

Quarterly Publication

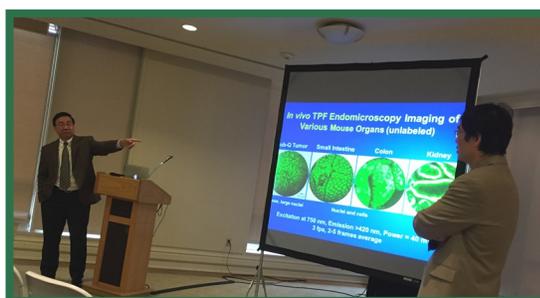
Issue 01 Fall 2016

## Prematurity Research Center “Thinks” Outside the Box

The inaugural Prematurity Think Tank Symposium was held April 20-21, 2016 at the Washington University School of Medicine campus. This event was designed to foster new collaboration by bringing together outside investigators as an expert panel to conceptualize, deliberate, and analyze the transdisciplinary approach to preterm birth research performed at the March of Dimes Prematurity Research Center (PRC). With diverse research backgrounds, the expert panel included Jerome Strauss, MD, PhD (Virginia Commonwealth University); Xingde Li, PhD (Johns Hopkins University); Marcus Raichle, MD (Washington University); and Till Roenneberg, PhD (Ludwig-Maximilian University). The symposium included a lecture series, breakout sessions, and group discussions on current and future PRC projects.

Approximately 100 people attended the lecture series, including faculty, staff, and students from across the Washington University campuses. Members of the local and national March of Dimes offices were also present. Audience members heard from the expert panel and the PRC investi-

gators on a variety of research projects and how they relate to preterm birth. Following the lecture series, internal breakout sessions convened. Each expert was paired with one of the three research themes to hear about the pro-



*Xingde Li, PhD from Johns Hopkins and Lihong Wang, PhD from Washington University*

gress of the projects and give feedback. The breakout sessions helped PRC investigators focus on new elements of the research projects and address current challenges.

On the second day of the symposium, the group assembled to discuss what was learned and next steps for each PRC project. The invited guests were enthusiastic about providing guidance on hypotheses and outcomes to measure, and have remained in contact with the investigators, with plans to continue collaborations and discussions. The next Prematurity Think Tank Symposium will be held in 2018.

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### Upcoming Events

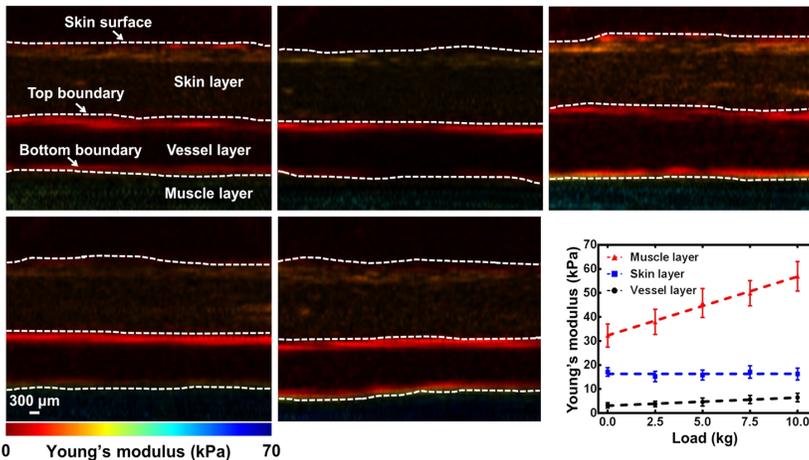
- January 23-28, 2017**  
Society for Maternal-Fetal Medicine 37th Annual Meeting  
Las Vegas, NV
- March 15-18, 2017**  
Society for Reproductive Investigation 64th Annual Scientific Meeting  
Orlando, FL

For more information about the March of Dimes Prematurity Research Center at Washington University in St. Louis please visit:

<http://prematurityresearch.org/washu-stlouis/>

## Publication Highlight

Engineers have moved the field of photoacoustic elastography forward in Lihong Wang's lab in Biomedical Engineering at Washington University in St. Louis.



“We have developed a new generation of photoacoustic elastography which further improves the technology. The previous generation only produces a relative measure of stiffness and cannot monitor cervical stiffness at different time points. By adding a reference stress sensor, the new generation, named quantitative photoacoustic elastography (QPAE), provides a numeric measure of tissue stiffness on an absolute scale. It allows long term monitoring of cervical stiffness during pregnancy,” said Pengfei Hai, first author on the project.

QPAE of a human biceps muscle *in vivo*.

Photoacoustic elastography measures tissue stiffness by adding a virtual sense of touch to photoacoustic imaging. By observing differences in tissue deformation under pressure, photoacoustic elastography distinguishes soft regions from rigid ones. This information is useful because alterations in tissue stiffness are often associated with disease. It generates a precise map of tissue stiffness, providing physicians with accurate data that can be used for diagnosis.

Cervical stiffness changes dramatically during pregnancy. An early change in this stiffness may be an indicator of preterm birth. By using photoacoustic endoscopy with elastography to measure cervical stiffness, obstetricians may have a better understanding of how cervical changes happen in preterm vs. term births.

The work, supported in part by the March of Dimes Prematurity Research Center, can be found at:

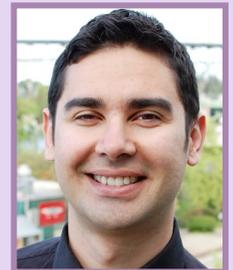
Hai P, Zhou Y, Gong L, Wang LV. *Quantitative photoacoustic elastography in humans*. J Biomed Opt. 2016 Jun 1;21(6):66011

Hai P, Yao J, Li G, Li C, Wang LV. *Photoacoustic elastography*. Opt Lett. 2016 Feb 15;41(4):725-8.

### March of Dimes Preterm Birth Scholars Program

In May of 2015, we announced a call for applications for the March of Dimes Preterm Birth Scholars Program, a two-year program for young investigators (MD, PhD, or equivalent) to be immersed in intense multi-disciplinary training among the three PRC research themes, with mentorship from one of the PIs. Candidates with intense interest in preterm birth were considered from all scientific fields.

After reviewing all candidates, we are happy to welcome **Utku Baran, PhD**, as the first Preterm Birth Scholar at Washington University. He joined Lihong Wang's lab in July 2016 after completing his PhD in Electrical Engineering at the University of Washington in Seattle. He has over three years of experience in biomedical optics, 15 first-authored journal publications to date, and has developed innovative designs and algorithms resulting in 1 granted and 2 pending US patents. He has extensive experience working with clinicians and human subjects developing quantitative optical imaging technologies for dermatology and neuroscience applications, and looks forward to applying his skillset to preterm birth research. Welcome, Dr. Baran!



Utku Baran, PhD

## Pilot Grant Funding Mechanism Announces Two New Awardees

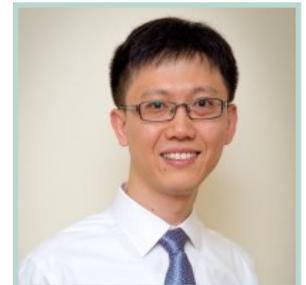
This past spring, the PRC Education Core called for applications to the Transdisciplinary Developmental Funding program. Faculty in any discipline within the Washington University community were encouraged to apply, to explore high-risk ideas related to preterm birth that will generate preliminary data for subsequent extramural applications to the NIH or to non-governmental foundations.



*Molly Stout, MD*

**Molly Stout, MD**, of the department of OB/GYN, was awarded one grant, for her proposal entitled “Preterm Birth: Interface Between Viruses, Bacteria, and the Maternal Host.” This grant will allow investigators to examine the connection between vaginal viral communities, either by themselves or through their interaction with the vaginal microbiome and maternal host, and preterm birth. Dr. Stout will pursue this work with co-investigators Kristine Wylie, MD (Pediatrics), George Macones, MD (OB/GYN), Methodius Tuuli, MD (OB/GYN), and Todd Wylie (Pediatrics). The analysis will capitalize on a completely assembled prospective cohort of pregnant women with full clinical data, completed obstetric outcomes, and serially collected vaginal samples.

The second proposal funded is titled “Noninvasively measure the cervix mechanical properties using magnetic resonance elastography,” by **Yong Wang, PhD**, of the department of OB/GYN. Co-investigators include Alison Cahill, MD (OB/GYN), Philip Bayly, PhD (Mechanical Engineering), and Qing Wang, PhD (Radiology). The goal of this proposal is to utilize MRI and shear wave technology to examine cervical remodeling, which Dr. Wang hopes will inform the understanding of how the cervix changes during pregnancy.



*Yong Wang, PhD*

These pilot awards were funded at \$25,000 for one year, beginning June 15, 2016, with matching funds from the department. A second year of support will be based on a progress report, yielding a potential for \$100,000 per grant.

In 2015, pilot grants were awarded to Zorimar Rivera-Nunez, PhD (Brown School) and, jointly, to Christopher Smyser, MD (Neurology and Pediatrics) and David Limbrick, MD, PhD (Neurosurgery and Pediatrics).

## Fox 2 News Interviews Emily Jungheim



In August, Emily Jungheim, MD, a reproductive endocrinologist and Theme 3 investigator, interviewed with Fox 2 News to discuss a study currently underway at Washington University. Dr. Jungheim and the other Theme 3 investigators are looking to see if any association exists between the disruption of circadian rhythm during pregnancy and preterm birth. The participants in this study have hormone levels measured in their saliva before and during

pregnancy, and wear activity watches to track exercise and sleep patterns. This study targets women who are looking to become pregnant and follows them throughout pregnancy until delivery. For more information on participation in this study, call or text 314-250-0360 or email [timetodeliver@wudosis.wustl.edu](mailto:timetodeliver@wudosis.wustl.edu).

## Thank You to Barnes Jewish Hospital!

In the fall of 2015, Barnes Jewish Hospital generously donated space in the OB/GYN clinic in the Center for Outpatient Health to the Prematurity Research Center for a new patient exam room, to be exclusively used for participants of PRC research studies. This past summer, the exam space was renovated to house all necessary equipment for both clinical and research projects. The new room will be utilized as a space for all future PRC clinical studies, including the 1000 Women Cohort which begins in 2017. The cohort will be recruited over the course of two and a half years, to study various measurements in women throughout the duration of their pregnancies in order to determine

which ones correlate to preterm birth. Because participants will come in for approximately six additional study visits (timed with their regular prenatal OB appointments), having a dedicated space is paramount for patient comfort. The new exam room will allow up to 40 study visits per week without interrupting usual clinic practices.



### Investigator Highlight



*Phillip Cuculich, MD*

Phillip Cuculich, MD, Associate Professor of Medicine in the Cardiovascular Division at Washington University School of Medicine is one of the leaders of Theme 2, working to develop a noninvasive electrical imaging tool to study uterine contractions and preterm birth. Dr. Cuculich comes to Theme 2 from a cardiac electrophysiology background, where he treats patients with heart rhythm disorders. In collaboration with Dr. Yoram Rudy (Biomedical Engineering), Dr. Cuculich has developed a noninvasive cardiac imaging method called electrocardiographic imaging, or ECGI, which allows panoramic electrical mapping of the heart in a single beat. In partnership with the Theme 2 leaders (Dr. Alison Cahill, Dr. Yong Wang, Dr. Alan Schwartz), Dr. Cuculich has applied similar noninvasive electrical mapping principles to study the electrical activation of the uterus. The team has been working for over two years to develop and test this new system, called electromyometrial imaging, fondly known as EMMI. The ultimate goal is to assess whether an “electrical maturation” of the uterus can be measured and how this maturation contributes to preterm birth mechanisms. Clinically, EMMI may help rapidly triage patients with premature uterine contractions and may open new avenues for electrically based therapies to halt the progression of labor that results in premature birth. “We are looking for ways to move human health forward on a global scale by applying concepts from the heart to the uterus, and if we get it right, it will make a dramatic impact.”

***“We are looking for ways to move human health forward on a global scale, and if we get it right, it will make a dramatic impact.”***

Dr. Cuculich enjoys exploring how different fields of medicine and science can be combined to drive new clinically-oriented discoveries. His other main areas of research explore ways to use cancer therapies to treat heart rhythm disorders. Outside of work, he enjoys raising his three sons, Bennett (9), Reid (4) and Grant (2), with his wife, Jennifer, who happens to be a neonatologist and genetic epidemiology researcher in the Department of Pediatrics. “Jen cares deeply for the premature babies and their families. Selfishly speaking, if EMMI can help prevent prematurity, it could make my wife’s job easier!”

## National Academy of Medicine Elects George Macones



*George Macones, MD, MSCE*

George Macones, MD, MSCE, program director for the Prematurity Research Center, was recently elected to the National Academy of Medicine, a part of the National Academy of Sciences. Dr. Macones is the Mitchell and Elaine Yanow Professor and chairman of the Department of Obstetrics and Gynecology at Washington University School of Medicine. He is among 79 other physicians, nationally and internationally, whose election was announced October 17, 2016. The National Academy of Medicine elects new members based on their contributions to public health, health care, and medical science. Dr. Macones is the author of over 300 scientific articles, and is known for his extensive work on vaginal deliveries after cesarean section, and on developing guidelines to monitor fetuses during labor.

### Presentations and Posters

- 11/15/15: Junjie Yao, Photoacoustic imaging with superb resolution, speed, and sensitivity. 9th IEEE International Conference on Nano/Molecular Medicine and Engineering, Waikiki Beach, HI
- 2/13/16: Junjie Yao, Reversibly switchable photoacoustic tomography using a genetically-encoded near-infrared phytochrome. 2016 SPIE Photonics West Conference, San Francisco, CA
- 2/14/16: Pengfei Hai, Vascular elastic photoacoustic tomography in humans. 2016 SPIE Photonics West Conference, San Francisco, CA
- 3/17/16: Carmel Martin-Fairey, Clock genes regulate circadian gating of parturition and gestation length. Society for Reproductive Investigation 63rd Annual Scientific Meeting, Montreal, QC, Canada
- 3/19/16: Carmel Martin-Fairey, Chronotype changes during pregnancy. Society for Reproductive Investigation 63rd Annual Scientific Meeting, Montreal, QC, Canada
- 3/19/16: Darcey Broughton and Emily Jungheim, Shifts to and from Daylight Saving Time and In Vitro Fertilization (IVF) Outcomes. Society for Reproductive Investigation 63rd Annual Scientific Meeting, Montreal, QC, Canada
- 4/20/16: Lihong Wang, High-speed functional photoacoustic endoscopy for assessment of cervical remodeling. Prematurity Think Tank Symposium, St. Louis, MO
- 4/20/16: Phillip Cuculich, Three-dimensional electrophysiology of the uterus. Prematurity Think Tank Symposium, St. Louis, MO
- 4/20/16: Erik Herzog, Chronodisruption and risk of preterm birth. Prematurity Think Tank Symposium, St. Louis, MO
- 5/1/16: Lihong Wang, High-speed functional photoacoustic endoscopy for assessment of cervical remodeling. Pediatric Academic Societies Meeting, Novel Imaging Technologies to Study Preterm Birth Symposium, Baltimore, MD
- 5/1/16: Phillip Cuculich, Three-dimensional electrophysiology of the uterus. Pediatric Academic Societies Meeting, Novel Imaging Technologies to Study Preterm Birth Symposium, Baltimore, MD
- 5/4/16: Erik Herzog, Chronodisruption and the risk of preterm birth. MOD PRC-Ohio Collaborative Data Meeting, Via WebEx
- 5/23/16: Carmel Martin-Fairey, Chronodisruption and risk of preterm birth. Society for Research on Biological Rhythms Annual Meeting, Palm Harbor, FL
- 5/23/16: Vania Carmona-Alcocer, Otogeny of circadian synchrony in the SCN. Society for Research on Biological Rhythms Annual Meeting, Palm Harbor, FL
- 5/24/16: Erik Herzog, Assembling a Clock System: Otogeny of Circadian Synchrony in the SCN. Society for Research on Biological Rhythms Annual Meeting, Palm Harbor, FL
- 5/26/16: Sarah England, Unlocking the Mysteries of Preterm Birth. MOD Stewardship Event, Kansas City, MO
- 6/1/16: George Macones, Unlocking the Mysteries of Preterm Birth. MOD Regional Leadership Meeting, St. Louis, MO
- 9/21/16: Erik Herzog, Assembling internal time: Circadian synchronization in utero. Center for Chronobiology Symposium, Cincinnati Children's Hospital, Cincinnati, OH