

**Research Institute** 

# 2017 YEAR IN REVIEW

# DISCOVER. INNOVATE. TRANSLATE.

# *"All intellectual teaching and learning arise from preexisting knowledge."*

- Fundamental concepts of Aristotle's theory of scientific knowledge.



#### Mission

We enrich lives through discovery, translation and application of scientific knowledge that improves health and well-being.

#### Vision

We will innovate and define the future of health care for generations. Our research will be the source of innovation for the future of disease and injury prevention and integrated health care locally and globally.

#### Values

Discovery – Will be the foundation of the overall activities of the research group.

Translation – A major effort will be made to apply our discoveries in the health care setting.

Dissemination – Results of work done will be distributed broadly on a timely basis. Teamwork - Will be a hallmark of the research group.

Excellence - Will be the standard for all research and program activities.

Collaboration - Partnerships both internal and external will be sought and encouraged.

#### From the Executive Director

The quest for biomedical knowledge discovery and innovation has been ingrained in the fabric of Marshfield Clinic since its inception. A century ago, its founding physicians stressed the value of patient care conducted hand-in-hand with research and education. This fundamental philosophy has stood the test of time and was further advanced by Melvin Laird, a lifelong champion of translational research at Marshfield Clinic. His passion for research set the stage for the innovative and cutting edge research currently being conducted at Marshfield Clinic Research Institute (MCRI) and for the many pioneering endeavors sure to follow.

Mr. Laird often said, "All the research in the world is not worth very much if you don't get it to the patients." This philosophy of translating research into care delivery is deeply embedded in how I perceive MCRI's role.

The ever-changing health care environment presents challenges. However, I strongly believe that our Institute has embarked on a unique journey focused around better integration and translation of medical research into patient care, thereby supporting the mission of our health system. It was an active year at MCRI, highlighted by several translational and applied research initiatives.

MCRI continues to collaborate with the University of Wisconsin Institute for Clinical and Translational Research (ICTR) as part of a five-year renewal of the Clinical and Translational Science Award from the National Center for Advancing Translational Science. MCRI will receive \$3.4 million over the next five years to support the mission of ICTR and to support the clinical and translational activities within our health system. In an effort to foster clinician-led research collaboration, MCRI made two research awards this year. The first award was to Dr. Paula Aston, neurologist, collaborating with Dr. Sanjay Shukla, microbiologist, for their research on the role of the microbiome in multiple sclerosis. The second award was to Dr. Seung (David) Kim, pathologist, collaborating with Dr. Scott Hebbring, geneticist, focusing on the exploration of telomere biology in seborrheic keratosis and cancer, utilizing genome-wide/phenome-wide association studies and tissue-based techniques.

MCRI epidemiology research staff conducted outreach to doctors and parents of adolescents to promote human papillomavirus (HPV) vaccination throughout Marshfield Clinic Health System. This effort, funded by the Centers for Disease Control and Prevention, demonstrated an increase in HPV vaccination rates among pre-teens system-wide. MCRI researchers continue to be part of a CDC-sponsored network called the "Vaccine Safety Datalink," and focused on the occurrence of blood clots (deep vein thrombosis) after flu vaccination in older adults and the risk of miscarriage in women who received the flu vaccine in early pregnancy during the 2010-11 and 2011-12 flu seasons.

Under the leadership of Dr. Jaime Boero and his research team, MCRI was one of 31 sites in the U.S. and Europe that participated in a breakthrough treatment of moderate to severe central sleep apnea in adult patients. Dr. Adedayo Onitilo and oncology research staff engaged in a Molecular Analysis for Treatment Choice (MATCH) clinical trial which provided a new treatment for some of our cancer patients by precise targeting of tumors based on their molecular sequencing. Dr. Murray Brilliant was instrumental in MCRI receiving a \$5.3 million grant to implement the National Institutes of Health's *All of Us* Research Program in Wisconsin, reflecting MCRI and our health system's commitment to providing a leadership role in this statewide approach to the national Precision Medicine Initiative.

The Wisconsin Infant Study Cohort (WISC) was successfully renewed for another grant cycle and will follow 400 children from birth to the age of eight, studying immune outcomes such as asthma, hay fever (allergies) and atopic dermatitis (eczema). As part of WISC, researchers from MCRI are focused on better understanding how early life exposures, like the farm environment, directly contribute to healthier immune outcomes.

It is an honor to lead a top-notch research enterprise like Marshfield Clinic Research Institute, and I am so thankful to be part of a unique health system that is interested in learning through research like Marshfield Clinic Health System.



Amit Acharya, B.D.S., M.S., Ph.D. Executive Director Marshfield Clinic Research Institute

#### AAHRPP grants re-accreditation

In December 2014, Marshfield Clinic Research Institute was granted full accreditation by the Association for the Accreditation of Human Research Protections Programs (AAHRPP). Accreditation indicates that MCRI follows rigorous standards for ethics, quality and protections for human research. MCRI's research participants, peers, potential sponsors, government agencies and the general public can be assured that the institute is among the world's most respected, trustworthy research organizations. Re-accreditation activities in 2017 included a site visit and review of all human subject research-related policies, procedures and training materials. The final application package contained nearly 200 documents, totaling more than 1,200 pages. AAHRPP announced Dec. 18 that MCRI had earned full re-accreditation for the next five years.



### BIOMEDICAL INFORMATICS RESEARCH CENTER

#### Big data, big impact

Since earning my Ph.D. in computer science from the University of Wisconsin-Milwaukee, I have been on a quest to improve patient diagnosis and treatment by using advanced computational algorithms. Computational health informatics is a blossoming field that streamlines the health care process by utilizing information technology and machine intelligence to store, retrieve and analyze massive amounts of clinical data collected when care is provided to patients.

Helping people worldwide and doing it more efficiently is the fundamental reason I pursued health informatics. Health informatics shapes the quality of services provided by the health care industry. I was honored to have played a key role in the development and enhancement of an integrated big data analytics framework within Marshfield Clinic Research Institute, particularly for adverse drug events (ADEs) analyses from big data biomedical literature and social media.



I am passionate about diverse biomedical data, machine intelligence and its applications in health care, and I have extensive research experience in conducting computer vision mechanisms with a key focus on medical image analysis. Computational health informatics provides me an opportunity to make a positive impact on many people, beyond what I ever could have imagined.



Ahmad P. Tafti, Ph.D. Associate research scientist

#### Transforming research and patient care with major technology gift

A high performance computing system (HPC) donated to Marshfield Clinic Research Institute from Milwaukee Institute, Inc., will advance research and innovative treatment options throughout Marshfield Clinic Health System. The HPC will transform the institute's ability to analyze patient health data and develop predictions that will assist physicians in identifying adverse events and ways to better care for patients. "That means science done in our lab can be used quickly by providers to help patients during their appointments," said Peggy Peissig, Ph.D., director of MCRI's Biomedical Informatics Research Center. "Patients will receive the right treatments, at the right dose, at the right time."

This means that a patient suffering from a particular disease can avoid a medication that could have an adverse effect, can learn if they are susceptible to a certain type of cancer based on their genetic make-up and can learn these things more quickly than ever before.

Using research to inform and transform patient care sets MCHS apart from other health care organizations. The HPC gift harnesses the power equivalent to hundreds of computers to solve problems and analyze large amounts of data more efficiently than a single computer.

### CENTER FOR CLINICAL EPIDEMIOLOGY AND POPULATION HEALTH

# Population health is still about individuals

I became interested in the causes of health outcomes and diseases in populations, and behavioral epidemiologic research in particular, after spending several years as a counselor in Minneapolis.

I paid careful attention to what patients were going through and offered advice and tools where I could to make their personal growth and change easier. Later, I designed programs to help large groups of people lose weight, quit smoking or use medications appropriately. The idea of such programs was that they would save health care payers money down the road because participants would have fewer visits to the hospital for heart attacks, strokes or diabetes. I quickly realized that evaluations of disease prevention programs, even the best ones, are scarce and often lack scientific rigor.

So I transitioned to research, where my work focuses on the applied side of epidemiology. Most of my larger studies are embedded in the health care system.

#### These include:

- Evaluating established preventive therapies like aspirin
- Testing new clinical counseling programs to help patients lose weight
- Implementing evidence-based practices to help reduce rural health disparities such as diabetes telemedicine and HPV vaccine promotion

Communicating research findings to the medical and scientific community, usually by a conference presentation or journal article, keeps me busy and can be very fulfilling. However, I mainly do this work because I enjoy a good story, just like back in my counseling days.

Whether it stems from my own work or that of my colleagues, I love seeing a graph showing a healthier trend over time or hearing from a doctor about how one of our programs helped their patient. I love learning how health care leaders in the U.S. started doing things differently based on what we discovered here in our "backyard" of north-central Wisconsin. Feeling useful toward a small part of that is reward enough for me.



Jeffrey VanWormer, Ph.D. Research scientist

#### Monitoring the safety of the influenza vaccine

Every winter the influenza virus causes thousands of deaths and hospitalizations. Flu vaccines have an excellent safety record, but it is important to monitor them since they are given every year and are frequently updated, said Edward Belongia, Ph.D., director for Center for Clinical Epidemiology and Population Health (CCEPH). CCEPH researchers are part of a CDCsponsored network called, "Vaccine Safety Datalink." In 2017 they published two studies on flu vaccine safety. The first study looked at the occurrence of blood clots (deep vein thrombosis) after the flu vaccination in older adults, and the results were reassuring: flu vaccine did not increase the risk of a blood clot or complication. This study was published in the journal Vaccine.

The second study looked at miscarriages in women who received the flu vaccine in early pregnancy during the 2010-11 and 2011-12 flu seasons. A previous study did not find any link between miscarriage and flu vaccination, but there was concern that the new H1N1 virus, which caused the 2009 pandemic, might be different. In this study, there was a significant association between miscarriage and flu vaccination in the previous 28 days. This was only seen in women who were also vaccinated in the prior season. These results do not prove that the flu vaccine caused miscarriages, but further research is needed. Results were published in Vaccine.

### **CLINICAL RESEARCH** CENTER

# 'I could have gone anywhere for care, but I came here.'

I always felt like an anomaly in nursing school. While most of my classmates aspired to work in fast-paced intensive care units and emergency departments or critical care units, I did not. My detailoriented mind was better suited to clinical research and its intricacies and propriety of protocols, and my curiosity hungered for a glimpse into the future of oncology treatment options.

More than that, I have noticed for my patients that research promises a sense of hope for the present. It also strikes to remind us of the past - of an individual's resilience in facing one of the most devastating diagnoses of the human condition.

Not long after I started, taking delight and enthusiasm into finding eligible patients, one of the oncologists called us inside an exam room to one of his patients. This patient, like many of our patients, chose a clinical trial for care and had been in complete remission. We learned that many years prior he had been confronted with a diagnosis of malignant melanoma - a disease characterized as both aggressive and, quite simply, with a questionable fate.

The man had come for a followup visit and, amid sharing his story, told us, "I could have gone anywhere in the world for care."

As he rattled off renowned cancer centers all over the nation, he stated, "But I came here to Marshfield Clinic. Five minutes away from my backyard, and I couldn't be more thankful."

If it's not the moral mission of research and success that has continuously captivated me, it is that of being witness to my colleagues' passion for research. Only a few weeks into my new role as a clinical research nurse. I was present to one of my colleagues' self-created fundraiser, Aim for a Cure. This fundraiser supports the work we all do for our patients and the reason why, for so many of our patients who invite us into the most vulnerable and trying times of their lives, they choose a place close to home - a place that allows us every day to execute our passion and aim to provide a cure.



Tiffany Bredeck, R.N. Research nurse

#### Trial leads to breakthrough treatment of sleep apnea

Marshfield Clinic Research Institute was one of 31 sites in the U.S. and Europe that participated in a breakthrough treatment of moderate to severe central sleep apnea (CSA) in adult patients.

CSA is a serious breathing disorder that disrupts the normal breathing pattern during sleep and negatively affects quality of life and overall cardiovascular health. CSA results from the brain's inability to send appropriate signals to the respiratory muscles to stimulate breathing. Dr. Jaime Boero implanted the remedē System (Respicardia, Inc.) in seven patients and randomized them 1:1 to the treatment or control group. On Oct. 10, the remedē System, a transvenous implantable neurostimulation system that stimulates the phrenic nerve and engages the diaphragm to restore natural breathing during sleep in patients with central sleep apnea, received FDA approval.

HIGHLIGHTS

# 'That one child has changed the course of my career.'

Shortly after beginning my practice of pediatric nephrology, I was confronted with a very unusual case of a child born with polycystic kidneys and extra fingers and toes. That one child has changed the course of my career.

Her correct diagnosis took a while to figure out, but finally we landed upon a rare disease called Bardet-Biedl syndrome (BBS), a genetic disorder that affects essentially every organ system of the human body.

This child, now an adult, has taught me a great deal over the years. One small protein in her cells located inconspicuously in a previously ignored cell organelle called a cilium resulted in kidney failure, severe vision loss, obesity, scoliosis, extra fingers and toes, learning disabilities and much more.

Over the last six years I have been privileged to help create a BBS Multispecialty Clinic for very special individuals such as this young lady. At the same time, a specialized registry called the Clinical Registry Investigating BBS (CRIBBS) was designed to track the health of nearly 400 individuals with BBS living on six continents.

At Marshfield Clinic Research Institute, we have pioneered the investigation of BBS including:

- 1. A novel therapy for obesity
- 2. Investigating sleep patterns
- 3. Categorizing skin disorders and speech disruption
- 4. Publishing novel information on renal transplant outcomes
- 5. Authored reviews on oral and systemic health

We are now moving forward with the development of a Center of Excellence for BBS research. All because of one child, and the creativity and insight housed here in the Institute.



Robert Haws, M.D. Multispecialty director

#### Treating obesity in rural populations

Obesity is a major health concern across the country, particularly in rural areas like north-central Wisconsin. In collaboration with the University of Kansas, Marshfield Clinic is participating in the RE-POWER study to understand how health care systems can best help overweight adults. Three behavioral obesity treatments are being compared, including:

- 1. Individual counseling
- 2. Group counseling
- 3. Group counseling delivered remotely by telephone

Weight loss and other outcomes such as blood pressure, cholesterol and glucose will be measured over two years to determine which treatment is the most beneficial. Early results have been encouraging in that most patients have lost around 10 percent of their body weight over the first 6-12 months of treatment. How well participants stay engaged in weight management activities during the second year will likely determine which treatment is most effective.

## CENTER FOR HUMAN GENETICS

#### Genetics research: Few diseases are random

I have always wanted to be a scientist. My scientific interests have morphed from turning over actual rocks to see what was crawling beneath, to turning over metaphorical rocks to make discoveries in genetics.

My interests in genetics began during my sophomore year in high school and has held strong ever since. Our lab currently focuses on "disease agnostic" approaches to human disorders, which groups patients by their genetic similarities rather than by disease symptoms or what parts of their bodies are affected.

This includes "phenome-wide" strategies that leverage Marshfield Clinic Health System's electronic health record (EHR) to study thousands of clinical diseases simultaneously. For example, we published a manuscript in 2014 describing a method that identified more than 8,000 pairs of twins in Marshfield Clinic's EHR. With all twins linked to extensive disease information through the EHR. we now show with hard evidence that few diseases are ever random: many of these diseases included conditions with unappreciated genetic causes.

While combing over our extensive twins data, we identified and further genetically evaluated a condition called seborrheic keratosis. Seborrheic keratosis results in benign skin lesions and shares a common link with breast cancer, ovarian cancer and glioma according to our genomic studies. We presented our phenome-wide twins study and genomic study of seborrheic keratosis at the 2017 American Society of Human Genetics conference.



Going beyond twins, we published an additional manuscript demonstrating our ability to identify all other family relationships in Marshfield Clinic's EHR. We now can align more than 800,000 Marshfield Clinic patients into more than 180,000 families representing one of the world's largest sets of families linked to extensive disease information.

Not surprisingly, preliminary phenome-wide analyses of these families show similar trends to what was observed in twins. Our future research will use this database to identify diseases and families to recruit for genomic study. With extensive family and disease data embedded in the electronic health record, it may now be possible to generate family histories automatically for thousands of diseases to help manage disease risk and treatment. Understanding how EHR-linked family data can be used in clinical care, while protecting patient rights and privacy, will also be the subject of future research.



Scott Hebbring, Ph.D. Geneticist

### **HIGHLIGHTS**

#### All of Us: \$5.3 million grant puts MCRI at forefront of precision medicine



The Center for Human Genetics, led by Murray Brilliant, Ph.D., was awarded a \$5.3 million grant to implement the National Institutes of Health's All of Us Research Program in Wisconsin. As the lead site, MCRI will share grant funds and collaborate with the University of Wisconsin School of Medicine and Public Health and Medical College of Wisconsin to advance research in precision medicine. All of Us, Wisconsin is an ambitious, statewide approach to the national program for disease treatment and prevention that involves taking into account individual variability in biological makeup, environment and lifestyle for all people.

Marshfield Clinic's inclusion in the All of Us Research Program serves as evidence of the tremendous work done in the Personalized Medicine Research Project, launched in 2002. This incredibly important work positions Marshfield Clinic at the forefront of an area of medicine that will add to medical knowledge on a national and worldwide scale, and will ultimately help define the future of health care. The Personalized Medicine Research Project was the first and largest population-based genetic research biobank in the U.S at the time of launch, involving more than 20,000 central Wisconsin residents.

#### Fostering clinician-led research collaborations

Neurologist Dr. Paula Aston and pathologist Dr. Seung (David) Kim were recipients of the two Clinician-Scientist Collaborative Research Awards funded in 2017. The award was designed to provide protected time for research by clinicians and pairs Marshfield Clinic physicians with MCRI scientists to work on a two-year project. Two scientists in the Center for Human Genetics were named as coprincipal investigators on this year's awards.

Sanjay Shukla, Ph.D., will work with Dr. Aston to investigate whether the gut microbiome of multiple sclerosis patients is different from that of healthy controls and whether treatment for multiple sclerosis leads to a gut microbiome profile similar to that of healthy individuals. Scott Hebbring, Ph.D., and Dr. Kim will collaborate to examine telomere length and the expression of telomerase, an enzyme that regulates telomere length, in tissues from patients with seborrheic keratosis, a benign skin disease, as well as from patients with breast cancer. The aim is to gain insights that could be used to improve treatments for these diseases.

#### Understanding the genetic causes of autism

Dr. Steve Schrodi is lead statistical geneticist on a national study designed to discover DNA variants responsible for structural and functional neuroimaging patterns in autism spectrum disorders. Autism is highly heritable and genes identified from this study will provide insight into the molecular pathophysiology of autism. Also, Dr. Schrodi developed a statistical framework to optimize the design of genetic association studies using electronic health record information, thereby increasing the efficiency of these studies.





#### National Farm Medicine Center (NFMC)

Focuses on agricultural safety and health research, education, outreach. Edits Journal of Agromedicine.



Rate of non-fatal injuries to children in U.S. agriculture has dropped 60% since NFMC established the federally-funded National Children's Center in 1997.

#### **Biomedical Infomatics Research Center (BIRC)**

BIRC scientists study data collected by Marshfield Clinic Health System and use it to support better patient care.





#### Institutional Review Board (IRB)

Approves, monitors and reviews all research conducted within Marshfield Clinic Health System. Protects research participants' rights and welfare.

## Exernally-Funded Projects in 2017: \$17 million

professionals throughout the Marshfield Clinic system are engaged in medical research. The mission of MCRI is to, "discover and communicate scientific knowledge that substantially improves human health and well-being."

#### Clinical Medicine & Research (CM&R)

An indexed journal (http://www.clinmedres.org/) published by Marshfield Clinic Health System; edited within the Research Institute for 15 years.

Received manuscripts from 19 countries, reviewed by experts in **36** countries.



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#### Center for Human Genetics (CHG)

CHG focuses its research on the structure of the human genome and the hunt for genes that influence human health disorders.



Personalized Medicine biobank: 8,228 unique DNA samples directly genotyped in 2017 for more than 500,000 genetic markers.

#### Integrated Research and Development Laboratory (IRDL)

Supports research projects being undertaken within Marshfield Clinic Health System, as well as with external collaborators in industry and academia.



## NATIONAL FARM MEDICINE CENTER

#### Cultivating safety on the farm

Our farm was on a side road, and everyone around us was either family or long-time neighbors. We had many neighborhood kids, so finding teams for kickball and softball was no problem. We'd pedal our bikes to the lake to go swimming. And of course, we worked. Baling hay, feeding cows, picking potatoes, collecting maple sap, dragging out Christmas trees – the type of work changed with the season, but there was always work to do.

Amongst all this work, no one talked about farm safety. The day my 2-year-old brother fell off the front of the hay wagon and was run over. I had no idea that he shouldn't have been on the wagon. A couple years later, when my teenage cousin got his arm caught in the hay baler, I didn't realize that he should have called an adult rather than try to fix the baler himself. As a child, I didn't see the danger of the farm; I saw one really big playground where I sometimes had to work too. Luckily, my brother and my cousin weren't permanently injured.

Looking back, I shudder at some of the things we did. As an adult working as a youth agricultural safety specialist, lots of child agricultural injury and fatality "accidents" cross my desk. I've learned how truly dangerous the farm worksite is.

For youth working in agriculture, the number of fatalities is higher than in all other occupations combined. Many of these injuries and deaths are associated with youth performing work that does not match their developmental abilities.

To address this problem, the National Farm Medicine Center/ National Children's Center for Rural and Agricultural Health and Safety developed the Agricultural Youth Work Guidelines (cultivatesafety. org/family-farms). The guidelines can be used by adults to determine if a youth is able to safely perform a job, learn about supervisor responsibilities and to determine hazards and protective strategies specific to various jobs.

These guidelines help us safeguard our farm kids, while enabling them to reap the benefits of living and working on farms. If the guidelines had been available when I was young, perhaps my cousin and brother wouldn't have had to learn safety the hard way.





Marsha Salzwedel, M.S. Youth agricultural safety specialist

#### Farming as medicine: Child asthma study joins national network

**HIGHLIGHTS** 

The National Institutes of Health announced an important initiative in 2016 to bring together studies throughout the U.S. in order to learn more about diseases, such as asthma and allergies, that affect many children. The Wisconsin Infant Study Cohort (WISC) has now joined with 11 other studies to learn about environmental influences on allergies and asthma during childhood, said MCRI site Principal Investigator Dr. Casper Bendixsen. This new study is called CREW (Children's Respiratory Research and the Environment Workgroup), and includes studies from mostly urban areas and suburban areas throughout the U.S. As part of CREW, the WISC study will be sharing and comparing information about early life environmental exposures and its effects on children's health. WISC is the only participating study in rural America. WISC was successfully renewed for another grant cycle, and will follow 400 children from birth to the age of eight, studying immune outcomes such as asthma, hay fever (allergies) and atopic dermatitis (eczema). WISC will allow researchers to better understand how early life exposures like the farm environment directly contribute to healthier immune outcomes.

## CENTER FOR ORAL AND SYSTEMIC HEALTH

#### At the intersection of medicine, dentistry and informatics

When I interviewed with the Center for Oral and Systemic Health (COSH), I was impressed with the diversity of projects and the rapid translation from research to application, with patient care being the target.

The effort to combine both medical and dental information was something I had never heard before, but made so much sense. I instantly knew this was something I'd like to do. My role on the DentaSeal project (Dental Sealant Registry) is that of an application developer. I have been involved in the planning, development and release process of DentaSeal from the beginning. DentaSeal is the first project where I have had the opportunity to work with a software development team, and it has been quite an experience.

Through this project, and working with the COSH team on numerous other projects, I have gained invaluable knowledge about informatics, and specifically how it applies to oral health. I highly respect the motivation and drive of the COSH team. It encourages me to give more than 100 percent to see all projects succeed, and put us on the map in the field of oral and systemic informatics research.



Harshad Hegde, M.S. Informatics research architect

#### Bridging medical and dental care

As co-investigator on the Integrated Care Model project, I have been involved with conducting crosssectional studies in Wisconsin to assess the current awareness, knowledge and behavior of medical providers, dental providers and patients towards the association of diabetes and periodontal disease.

My passion and motivation in this research was driven by my interest in creating new ideas and my experience at Marshfield Clinic Research Institute, as well as past work experiences. Comments from research participants about oral-systemic connections have broadened my horizon.

For example, one participant asked if there was any relation between vitamin deficiency and periodontal disease. Some of them asked about association between root canal treatment and cardiovascular disease. I truly believe that my passion, research interests, new ideas and ongoing research - coupled with guidance provided by colleagues who take the role of mentors, friends and learners - helps me to make a positive contribution to the field of health care and informatics.



Neel Shimpi, Ph.D. Associate research scientist

#### Developing a medical-dental model to manage diabetes

Delta Dental of Wisconsin awarded a research grant to the Center for Oral and Systemic Health (COSH) to develop a medical-dental integrated care model to better manage and coordinate care for patients with diabetes and their oral health. Dr. Amit Acharya, founding director of COSH, who is trained as a general dental surgeon and an informatics scientist, will lead the initiative.

Diabetes is a major health concern. More than 29 million people in the U.S. have diabetes - about one out of every 11 people. One out of two people above the age of 30 have some form of periodontal gum disease. Diabetes has a negative effect on periodontal health.

"These are staggering numbers," said Dr. Acharya. "There is a great opportunity here for the medical and dental professions to be working together. Dental providers can screen for undiagnosed dysglycemic individuals and refer their patients to their medical colleagues, while medical providers can look for early signs of diabetes in the mouth and refer their patients to dental providers to receive better oral health."

## **INTEGRATED RESEARCH & DEVELOPMENT LAB**

# An eclectic team: hard to describe, impossible to do without

Two recent job recruits asked, "What is a typical day in the Integrated Research and Development Laboratory (IRDL)?" The quick answer is that there is no typical day, week nor month in IRDL.

Typically juggling 50 studies, IRDL team members can be challenged with working in multiple studies within a day, or a single study for months. These studies require an intricate system of cross-trained staff who rely upon each other to ensure that our commitments are completed accurately and on time. Our collective schedule flexes from our intense domestic flu surveillance during the northern hemisphere's winter months to our international studies that pick up during the summer. We are also involved in tick-borne disease and blastomycosis studies during their respective seasons. Our support of the Marshfield Clinic Research Institute's clinical trials can start at 7 a.m. and end after 9 p.m. Our work days for certain projects expand to the entire year.

Some studies require our team to ensure proper receipt, processing, extraction and analysis of sample types including nasal swabs, sputum, blood and even feces. Some procedures simply require ensuring proper transit to any of our collaborative partners following strict IATA shipping guidelines that guarantee the sample is received in perfect condition for analysis in their labs. Additionally, there is the rigor of working under a check, double-check and triple-check practice during our comprehensive auditing processes demanded by FDA-approved protocols.

Trying to explain to new hires how this eclectic staff interacts is a challenge. A team member may function as a team leader on a specific project, while supporting a colleague on a different project. This high level of communication, mutual respect and reliance upon each other could possibly explain the mean tenure in our team of nearly 16 years!

The positive energy of the IRDL team extends to our relationships with the different MCRI centers, and our external partners, to make them successful in their research interests.



Steve Kaiser Lab operations manager

# Seeking better treatment of blastomycosis

Jennifer Meece, Ph.D., director of the Integrated Research and Development Laboratory, utilized her 2016 Sebold Award honoraria to support a research project with graduate student Klaire Laux focusing on blastomycosis, a fungal infection found in Wisconsin. Expanding on Dr. Meece's recognition of two species of blastomycosis, this research identified the clinically-relevant differences in patient demographics and clinical symptoms between these two species. Future research will focus on diagnostic differences and genetic variability in relation to how these two species clinically present for better treatment options for MCHS patients.

# Supporting STEM Scouts in our community

MCRI sponsors the Marshfield chapter of Boy Scouts of America's Science, Technology, Engineering and Math (STEM) program. The chapter is led by MCRI staff and dedicated to Donna David, a former IRDL member who was fatally struck while bicycling. David was a scientist and educator who shared her love of science with others. STEM Scouts utilizes hands-on lab projects to introduce concepts to energetic third through fifth grade aspiring scientists.



HIGHLIGHTS

### HIGHLIGHTS

# Helping young people perform farm work safely



The National Children's Center for Rural and Agricultural Health and Safety released a set of Agricultural Youth Work Guidelines (AYWG) to assist parents and others in assigning appropriate tasks for youth who live or work on farms and ranches. Since 2001, there has been a steady decline in the number of non-fatal injuries to farm youth. Nonetheless, about every 3 days in the U.S., a youth dies in an agricultural incident, said AYWG project leader Marsha Salzwedel, M.S. For youth younger than 16 working in agriculture, the number of fatal injuries is consistently higher than all other industries combined. The voluntary guidelines are based on childhood growth and development, agricultural practices, principles of childhood injury and agricultural and occupational safety. The guidelines can be printed, downloaded or used interactively at www.cultivatesafety.org.

#### Protecting research participants

This past year marked the first time since the early 1980s that federal human subject regulations have been updated. Marshfield Clinic Research Institute teamed with UW-Madison and Public Responsibility in Medicine and Research (PRIM&R) to co-sponsor a day-long workshop on IRB preparedness for the implementation of the newly revised Common Rule (45 CFR 46). The workshop was presented free of charge to attendees, and staff from every registered IRB in Wisconsin were invited. Keynote speaker John Baumann, Ph.D., associate vice president for Research Compliance at Indiana University, gave an overview of potential challenges presented by the rule changes. A similar workshop will be hosted by MCRI in 2018 after the new Common Rule has been implemented.

# Mentoring the next generation of researchers



Since 1974, MCRI has offered summer research internship opportunities to students, supported almost entirely through philanthropy. The primary goal of this highlycompetitive program is to provide a mentored, hands-on research experience for college undergraduate, graduate, dental and medical students considering a career in research. Students work with a research scientist on an independent project and contribute to all aspects of the researchprocess. In 2017, the program provided 10 interns with research projects in the areas of genetics, cultural/medical anthropology, epidemiology, biomedical informatics, oral and systemic health and laboratory/ clinical research.

#### Partnering with the University of Wisconsin



The *All of Us* Research Program in Wisconsin is one example of collaboration between Marshfield Clinic Health System and the University of Wisconsin. This photo shows researchers from MCRI, University of Wisconsin School of Medicine and Public Health and Medical College of Wisconsin attending a national *All of Us* meeting in Bethesda, Maryland. In another initiative, the Health System will receive \$3.4 million over the next five years from the University of Wisconsin Institute for Clinical and Translational Research (ICTR) to support research projects at the University and Health System.

# GIVING THE GIFT OF RESEARCH

A child undergoing cancer treatment. A scientist searching for a cure. A student training to become a doctor. These are the people you support when you make a gift of any size to Marshfield Clinic Health System Foundation.

As a nonprofit organization, MCHS Foundation relies on sustaining support from difference-makers like you to fund patient care, research and education programs.

In 2017, more than \$1.9 million was raised for research alone through MCHS Foundation.

#### Gifts at work

- Dr. Robert Haws' Clinical Registry Investigating Bardet-Biedl Syndrome (CRIBBS) has exceeded 300 participants. Dr. Haws is using CRIBBS to work with the National Institutes of Health to study the long-term health of people with Bardet-Biedl Syndrome.
- Jennifer Meece, Ph.D., is conducting a blastomycosis study in Wisconsin patients and among various races/ethnic groups.
- The National Farm Medicine Center is working with the Mike Biadasz Farm Safety and Education Memorial Fund to implement a Wisconsin manure gas monitor rebate program. Continued research in this field is on the horizon.
- Marshfield Clinic Health System, through the Institute, is one of three Wisconsin health care systems involved in the *All of Us* Research Program in Wisconsin, a precision medicine initiative through the NIH. Philanthropy is helping to drive continued precision medicine research.
- Each year, the Center for Clinical Epidemiology and Population Health plays a key role in nationwide studies of flu vaccine effectiveness.
- The Center for Oral and Systemic Health is studying links between diabetes and dental disease.

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#### Mike Biadasz Manure Gas Monitor Rebate Program



The Biadasz family presents a check for \$40,000 to implement the Mike Biadasz Manure Gas Monitor Rebate Program. Wisconsin farmers can contact farmforeverrebates@gmail.com to apply for a rebate that partially covers the cost for renting a portable gas monitor device that detects gas levels and alerts them when potentially lethal levels are reached.

#### THERE ARE MANY WAYS YOU CAN HELP.

Please contact Matt Faber, 715-387-5901, faber.matt@marshfieldclinic.org

#### Precision medicine fellowship established



Sally Ebenreiter, longtime supporter of Marshfield Clinic Health System, has again stepped forward with a generous donation, this time with a \$300,000 gift supporting a precision medicine research fellowship. Sally and her late husband Tom began supporting cancer research after they first were treated at Marshfield Clinic more than 30 years ago. The couple gave the lead gift to help establish the Tom and Sally Ebenreiter Distinguished Physician/Scientist Endowment in Oncology Research in 2014, currently held by Dr. Adedayo Onitilo, oncology service line director, Marshfield Clinic.

#### Midwest Athletes Against Childhood Cancer



Local athletes, a championship coach and friends of Marshfield Clinic Health System gathered in May to celebrate a \$50,000 grant for pediatric oncology research from Midwest Athletes Against Childhood Cancer (MACC), Inc. With the grant, MCHS became the first research institution in nine years to be selected to partner with the MACC Fund.

#### ALS Steps for Hope



More than 300 people from across Wisconsin came together in early September to support ALS research as well as families, friends and coworkers who have been stricken by the disease. Thanks to support from area businesses like the Boson Company, the ALS Steps for Hope group raised more than \$22,000 for research.

#### **Golf for Research**



The 19th annual Golf for Research, presented by Solarus, was held in August at Lake Arrowhead Golf Club. Event sponsors, golfers and volunteers raised more than \$69,000 for cancer research at Marshfield Clinic Research Institute, bringing the event's cumulative total to more than \$1 million. 128 golfers and 35 volunteers took part in memorializing loved ones and honoring all touched by cancer. V&H Trucks CEO Terry Frankland has led Golf for Research efforts for many years. Ryan Dieringer, a cancer survivor, and his family were this year's special guests.

### ON THE SHOULDERS OF GIANTS

#### SETTING THE COURSE



Fritz Wenzel's vision, energy lead MCRI transition

"When I was asked to come back, the word 'no' was not in my vocabulary. We did a lot of good things the past two years."

- Fritz Wenzel

Frederick "Fritz" Wenzel made it his life's work to serve Marshfield Clinic and ultimately hundreds of thousands of patients during the course of his career.

After serving as interim executive director of the Marshfield Clinic Research Institute from November 2015 to August 2017, Dr. Wenzel passed the gavel to Amit Acharya B.D.S., Ph.D., a renowned research scientist and founding director of the Center for Oral and Systemic Health. Dr. Acharya assumed this new role July 10.

Wenzel, just several weeks shy of his 87th birthday, was honored at MCRI's all-staff meeting July 19. A brief video presentation included photos of him doing three of his favorite things – his work at the Clinic, hiking mountains and sailing.

A University of Wisconsin-Stevens Point graduate, he began his career in medical research and was the first executive director for Marshfield Clinic Foundation for Medical Research and Education. He then became executive director for Marshfield Clinic in 1976, serving in that role until 1993. Under his leadership, Marshfield Clinic established a regional health care system, a health maintenance organization and community health center.

Wenzel brought a national reputation in research, management, leadership, health care policy and education to the interim role which informed how MCRI leadership chose the path forward over the ensuing year and a half.

"While the journey was brief, we accomplished a great deal these past months, through the cooperation of the staff," Dr. Wenzel said. "The Institute directors and administrators played a central role in that effort working with a staff of dedicated scientists and all those who contribute to the operation. applaud your efforts as you thinned the walls of the silos and developed strong communication across the entire Institute. And the Institute will rise to an even greater level under the leadership of Dr. Acharya."

He led the organization through its strategic planning initiative by examining the future needs of MCRI and harmonizing it with the planning for MCHS. He worked alongside Mel Laird and Dr. Murray Brilliant to pursue the All of Us, Wisconsin National Institutes of Health grant as well as secured donated funds for the Precision Medicine Initiative. Wenzel's positivity set the tone and his energy laid the groundwork for the next stage of growth for MCRI.

"I want to sincerely thank Fritz for his selflessness and invaluable leadership," Dr. Acharya said. "He has been our guiding light and without him we would not be here. We are grateful for the time and knowledge he was willing to share with us."

#### 'THE MAN FROM MARSHFIELD'



Melvin Laird shaped American health care, research

The way to make progress is "by focusing on partnership rather than partisanship."

- Melvin Laird

Melvin Laird is remembered as one of the most important people in American politics in the 20th century, but his true passion was his hometown of Marshfield.

Known as "The Man from Marshfield," the former Congressman, Secretary of Defense and long-time Marshfield Clinic and medical research supporter, was honored Nov. 16 on the one-year anniversary of his passing at age 94.

Laird's impact on the Clinic and health care left an enduring mark that will benefit future generations. That impact was highlighted during a series of presentations at Marshfield Center honoring Laird.

"Mr. Laird was a force of nature and shaped our organization to where we are today," said Marshfield Clinic Research Institute Director Amit Acharya, B.D.S., Ph.D. "His passion for research and lifelong support of Marshfield Clinic set the stage for all the innovation and cuttingedge research currently being conducted, as well as future work at MCRI."

Laird and Democrat Congressman John E. Fogarty from Rhode Island formed a bipartisan alliance to expand federal funding for medical research projects and institutions - including the National Institutes of Health (NIH), National Library of Medicine and the Centers for Disease Control and Prevention.

The relationship with the NIH continues today as the Clinic has received other grants over the years and anticipates another significant grant in the near future. Even at his advanced age, Laird served as the Clinic's liaison to federal leaders who helped secure grants and provided a listening ear when it came to health care policy, often as the result of Laird's handwritten notes and phone calls.

Nationally, he promoted the expansion of health research programs and facilities across the U.S., including in Wisconsin. Laird's impact on health care was felt internationally as he was reappointed by three U.S. presidents from 1956-67 to serve as a delegate to World Health Organization.

Laird visited Wisconsin shortly after Congress passed the Health Maintenance Organization Act of 1973 and spoke to local physicians about this "wave of the future." Clinic physicians listened and created the Greater Marshfield Community Health Plan, which later became Security Health Plan of Wisconsin, Inc.

"He had a love and devotion to the state and people of Wisconsin with a desire to help them in any way he could. That was first and foremost," said son David Laird, one of three Laird children in attendance. "His true passion was health care. This passion was lit by his lifelong relationship with doctors and staff of Marshfield Clinic."



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