I’m excited about the future of research at March of Dimes, the foundation of our mission to improve the health of all moms and babies. The centerpiece of that mission is an integrated research agenda to address the multi-faceted maternal-infant health crisis facing our nation. This new agenda will look to both medical and social science research, with an emphasis on translational science, to evaluate and increase our understanding of the numerous factors that impact maternal and infant health, and help us develop programs and policy solutions to create positive change.

In this issue, we showcase one of the numerous grants currently underway through our Prematurity Research Centers. Thanks to extensive research on the placenta, we’ve increased our spectrum of understanding from the first molecules that mediate implantation at the start of pregnancy to immune tolerance of the genetically foreign placenta and baby to the pathways involved in preeclampsia, which can result in preterm birth. We look forward to the possibility of one day having effective treatments and new protocols based on this newfound knowledge.

We also debut three more stories—two about researchers who are diligently working on promising new areas of inquiry. The first research account details the effort to formulate a novel non-opioid neonatal abstinence syndrome (NAS) treatment and delivery option in newborns for clinical trials and FDA approval. The second feature is about how adding metabolomics to our integrative approach to prematurity research is helping us zero in on prematurity’s biological triggers. Finally, we’d like to introduce you to a some of our most inspiring donors whose work spans a dozen years, one of whom happens to be the board chair in Arizona and New Mexico.

As always, thank you for your kindness and generosity as you join us to fight for all families. Please enjoy reading the stories of these very special people.
March of Dimes is pleased to announce the recipient of the 2020 March of Dimes and Richard B. Johnston, Jr., MD, Prize in Developmental Biology is Dr. Susan Fisher for her breakthrough research in human placental biology.

The March of Dimes and Richard B. Johnston, Jr., MD, Prize in Developmental Biology recognizes an outstanding scientist who significantly advanced our understanding of the course of pregnancy, prenatal development and parturition. Dr. Susan Fisher has made a career of doing exactly that. Her most recent research on the human placenta and its role in preeclampsia and other events that lead to preterm labor, for which the Prize was awarded, stands on the shoulders of her lifetime of achievement.

“We’re delighted to honor Dr. Fisher with this year’s Prize,” said Dr. Rahul Gupta, Senior Vice President and Chief Medical and Health Officer and Interim Chief Scientific Officer at March of Dimes. “Her extensive research has transformed our understanding of the important role of the placenta in a healthy pregnancy, and fetal health and development.”

Dr. Fisher received her undergraduate degree from Hope College, where she began her research career as a plant biologist. Her work using biochemical approaches to study hormonal control of pea seedling growth ignited what would become a life-long fascination with laboratory-based investigations focused on development. But it was during her senior year that she began studying human rather than plant biology, and she quickly became excited about making contributions with direct medical relevance. She started a PhD program in human anatomy at the University of Michigan where she became acquainted with one of the human body’s most complex and enigmatic organs: the placenta. Ever since, she’s investigated mechanisms of human development, work that engaged her through the rest of graduate school and postdoctoral training at the University of Kentucky, and which continues to this day. She’s received numerous grants and awards for her discoveries. Along the way she rose through the ranks to become a full professor of Obstetrics, Gynecology and Reproductive Sciences at the University of California San Francisco.

Through extensive research on the placenta, Dr. Fisher has increased our knowledge of everything from the first molecules that mediate implantation at the onset of pregnancy to immune tolerance of the genetically foreign placenta and baby to the pathways involved in preeclampsia, which can result in preterm birth. It’s for her major and impactful scientific contributions—primarily in human placental biology, but also in stem cell-based, regenerative medicine therapies—that Dr. Fisher was awarded the Prize, one among many. Her work is published in more than 200 manuscripts reporting primary data as well as numerous reviews in top-tier journals. She’s also made a major commitment to graduate education and mentoring future generations of scientists. Her contributions extend outside the laboratory, serving her profession by increasing public awareness about the science of pregnancy.

Established in 1996, the Prize is named in recognition of Dr. Johnston, a former Medical Director at March of Dimes. Dr. Susan Fisher joins an impressive roster of more than 20 seminal researchers who’ve received this annual award. This Prize is part of March of Dimes’ efforts to spearhead and promote achievements in actionable science that turn observations from the laboratory into interventions that support the March of Dimes mission to fight for healthy moms and strong babies.
SUSAN FISHER, Ph.D.
Professor in Obstetrics, Gynecology and Reproductive Sciences
University of California, San Francisco
Doctors, nurses, social workers, psychologists and other caregivers see the tragedy of neonatal abstinence syndrome (NAS) happen daily right before their eyes. Babies become impacted when they’re exposed to heroin, morphine and other opiates in utero. And the moment they’re born or shortly afterwards, they begin suffering from the symptoms of withdrawal.

That’s also when treatment may begin—the same treatment as adults with a substance use disorder—a pharmacological cocktail that could include morphine, methadone, buprenorphine, clonidine and phenobarbital. All these drugs are unpleasant at best, and dangerous if not used appropriately. Their effects are much worse in babies because their immature nervous systems are much more sensitive and the long-term impacts are largely unknown.

Treating babies with these powerful drugs doesn’t sit well with many practitioners, but there aren’t any alternatives. That is, until Dr. Dean Carson’s research into neurodevelopmental and substance use disorders and his testing of the neuropeptide oxytocin as a possible treatment began to give reason for hope. His results were so promising that he shared them with Dr. Jonathan Davis, the Chief of Neonatology at Tufts who was also dissatisfied with the treatment options in the armamentaria. Dr. Davis emphasized that what was needed was one drug to treat a multitude of different withdrawal syndromes rather than the use of multiple drugs to treat the very complex withdrawal syndrome in these babies.

Which was exactly what Dr. Carson was doing: conducting research, not just on opioid withdrawal in the babies, but also withdrawal symptoms from other drugs, including benzodiazepines and antidepressants. It turned out that oxytocin had a positive effect across all of these different withdrawal syndromes in his animal models. As a bonus, he was also able to show that oxytocin actually improved developmental outcomes for anxiety, memory and social behavior.

Dr. Carson has been headed in this direction since he was an undergraduate at Australia’s University of New South Wales. Since then, he received his Ph.D. in neuropharmacology at the University of Sydney, completed postdoctoral training in pediatric psychopharmacology at Stanford University and has published extensively on the topic of oxytocin as a potential therapy for neurodevelopmental and substance use disorders. He understands the history of oxytocin, its use in obstetrics, and that it’s generally been shown to be safe and effective across a broad range of clinical indications in children and even infants. And that’s what’s especially important when treating a baby.

“It would be ideal if babies were never exposed to these drugs in the first place, but unfortunately they are. And currently treatments are suboptimal—there’s nothing at present that’s going to be able to effectively treat them in utero,” said Dr. Carson. “The first step is to conduct the appropriate clinical trials to determine the actual safety and efficacy profile of this novel treatment option, and then work towards getting FDA approval. March of Dimes is helping fund that effort.”

Dr. Carson’s work will begin with the development of the formulation specifically suited to a neonatal population that will then be taken into the clinic for testing.

Like most of the research March of Dimes funds, Dr. Carson’s work has a transdisciplinary aspect to it. Beyond OB/GYNs and neonatologists, he works closely with basic scientists, obstetricians, neonatologists, endocrinologists, urologists, psychiatrists, anesthesiologists and social scientists, as well. “We need to understand this complex disorder and every facet of the patient population,” he said. “That means considering the challenges faced by other disciplines outside of medicine, like social workers who are trying to help the babies transition out of the hospital and into home care. Having a non-narcotic treatment option that’s safe and effective will help with that transition.”

It’s estimated that 1 baby every 15 minutes is born with NAS in the U.S.—and that number seems to be increasing. March of Dimes is proud to work with Dr. Carson on his unique work in an area of such high unmet need. Clearly, these babies are caught in the crossfire of the opioid epidemic. They deserve a better chance at a healthy existence.
DEAN S. CARSON, Ph.D.
President and CEO of Katana Pharmaceuticals Inc.
ADDING METABOLOMICS TO OUR INTEGRATIVE APPROACH TO PREMATURITY RESEARCH

A Q&A with Karl Sylvester, MD, by Laura Hedli, Writer, Stanford University School of Medicine

How do your efforts with the Stanford Metabolic Health Center interface with those of the Stanford Prematurity Research Center (PRC)?

Dr. Sylvester: I think they’re very complimentary. Because of my membership in the PRC and also serving as a Co-Director of the Metabolic Health Center, I see really tight synergy.

There’s a multi-omics focus to a lot of what takes place in the PRC. One of those technologies is metabolomics, which we’re utilizing to profile the normal trajectory of a growing, developing fetus and for determining when that pattern is abnormal so that we can estimate a potential risk of preterm birth or growth restriction. Using one blood draw, we feel it will be possible to simultaneously create diagnostic and prognostic tests for pregnancy while simultaneously assessing a developing fetus for risk of acquired diseases of the newborn. Early on, we’ve derived very compelling data models using a metabolomics platform.

If we can make progress toward reducing preterm birth to an irreducible minimum, the question becomes: What can we say about the preterm or growth restricted newborn’s health risk after birth?

We think there’s a common theme that’s emerging: In a deliberate way, size matters. The smaller the newborn baby in terms of birth weight, the more biologic fragility, the more clinical risk. Now, we’re beginning to quantify those size-based risks through the lens of altered metabolism, and possibly provide the biologic mechanism for size-based risk. It will get really exciting when we come back to the strategy that the PRC has taken around prematurity and we start pulling in other omics and other molecular data pieces to solve the puzzle of prematurity and low-birthweight newborns.

How can you use metabolomics to assess a newborn’s risk?

Dr. Sylvester: Metabolomics may allow us to:

1. Quantify the degree of metabolic alterations in preterm and low-birthweight newborns at birth.
2. Understand the impact of microbial exposures and the required colonization of the newborn gut at birth. The microbiome of the gut is a whole area of focus for prematurity.
3. Assess the impact of type of birth, whether C-section or vaginal.
4. Understand how the NICU environment impacts for better or worse the metabolic machinery contributing to health or disease in the newborn.
5. Determine the impact of what and how much a newborn is fed on that newborn’s health and disease risk profile.

We’re very interested in developing the tools to determine a newborn’s comprehensive health and disease risk profile. Our anticipation is that these tools and the understanding they bring will enable us to develop strategies that will impact not only the newborn’s health trajectory but will persist across the lifespan.

I know you have an interest in probiotics for the newborns. Tell me more about how they may help alter a baby’s metabolism for the better.

Dr. Sylvester: To complement clinical care like feeding a newborn baby a specific probiotic with a known mechanism of action in the gut, we’re interested in developing the molecular tools to understand how that gut microbe is able to alter the majority of metabolites being produced in the gut. Because of the manner by which the probiotic metabolizes mother’s breast milk, the
metabolic by-products of this relationship have a significant health-benefitting effect. One of the many additional benefits of the probiotic is that it prevents its potentially trouble-causing cousin microbes from being able to move in and colonize the newborn’s gastrointestinal tract.

I think the example of probiotics highlights the types of insight into intervention based upon the biology of metabolism that we’d like to provide using metabolomics. Since growth and nutrition are so critical to a baby’s earliest weeks and months, this represents a tremendous opportunity that metabolomics is helping us to understand and quantify.

What do you think is underappreciated about metabolism in relation to prematurity?

Dr. Sylvester: The current metrics of healthy growth are based upon population norms that are unlikely to be universally applicable. Measurements of length, weight and head circumference have been used to describe “normal,” but what constitutes normal is different depending on the standard and the specifics of the population to which they are applied. We have some early data to suggest those measurements are not as sensitive as perhaps molecular or metabolic indicators are when we think in terms of understanding healthy growth and risk of disease. We are beginning to re-think some long-held clinical strategies, and develop a finer way to interpret how newborns are thriving from a metabolism perspective in the critical first weeks of life.

For the full study, see the link below:
KARL SYLVESTER, MD
Professor of Surgery (Pediatric Surgery)
Stanford University Medical Center
AFTER THE NICU, GIVING BACK

Too many new families start out in the NICU. Sixteen years after their own NICU ordeal, Kelly and Dave Damron are still working to spare others the same experience.

Kelly and Dave Damron’s twin girls, Kaley and Ashley, are now 16—but they were born at just 30 weeks. Ashley had few problems, but her older sister wasn’t so lucky. While both girls spent seven weeks in the NICU, Kaley contracted necrotizing enterocolitis, or NEC, a life-threatening disease that attacks the intestines of preterm babies. That happened on day nine.

In week four, doctors removed a significant portion of Kaley’s large intestine, which caused significant scarring, followed by nearly six months with a colostomy bag. She had a final operation when she no longer needed the bag and she’s been a normal, healthy kid ever since. In fact, both girls are now thriving teenagers involved in sports and after-school activities.

Even though Dave, Kelly and their twins endured what no family should have to, they all survived. That experience changed them in many ways—one of which was to raise awareness and empathy for other families who have to undergo their own version of that trial.

“We did the very first March for Babies after the twins were born and literally have done every walk since. That’s kind of where our volunteerism started,” said Kelly. “We served on different committees here and there, and then later, Dave joined the board for the Arizona/New Mexico region, and is currently serving his third year as Board Chair. So we’ve really been involved with March of Dimes pretty much continuously since we brought the girls home. We wanted to do something that would spare other parents the ordeal we went through.”

At March of Dimes, we believe every mom, baby and family deserves the best possible start. That’s why this research into eliminating preterm birth is so important, and why donors like the Damrons are so vital to the cause. Their commitment and generosity are unmatched and make the difference for so many families like them.

“The birth of your children obviously changes your life, but our experience in the NICU took that to a whole other level,” said Dave. “Couples go through an emotional and medical rollercoaster when they’re in the NICU. And it just ripped us apart to see parents going through experiences that were far worse than what we were going through—and that’s saying something, given the surgeries Kaley had to have. We don’t want anybody to go through that. That’s why we’ve stayed involved with March of Dimes for as long as we have.”
KELLY, DAVE, KALEY AND ASHLEY DAMRON, thriving prematurity survivors
Congratulations to March of Dimes current grantees who include experts working on everything from development of antibodies to prevent NEC and an aspirin regimen for preeclampsia to addressing racial and health disparities in birth outcomes and so much more.

- Khosrow Adeli, Ph.D., The Hospital for Sick Children
- Rupsa Boelig, MD, Ph.D.
- Dean Carson, Ph.D., Katana Pharmaceuticals
- Jennifer Condon, Ph.D., Wayne State University
- Andrea Edlow, MD, MSc, Harvard Medical School
- Richard Frank, Ph.D., Harvard Medical School
- Professor Ehud Gazit, Tel Aviv University
- Anu Manchikanti Gomez, Ph.D., MSc, UC Berkeley
- Drew Hall, MS, UCSD
- Timothy Hand, MD, CHOP
- Margaret Hicken, Ph.D., University of Michigan
- Elizabeth Howell, MD, MPP, University of Pennsylvania
- Haiden Huskamp, Ph.D., Harvard Medical School
- Fleda Jackson, Majaica, LLC
- Kelly Jones, Ph.D., Institute for Women’s Policy
- Deborah Karasek, Ph.D., UCSF
- Michael Kramer, Ph.D., Emory School of Medicine
- Miriam Kupperman, Ph.D, UCSF
- Louise Laurent, MD, Ph.D.
- Michael J. Morowitz, MD
  UPMC Children’s Hospital of Pittsburgh
- Sam Parry, MD, University of Pennsylvania
- Rebecca Simmons, MD, University of Pennsylvania
- Norman Waitzman, Ph.D., University of Utah

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For more information on how you can be a part of this effort, please contact:

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