

Beyond the biopsy

Monitoring heart transplant rejection with a blood test

For patients who've had a heart transplant, the first postoperative year is filled with as many as a dozen biopsies to check for allograft rejection. The current gold standard for monitoring rejection is catheter-based endomyocardial biopsy (EMB), which is associated with some risk and considerable expense. In addition, a single tissue sample doesn't always identify rejection underway in other parts of the heart. Yet early detection of rejection is critical in improving outcomes.

A BETTER WAY

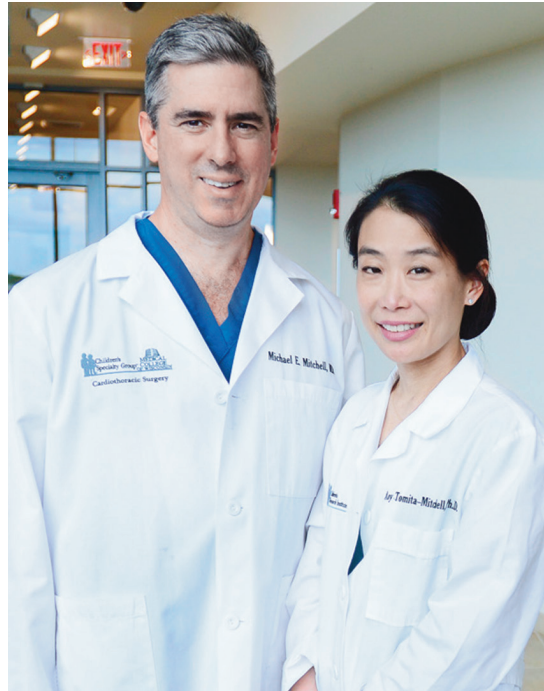
A new blood test developed by a team led by Michael E. Mitchell, MD, cardiothoracic surgeon at the Herma Heart Institute at Children's Hospital of Wisconsin, and Aoy Tomita-Mitchell, PhD, professor of pediatric cardiothoracic surgery and biomedical engineering at the Medical College of Wisconsin and investigator for the Children's Hospital of Wisconsin Research Institute, could dramatically improve the identification of early transplant rejection.

The test uses quantitative genotyping to measure donor-specific cell-free DNA (cf-DNA), fragments of normal cell turnover, cellular injury and inflammation. The fraction of cell-free DNA increases with injury to the donor organ, providing an early warning system of potential rejection.

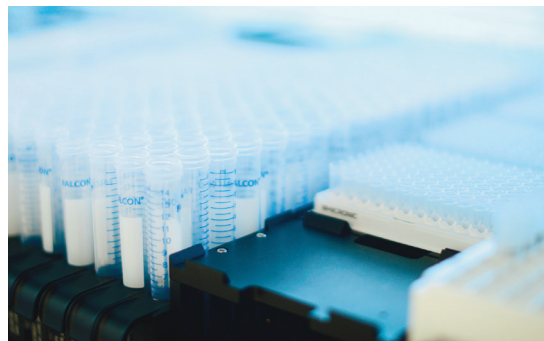
A PROMISING START

Dr. Mitchell was the principal investigator on a prospective, blinded pilot study that collected 53 blood and biopsy samples from 32 pediatric transplant patients who had undergone

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Michael E. Mitchell, MD, and Aoy Tomita-Mitchell, PhD, are each inventors of the DNA-based test and each hold leadership positions at TAI Diagnostics, Inc., as the chief clinical advisor and the chief scientific officer, respectively.



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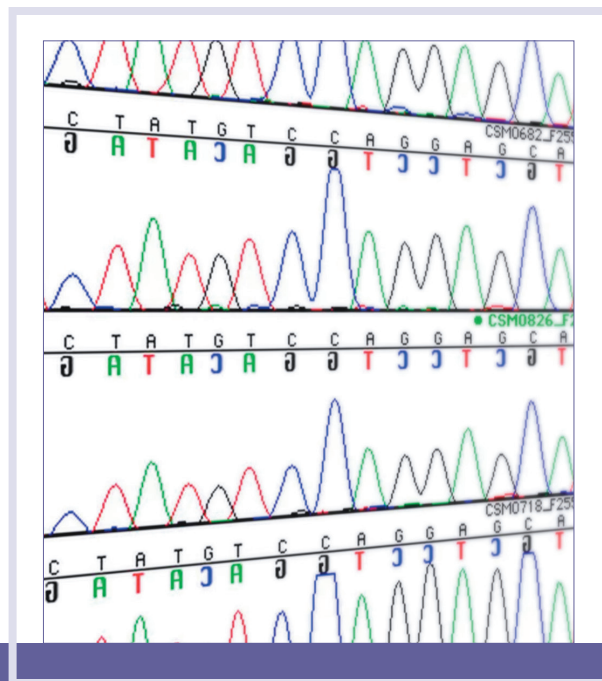
scheduled surveillance EMB, unscheduled diagnostic EMB because they were symptomatic, or those with proven rejection (samples collected before, during and one week after treatment). Find the study at ncbi.nlm.nih.gov/pmc/articles/PMC4988656.

All patients diagnosed with rejection demonstrated elevated levels of donor cf-DNA, with no rejection seen in those with levels less than 1%. In conclusion, results showed that quantifying cf-DNA “constitutes a sensitive, rapid and cost-effective non-invasive tool potentially suitable for rejection surveillance as an alternative to EMB.”

“We’re hoping to dramatically decrease the need for surveillance biopsy, which is invasive and potentially dangerous, while also increasing the frequency of monitoring so we can ensure the health of the donor heart,” Dr. Mitchell says. “The earlier you identify rejection, the more likely it is that you can stop it.”

Dr. Mitchell and his team are now investigating the test in a larger clinical trial involving 480 adult and pediatric heart transplant patients at five hospitals around the country. Find the trial at clinicaltrials.gov/ct2/show/NCT02109575.

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The blood test uses quantitative genotyping to measure donor-specific cell-free DNA.

In good company

Michael E. Mitchell, MD, is a cardiothoracic surgeon at Children’s Hospital of Wisconsin and a professor and section chief of pediatric cardiothoracic surgery at the Medical College of Wisconsin. Dr. Mitchell has a special interest in neonatal cardiovascular surgery, pediatric valve reconstruction, heart transplantation and tracheal reconstruction.

Aoy Tomita-Mitchell, PhD, is a medical researcher at Children’s Research Institute and a professor of pediatric cardiothoracic surgery and biomedical

engineering at the Medical College of Wisconsin. Dr. Tomita-Mitchell has a special interest in cell and developmental biology, heart disease and solid organ transplantation.

In addition to dedicating their careers to Children’s, the couple co-founded TAI Diagnostics, Inc., a biotechnology company that uses proprietary technology to test for donor rejection in a more accurate and less invasive manner, potentially improving the lives of transplant patients everywhere.

Children’s Hospital of Wisconsin has a financial interest in TAI Diagnostics, Inc.

The value of collaboration

When we work together to care for children, everyone benefits

Collaboration is one of Children's Hospital of Wisconsin's five core values. When effective collaboration is practiced, everyone benefits, according to Carey A. Ehlert, MD, a neonatologist at Children's, director of provider experience for Children's Specialty Group and associate professor of Neonatology at the Medical College of Wisconsin.

PRACTICING COLLABORATION

Collaboration occurs across all functions at Children's, from patient care and advocacy to hospital initiatives and policies. "By having a network of people around us who are experts in their individual fields, we can all come together to provide the best care for our patients and our families," Dr. Ehlert explains. "That includes working both internally with each other and externally with our referring providers."

Bringing that network together requires keeping the lines of communication open. We communicate with providers regularly at Children's weekly grand rounds, and we also reach a broad range of providers via continuing medical education events throughout the year.

To collaborate effectively, we must recognize that communication goes both ways. "We have to keep our minds open to all the different perspectives that others bring to the table," Dr. Ehlert adds. "We have to stay curious, and by doing so, we continue to learn from each other."

In this spirit, Children's also continues to seek feedback from referring providers, with two quick specialty-specific surveys and the bi-annual referring provider survey coming out later in 2019. "We are the only organization that is taking that specialty-specific approach to

referring provider feedback that we know of," Dr. Ehlert says.

PATIENTS BENEFIT THE MOST

Working with specialists within the hospital and reaching out to referring providers results in the best quality of care for patients. Referring providers have a deep understanding of their patients, and we work to make sure that knowledge and history is seamlessly transferred. "It gives our specialist the opportunity to understand the entire patient and what could be contributing to the specific problem for which they're coming to us," Dr. Ehlert says.

Learn more about the values that guide and inspire us at chw.org/about/mission-and-values.

ONGOING EFFORTS

Children's has several upcoming opportunities for continuing education, including the Best Practices conference in March. (See page 13.) Look for communications about referring provider surveys to come by email later this year.

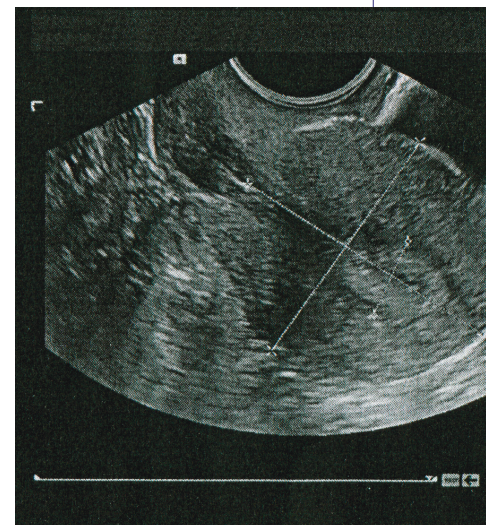


Cutting-edge heart care begins before birth

Over the past decades, Children's Hospital of Wisconsin has built one of the premier fetal heart programs in the country. Today, all fetal cardiac imaging is performed in the Fetal Concerns Center, located right across the hall from the Herma Heart Institute, and Children's renowned cardiology care spans from the fetal stage through adulthood.

Pediatric Rounds interviewed Michele Frommelt, MD, about the program's innovations in imaging, diagnosing and treating fetal heart conditions.

Read the article at chw.org/fetal-heart.



Comprehensive spine care

Focused, multidisciplinary program surrounds patients with care

A number of conditions can affect a child's spine

health and function as they develop from birth through adolescence. Fortunately, Children's Hospital of Wisconsin has a comprehensive, multidisciplinary program that can address all spine disorders, whether they are congenital, idiopathic, or the result of illness or injury.

A UNIQUE PROGRAM

Children's holistic spine program is unique in how we leverage expertise from multiple specialties. Patients and families referred to the spine program will experience a seamless coordination of care, removing the stress of finding specialists or bridging communications between physicians. Referring providers will also be kept apprised of treatment decisions.

Specialties including orthopedics, neurosurgery, physical medicine and rehabilitation, sports medicine, and physical and occupational therapy all contribute dedicated spine specialists to the program. Experienced triage nurses will assist referred families in finding the right level and type of care, while our nurse navigators will help guide patients and families through their care experience.

WHAT WE TREAT

Here are some of the common neck and spine conditions the specialists at Children's can address:

- Birth injuries of the neck, back or spine
- Congenital deformity or malformation
- Head and spine trauma
- Scoliosis
- Spina bifida
- Spondylolisthesis
- Spondylolysis
- Sprains or strains in the back, neck or spine

Learn more about the spine program and find a full list of conditions we treat at chw.org/spine. You may submit a referral to the spine program through the EHR, or call Children's directly at (414) 33-SPINE (77463).



Fracture care close to home

Same-day fracture care is available with Children's Hospital of Wisconsin's pediatric orthopedic specialists at four convenient locations with expansion to Kenosha once a week. Care is simplified and streamlined thanks to onsite services such as radiology, which allow for evaluation, imaging, treatment planning and immobilization all in one visit.

Because our orthopedists are pediatric specialists, they are able to evaluate every fracture for injury to or near the growth plate. Damage to the growth plates can cause long-term problems as the bone and joints develop, if not treated appropriately. Providers who focus on adults or in standard ERs may overlook these subtle but important differences in pediatric fracture care.

When families reach out with concern about a fracture, direct them to Children's Hospital in Milwaukee — with locations in Milwaukee, Delafield, Greenfield and Mequon — for the best in pediatric fracture care.

Learn more about our Orthopedics program and locations at chw.org/orthopedics.

