of Dimes the significant gift of time, leadership level gifts and guidance based on their professional and personal expertise to ensure each initiative with their involvement was and is successful. Their incredible commitment to service to March of Dimes was honored in 2022 when Fred and Emma were awarded the Elaine Whitelaw Volunteer Service Award, the most prestigious award March of Dimes presents to recognize a lifetime of distinguished volunteer service.

“We have gotten more from March of Dimes than we have given,” they said. “We have learned so much in our journey in terms of philanthropy, working with a mission driven organization and being involved with the research. We are helping support a mission we are still passionate about while participating in March of Dimes’ success.”