

Directors' Report



Dr. Bob Steiner,
MCRF Exec. Dir.

We could title this edition of Research Matters, "MCRF Goes to the White House." I'll explain. President Obama, in his recent State of the Union Address, mentioned his desire to launch a "Precision Medicine" initiative. This is the new name for what has been called Personalized Medicine. As many of you know, MCRF has been a leader nationally in Personalized Medicine, and is the home of the Personalized Medicine Research Program (PMRP). Fortunately, this is not a closely held secret. Dr. Francis Collins, Director of NIH, called Dr. Murray Brilliant, Center Director, Center for Human Genetics, MCRF before the announcement to discuss where the field of Precision Medicine is going. Next thing we knew, Murray was invited to the

White House for the President's announcement of the initiative. Following that, Murray was also invited to a workshop for Precision Medicine, sponsored by NIH. We have high hopes for Marshfield Clinic Health System/MCRF and our patients' participation in a new Precision Medicine Initiative. We're also delighted that Dr. Brilliant was able to represent all of us at the White House and NIH this past month; it was an honor for him and his colleagues here. We hope to have Dr. Brilliant explain what Precision Medicine is, and the promises it holds in the coming months.



Dr. Steve Ziemba,
MCRF Assoc. Dir.

MCRF and MCHS leadership, scientists, BOT members, physician-investigators and other stakeholders engaged in a strategic planning retreat on Jan 28 and 29. The retreat was focused on assessing the current internal and external environments of MCRF and making determinations of opportunities and challenges for the next three to five years, in order to position ourselves for success during this upcoming time period. The retreat was considered valuable and successful, in that it provided open discourse both within MCRF and between MCRF and MCHS. It also demonstrated everyone's common goal of advancing research within our Health System.

The retreat is only one part of the strategic planning process, though it is a large component. We are presently working with our facilitators (The Improve Group) in finalizing the summary report from the retreat. The next steps are to use this and other information to develop and approve our actual strategic plan, and more importantly, to implement it. We are at a critical point in our future, but the involvement, interest, and determination of those at the retreat as well as others who were not able to attend, have already marked this process as one that will only meet with success.

As always, thank you all for the work you do!

Marshfield Clinic Research Foundation Researcher Attends President Obama's White House Announcement for Precision Medicine Initiative



National Institutes of Health Director Francis Collins, MD, PhD (left) with Murray Brilliant, PhD (right)

Marshfield Clinic has been involved in personalized medicine database development for more than a decade, allowing providers to tailor health care to an individual's precise genetic profile.

This approach played an integral role in President Barack Obama's new Precision Medicine Initiative and for that, Murray Brilliant, PhD, director, Center for Human Genetics, was a guest at the Friday, Jan. 30, White House announcement in which the president shared how this bold new research effort will revolutionize health care. Obama first announced the initiative in his State of the Union address.

Precision medicine is an innovative approach to disease prevention and treatment that takes into account individual differences in people's genes, environments and lifestyles. It gives clinicians tools to better understand complex mechanisms underlying a patient's health, disease or condition and to better predict which treatments will be most effective.

The Precision Medicine Initiative objectives include:

- Accelerating biomedical discoveries.
- Investing in the design and testing of effective, tailored treatments for cancer.
- Creation of a voluntary national research cohort of 1 million people.

Brilliant oversees Marshfield Clinic's Personalized Medicine Research Project (PMRP), created in 2001, that now has a database of more than 20,000 volunteers. PMRP is one of the largest population-based genetic research projects in the U.S. The Clinic now uses information gained from years of PMRP studies to predict which patients will have adverse reactions to commonly prescribed anticoagulant and cholesterol-lowering medications based on their genetic make-up and medical history.

"PMRP was designed to understand genetic underpinnings of disease and we have now developed one of the first programs that demonstrated precision medicine works and is effective," Brilliant said. "This method was researched and a pilot project is now being implemented. We demonstrated this works in small groups and believe we are able to generalize this for all of our patients."

One way patients benefited from the new implementation of precision medicine was through a study of genetic variation in genes associated with drug reactions. Based on their medical records, patients who were likely to go on certain commonly prescribed anticoagulant and cholesterol-lowering medications were first tested for how they are likely to respond to the medication. Patients at risk for a bad reaction have an alert in their electronic health record that notifies their provider about a possible adverse reaction when a prescription for that drug is written and then an alternative therapy is recommended. *(continued on next page)*

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Precision Medicine Initiative *(continued from previous page)*

“We can look at their genetic variations, but also their clinical conditions and outcomes of care to develop precise, almost fingerprint-like unique medical care for each individual based on genetic and other risk factors,” Brilliant said. “Employing precision medicine can insure that our patients get better health care with fewer bad outcomes.”

Brilliant’s invitation to the White House started a month ago when National Institutes of Health Director Francis Collins called him and spoke about the potential for this announcement. “He mentioned the pioneering work done at Marshfield Clinic with PMRP and how we showed the power of this approach,” Brilliant said. “We’re not the only ones doing this now, but we were one of the first and best.”

Brilliant said the foresight of Clinic leaders, researchers, scientists, providers and staff who started PMRP more than 15 years ago and continued its work through today deserve credit. “What pleases me most is the recognition of what we’re doing at Marshfield Clinic is cutting edge, so cutting edge that we were invited to participate in this announcement,” Brilliant said. “I hope the Clinic participates in the president’s initiative and we’re able to recruit some of those one million patients for this new effort.”

Compliance Corner



Linda Jaros, RCO

I wanted to take this opportunity to introduce myself as MCRF’s new Research Compliance Officer. Many of you have worked with me in my previous role as IRB Administrator, but I wanted to put a face with my name for those of you who have not. Each of you is encouraged to contact me if you have any concerns about the compliance of the MCRF research program. Compliance encompasses federal regulations, institutional policies, issues of potential conflicts of interest or research misconduct.

The Research Compliance Department is available as a resource to you for consulting on quality improvement activities for your offices and centers. From organizing research records, to policy and procedure writing, to preparing for an external audit, we are available to assist with your needs.

Some of my first priorities include: policy development, including simplification of MCRF’s Non-Compliance policy, work on implementing simplified HIPAA Authorization template language, education to clinical investigators about various aspects of research compliance, and visiting Center meetings to meet all of you.

Screening Detects Potential Skin Cancers at Wisconsin State Cranberry Growers Association Trade Show

Physicians identified several suspected skin cancers, including at least one potentially deadly melanoma, and an even larger number of pre-cancerous lesions among 54 people who participated in free skin cancer screening during the Wisconsin State Cranberry Growers Association Winter Trade Show, Jan. 21, at the Holiday Inn, Stevens Point. Nearly half the people screened were referred to their healthcare providers for follow-up. *(continued on next page)*

Skin Cancer Screening *(continued from previous page)*

The National Farm Medicine Center (NFMC) offered the screening in conjunction with the Marshfield Clinic Dermatology Department. "This is an at-risk population, given their occupation exposes them constantly to the sun's damaging rays," said dermatology resident Tyler Conway, MD. "It is important for these cranberry growers and their families to pay attention to changing skin lesions and bring these to the attention of a healthcare professional."

Dr. Conway and dermatologist Alexandra Carley, MD, conducted the screening, the first NFMC has done with cranberry growers. "I think having Marshfield Clinic offering free skin cancer screening was a great idea," said Jessica Rezin, a central Wisconsin grower. "Cranberry growers, like all farmers, spend a lot of time out in the sun."

Previous screening done at Wisconsin Farm Technology Days yielded a research paper by Dr. Carley and Department Chair Erik Stratman, MD, soon to be published in the peer-reviewed *Journal of Agromedicine*. The earlier skin cancer is detected, the more successfully it can be treated. Skin cancer is the most common form of cancer in the United States, with 1 in 5 people developing it. "Of all the cancers farmers and growers are at risk for, skin cancer is the No. 1 cancer that can be diagnosed quickly and cured," said Matthew Keifer, MD, Director of the National Farm Medicine Center.

National Farm Medicine Center screenings in 2015 are being made possible through philanthropic support provided to Marshfield Clinic through the Auction of Champions Fund a Need program. Please check the NFMC website for upcoming screenings, <http://www3.marshfieldclinic.org/nfmc/>.

Recent Publications, Grants, and Awards

This column is to highlight recent accomplishments of MCRF researchers and MC clinical investigators.

Please select the hyperlinks to view recent [publications](#) and [January](#) grant awards.



Peggy Peissig, PhD, Principal Investigator, received notification of funding for a UO1 award submitted through Auburn University and in collaboration with the University of Wisconsin - Madison. This subcontract will support the participation of the Marshfield Clinic Research Foundation in the Post Market Surveillance of Authorized Generic and Generic Drug Products. Local Co-Investigators include Richard Berg, MS and Michael Caldwell, MD. The purpose of this study is to evaluate existing data and to develop new methods to monitor the drug safety, efficacy, usage, and substitution patterns of authorized generic drugs in different therapeutic categories in comparison with those of brand name drugs and other generic drugs. The outcome of this study will help determine whether any potential bias against generic drugs is involved in generic drug complaints and affects generic substitution. *(continued on next page)*

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Recent Publications, Grants, and Awards *(continued from previous page)*



Edward Belongia, MD, director of the Center for Clinical Epidemiology and Population Health, was featured in numerous stories about the effectiveness of this year's flu vaccine. Along with media interviews ([Marshfield News Herald](#), [CIDRAP](#), [WSAW](#)), Dr. Belongia served as an expert source for the [Canadian Press](#), which distributes news stories throughout Canada. For more information pertaining to CDC's interim report on this year's flu vaccine effectiveness, visit [ABC News](#) and the [CDC Morbidity and Mortality Weekly Report](#).

If you have recently published an article or received a grant or an award and want it included in the next issue of *Research Matters*, please contact Alexis Tavano at tavano.alexis@mcrf.mfldclin.edu.

Marshfield Clinic Receives \$620,000 Grant to Improve Adolescent HPV Vaccine Rates



Marshfield Clinic Research Foundation (MCRF) has received a \$620,000 grant to promote vaccination against a common infection that can cause cancer. The two-year project, funded by the Centers for Disease Control and Prevention (CDC), will supplement existing activities at Marshfield Clinic aimed at increasing adolescent human papillomavirus (HPV) vaccination rates.

"Increasing HPV vaccine uptake is a public health priority. The more adolescents who are vaccinated now, the more people we can protect against HPV-related cancers like cervical cancer in the future," said Huong McLean, PhD (above, left), one of the study's lead investigators at MCRF.

HPV is actually a group of more than 100 kinds of viruses. Most HPV infections are harmless, but some can lead to cancer or genital warts. An estimated 79 million Americans are infected with HPV, with 14 million new infections each year. Like several other infections such as meningitis or pertussis, HPV can be prevented with a safe and effective vaccine.

"Prior research suggests there is often hesitation with the HPV vaccine. Some parents aren't sure how safe it is or if it is worthwhile for their child, so they hold off on it," said Jeffrey VanWormer, PhD (above, right), one of two epidemiologists leading the study at MCRF's Center for Clinical Epidemiology and Population Health. "But no studies on this topic have been conducted in our area of Wisconsin yet, so we know very little about what influences the decision to get the HPV vaccine here."

Three doses of HPV vaccine are recommended for 11- and 12-year-old girls and boys. The vaccine is most effective when received before a person is exposed to an infection, and immune response to the vaccine is better in younger adolescents. Currently in the U.S., less than 40 percent of adolescent girls and 14 percent of adolescent boys get all three required doses of the HPV vaccine. *(continued on next page)*

HPV Vaccine Rate Grant *(continued from previous page)*

“The HPV vaccine is safe and effective, but very few adolescents have received the vaccination to prevent these serious diseases that HPV causes,” McLean said. “What we learn from this project may inform how other health care systems can reduce the burden of HPV infection in the patient populations they serve, which could eventually help decrease the rates of some cancers.”

[Visit the CDC's fact sheet](#) to learn more about HPV, including symptoms and prevention measures such as the HPV vaccine.

Center for Human Genetics Scientist Published



The *Journal of Medical Genetics* published the manuscript of CHG Associate Research Scientist Min (Max) He, PhD, entitled “SeqHBase: a big data toolset for family based sequencing data analysis” in January 2015. Several other Marshfield investigators contributed to the project: Thomas (Nate) Person, Scott Hebring, Zhan (Harold) Ye, Steve Schrodi, Elizabeth McPherson, Peggy Peissig, Murray Brilliant, and Ethan Heinzen (MCRF 2014 summer intern).

A short summary of the article: High-throughput sequencing technologies are now increasingly used to find disease genes, but it is difficult to infer biological insights from massive amounts of data in a short period of time. We developed a software framework called SeqHBase to help quickly identify disease genes. SeqHBase was developed based on Apache [Hadoop](#) and [HBase](#) infrastructure, which works through distributed and parallel manner over multiple data nodes. Its input includes coverage information of 3 billion sites, over 3 million variants and their associated functional annotations for each genome. With 20 data nodes, SeqHBase took about 5 seconds for analyzing whole-exome sequencing data for a family quartet and approximately 1 minute for analyzing whole-genome sequencing data for a 10-member family. We demonstrated SeqHBase’s high efficiency and scalability with several real sequencing data sets.

The full article can be read at: <http://img.bmj.com/content/early/2015/01/13/jmedgenet-2014-102907?eaf>

Collaborative Research Pilot Award Recipients Announced



Last summer marked the release of a novel award program between Marshfield Clinic Research Foundation (MCRF) and UW Madison, the *Marshfield Clinic/MCRF-UW Madison Collaborative Research Pilot Award*. Co-PIs Sanjay Shukla, PhD (MCRF, pictured on left), and Warren Rose, PharmD (UW, pictured on right), along with co-investigators Steven Schrodi, PhD (MCRF), and Jens Eickhoff, PhD (UW), will receive this award for their project, *Biomarkers of Staphylococcus aureus bacteremia*. This first-of-its-kind

award builds upon research interests and infrastructure of both partners, and serves as a catalyst for larger research endeavors of the UW ICTR partnership. The RFA required a single Principal Investigator at both institutions, meaningful and necessary collaboration, and innovation and health impact. *(continued on next page)*

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Collaborative Research Pilot Award *(continued from previous page)*

The proposed study focuses on identifying host genetic susceptibility markers that correlate with short-term *Staphylococcus aureus* bacteremia versus the prolonged bacteremia that can lead to death. *S. aureus* bacteremia is a common condition in elderly hospitalized patients, and thousands of people die from it each year in the United States. Because some patients are able to resolve this bacteremia better than others, host genetic and immune responses are thought to play a role.

The study received a lot of enthusiasm from the reviewers and the ICTR committee because of the project significance, a recognition of an existing productive collaboration between Drs. Shukla and Rose, and its potential to provide sufficient evidence for future federal grant applications. This study also exemplifies the UW ICTR focus on Team Science.

Individual investigators are bringing unique expertise to the table and will be able to address complex diseases using multi-institutional resources. The study will utilize the biobank of *S. aureus* bacteremia samples maintained by Warren Rose at UW-Madison. Dr. Shukla and his colleagues from MCRF will use their infrastructure resources and expertise to identify host genetic susceptibility markers from patient DNA, while the team led by Dr. Rose will examine host antibody responses against common toxins from this pathogen. Together, the UW and MCRF investigators will derive a statistical model to predict patient outcomes (short-term bacteremia or prolonged bacteremia including death).

This study is a continuation of a genome-wide association study conducted by Shukla and others from Marshfield that investigated genes associated with susceptibility to *S. aureus* infections of all types.

Use of Donated Funding

MC/MCRF is the beneficiary of donations from grateful patients that are expected to be used for conducting disease specific research. Through MCRF's [Internal Funding](#) policy, employees of MC can apply for access to these donated funds by submitting a research proposal to the Research Committee for scientific merit review. The "Research Committee – Full Proposal Application - Projects Requesting Funds" is located at: http://srdweb1/clinic/policies/form_results.asp?FL=Yes&L=R&typeEntity=clinic. The level of base funding available per project is currently \$50,000. (When practicing clinicians are participating in the research, an additional \$15,000 per project may be awarded to compensate for their time and effort.)

Pre-proposals are required to be submitted for review in advance of submitting a full proposal. Applications may be submitted any time prior to the start of each quarterly cycle, with new cycle dates beginning on the 16th of March, June, September and December. Applications are reviewed in the order they are received during the cycle, so it can be advantageous to submit proposals earlier in the cycle than later.

A listing of [disease specific funds](#) available can be found on the Research Mentor intranet landing page, with a link titled "Donated Funds Available for Research". Questions regarding this funding mechanism can be directed to Deb Hansen (ext. 7-9130).

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AgrAbility of Wisconsin Summit Set



AgrAbility of Wisconsin, together with the National Farm Medicine Center, is pleased to announce the upcoming AgrAbility of Wisconsin Summit. The event will take place Monday, March 16th, 2015, with registration starting at 9:00 AM. Lunch will be provided, and the event will run until 2:30 PM at the Froehle Auditorium at the Marshfield Clinic in Marshfield, WI. All are welcome to attend.

“We are very excited about this year’s summit,” said Hannah Gerbitz, Outreach Specialist for AgrAbility. “With our new grant in place, as well as some new staff members, we are ready to take our summit to new heights. Our team looks forward to providing our farmers with the opportunity to network, think about their financial future, and learn more about the agriculture topics that are affecting farmers today.”

The day-long program gives participants an opportunity to network and learn about resources available through AgrAbility and other Wisconsin programs. Topics to be covered include pain management, finances and farm transitions, Easter Seals and AgrAbility farm technology, and hot topics in agriculture. These presentations and discussions will be led by farmers and agriculture industry members. New this year will be a visit from Alice in Dairyland.

Registrations will be accepted until March 10th. Call 608-262-9336, email aaw@mailplus.wisc.edu, or click [here](#) to reserve your space today and get additional information.

AgrAbility of Wisconsin is a partnership that combines the disability expertise of Easter Seals Wisconsin with the educational networking capabilities of the UW-Extension to provide a comprehensive program for farmers and their families affected by disabilities. AgrAbility helps farmers and their families continue to farm safely and successfully.

AgrAbility of Wisconsin Promotes Success in Agriculture for Farmers with Disabilities. For more information, contact our office at 608-262-9336 or visit <http://bse.wisc.edu/agrability>.

Agritourism Safety Website Unveils Upgrades

Salzwedel honored by national agritourism association



A national survey of agritourism operators conducted by the National Children’s Center for Rural and Agricultural Health and Safety guided major updates to “Integrating Safety into Agritourism” (www.safeagritourism.com), and provided new information on activities offered and safety resources desired.

National Children’s Center Project Manager for Agritourism Marsha Salzwedel announced the website’s upgrades at the North American Farm Direct Marketing Association (NAFDMA) Convention, held Feb. 1-6 in

Nashville and Knoxville, TN.

“As agritourism continues to grow in popularity, implementing safety strategies to help maximize fun and minimize liability is increasingly important,” Salzwedel said. *(continued on next page)*

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Agritourism Safety Website Upgraded *(continued from previous page)*

Safety took center-stage at the convention when NAFDMA Executive Director Charlie Touchette presented Salzwedel the organization's "Outstanding Leadership" award. Salzwedel credited the entire Children's Center team for the long term, mutually beneficial relationship with NAFDMA.

The survey was conducted in the spring of 2014. An advisory team of farmers, agritourism association professionals, computer programmers and safety professionals used results of the survey to develop new content and redesign the homepage into walkthroughs, checklists and resources. Complete results of the survey are embargoed pending publication in a research journal. Virtual walkthroughs now cover 15 key areas of agritourism including new walkthroughs on farmers' markets, inflatables and large animal safety.

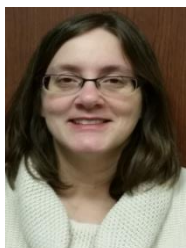
Farm Center Welcomes Project Manager



Bryan Weichelt, MS, MBA, PMP, joined the Farm Center last fall as a project manager, bringing information and communication technology expertise. He is leading research projects for both the National Children's Center and Farm Center. Weichelt comes to the Center from the Biomedical Informatics Research Center. He is a fourth generation farmer, growing up on a family dairy that is still operational. He and his wife, Stacey, welcomed identical triplet boys to the world in October 2014. Weichelt served eight years in the Army National Guard, three years active duty, and one 12-month tour in Iraq as a platoon leader. He plans to finish his PhD in Biomedical and Health Informatics later this year.

IRB Welcomes New Staff

MCRF is thrilled to announce new leadership for the Institutional Review Board (IRB). For those not familiar, the IRB is a committee of scientists, non-scientists, and community representatives charged with maintaining oversight of research studies that involve human subjects, such as clinical trials, with a focus on ethical conduct and the protection of the rights of individuals enrolled to studies.



Anna Schotthoefer, PhD



Matthew Hall, MD



Lori Scheller

Anna Schotthoefer, PhD, has been appointed as Chair of the IRB of MCRF, a role previously held by Jonathan Reeser, MD, until his retirement. Schotthoefer is a Project Scientist with the Integrated Research and Development Laboratory and is active in research on tick-borne illnesses, particularly Lyme Disease, Anaplasmosis, and others. Her role as an active scientist provides perspective on the balance of human subjects protection in scientific work. *(continued on next page)*

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IRB Staff *(continued from previous page)*

Matthew Hall, MD was appointed as Vice Chair of the IRB of MCRF effective January 1, 2015. Hall is a practicing Infectious Disease physician for Marshfield Clinic. He was previously an active IRB member from Sept. 2005 through Oct. 2010 and recently rejoined as of Dec. 2014.

Lori Scheller has been selected as the new IRB Administrator, replacing Linda Jaros who has moved into the role of Research Compliance Officer. Lori has over ten years of experience as an IRB Administrator with Aspirus, and was previously a Research Coordinator with MCRF as well as a Research Manager and Instructor in Clinical Research with other institutions. As such, she provides a blending of experience in research and regulatory requirements that will be of vital importance in helping to ensure quality research of MCRF.

In Addition:

- **Continuing Education Opportunity:** On March 19th, from 7-8AM in East Wing 5 and via MediaSite, the Marshfield Clinic Investigational Drug Program (IDP) will present on the following: 1) Describe the scope of practice for the IDP team; 2) Review highlights of most common policies and procedures and how to access full documents; 3) List the labeling requirements for investigational drugs; 4) Discuss the importance of accurate record keeping/continuous quality improvement; and 5) Explain the expectations for non-IDP pharmacists and technicians in investigational drug dispensing.
- As part of the CDC BRAVO (Boosting Recommended Adolescent Vaccines On-time) study, CCEPH has invited Dr. Jim Conway to speak about the HPV vaccine during the Grand Rounds presentation on Friday, February 20, 2015. Topics will include importance of HPV vaccine, current HPV vaccine uptake, and strategies of recommendation to improve coverage rates. All are welcome to join. Grand Rounds takes place at 12:00PM in the Froehlke Auditorium.
- The next Full Foundation meeting is scheduled for March 12, 2015 at 10AM in the Froehlke Auditorium. Questions can be routed or emailed to Jeanette Normington at 1R3 or normington.jeanette@mcrf.mfldclin.edu.
- The next Board of Trustees meeting will be held on May 14, 2015 at 6PM in the Laird 50 conference room.
- For the latest issue of the UW-Madison newsletter, *ICTR Today*, please click here: <https://ictr.wisc.edu/Newsletters>.
- *Research Matters* is always accepting announcements. Your contributions are greatly appreciated.

Contributors to this issue: Bobbi Bradley, Deb Hansen, Scott Heiberger, Linda Jaros, Cathy Marx, Dr. Bob Steiner, Lori Weigel, Michelle Wellsandt, Dr. Steve Ziemba

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