

Research Report 2016



A Message from Executive Vice President Gilbert White, II, MD, Chief Scientific Officer



2016 was another strong year for research. Grant revenues for the year were \$14.999M, just missing \$15M and exceeding budget by over \$2M. New National Institutes of Health (NIH) grants or competitive renewals were obtained by Magda Chrzanowska, Demin Wang, Bonnie Dittel, Jieqing Zhu, Hardy Weiler, Veronica Flood, Weiguo Cui, Yan Qing Ma, and Herve Falet, and the transfer of two grants by Karin Hoffmeister. These 11 new NIH grants total \$14.145M over their lifetime. Matt Riese received our sixth Bridge Award from the American Society of Hematology, more than any other institution in the country. New industry sponsored research grants total \$1.485M.

We added five new faculty members: Karin Hoffmeister and Herve Falet, a wife and husband team from Harvard with an interest in platelet formation and platelet transfusion; Veronica Flood, a Medical College of Wisconsin (MCW) Pediatric Hematologist with an interest in von Willebrand disease; Karen Carlson, an MCW Hematologist-Oncologist with an interest in leukemia and blood formation; and Lynn Malec, a Hematologist-Oncologist from the University of Pittsburgh with an interest in hemophilia and bleeding disorders. This brings to 42 the total number of research faculty: 27 in the basic science track, 9 in the clinical investigator track, and 6 in the laboratory investigator track.

Two noteworthy developments occurred during the year. First, under a charge from CEO Jackie Fredrick, we developed a plan to integrate basic and clinical research. This plan, ultimately called Research 2025, proposes to

unite basic and clinical research under the Executive Vice President for Research, with Peter Newman and Tom Abshire as part of this new leadership team. This will better enable us to forward and back translate research with clinical care. Key parts of Research 2025 are growing the endowment to \$115M and the addition of up to 9 more researchers. This integration will begin in 2017.

Second, Peter and Joan Ziegler and their children created the R. Douglas Ziegler Innovation Award and Lecture to honor Peter's father, Doug Ziegler, and the role he played at BloodCenter and the BRI for more than 30 years. The R. Douglas Ziegler Lecture will be an annual invited event delivered by a noted individual on a topic related to innovation in science. The R. Douglas Ziegler Innovation Awards will be competitively awarded to BloodCenter scientists for innovative work.

Individual accomplishments during the year were numerous. Alan Mast, M.D., Ph.D., was elected Chair of the next Hemostasis Gordon Conference to be held in the summer of 2018. Magda Chrzanowska was named the second Aster Scholar, recognizing her appointment to an NIH review panel and her success in renewing her grant. Bonnie Dittel received the 2016 Stephen C. Reingold Award from the National Multiple Sclerosis Society. Jeremy Wood in Dr. Mast's lab received the Brinkhous Award from the American Heart Association's Arteriosclerosis, Thrombosis, and Vascular Biology Council, the award to the top young investigator at the annual meeting. Tom Abshire, M.D., received the Lusher-Shapiro

Continued: A Message from Executive Vice President Gilbert White, II, MD, Chief Scientific Officer

Award from the American Thrombosis and Hemostasis Network (ATHN). Dr. Abshire was the 3rd Chair of the ATHN Board but actually was responsible for the funding that led to the creation of ATHN. As Chair, he oversaw development of the database and laying out the case to centers to use the database. Laura Savatski, Technology Transfer Officer for BCW, was nominated to the Board of Directors for the Association of University Technology Managers (AUTM). Anand Padmanabhan, M.D., Ph.D., received the 2016 National Blood Foundation Award for Innovative Research for his work with Dr. Richard Aster on the diagnosis of Heparin-Induced Thrombocytopenia. This award is given to young investigators who show unusual promise in their work. Debra Newman joined the National Heart, Lung, and Blood Institute's Program Project Parent Committee, while Magda Chrzanowska, Roy Silverstein and Bob Montgomery continue to serve on NIH review panels. Andrea Brown and Michael Frohna served on the planning committee for the annual Association of Independent Research Institutes (AIRI) Conference.

Three students, Devi Prasad Ramakrishnan from Roy Silverstein's lab, Danying Liao from Peter Newman's lab, and Kelsey Swartz from Alex Minella's lab completed their PhD degree in 2016. Jack Gorski celebrated his 30th year with the organization.

The 14th Annual Aster Lecture was delivered on June 16th by Dr. Paul Kubes, the Calvin, Phoebe and Joan Snyder Chair in Critical Care Research and Director of the Snyder Institute at the University of Calgary in Canada and an international expert in confocal microscopy. His talk, titled "Visualizing Innate Immunity in vivo," was amazingly artistic and his work was highly innovative. The 15th Annual Mosesson Lecture was delivered on October 6th by Dr. John Griffin. Dr. Griffin is Professor in the

Department of Molecular and Experimental Medicine at the Scripps Research Institute and Professor of Medicine at the University of California at San Diego.

The 10th Annual Center for Human Immunology Symposium was held October 27th at the Blood Research Institute. The symposium featured renowned speakers from the National Institutes of Health, University of Michigan, University of Chicago, University of Toronto, Emory University and the Medical College of Wisconsin. Bonnie Dittel, Renren Wen, and Jack Gorski organized this year's meeting.

The Scientific Advisory Board reviewed the Immunology program in September. Progress in the development of new mechanisms for attracting and supporting postdoctoral fellows was viewed positively. The SAB also liked the increase in industry sponsored research but felt we were capable of even more. The grant successes over the past three years were considered important and impressive. They were enthusiastic about the programs presented by the young investigators in the immunology program and about the growth of the program. The External Advisory Board reviewed the clinical research program in June. The junior clinical researchers have been successful in obtaining pilot and mentored career grants.

At years' end, there were 48 trainees in the BRI. In 2016, all of our T32 Training Grant positions were filled. We awarded a third and fourth Directors Fellow, supported by the fund from Genevieve and Scott Harkness to Melissa Lee-Sundlov in the lab of Karin Hoffmeister and Ryan Zander in the lab of Weiguo Cui. The availability of these named fellowships is helping to attract stronger trainees to our laboratories and help us fulfill the recommendation from our external Scientific Advisory Board that we

build upon our current applicant pool. Six new graduate students (Peter Volberding in Weiguo Cui's lab, Theresa Bluemn in Alex Minella's lab, Lixun Guan and Lan Luo in Demin Wang's lab, Ming Yue in Deb Newman's lab, and Azza Abdelaal in Sandra Haberichter's lab) selected the BRI as their place to train.

Transfusion Medicine

Transfusion Medicine research has a long history at BloodCenter, reflecting its basic mission to provide a safe and effective supply of blood products for patients who require transfusion.

Effective transfusion therapy requires knowledge of the biology and physiology of blood, satisfactory methods for collecting and storing blood cells with maximum preservation of function, and an understanding of the many diseases in which transfusion of blood components can be beneficial.

Research conducted by the Transfusion Medicine group addresses each of these areas. Investigators in the Transfusion Medicine Program study basic biology and clinical implications of a range of transfusion-related issues. In 2016, Drs. Karin Hoffmeister and Herve Falet joined the BRI from Harvard University to develop a program in glycobiology (biology of sugar molecules) in which they will address fundamental questions relevant to blood cell physiology and blood preservation.



Richard H. Aster, MD

CEO Emeritus and Senior Investigator, Blood Research Institute
Professor, Department of Medicine, Medical College of Wisconsin (MCW)
MD, University of Michigan 1957
Hematology, Harvard University 1965
Faculty, Harvard 1964-1970
Employed at BloodCenter of Wisconsin: 1971



Awards and Honors

- Founder, Great Lakes Hemophilia Foundation
- Founder, National Blood Foundation and Americas Blood Centers
- Founder, BloodCenter Research Foundation

Funding

R01 HL1362947 "Hemorrhagic Diseases"

Publications

1. Bougie DW, Nayak D, Aster RH. Immune destruction of human platelets in the NOD-scid mouse. *Transfusion* 56:2648-2649, 2016

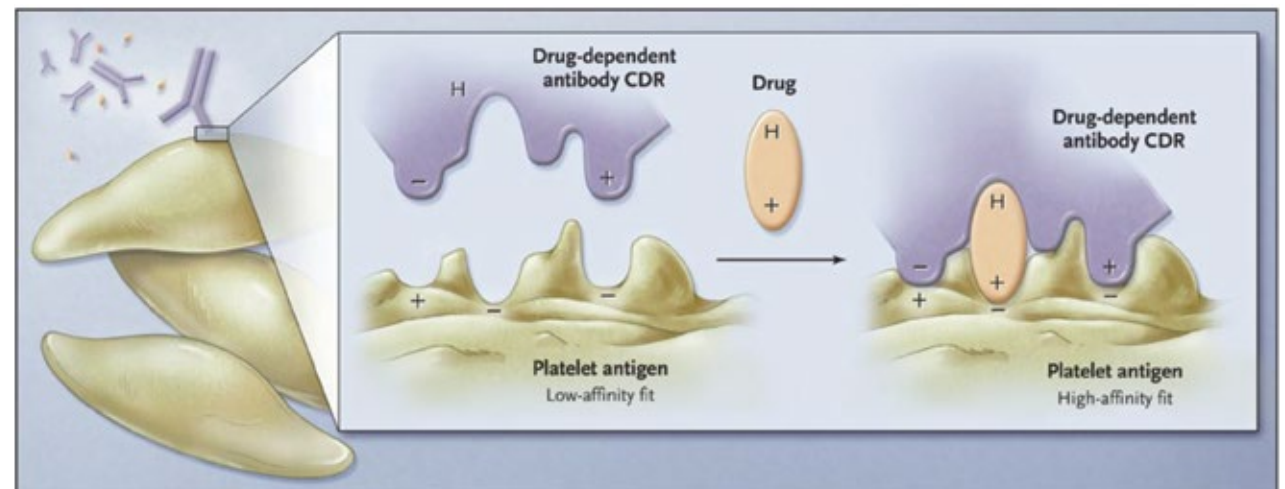
2. Falk G, Winans CG, Bowens K, Bougie DW, Curtis BR, Aster RH. An unexpected development after surgery - Post transfusion pupura! *Am J. Hematol* 91:848-851, 2016

3. Fuentes RE, Zaitsev S, Ahn HS, Hayes V, Kowalska MA, Lambert MP, Wang Y, Siegel DL, Bougie DW, Aster RH, Myers DD, Stepanova V, Cines DB, Muzykantov VR, Poncz, M., A chimeric platelet-targeted urokinase prodrug selectively blocks new thrombus formation. *J Clin Invest* 126:483-494, 2016

4. Padmanabhan A, Jones CG, Curtis BR, Bougie DW, Sullivan MJ, Peswani, N, McFarland JG, Eastwood D, Wang, D, Aster RH. A novel PF4-dependent platelet activation assay identifies patients likely to have heparin-induced thrombocytopenia/thrombosis (HIT). *Chest* 150:506-515, 2016

Research Interests

Immune destruction of red blood cells, white blood cells, and platelets is a major cause of morbidity and mortality in patients. Dr. Aster's work is aimed at understanding the causes of blood cell destruction by autoantibodies, drug-induced antibodies, and antibodies triggered by blood transfusion or exposure to fetal blood cells during pregnancy. Recent studies in his laboratory have shown that metabolites generated in the body following exposure to various drugs are capable of inducing antibodies that cause platelet destruction and bleeding. Findings made in these and related studies are defining new methods for antibody detection to improve diagnosis and treatment in patients with antibody-induced blood cell destruction.



Rachel Bercovitz, MD, MS

Associate Medical Director, Assistant Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor of Pathology and Pediatrics, Medical College of Wisconsin
MD, University of Illinois College of Medicine, 2005
Employed at BloodCenter of Wisconsin: 2012



Research Interests

Dr. Bercovitz joined the Medical Sciences Institute (MSI) faculty in August 2012. Her primary research interest is in understanding the role platelet defects (both qualitative and quantitative) play in bleeding issues in pediatric patients and developing diagnostic tools and therapeutic protocols that will minimize bleeding risk as well as exposure to blood transfusions. She is engaged in a collaborative study between the Blood Research Institute and the Herma Heart Center and Department of Pediatrics of Children's Hospital of Wisconsin to define bleeding risks and effectiveness of platelet transfusions in children undergoing cardiac surgery.

Awards and Honors

- Member, American Academy of Pediatrics 2016
- Member, American Heart Association 2016
- Member, Hemostasis and Thrombosis Research Society 2016

Publications

1. Bercovitz RS, Brenner MK, Newman DK. A whole blood model of thrombocytopenia that controls platelet count and hematocrit. *Ann Hematol* 2016 Oct; 95(11):1887-94. PMID: 27515424
2. Bercovitz RS, Josephson CD. Transfusion Considerations in Pediatric Hematology and Oncology Patients. *Hematol Oncol Clin North Am.* 2016 Jun;30(3):695-709. Review. PMID: 27113005
3. Brenner MK, Clarke S, Mahnke DK, Simpson P, Bercovitz RS, Tomita-Mitchell A, Mitchell ME, Newman DK. Effect of 22q11.2 deletion on bleeding and transfusion utilization in children with congenital heart disease undergoing cardiac surgery. *Pediatr Res.* 2016 Mar;79(2):318-24 PMID: 26492284

Brian Curtis, PhD, D(ABMLI), MT(ASCP) SBB, Investigator



Research Interests

Antibodies specific for antigens carried on blood platelets and white blood cells (neutrophils) cause thrombocytopenia and neutropenia (low neutrophil count) in various immune disorders and can be difficult to identify. Work in Dr. Curtis' laboratory has led to improved methods for detecting such antibodies and to new understanding of the blood disorders in which they are involved. Recent work led to the molecular characterization of a neutrophil antigen designated HNA-3a, a common target for antibodies that cause transfusion-related acute lung injury (TRALI) – a serious complication of blood transfusion. Other studies have led to improved methods for detecting platelet and

Director, Platelet & Neutrophil Immunology Lab, BloodCenter of Wisconsin
Senior Clinical Laboratory Director, BloodCenter of Wisconsin
Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Adjunct Professor, Clinical and Translational Science Institute, Medical College of Wisconsin
PhD, University of Wisconsin-Milwaukee, 2010
Employed at BloodCenter of Wisconsin: 1992

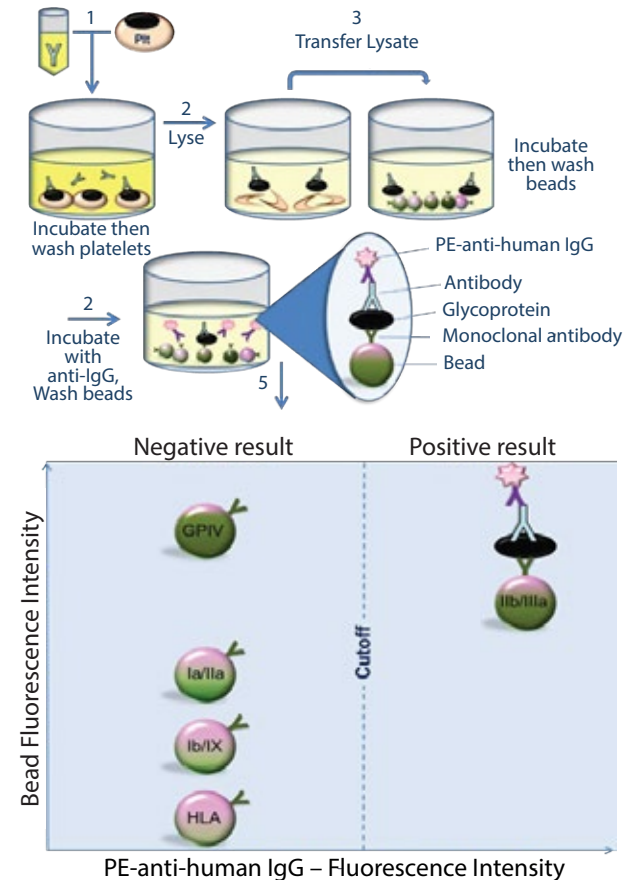
neutrophil antibodies for diagnostic purposes. Dr. Curtis is Director of the Platelet and Neutrophil Immunology Laboratory of BloodCenter of Wisconsin and applies his research findings to improve the effectiveness with which this laboratory enhances medical care for patients referred for diagnostic testing.

Awards and Honors

- Member, American Society of Hematology (ASH) 2016
- Member, International Society of Blood Transfusion (ISBT) 2016
- Member, International Society of Thrombosis & Hemostasis (ISTH) 2016

Publications

1. Curtis BR, Roman AS, Sullivan MJ, Raven CS, Larison J, Weitekamp LA. Two cases of maternal alloimmunization against human neutrophil alloantigen-4b, one causing severe alloimmune neonatal neutropenia. *Transfusion*. 2016 Jan;56(1):101-6. PMID: 26332036
2. Falk G, Winans CG, Bowens K, Bougie DW, Curtis BR, Aster RH. An unexpected development after surgery-post-transfusion purpura! *Am J Hematol*. 2016 Aug;91(8):848-51. PMID: 27159228
3. Zhang N, Zhi H, Curtis BR, Rao S, Jobaliya C, Poncz M, French DL, Newman PJ. CRISPR/Cas9-mediated conversion of human platelet alloantigen allotypes. *Blood*. 2016 Feb 11;127(6):675-80. PMID: 26634302



Gregory Denomme, PhD

Director, Immunohematology and Transfusion Services, BloodCenter of Wisconsin
Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
PhD, Microbiology and Immunology, University of Western Ontario, 1993
Employed at BloodCenter of Wisconsin: 2009



Research Interests

Dr. Denomme is Director of BloodCenter's Immunohematology and Transfusion Service Laboratory, a division of BCW Clinical Laboratories. He is an immunology and immunohematology-trained scientist with interests in the immune response to red cell antigens, the expression of blood groups, and bench-to-bedside studies in immunohematology. His work integrates the immunogenetics with transfusion medicine to explore the genetic basis of blood group expression and the functional polymorphisms underlying the pathology of immune-mediated red cell hemolysis.

Awards and Honors

- Member, American Association of Blood Banks (AABB) 2016
- Board Member, International Society of Blood Transfusion, Red Cell Immunogenetics and Blood Group Terminology Workgroup 2016
- Member, International Collaboration for Transfusion Medicine Guidelines 2016

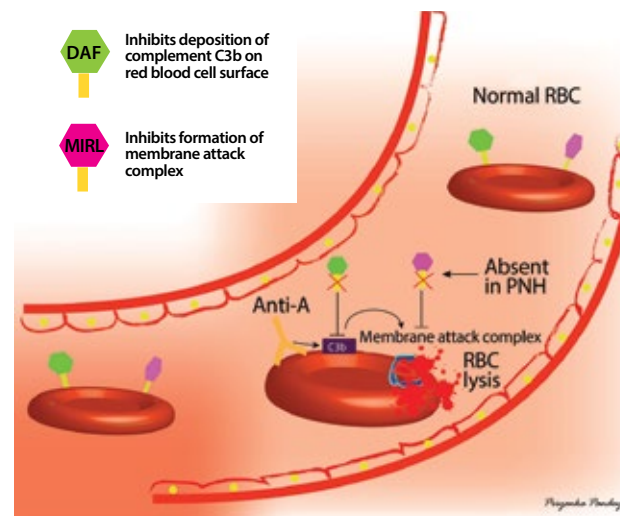
Funding

Commonwealth Transfusion Foundation 2016

Publications

1. Flegel WA, Castilho L, Heaton WA, Keller MA, Klapper EB, Lane WJ, Pirenne F, Shehata N, Stack G, St-Louis M, Tormey CA, Wagner FF, Waxman DA, Denomme GA. Molecular immunohaematology round table discussions at the AABB Annual Meeting, Anaheim 2015. *Blood Transfus.* 2016 Jul 29;1-9. PMID: 27483480
2. Flegel WA, De Castilho SL, Keller MA, Klapper EB, Moulds JM, Noizat-Pirenne F, Shehata N, Stack G, St-Louis M, Tormey CA, Waxman DA, Weinstock C, Wendel S, Denomme GA. Molecular immunohaematology round table discussions at the AABB Annual Meeting, Philadelphia 2014. *Blood Transfus.* 2016 Sep;14(5):425-33. PMID: 26710354
3. Srivastava K, Polin H, Sheldon SL, Wagner FF, Grabmer C, Gabriel C, Denomme GA, Flegel WA. The DAU cluster: a comparative analysis of 18 RHD alleles, some forming partial D antigens. *Transfusion.* 2016 Oct;56(10):2520-2531. PMID: 27480171

Antibody mediated lysis of PNH red blood cell clone



Joshua Field, MD, MS

Medical Director, BloodCenter of Wisconsin
Investigator, Blood Research Institute
Associate Professor of Medicine, Medical College of Wisconsin
Medical Director, Adult Sickle Cell Disease Clinic, Froedtert Hospital
MD, Carver College of Medicine, University of Iowa, Iowa City, IA, 2001
Employed at BloodCenter of Wisconsin: 2010



Awards and Honors

- Ad hoc reviewer: Special Emphasis Panel Zika Virus, NHLBI 2016
- Member, American Society of Hematology; Committee on Quality 2016
- Ad hoc Reviewer: Clinical Trials Review Committee, NHLBI 2016

Funding

R01 HL111969 "Biomarkers of Inflammation and Vaso-Occlusion in Sickle Cell Disease"

P50 HL110790 "A Controlled Clinical Trial of Regadenoson in Sickle Cell Anemia"

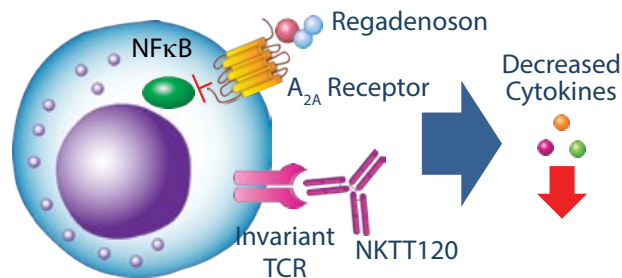
Publications

1. Karafin MS, Dogra S, Rodeghier M, Burdick M, Mehrad B, Rose CE, Strieter RM, DeBaun MR, Strunk RC, Field JJ. Increased circulating fibrocytes are associated with higher reticulocyte percent in children with sickle cell anemia. *Pediatr Pulmonol.* 2016 Mar;51(3):295-9 PMID: 26130026
2. Karafin MS, Sachais BS, Connelly-Smith L, Field JJ, Linenberger ML, Padmanabhan A. NHLBI state of the science symposium in therapeutic apheresis: Knowledge gaps and research opportunities in the area of hematology-oncology. *J Clin Apher.* 2016 Feb;31(1):38-47. PMID: 25940408
3. Karafin MS, Singavi AK, Irani MS, Puca KE, Baumann Kreuziger L, Simpson P, Field JJ. Red cell storage age policy for patients with sickle cell disease: A survey of transfusion service directors in the United States. *Transfus Apher Sci.* 2016 Feb;54(1):158-62 PMID: 26775259

Research Interests

Dr. Field is concerned with clinical aspects and optimization of treatment for adults with sickle cell disease (SCD). He currently is principal investigator on a multi-center trial to evaluate effectiveness of the adenosine_{2A} receptor agonist regadenoson, an inhibitor of inflammation that may be useful for treatment of blood vessel occlusion in SCD, as well as a trial to evaluate the cysteinyl leukotriene receptor antagonist, montelukast. Dr. Field also is examining a novel imaging modality, contrast-enhanced ultrasound, for the measurement of microvascular blood flow in patients with SCD. Preliminary results suggest that this approach can reliably measure blood flow at the capillary level and may be ideal for measuring outcomes in therapeutic trials.

Regadenoson and NKTT120 target iNKT cells



Agent	Class/mechanism	Route	Half-life	Schedule	VO approach
Regadenoson	A _{2A} R agonist/ iNKT cell inhibitor	IV	5 minutes	CIVI during VO	Treatment
NKTT120	Humanized monoclonal antibody/ iNKT cell inhibitor	IV	11 days	Undetermined (goal every 3 months)	Prevention

Shanice Williams

When she was two years old, Shanice was diagnosed with sickle cell disease, a painful disorder that deprives red cells of oxygen, and which caused her to miss out on the experiences most kids take for granted.

“I pretty much lived in the hospital during my entire childhood,” say Shanice.

As a young adult, Shanice became a patient of BCW Medical Director Dr. Josh Field and began receiving blood transfusions every four to six weeks. These treatments eased her pain, allowed her to graduate high school and work part-time as she goes to nursing school.

“Now, I know how to better control my disease,” says Shanice. “Thanks to these treatments, I can live a normal life.”



Hervé Falet, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
PhD, Paris Descartes University, 1997
Medicine, Brigham and Women's Hospital, Harvard Medical School, 2001
Employed at BloodCenter of Wisconsin: 2016



Research Interests

Dr. Hervé Falet received his master's and doctoral degrees from Paris Descartes University and completed his postdoctoral fellowship at Brigham and Women's Hospital. He joined the Blood Research Institute faculty in 2016. His primary research interests are associated with blood platelet production (thrombopoiesis) and function.

Platelets circulate in blood at a concentration of 150,000-450,000/ μ l that is maintained by a fine balance between production and clearance. At sites of vascular injury platelets respond to external stimuli by rapidly changing shape and recruiting other platelets. Deficient platelet production, due to genetic causes, secondary to cancer

therapy, or from unknown etiology, poses significant risks of mortality, mostly due to bleeding.

Blood platelets are produced in the bone marrow by megakaryocytes in a unique process that requires extensive intracellular membrane rearrangements. These include the formation of the demarcation membrane system, the surface-connected membrane extension that invaginates into the cell body and further develops to provide membranes for future platelets.

At the Blood Research Institute, Hervé investigates the roles of novel membrane binding and deforming proteins in the formation and organization of the megakaryocyte demarcation membrane system. He anticipates that his studies will yield basic information related to megakaryocyte and platelet biology, and lead to the development of new approaches to reestablish thrombopoiesis in the setting of thrombocytopenia (low platelet count).

Awards and Honors

- Bridge Grant Award, American Society of Hematology 2016
- Bridge Grant Award, Brigham Research Institute 2016
- Member, International Society on Thrombosis and Hemostasis 2016

Funding

R01 HL126743 "Endocytosis in Platelet and Megakaryocyte Biology"

Publications

1. Crescente M, Pluthero FG, Li L, Lo RW, Walsh TG, Schenk MP, Holbrook LM, Louriero S, Ali MS, Vaiyapuri S, Falet H, Jones IM, Poole AW, Kahr WH, Gibbins JM. Intracellular Trafficking, Localization, and Mobilization of Platelet-Borne Thiol Isomerases. *Arterioscler Thromb Vasc Biol.* 2016 Jun;36(6):1164-73. PMID: 27079884
2. Hoffmeister KM, Falet H. Platelet clearance by the hepatic Ashwell-Morrell receptor: mechanisms and biological significance. *Thromb Res.* 2016 May;141 Suppl 2:S68-72. PMID: 27207430
3. Li R, Hoffmeister KM, Falet H. Glycans and the platelet life cycle. *Platelets.* 2016 Sep;27(6):505-11. PMID: 27135356

Jerome Gottschall, MD

Senior Medical Director, BloodCenter of Wisconsin
Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Professor of Pathology, Department of Pathology, Medical College of Wisconsin
MD, Ohio State University College of Medicine, 1974
Employed at BloodCenter of Wisconsin: 1979



Research Interests

Dr. Gottschall is a Co-Principal Investigator on the Recipient Epidemiology and Donor Evaluation Study-III (REDS III) sponsored by the National Heart Lung and Blood Institute in which BloodCenter is one of several participating organizations. REDS III includes studies on blood safety, blood availability, HIV transmission and other transfusion-related studies. REDS-III will utilize large donor, component and recipient databases to help answer important transfusion-related questions. Among subjects to be studied are alloimmunization (immunization against transfused blood cells), impact of blood donation on donor iron levels, benefits of red cell transfusion in the elderly, and transfusion of various blood products in distinct clinical settings. Dr. Gottschall also is concerned

with the clinical aspects of immune hemolytic anemia and in the status of iron levels in repeat blood donors. In 2015, Dr. Gottschall participated as co-author on two important articles, published in *Lancet Haematology* and *Transfusion*, about the importance of red cell genotyping for transfusion medicine. An avid athlete throughout his entire life, Dr. Gottschall says sports have taught him three critical life skills that he uses in his medical work and throughout his life: discipline; persistence; and setting goals.

Awards and Honors

- Member, College of American Pathologists 2016
- Member, American Association of Blood Banks (AABB) 2016
- Member, American Society of Hematology 2016

Publications

1. Hendrickson JE, Roubinian NH, Chowdhury D, Brambilla D, Murphy EL, Wu Y, Ness PM, Gehrie EA, Snyder EL, George Hauser R, Gottschall JL, Kleinman S, Kakaiya R, Strauss RG; National Heart, Lung, and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study (REDS-III). Incidence of transfusion reactions: a multicenter study utilizing systematic active surveillance and expert adjudication. *Transfusion*. 2016 Oct;56(10):2587-2596. PMID: 27460200
2. Punzalan RC, Gottschall JL. Use and Future Investigations of Recombinant and Plasma-Derived Coagulation and Anticoagulant Products in the Neonate. *Transfus Med Rev*. 2016 Oct;30(4):189-96. Review. PMID: 27576087

Matthew Karafin, MD

Associate Medical Director, Medical Sciences Institute, BloodCenter of Wisconsin
Junior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor of Pathology, Medical College of Wisconsin
MD, Carver College of Medicine, University of Iowa, Iowa City, IA, 2007
Transfusion Medicine Fellowship, Johns Hopkins Hospital, 2011
Anatomical and Clinical Pathology Residency, Johns Hopkins Hospital, 2012
Employed at BloodCenter of Wisconsin: 2012



Research Interests

Dr. Karafin's research interests include the use of red cell transfusion to control pain in patients with sickle cell disease, etiology and prevention of red cell alloimmunization and iron overload, benefits and risks of red cell storage for patients with sickle cell disease, benefits and risks of red cell transfusions in the elderly, and the etiology and prevention of transfusion reactions.

Awards and Honors

- Member, American Society for Apheresis (ASFA) 2016
- Ad hoc Journal Reviewer, Transfusion Medicine Reviews, Transfusion 2016
- Member, American Society for Clinical Pathology (ASCP) 2016

Publications

1. Karafin MS, Dogra S, Rodeghier M, Burdick M, Mehrad B, Rose CE, Strieter RM, DeBaun MR, Strunk RC, Field JJ. Increased circulating fibrocytes are associated with higher reticulocyte percent in children with sickle cell anemia. *Pediatr Pulmonol.* 2016 Mar;51(3):295-9 PMID: 26130026
2. Karafin MS, Sachais BS, Connelly-Smith L, Field JJ, Linenberger ML, Padmanabhan A. NHLBI state of the science symposium in therapeutic apheresis: Knowledge gaps and research opportunities in the area of hematology-oncology. *J Clin Apher.* 2016 Feb;31(1):38-47. PMID: 25940408
3. Karafin MS, Singavi AK, Irani MS, Puca KE, Baumann Kreuziger L, Simpson P, Field JJ. Red cell storage age policy for patients with sickle cell disease: A survey of transfusion service directors in the United States. *Transfus Apher Sci.* 2016 Feb;54(1):158-62 PMID: 26775259

Anand Padmanabhan, MD, PhD,

Associate Investigator, Blood Research Institute
Medical Director, Therapeutic Services, BloodCenter of Wisconsin
Associate Professor of Pathology, Medical College of Wisconsin
MD, Thanjavur Medical College, Thanjavur, TN, India, 2000
PhD, Brown University, 2006
Employed at BloodCenter of Wisconsin: 2010



Awards and Honors

- National Blood Foundation Award for Innovative Research, AABB Annual Meeting 2016
- HIT research paper published in the journal Chest – also selected as the featured paper for discussion for the Chest September podcast 2016
- HIT research presented at the Annual Meeting of the American Society of Hematology (ASH) 2016

Publications

1. Padmanabhan A, Jones CG, Curtis BR, Bougie DW, Sullivan MJ, Peswani N, McFarland JG, Eastwood D, Wang D, Aster RH. A novel PF4-dependent platelet activation assay identifies patients likely to have heparin-induced thrombocytopenia/thrombosis (HIT). Chest. 2016 Sep;150(3):506-15. PMID: 26905366
2. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, Dunbar NM, Witt V, Wu Y, Shaz BH. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. J Clin Apher. 2016 Jun;31(3):149-62. PMID: 27322218
3. Karafin MS, Sachais BS, Connelly-Smith L, Field JJ, Linenberger ML, Padmanabhan A. NHLBI state of the science symposium in therapeutic apheresis: Knowledge gaps and research opportunities in the area of hematology-oncology. J Clin Apher. 2016 Feb;31(1):38-47. PMID: 25940408

Research Interests

Heparin is widely used to prevent and treat thrombosis, but some patients given this otherwise useful anticoagulant become immunized and produce antibodies that cause thrombocytopenia (heparin-induced thrombocytopenia, HIT). The low platelet counts rarely cause bleeding but some affected individuals experience thrombosis, which can be life threatening. Dr. Padmanabhan is engaged in studies to define the properties of heparin-induced antibodies that are most likely to cause thrombosis. Findings made are expected to advance the understanding of HIT and to improve laboratory diagnosis and safety of anticoagulation with heparin.

A close-up photograph of a person wearing a white lab coat and blue nitrile gloves. They are carefully handling a red blood bag with a white label. The bag is being held over a metal tray that contains several other similar blood bags. The background is slightly blurred, showing a laboratory environment with stainless steel surfaces and equipment.

Glycomics Center

The Glycomics Center, led by new faculty member, Karin Hoffmeister, opened its doors in 2016 for the Blood Research Institute. Analogous to Genomics and Proteomics, Glycomics focuses on defining the structures and functions of complex carbohydrates (sugars), as found in glycoproteins, glycolipids, and glycosaminoglycans.

Complex carbohydrates are important in many physiological processes and alterations in glycosylation are associated with vast numbers of blood related and unrelated diseases and disorders. The specific focus of the Center is to harness genomic with glycomic approaches with an emphasis on exploring transcriptional and epigenetic regulatory mechanisms of carbohydrate synthesis in health and disease. The data will help to understand and predict molecular mechanisms of carbohydrate expression and recognition by proteins important in human biology and disease. The Center will bring together scientists at BloodCenter and other institutions to understand the role that sugars play in biology.

Karin Hoffmeister, MD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Lecturer on Medicine, Harvard Medical School, Brigham and Women's Hospital
Associate Professor of Pediatrics, Boston Children's Hospital
MD, Technical University of Aachen, Aachen, Germany, 1993
Doctor of Medicine, Doctoral Research Program, Technical University of Aachen, 1995
Employed at BloodCenter of Wisconsin: 2016



Research Interests

Dr. Hoffmeister investigates how glycans regulate hematopoiesis and end-effector blood cells, including platelets. The general theme of Dr. Hoffmeister's research is to better understand the role of carbohydrates in hematopoietic stem cells, megakaryocytes and platelet function, survival, and interaction with other blood cells. Carbohydrate biosynthesis in nucleated cells is a highly regulated process involving several hundred glycosyltransferases. Correct glycan biosynthesis depends on the correct architecture and topology of the endoplasmic reticulum (ER) and Golgi apparatus. During maturation, differentiation and inflammation programmed remodeling of cell surface glycans

takes place by the regulated expression of specific glycosyltransferases to regulate different biological functions. Our studies expand towards defining glycosyltransferases cell-specific transcriptional regulatory mechanisms during hematopoiesis to combine phenotypic surface carbohydrate expression with genomic and epigenetic data in hematopoietic cells.

Awards and Honors

- Member, Hemostasis and Thrombosis Study Section 2016
- Member, Transfusion Medicine Study Section, special panel 2016
- Member, American Society of Hematology 2016

Funding

R01 HL089224-10 "Carbohydrate Mediated Platelet Clearance"

P01 HL107146-06 "Biosynthesis and Function of Lactosaminyl Glycans in Hematopoiesis"

U54 HL119145-04 "Novel Approaches for Platelet Storage B-Bic Drive"

Publications

1. Fischer K, Otori S, Meral FC, Uehara M, Giannini S, Ichimura T, Smith RN, Jolesz FA, Guleria I, Zhang Y, White PJ, McDannold NJ, Hoffmeister K, Givertz MM, Abdi R. Testing the efficacy of Contrast Enhanced
2. Ultrasound in detecting transplant rejection using a murine model of heart transplantation. *Am J Transplant.* 2016 Dec 23. PMID: 28009476.

3. Lee-Sundlov MM, Ashline DJ, Hanneman AJ, Grozovsky R, Reinhold VN, Hoffmeister KM, Lau JT. Circulating blood and platelets supply glycosyltransferases that enable extrinsic extracellular glycosylation. *Glycobiology.* 2016 Oct 26. PMID: 27798070.
4. Li R, Hoffmeister KM, Falet H. "Glycans and the platelet life cycle. *Platelets.* 2016 Sep;27 (6):505-11. PMID: 27135356.
5. Hoffmeister KM, Falet H. "Platelet clearance by the hepatic Ashwell-Morrell receptor; mechanisms and biological significance. *Thromb Res.* 2016 May; 141 Suppl 2:S68-72. PMID: 27207430.



Thrombosis, Hemostasis & Vascular Biology

The Thrombosis, Hemostasis and Vascular Biology Program is concerned with cellular and molecular mechanisms of normal blood clotting, pathological thrombosis, and events impacting the integrity of the blood vessels that transport blood throughout our body.

Studies conducted in the laboratories of the BRI range from basic scientific investigations of blood coagulation and platelet function, to the pathophysiology, treatment, and diagnosis of bleeding and clotting disorders.

Thomas C Abshire, MD

Executive Vice President, Medical Sciences Institute and Chief Medical Officer, BloodCenter of Wisconsin
Senior Investigator, Blood Research Institute
Professor of Pediatrics and Medicine, Medical College of Wisconsin
MD, Tulane University School of Medicine, 1979
Pediatrics, David Grant USAF Medical Center, Travis AFB, CA, 1979-82
Pediatric Hematology, University of Colorado Health Science Center, 1985-88
Employed at BloodCenter of Wisconsin: 2009



Gill at the Comprehensive Center for Bleeding Disorders in Milwaukee and will prospectively assess the usefulness of a new diagnostic tool—the quantitative bleeding score—in predicting the severity of bleeding during and after surgery in two common procedures: tonsillectomy and wisdom tooth extraction.

Awards and Honors

- Inaugural Lusher-Shapiro Award, ATHN, October 2016
- Best Doctors in America 2016
- Member, American Society of Hematology 2016

Funding

R01 HL112614 "Comparative Effectiveness in the Diagnosis of VWD"

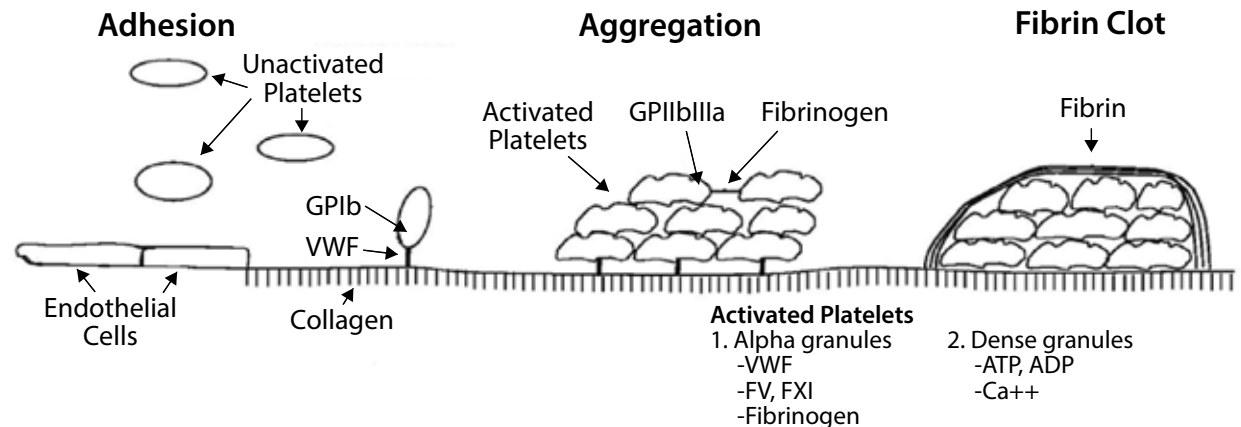
Publications

1. Boylan B, Rice AS, Neff AT, Manco-Johnson MJ, Kempton CL, Miller CH; Hemophilia Inhibitor Research Study Investigators. . . Abshire TC. Survey of the anti-factor IX immunoglobulin profiles in patients with hemophilia B using a fluorescence-based immunoassay. *J Thromb Haemost.* 2016 Oct;14(10):1931-1940. PMID: 27501440
2. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissing C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillcrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood.* 2016 May 19;127(20):2481-8. PMID: 26862110

Research Interests

One of Dr. Abshire's major research interests involves conducting clinical trials in patients with bleeding and thrombotic disorders with the aim of defining disease characteristics and evaluating new approaches to treatment. A recent focus is the evaluation of mild bleeding conditions in both children and adults, particularly those affected by von Willebrand Disease (vWD). With Bob Montgomery, MD, Tom Abshire and a team of investigators from 12 Centers across North America have started the third year of a study funded by the NIH entitled "Comparative Effectiveness in the Diagnosis of VWD" which is focusing on new diagnoses of vWD. The third aim of this grant is being led by Dr. Joan

Platelet-Vessel Interaction



Lisa Baumann Kreuziger, MD, MS

Associate Medical Director/Assistant Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Dept. of Medicine, Division of Hematology/Oncology, Medical College of Wisconsin
MD, University of Wisconsin School of Medicine and Public Health, 2006
Employed at BloodCenter of Wisconsin: 2013



patients will develop thrombotic complications including stroke or LVAD failure. Dr. Baumann Kreuziger was awarded a pilot grant from the Clinical and Translational Sciences Institute to evaluate potential mechanisms of thrombosis in patients with left ventricular assist devices.

Awards and Honors

Member, International Society on Thrombosis and Hemostasis 2016

Member, Institute for Clinical Systems Improvement, Dabigatran Working Group 2016

Member, American Society of Clinical Oncology 2016

Research Interests

Venous thromboembolism occurs in more than a half million Americans every year. Anticoagulation after venous thrombosis can prevent recurrence but is associated with a risk of bleeding. Dr. Baumann-Kreuziger aims to define the best treatment course for cancer patients with thrombosis associated with catheters and determine if a biomarker can be used to predict recurrence. Identification of a biomarker would allow anticoagulation to be individualized based on each patient's risk profile. Patients with heart failure who require implanted left ventricular assist devices (LVADs) are another group that is at high risk for bleeding and thrombotic complications. Despite use of anticoagulant and antiplatelet medications, approximately 10% of LVAD



Patient:

- Heart Failure
- Coagulation System
- Infection



Device:

- Material Interaction
- Shear Force



Management:

- Anticoagulant
- Antiplatelet
- Transfusion



Thrombosis:

- Initiation Events
- Time course
- Propagation
- No Model

Goal:
Prevention & Treatment

Magdalena Chrzanowska, PhD, FAHA

Investigator, Blood Research Institute
Associate Adjunct Professor in Pharmacology and Toxicology, Medical College of Wisconsin
Research Member, Medical College of Wisconsin Cancer Center
Medical College of Wisconsin Cardiovascular Center
PhD, University of North Carolina at Chapel Hill, 1996
MSc, Jagiellonian University, Krakow, Poland, 1991
Employed at BloodCenter of Wisconsin: 2005



causing hypertension and the narrowing and hardening of the blood vessel wall in atherosclerotic disease. In 2015, Dr. Chrzanowska succeeded in obtaining the renewal of grant support from the National Institutes of Health for her work.

Awards and Honors

- Affiliate member, Clinical and Translational Science Institute of SE Wisconsin 2016
- Affiliate Member, Medical College of Wisconsin Cardiovascular Center 2016
- Member, Medical College of Wisconsin Cancer Center, Cancer Cell Biology Research Program 2016

Funding

R01 HL111582 "Rap1 in Endothelial Homeostasis"

Publications

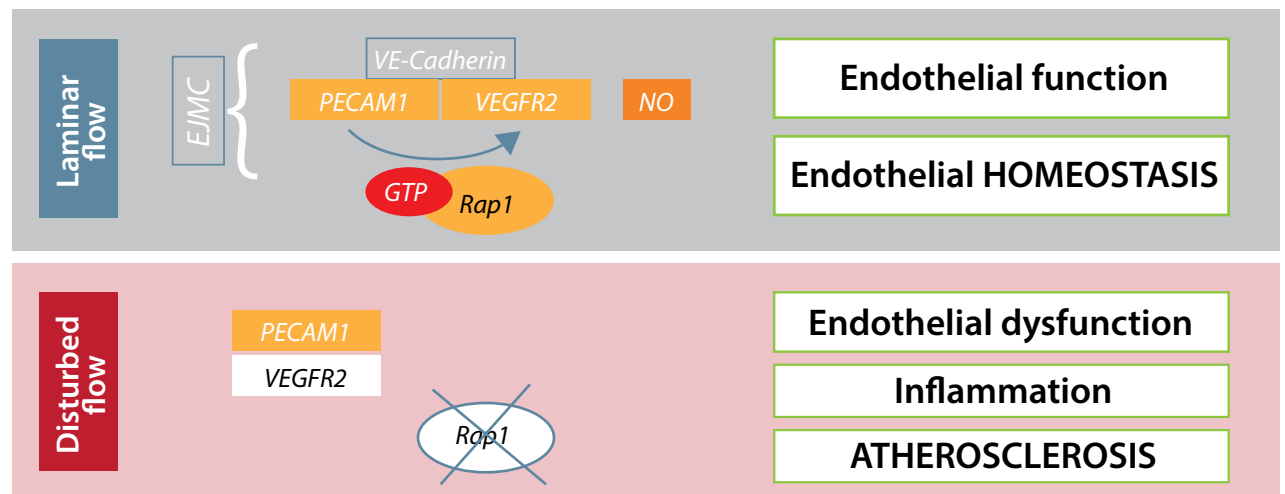
1. Rana U, Liu Z, Kumar SN, Zhao B, Hu W, Bordas M, Cossette S, Szabo S, Foeckler J, Weiler H, Chrzanowska-Wodnicka M, Holtz ML, Misra RP, Salato V, North PE, Ramchandran R, Miao QR. Nogo-B receptor deficiency causes cerebral vasculature defects during embryonic development in mice. *Dev Biol.* 2016 Feb 15;410(2):190-201. PMID: 26746789
2. Wang H, Han X, Bretz CA, Becker S, Gambhir D, Smith GW, Samulski RJ, Wittchen ES, Quilliam LA, Chrzanowska-Wodnicka M, Hartnett ME. Retinal pigment epithelial cell expression of active Rap 1a by scAAV2 inhibits choroidal neovascularization. *Mol Ther Methods Clin Dev.* 2016 Aug 24;3:16056. PMID: 27606349

Research Interests

Endothelial cells (EC) cover the inner surface of blood vessels and perform many critical functions, such as preventing leakage of blood cells and plasma from the circulation, preventing inappropriate blood clotting, regulating selective transfer of cells and substances into and out of blood vessels, and maintaining the correct blood pressure.

Importantly, EC can adapt their functions to their environment, by sensing blood flow and the presence of inflammatory signals.

Dr. Chrzanowska studies how a protein designated Rap1 regulates the response of EC to changes in blood flow and inflammation. Her work helps understand the processes



Kenneth Friedman, MD

Medical Director Hemostasis Reference Lab, Diagnostic Labs, BloodCenter of Wisconsin
Associate Investigator Blood Research Institute, BloodCenter of Wisconsin
Assistant Medical Director Comprehensive Center for Bleeding Disorders
Associate Professor of Internal Medicine and Pathology, Medical College of Wisconsin
MD, SUNY Upstate Medical University, Syracuse, NY, 1980
Employed at BloodCenter of Wisconsin: 1997



Research Interests

Thrombotic microangiopathies are a collection of diseases characterized by formation of platelet/protein aggregates that obstruct the microcirculation, resulting in multi-organ dysfunction. Microthrombi in thrombotic thrombocytopenic purpura are rich in von Willebrand factor as a consequence of deficiency of the von Willebrand factor control enzyme ADAMTS13. Alternatively in atypical hemolytic uremic syndrome, the microthrombi are rich in fibrin as a consequence of disordered complement regulation and endothelial cell injury. The current focus of Dr. Friedman's research of thrombotic microangiopathies is the evaluation of patient plasma and genetic samples in order to identify patterns of disease, underlying risk factors and prognostic markers.

Dr. Friedman's other area of interest relates to utilization of plasma and genetic markers to better understand the mechanisms underlying the bleeding that occurs in patients with defects of von Willebrand factor.

Awards and Honors

- Co-Director, National Marrow Donor Program – BCW Branch 2016
- Best Doctors in America 2016
- Ad hoc Reviewer, Journal of Thrombosis and Hemostasis, Blood, and American Journal of Hematology 2016

Publications

1. Peyvandi F, Oldenburg J, Friedman KD. A critical appraisal of one-stage and chromogenic assays of factor VIII activity. *J Thromb Haemost.* 2016 Feb;14(2):248-61. Review. PMID: 26663865
2. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissing C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood.* 2016 May 19;127(20):2481-8. PMID: 26862110
3. Epperla N, Hemauer K, Friedman KD, George JN, Foy P. Congenital Thrombotic Thrombocytopenic Purpura related to a Novel Mutation in ADAMTS13 Gene and Management during Pregnancy. *Am J Hematol.* 2016 Jun;91(6):644-6. PMID: 26822222

Tracy & Charlie Christensen

Charlie's sunny smile is how he thanks his doctors at BloodCenter of Wisconsin for their discovery of his blood disorder, type 1C von Willebrand disease.

He inherited the disease from his mom, Tracy. She was diagnosed during her pregnancy by BloodCenter's Dr. Kenneth Friedman. Because of this accurate diagnosis and the treatment she received through research done at BloodCenter, Tracy experienced a safe delivery.

Tested and diagnosed with von Willebrand after he was born, Charlie's treatment included blood transfusions. Now 4 years old, Charlie and his family are able to celebrate his good health every day.



Veronica H. Flood, MD

Associate Professor of Pediatric Hematology, Medical College of Wisconsin
Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
MD, Tufts University School of Medicine, 1999
Employed at BloodCenter of Wisconsin: 2016



Research Interests

Dr. Flood is a pediatric hematologist and researcher at the Medical College of Wisconsin in Milwaukee. She received her medical degree from Tufts University School of Medicine, and went on to complete a residency in pediatrics at Phoenix Children's Hospital and a fellowship in pediatric hematology/oncology at Oregon Health and Science University.

She began her research career as an undergraduate studying primate genetics in the Department of Anthropology at Harvard University. Her academic career in hemostasis research includes work on the biology of von Willebrand factor (VWF). Dr. Flood is interested in how VWF interacts with two of its main partners, platelet GPIb

and collagen. Since collagen is exposed at sites of blood vessel injury, the VWF-collagen interaction is an important component of hemostasis. She is also interested in the genetics of von Willebrand disease (VWD). Through collaboration with Dr. Montgomery and the Zimmerman Program for the Molecular and Clinical Biology of VWD, Dr. Flood has worked on characterizing genetic changes in VWD, with particular attention to variants that affect platelet and collagen binding. Dr. Flood has been funded by the National Heart Lung and Blood Institute since 2010, initially through a K08 award and subsequently transitioned to independent funding through an R01 grant.

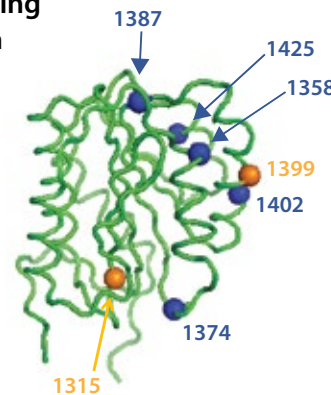
VWF A1 Domain Variants

Specific defect in binding types 4 and 6 collagen

- Type 1 VWD
- Type 2M VWD

Zimmerman Program subjects:

- 6% with A1 collagen defect
- <1% with A3 collagen defect
- 5% of type 1 subjects
- 19% of type 2M subjects



Flood et al, J Thromb Haemost 2012; Larsen et al, Haemophilia 2013

Awards and Honors

- Co-chair, Von Willebrand Disease Scientific Subcommittee of the ISTH 2016
- Secretary, Hemostasis and Thrombosis Research Society 2016
- Member, American Academy of Pediatrics 2016

Funding

R01 HL126810 "Mechanism of Type 4 Collagen Interactions with Von Willebrand Factor"

Publications

1. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissinger C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood*. 2016 May 19;127(20):2481-8. PMID: 26862110
2. Montgomery RR, Flood VH. What have we learned from large population studies of von Willebrand disease? *Hematology Am Soc Hematol Educ Program*. 2016 Dec 2;2016(1):670-677. PMID: 27913545
3. Cooper S, Sell S, Nelson L, Hawes J, Benrud JA, Kohlnhofer BM, Burmeister BR, Flood VH. Von Willebrand factor is reversibly decreased during torpor in 13-lined ground squirrels. *J Comp Physiol B*. 2016 Jan;186(1):131-9. PMID: 26481634

Joan Cox Gill, MD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Director, Comprehensive Center for Bleeding Disorders
Professor, Pediatrics and Medicine, Medical College of Wisconsin
Program Director, Hemophilia, Children's Hospital of Wisconsin
MD, Medical College of Wisconsin, 1976
Employed at BloodCenter of Wisconsin: 1991



Research Interests

Dr. Gill is engaged in clinical research concerning the diagnosis and treatment of bleeding and clotting disorders in both adult and pediatric populations. She is co-investigator of a study to evaluate the ability of bleeding questionnaires to predict surgical bleeding in tonsillectomies and molar tooth extractions; co-principal investigator of a study to characterize the pharmacogenetics of the anticoagulant warfarin in pediatric patients with thrombosis; and an investigator and member of the science and advisory committees of the CDC national study of the complications of hemophilia. Dr. Gill is chair of the Great Lakes Hemophilia Foundation Regional Committee to investigate treatment

guidelines in hemophilia and other bleeding disorders, and also directs several pharmaceutical contract research studies to evaluate replacement therapy products for patients with hemophilia and von Willebrand disease.

Awards and Honors

- Member, Science Committee, CDC Public Health Surveillance for Bleeding Disorders 2016
- Best Doctors in America 2016
- Medical Expert Panel; Federal Division of Vaccine Compensation 2016

Publications

1. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissing C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood*. 2016 May 19;127(20):2481-8. PMID: 26862110
2. Mahlangu J, Kuliczowski K, Karim FA, Stasyshyn O, Kosinova MV, Lepatan LM, Skotnicki A, Boggio LN, Klamroth R, Oldenburg J, Hellmann A, Santagostino E, Baker RI, Fischer K, Gill JC, P'Ng S, Chowdary P, Escobar MA, Khayat CD, Rusen L, Bensen-Kennedy D, Blackman N, Limsakun T, Veldman A, St Ledger K, Pabinger I; AFFINITY Investigators. Efficacy and safety of rVIII-SingleChain: results of a phase 1/3 multicenter clinical trial in severe hemophilia A. *Blood*. 2016 Aug 4;128(5):630-7. PMID: 27330001

3. Roberts JC, Morateck PA, Christopherson PA, Yan K, Hoffmann RG, Gill JC, Montgomery RR, Program Investigators TZ. Rapid discrimination of the phenotypic variants of von Willebrand disease. *Blood*. 2016 May 19;127(20):2472-80 PMID: 26917779

Sandra Haberichter, PhD

Investigator, Blood Research Institute, BloodCenter of Wisconsin
Director of Hemostasis Reference Laboratory, BloodCenter of Wisconsin
Associate Professor of Pediatrics, Medical College of Wisconsin
PhD, University of Wisconsin-Milwaukee, 1998
Fellowship, Blood Research Institute, BloodCenter of Wisconsin, 1998-2003
Employed at BloodCenter of Wisconsin: 1998



Research Interests

The plasma protein von Willebrand factor (VWF) plays a critical role in enabling blood platelets to interact with damaged blood vessels and stop bleeding. Genetically determined abnormalities of VWF function and synthesis cause von Willebrand Disease (VWD), a source of abnormal bleeding that affects about one percent of the general population. Dr. Haberichter's work is aimed at characterizing various genetic defects that cause VWD and defining how these defects affect the structure and function of the large, highly complex VWF molecule. Recent findings have shown that low VWF levels in patients with a sub-type of VWD, designated Type 1C, decrease VWF levels by shortening the survival of VWF in the circulation and have led to a novel laboratory

assay to diagnose this condition. Her current work is aimed at defining the molecular basis for accelerated clearance of VWF in patients with this form of VWD. Knowledge gained in these studies is expected to improve laboratory diagnosis and treatment of this common bleeding disorder.

Awards and Honors

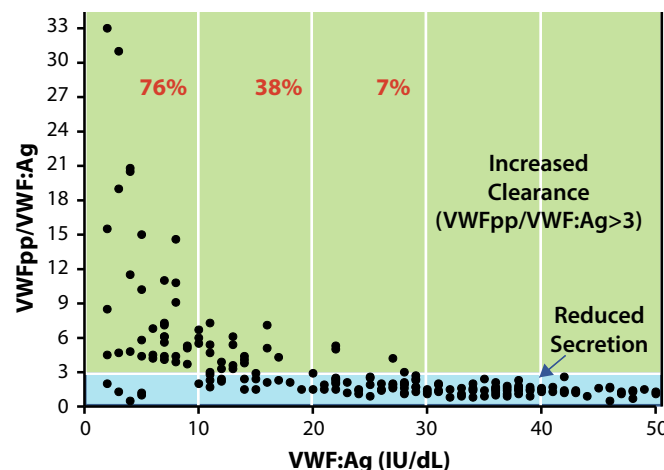
- Member, American Society of Hematology 2016
- Co-Chair, ISTH SSC scientific committee on von Willebrand Factor 2016
- Member, American Heart Association – Arteriosclerosis, Thrombosis and Vascular Biology Council 2016

Funding

P01 HL08158 "Zimmerman Program for the Molecular and Clinical Biology of VWD; Project 2: Molecular Mechanisms of VWF Alternation in Vitro/Vivo"

Publications

1. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissinger C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood*. 2016 May 19;127(20):2481-8. PMID: 26862110
2. White-Adams TC, Ng CJ, Jacobi PM, Haberichter SL, Di Paola JA. Mutations in the D'D3 region of VWF traditionally associated with type 1 VWD lead to quantitative and qualitative deficiencies of VWF. *Thromb Res*. 2016 Sep;145:112-8. PMID: 27533707



Increased VWF clearance in prevalent in moderately severe type 1 VWD.

VWFpp/VWF:Ag < 3 predicts reduced synthesis/secretion phenotype (blue).

VWFpp/VWF:Ag > 3 predicts increased plasma VWF clearance (green).

76% of subjects with VWF:Ag ≤ 10 IU/dL and 38% of subjects with VWF:Ag = 11-20 IU/dL have an increased VWF clearance phenotype (type 1C).

Shawn Jobe, MD, PhD

Medical Director, Comprehensive Center for Bleeding Disorders (CCBD),
Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Associate Professor, Department of Pediatrics and Cell Biology, Neurobiology, and Anatomy
PhD, Medical College of Wisconsin, 1998
MD, Medical College of Wisconsin, 1999
Employed at BloodCenter of Wisconsin: 2013



Research Interests

Platelets are required to stop bleeding, but inappropriate platelet adhesion and activation results in thrombosis. Dr. Jobe's group is working to understand how platelet activation is regulated. They have identified a novel platelet mitochondrial mechanism that transforms the platelet's function from proaggregatory to procoagulant. Work in Dr. Jobe's lab currently is focused on understanding how platelet mitochondrially-mediated events are regulated and how they function to regulate hemostasis and thrombosis. Changes in mitochondrial metabolism are linked closely with many diseases associated with aging including diabetes, atherosclerosis and hypertension. Insights gained through the study are

expected to provide novel avenues for the treatment and prevention of thrombosis in aging-related diseases. Platelet procoagulant activity also is important in the prevention of bleeding. In other work, researchers in Dr. Jobe's lab are investigating how these procoagulant platelet events might work to prevent bleeding in patients with severe hemophilia.

Awards and Honors

- Standing member American Heart Association Thrombosis/Hemostasis Study Section 2016 National Hemophilia Foundation Clinical Fellowship Advisory Board 2016
- Member, International Society on Thrombosis and Hemostasis 2016

Funding

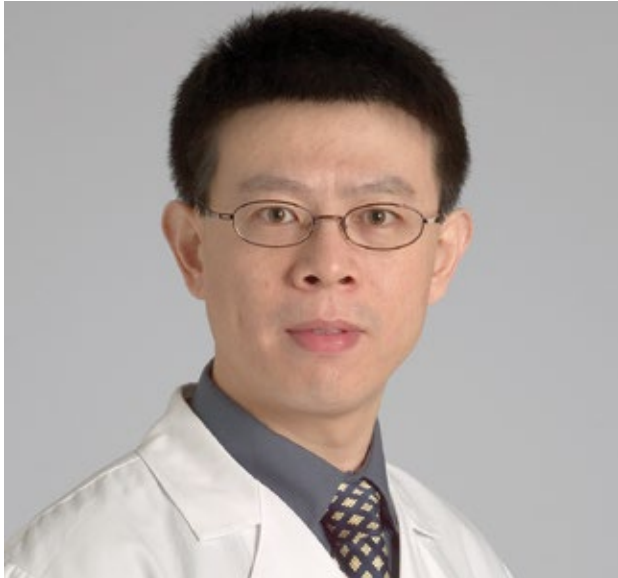
U54 HL112309 "Biological Variation in Hemophilia"

Publications

1. Matthiej, NJ, Gilio K, van Kruchten R, Jobe SM, Wieschhaus AJ, Chishti AH, Collins P, Heemskerk JW, Cosemans JM. Dual mechanisms of integrin $\alpha\text{IIb}\beta\text{3}$ closure in procoagulant platelets. *J Biol Chem*, 2013; 288 (19): 13325-35. PMID: PMC3650371.
2. Liu F, Clemmons W, Gamez G, Myers DR, Lam WA, Jobe SM. Mitochondrially-mediated integrin $\alpha\text{IIb}\beta\text{3}$ protein inactivation limits thrombus growth. *J Biol Chem*, 2013; 288(42):30672-81, MPCID: PMC3798537.

Yan-Qing Ma, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Dept. of Biochemistry, Medical College of Wisconsin
PhD, Chinese Academy of Sciences, 2004
Employed at BloodCenter of Wisconsin: 2011



Research Interests

Integrins comprise an extensive family of cell membrane proteins that are essential for cell-cell communication and signaling. In blood platelets, the integrin $\alpha\text{IIb}/\beta\text{3}$ undergoes complex intracellular and extracellular structural changes that enable these cells to adhere to damaged blood vessels and to each other to control bleeding. This process must be carefully regulated to enable hemostasis to be achieved without causing a clot to be propagated inappropriately. Dr. Ma's current work is aimed at understanding intracellular signaling cascades in platelets that control structural changes in integrin $\alpha\text{IIb}/\beta\text{3}$ during platelet activation. A particular goal is to define how kindlin-3, a key integrin regulator

in platelets, coordinates with upstream binding partners and creates a signaling network that regulates the platelet activation process. An important objective is to identify novel inhibitors of platelet function that can be useful for treatment and prevention of thrombosis.

Awards and Honors

- Member, Sigma Xi, the Scientific Research Society 2016
- Member, American Society of Hematology 2016
- Member, International Society on Thrombosis and Hemostasis 2016

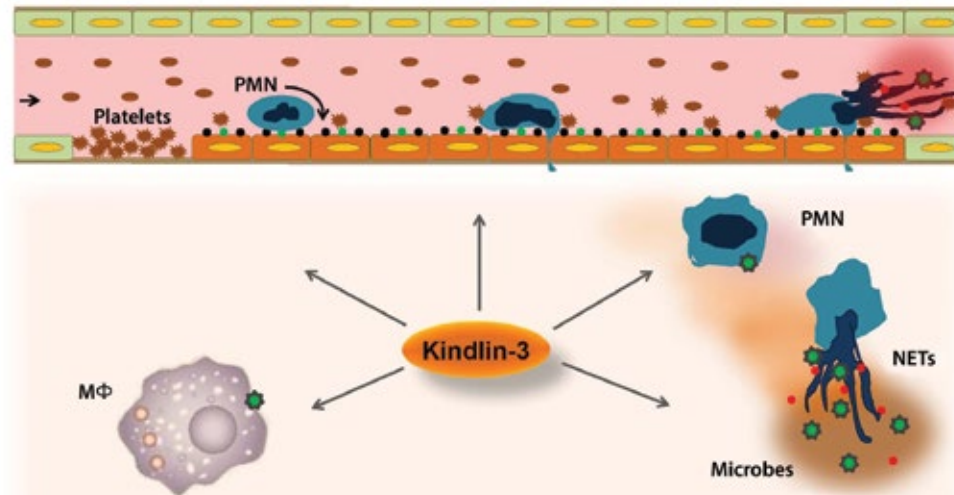
Funding

RO1 HL131654 "Kindlin-3 Signaling in Blood Cells"

Publications

1. Xu, Z., Cai, J., White, G.C., Chen, F., and Ma, Y.Q. Interaction of kindlin-3 and β2 -integrins differentially regulates neutrophils recruitment and NET release in mice. *Blood*, 2015; 126(3):373-7. PMID: PMC Journal – In Process.
2. Xu, Z., Chen, X., Zhi, H., Gao, J., Bialkowska, K., Byzova, T.V., Pluskota, E., White, G.C., Liu, J., Plow, E.F., and Ma, Y.Q. Direct interaction of kindlin-3 with integrin $\alpha\text{IIb}\beta\text{3}$ in platelets is required for supporting arterial thrombosis in mice. *Arterioscler Thromb Vasc Biol*, 2014; 34(9):1961-9. PMID: PMC4167429.

Kindlin-3 signaling in platelets and neutrophils



Lynn Malec, MD, MSc

Associate Medical Director of the Center for Comprehensive Bleeding Disorders, BloodCenter of Wisconsin MD, UW Madison School of Medicine and Public Health, 2006
Employed at BloodCenter of Wisconsin: 2016



Research Interests

Lynn Malec developed an interest in hemostasis during Internal Medicine and Pediatrics residency at the University of Pittsburgh Medical Center (UPMC)/Children's Hospital of Pittsburgh. This interest flourished during her fellowship in Pediatric Hematology/Oncology at Children's Hospital of Pittsburgh during which time she worked closely with Dr. Margaret Ragni to gain further expertise in the care of, and research involving, patients with congenital bleeding disorders across the age spectrum. During her fellowship, she pursued a Master's of Science in Clinical Research through the University of Pittsburgh Institute for Clinical Research Education. This rigorous

training furthered her interest in clinical research involving patients with bleeding disorders.

Dr. Malec's current research interests involve the investigation of inhibitor prevention and eradication in patients with hemophilia and the impact of prophylactic use in this patient population. She currently is investigating the role that recombinant factor VIII Fc fusion protein (rFVIII Fc) has in immune tolerance induction and is conducting a multi-site observational study to evaluate the efficacy and safety of rFVIII Fc administered every other day for ITI. Additionally, Dr. Malec recently was successful in competing for funding amongst a qualified pool of national junior investigators and has been awarded the 2016 DREAM Award through HTRS to explore the impact of extended half-life products in preventing joint bleeds and joint damage in patients with hemophilia. Dr. Malec is engaged in the care of adult and pediatric patients with disorders of hemostasis and thrombosis, as well as other benign hematologic conditions.

Awards and Honors

- Member, International Society on Thrombosis and Hemostasis 2016
- Member, American Society of Pediatric Hematology and Oncology 2016
- Member, Hemostasis and Thrombosis Research Society 2016

Publications

1. Malec LM, Moore CG, Bennett CM, Yee D, Kerlin B, Witmer C, Gunawardena S, Kulkarni R, Gupta S, Kouides P, Brown D, Bujnicki H, Ragni MV. Validation study of the composite score to identify von Willebrand disease in children. *J Ped Heme Onc* (in press).
2. Ragni MV, DiMichele DM, Hay CM, Malec LM, Seaman CD, Li J, Yabes JG, Butenas S, Brummel-Ziedins K. Thrombin generation and bleeding in haemophilia inhibitor patients during immune tolerance induction. *Haemophilia*. October 2015. doi: 10.1111/hae.12830 (Epub ahead of print). PMID: 26517283
3. Malec LM, Moore CG, Yabes J, Li J, Ragni MV. Postpartum haemorrhage in women with von Willebrand disease: an observational study of the Pennsylvania Health Care Cost Containment Council (PHC4) database. *Haemophilia*. September 2015. 21: e442-e445. PMID: 26189327

Alan Mast, MD, PhD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Medical Director, Medical Services, BloodCenter of Wisconsin
Associate Professor, Department of Pathology, Medical College of Wisconsin
Associate Professor, Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin
MD, Duke University, 1991
PhD, Duke University, 1991
Employed at BloodCenter of Wisconsin: 2003



Research Interests

Blood donation removes a large amount of iron that is contained in red blood cells. Therefore, many regular blood donors become iron deficient. In his clinical research, Dr. Mast studies the effect of blood donations on iron metabolism and iron deficiency in the donor. His clinical research program has found that recovery of iron stores following blood donation takes more than six months, emphasizing the need for blood donors to take iron pills following each donation. A study found that taking 19 mg iron (the amount of iron in a typical multiple vitamin with iron) for 60 days following each donation is a simple and effective means for donors to replace iron lost during blood donation. In his basic research,

Dr. Mast studies a protein designated “tissue factor pathway inhibitor (TFPI).” This protein plays a critical role in preventing blood from clotting inside blood vessels.

His basic research program has made several important discoveries about the molecular interactions between TFPI and blood coagulation proteins. These have led to new ideas about how bleeding and clotting disorders occur. TFPI alters bleeding severity in a disorder called hemophilia. Dr. Mast’s laboratory is working to develop new pharmaceutical agents that block TFPI activity as a treatment for hemophilia. A fellow in Dr. Mast’s group (Dr. Jeremy Wood) received the prestigious 2016 Kenneth Brinkhous Award from the American Heart Association.

Awards and Honors

- Member, American Society of Hematology Media Experts Subcommittee 2016
- Member, AABB Donor Health and Safety Committee 2016
- Member, Editorial Board: Blood Advances 2016

Funding

RO1 HL068835 “Characterization of an Isoform Specific Anticoagulant Function of TFPI-Alpha”

Publications

1. Mast AE. Tissue Factor Pathway Inhibitor: Multiple Anticoagulant Activities for a Single Protein. *Arterioscler Thromb Vasc Biol.* 2016 Jan;36(1):9-14. Review. PMID: 26603155

2. Mast AE, Bialkowski W, Bryant BJ, Wright DJ, Birch R, Kiss JE, D’Andrea P, Cable RG, Spencer BR. A randomized, blinded, placebo-controlled trial of education and iron supplementation for mitigation of iron deficiency in regular blood donors. *Transfusion.* 2016 Jun;56(6 Pt 2):1588-97. PMID: 26813849
3. Wood JP, Baumann Kreuziger LM, Desai UR, Mast AE. Blocking inhibition of prothrombinase by tissue factor pathway inhibitor alpha: a procoagulant property of heparins. *Br J Haematol.* 2016 Oct;175(1):123-32. PMID:27301751

Robert Montgomery, MD

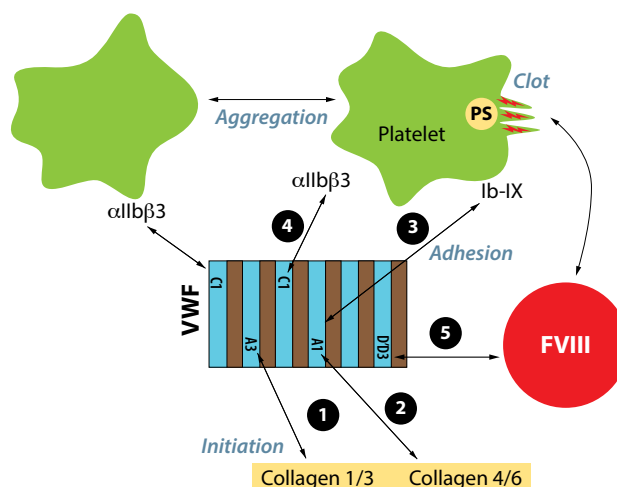
Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Attending Physician, Children's Hospital of Wisconsin
Professor of the Clinical and Translational Science Institute, Medical College of Wisconsin
Professor of Pediatric Hematology & Population Health – Epidemiology, MCW
Research Member, Hematologic Malignancy & Transplantation Research Program, MCW
MD, University of Pittsburgh Medical School, 1969
Employed at BloodCenter of Wisconsin: 1984



Research Interests

Hemophilia and von Willebrand Disease (VWD) are two major hereditary bleeding disorders that our laboratory studies. The abnormal protein in hemophilia is Factor VIII (FVIII) and in VWD it is von Willebrand factor (VWF). Although these are regulated by different genes, the two proteins bind together and help orchestrate the cessation of bleeding. In hemophilia we are exploring a unique form of gene therapy in which FVIII is induced to be synthesized and stored in platelets where it binds to VWF. This is not its normal site to be synthesized, but the platelet targets it to be released at the site where a blood vessel is damaged. This therapy can be effective even if the patient has begun to mount an immune

response that normally blocks FVIII (this occurs in 30% of hemophilia patients). Gene therapy using this approach could be used as an alternative to using FVIII by-passing therapeutics that can sometimes run into more than \$1M/yr. No one would have predicted that gene therapy could work in these individuals. Two other projects are directed at the molecular (DNA) causes of VWD.



Awards and Honors

- Executive Secretary, Hemophilia (and Thrombosis) Research Society of North America 2016
- Member, Medical and Scientific Advisory Board National Hemophilia Foundation 2016
- Chair, Fellowship Review Program, National Hemophilia Foundation 2016

Funding

RO1 HL112614 "Comparative Effectiveness in the Diagnosis of VWD"

PO1 HL081588 "Zimmerman Program for the Molecular and Clinical Biology of VWD"

PO1 HL044612 "Molecular & Cellular Mechanisms in Transfusion Medicine; Project 5: Critical Molecular Interactions of VWF and FVIII"

Publications

1. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissinger C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood*. 2016 May 19;127(20):2481-8. PMID: 26862110
2. Montgomery RR, Flood VH. What have we learned from large population studies of von Willebrand disease? *Hematology Am Soc Hematol Educ Program*. 2016 Dec 2;2016(1):670-677. PMID: 27913545
3. Roberts JC, Morateck PA, Christopherson PA, Yan K, Hoffmann RG, Gill JC, Montgomery RR, Program Investigators TZ. Rapid discrimination of the phenotypic variants of von Willebrand disease. *Blood*. 2016 May 19;127(20):2472-80 PMID: 26917779

Debra Newman, PhD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Associate Professor, Department of Pharmacology & Toxicology/Department of Microbiology and Molecular Biology, Medical College of Wisconsin
PhD, Biology, Marquette University 1989
Employed at BloodCenter of Wisconsin: 1989



Research Interests

Platelets are important in early wound healing, where they initially stick to damaged blood vessels and then aggregate with one another to form a platelet plug. Excessive bleeding occurs when platelet counts are low, or when platelets don't function well. Newborns who undergo heart surgery for congenital heart defects experience very severe bleeding. We want to know how much decreases in platelet count and function that occur during heart surgery contribute to severe bleeding in newborn heart surgery patients. This research will help physicians administer the right number of platelets at the right time to effectively control bleeding in this at risk population.

A major focus of research in our laboratory is Platelet Endothelial Cell Adhesion Molecule-1 (PECAM-1), which inhibits responses of many circulating blood cells, including platelets and T cells. T cells are immune cells that play an important role in clearing infections and eradicating tumors. We have recently discovered that PECAM-1 works with another potent T cell suppressor, Transforming Growth Factor β (TGF β), to inhibit T cell anti-tumor responses. Our current work is dedicated to developing a better understanding of how PECAM-1 and TGF β work together to inhibit T cell responses. This research will help us improve T cell-based therapies for treatment of cancer.

Awards and Honors

- Ad hoc Reviewer Journal of Biological Chemistry 2016
- Member, American Society of Hematology Committee on Scientific Affairs 2016
- Member, Interdisciplinary Program Executive Evaluation Committee, Medical College of Wisconsin 2016

Funding

PO1 HL044612 "Molecular & Cellular Mechanisms in Transfusion Medicine; Project 5: Critical Molecular Interactions of VWF and FVIII"

Publications

1. Bercovitz RS, Brenner MK, Newman DK. A whole blood model of thrombocytopenia that controls platelet count and hematocrit. *Ann Hematol* 2016 Oct; 95(11):1887-94. PMID: 27515424

2. Brenner MK, Clarke S, Mahnke DK, Simpson P, Bercovitz RS, Tomita-Mitchell A, Mitchell ME, Newman DK. Effect of 22q11.2 deletion on bleeding and transfusion utilization in children with congenital heart disease undergoing cardiac surgery. *Pediatr Res*. 2016 Mar;79(2):318-24 PMID: 26492284
3. Newman DK, Fu G, Adams T, Cui W, Arumugam V, Bluemn T, Riese MJ. The adhesion molecule PECAM-1 enhances the TGF- β -mediated inhibition of T cell function. *Sci Signal*. 2016 Mar 8;9(418):ra27. PMID: 26956486

Peter Newman, PhD

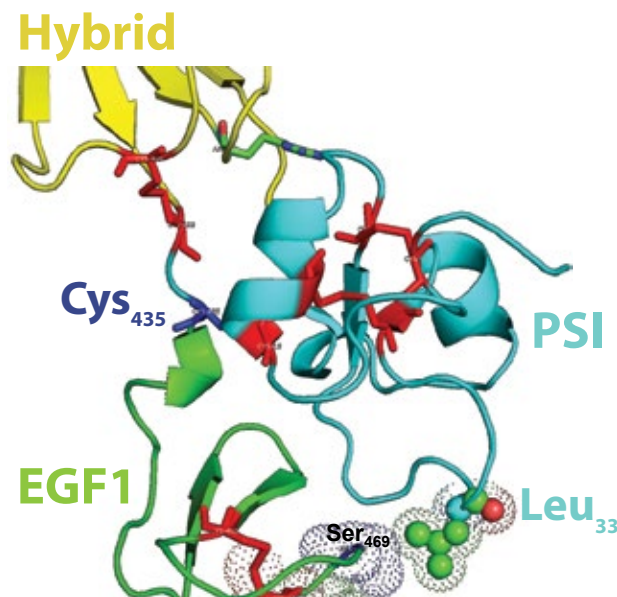
Associate Director/Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Professor, Department of Pharmacology, Medical College of Wisconsin
Professor, Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin
PhD, St. Louis University, 1983
Employed at BloodCenter of Wisconsin: 1983



Research Interests

Peter Newman's laboratory divides its attention between exploring the structure and function of the vascular cell adhesion and signaling receptor, PECAM-1, in platelets and endothelial cells (funded through a long-standing R01, now in its 28th year) and the generation of antigenically-distinct megakaryocytes and platelets from induced pluripotent stem (iPS) cells (funded through a 25 year-old Program Project grant from the NHLBI). Techniques range from CRISPR-mediated gene editing to protein crystallography to the development of animal models of platelet alloimmunity. While projects range from investigating the molecular basis of PECAM-1-mediated homophilic binding and the role

of carbohydrate residues in this process to exploiting recent advances in CRISPR gene editing technology to generate megakaryocyte progenitor cells, megakaryocytes, and platelets from induced pluripotent stem cells to create platelet alloantigen-specific cell lines capable of long-term self-renewal, cryopreservation, and distribution.



Awards and Honors

- Associate Editor, Arteriosclerosis, Thrombosis and Vascular Biology (ATVB) 2016
- Member, American Society of Hematology 2016
- Member, International Society on Thrombosis and Hemostasis 2016

Funding

- P01 HL044612 "Molecular & Cellular Mechanisms in Transfusion Medicine"
- R01 HL040926 "Molecular Biology and Function of PECAM-1"
- R01 HL130054 "Generation of Alloantigen-Specific Designer Platelets for Diagnostic and Investigative Use"

Publications

1. Lertkiatmongkol P, Paddock C, Newman DK, Zhu J, Thomas MJ, Newman PJ. The role of sialylated glycans in human PECAM-1-mediated trans-homophilic interactions and endothelial cell barrier function. *J Biol Chem.* 2016 Dec 9;291(50):26216-26225. PMID: 27793989
2. Paddock C, Zhou D, Lertkiatmongkol P, Newman PJ, Zhu J. Structural basis for PECAM-1 homophilic binding. *Blood.* 2016 Feb 25;127(8):1052-61. PMID: 26702061
3. Zhang N, Zhi H, Curtis BR, Rao S, Jobaliya C, Poncz M, French DL, Newman PJ. CRISPR/Cas9-mediated conversion of human platelet alloantigen allotypes. *Blood.* 2016 Feb 11;127(6):675-80. PMID: 26634302

Ruchika Sharma, MD

Assistant Professor of Pediatrics, Pediatric Hematology/Oncology, Medical College of Wisconsin
Associate Medical Director, Platelet and Neutrophil Immunology Laboratory, Medical Sciences Institute,
BloodCenter of Wisconsin
MD, Maulana Azad Medical College, New Delhi, India, 2008
Employed at BloodCenter of Wisconsin: 2016



Research Interests

Dr. Sharma's research interests are in clinical/ translational research in Pediatric Hemostasis and Thrombosis. She previously has studied thrombosis (blood clotting) in nephrotic syndrome, a major kidney disease in children. Dr. Sharma also has conducted clinical research in young women's hematology and mild bleeding disorders in children. Up to 20% of US women with Heavy Menstrual Bleeding have an undetected underlying bleeding disorder. Women with blood disorders have distinct healthcare needs, affecting health-related quality of life, morbidity and mortality. At BloodCenter she will continue her efforts in developing the Young Women's Hematology

program and study bleeding and clotting disorders in this unique patient population.

Dr. Sharma provides medical oversight to the Platelet Neutrophil Immunology Diagnostic Laboratory at the BloodCenter and clinical care to children and young adults with hematological disorders at Children's Hospital of Wisconsin.

Awards and Honors

- Outstanding Publication Award, Research Institute at Nationwide Children's Hospital, Columbus, OH 2016
- Member, American Society of Hematology (ASH) 2016
- Fellow of the American Academy of Pediatrics 2016

Publications

1. Sharma R, Stanek J, Koch T, Grooms L, O'Brien S. Effect of Intravenous Iron Therapy on Quality of Life in Non-Anemic Iron-Deficient Young Women with Fatigue. *Am J Hematol*. 2016 Oct; 91(10):973-7.

Qizhen Shi, MD, PhD

Investigator, Blood Research Institute, BloodCenter of Wisconsin
Associate Professor of Pediatric Hematology, Medical College of Wisconsin
MD, Fujian Medical University, Fuzhou, China 1990
PhD, Fujian Medical University, Fuzhou, China 1998
Molecular Hematology Fellowship, Medical College of Wisconsin 2000 - 2006
Employed at BloodCenter of Wisconsin: 2010



For optimal platelet-target FVIII gene therapy of hemophilia A with inhibitors, both platelet- and plasma-VWF are required. In related studies, she found that platelet-FVIII expression was optimized when platelet-derived VWF was present even without endothelial cell-derived VWF, suggesting that platelet-VWF is critical for optimal platelet-FVIII expression and storage in platelet α -granules. These studies are aimed at understanding why platelet-derived FVIII can still be effective in hemophilia A even with inhibitors, but the clinical efficacy of FIX is limited in hemophilia B mice in the presence of inhibitors.

Awards and Honors

- Member, American Society of Hematology 2016
- Member, American Society of Gene Therapy 2016
- Member, International Society of Thrombosis and Hemostasis 2016

Research Interests

Although hemophilia can be treated by transfusion, a cure remains elusive and antibodies raised against factor VIII (FVIII), the protein that is deficient in patients with the most common type of hemophilia, hemophilia A, often complicates patient management. Dr. Shi has demonstrated that targeting FVIII expression to platelets results in FVIII storage together with its carrier protein VWF in platelet α -granules and that platelet-derived FVIII (2bF8) corrects the murine hemophilia A phenotype even in the presence of high-titer anti-FVIII inhibitory antibodies (inhibitors). Dr. Shi found that VWF is essential for maintaining the clinical efficacy in platelet gene therapy of hemophilia A in the presence of inhibitors.

Funding

R01 HL102035 "Platelet Derived FVIII Gene Therapy of Hemophilia A"

Publications

1. Chen Y, Schroeder JA, Chen J, Luo X, Baumgartner CK, Montgomery RR, Hu J, Shi Q. The immunogenicity of platelet-derived FVIII in hemophilia A mice with or without pre-existing anti-FVIII immunity. *Blood*. 2016 Mar 10;127(10):1346-54P. PMID: 26668132

Roy Silverstein, MD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
John and Linda Mellowes Professor and Chair, Department of Medicine, Medical College of Wisconsin
MD, Emory University School of Medicine, 1979
Employed at BloodCenter of Wisconsin: 2011



state associated with these conditions as well as in accumulation of cholesterol in blood vessel walls, leading to atherosclerosis. The remarkable diversity of CD36 functions suggests that further work will have implications for treatment and/or prevention of arterial disease, thrombosis and cancer.

Awards and Honors

- Council member, Central Society for Clinical and Translational Research 2016
- Board member, American Society of Hematology 2016

Funding

- R01 HL111614 "Mechanistic Role of CD36 in Thrombosis"
- R01 HL126645 "MRP-14, CD36 and Thrombosis"

Publications

1. Ramakrishnan DP, Hajj-Ali RA, Chen Y, Silverstein RL. Extracellular Vesicles Activate a CD36-Dependent Signaling Pathway to Inhibit Microvascular Endothelial Cell Migration and Tube Formation. *Arterioscler Thromb Vasc Biol.* 2016 Mar;36(3):534-44. PMID: 26821945
2. Ren B, Best B, Ramakrishnan DP, Walcott B, Storz P, Silverstein RL. LPA/PKD-1-FoxO1 Signaling Axis Mediates Endothelial Cell CD36 Transcriptional Repression and Proangiogenic and Proarteriogenic Reprogramming. *Arterioscler Thromb Vasc Biol.* 2016 Jun;36(6):1197-208. PMID: 27013613
3. Zhu W, Gregory JC, Org E, Buffa JA, Gupta N, Wang Z, Li L, Fu X, Wu Y, Mehrabian M, Sartor RB, McIntyre TM, Silverstein RL, Tang WH, DiDonato JA, Brown JM, Lusis AJ, Hazen SL. Gut Microbial Metabolite TMAO Enhances Platelet Hyperreactivity and Thrombosis Risk. *Cell.* 2016 Mar 24;165(1):111-24. PMID: 26972052

Research Interests

Research by Dr. Silverstein's group concerns basic mechanisms underlying common vascular diseases, especially thrombosis, atherosclerosis and neoplastic angiogenesis, with particular emphasis on the role of a cellular receptor designated CD36 expressed on platelets, endothelial cells, macrophages and other tissues. Recent work has shown that CD36 acts as a negative regulator of new blood vessel formation (angiogenesis), a process critical to tumor growth. CD36 also enables the recognition by platelets and macrophages of danger signals generated in the body as the result of inflammation, oxidant stress, diabetes and cancer, and may play a role in the pro-thrombotic

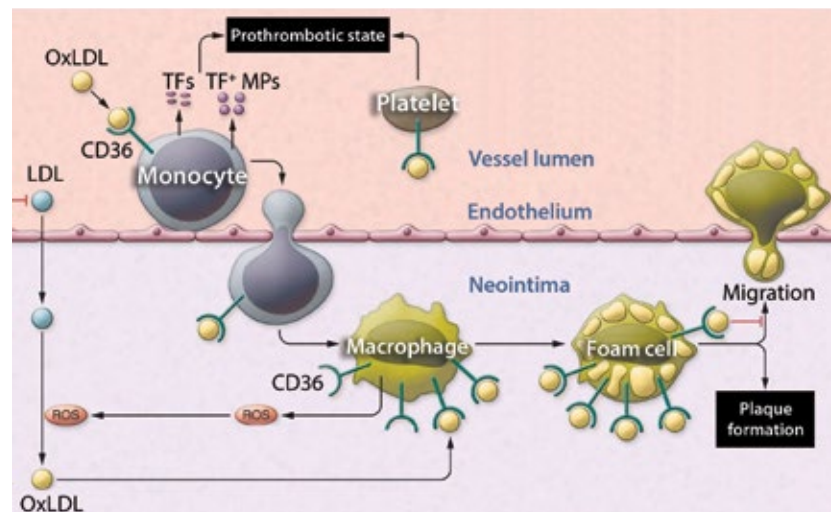


Fig 1. CD36 interactions with oxLDL on monocytes and macrophages regulates prothrombotic functions, ROS generation, foam cell formation and migration.

Hartmut Weiler, PhD

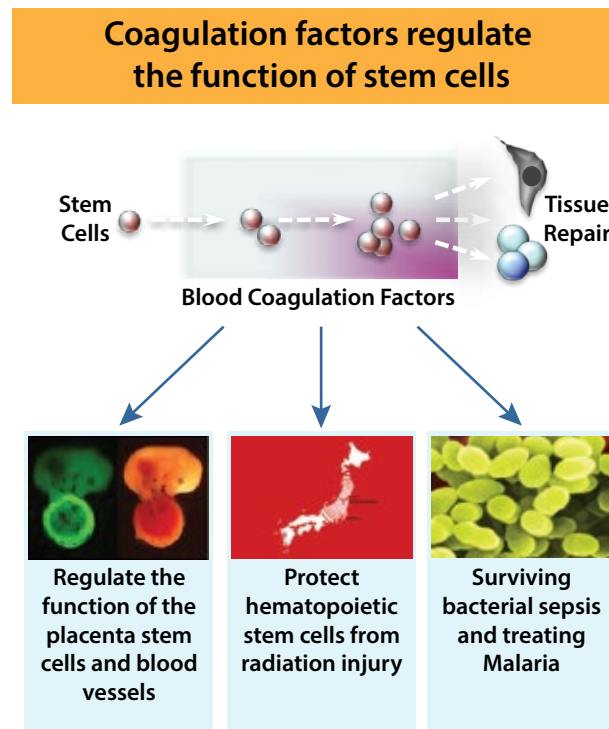
Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Associate Professor, Department of Physiology, Medical College of Wisconsin
Director, Transgenic Core Facility, Human Molecular Genetics Center, MCW
PhD, Technische Hochschule Darmstadt, Germany, 1989
Employed at BloodCenter of Wisconsin: 1997



Research Interests

Activation of the blood clotting system serves to stop bleeding when a blood vessel is injured, but is also a natural part of the body's response to infections, inflammation, and cancer, and plays an important role in embryonic development. In 2016, the National Institutes of Health supported work in Dr. Weiler's laboratory to develop innovative therapeutic interventions targeting blood coagulation pathways in diseases such as severe sepsis, malaria, and bone marrow failure after exposure to lethal doses of radiation. Dr. Weiler holds the Ziegler Family Chair for Research, and also directs the joint Transgenic Core Facility of the Medical College of Wisconsin (MCW) and the Blood Research Institute / BloodCenter of Wisconsin. The facility provides a

wide range of genome editing services facilitating the generation of genetically altered rodents serving as models for human disease.



Awards and Honors

- Member, American Society of Hematology 2016
- Member, American Heart Association 2016
- Member, International Society on Thrombosis and Hemostasis 2016

Funding

R01 HL130678 "Discovery of Novel Vascular Therapies Targeting PFEMP1-Mediated Cytoadhesion in Severe Malaria"

P01 HL044612 "Molecular & Cellular Mechanisms in Transfusion Medicine; Core C: Transgenic and Knockout Mouse Husbandry Core"

R01 HL117132 "Protein C Pathway Function in Hematopoiesis"

R01 HL133348 "Regulation of Innate Immunity by Coagulation Receptors"

Publications

1. Lin C, von der Thüsen J, Isermann B, Weiler H, van der Poll T, Borensztajn K, Spek CA. High endogenous activated protein C levels attenuates bleomycin-induced pulmonary fibrosis. *J Cell Mol Med* 2016 Nov;20(11):2029-2035. PMID: 27295971
2. Rana U, Liu Z, Kumar SN, Zhao B, Hu W, Bordas M, Cossette S, Szabo S, Foeckler J, Weiler H, Chrzanowska-Wodnicka M, Holtz ML, Misra RP, Salato V, North PE, Ramchandran R, Miao QR. Nogo-B receptor deficiency causes cerebral vasculature defects during embryonic development in mice. *Dev Biol.* 2016 Feb 15;410(2):190-201. PMID: 26746789
3. Rangrez AY, Eden M, Poyanmehr R, Kuhn C, Stiebeling K, Dierck F, Bernt A, Lüllmann-Rauch R, Weiler H, Kirchof P, Frank D, Frey N. Myozap Deficiency Promotes Adverse Cardiac Remodeling via Differential Regulation of Mitogen-activated Protein Kinase/Serum-response Factor and β -Catenin/GSK-3 β Protein Signaling. *J Biol Chem.* 2016 Feb 19;291(8):4128-43. PMID: 26719331

Gilbert White, II, MD

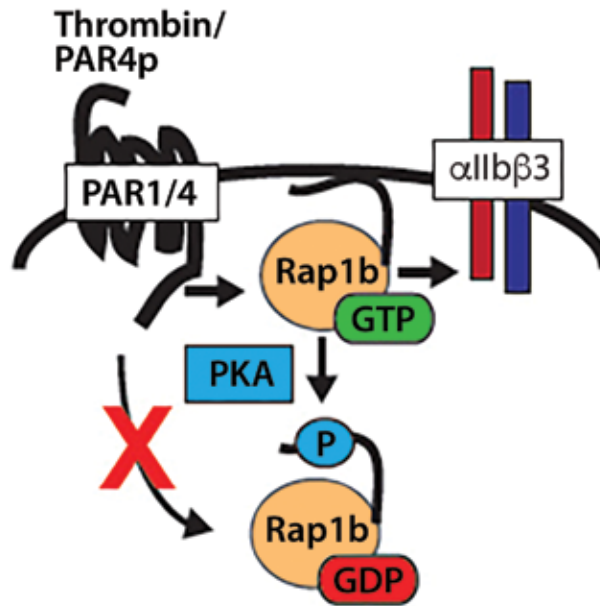
Senior Investigator/Director, Blood Research Institute, BloodCenter of Wisconsin
Richard H. and Sara E. Aster Chair for Medical Research
Professor, Dept. of Medicine, Biochemistry, and Pharmacology & Toxicology, Medical College of Wisconsin
MD, University of North Carolina, Chapel Hill, 1971
Employed at BloodCenter of Wisconsin: 2004



Research Interests

Work by Dr. White's group is aimed at understanding signaling pathways involved in the hemostatic responses by blood platelets. A current focus is the role of an intracellular protein, Rap1b, which is present in high concentrations in platelets and is critical for platelet aggregation and the activation of integrins that are critical for the platelet-platelet interactions needed to form a hemostatic plug. Rap1b also appears to be a critical target for cyclic AMP-dependent protein kinase (PKA) and phosphorylation of Rap1b by PKA is somehow involved in the inhibition of platelets by drugs that target the PKA pathway. Thus, Rap1b may function as a unique and critical, bi-directional modulator of platelet activation.

Understanding how Rap1b modulates platelet function will enable development of methods to selectively manipulate intracellular signaling pathways so as to prevent thrombosis without provoking hemorrhage in patients with impending heart attacks or strokes.



Awards and Honors

- Board member, American Society of Hematology (ASH) Bridge Grant Review Program 2016
- Member, International Society of Thrombosis and Hemostasis (ISTH) Awards and Honors Committee 2016
- Member, BEE/Council Working Group to Examine PPG Funding Mechanisms 2016

Funding

- CTSA (RFA RM07-007) "Clinical and Translational Science Award"
- 2T32 HL007209-36A1 "Research Training in Transfusion Medicine"
- 2T32 GM 080202-06 "Medical Scientist Training Program"

Publications

1. Key NS, Khorana AA, Mackman N, McCarty OJ, White GC, Francis CW, McCrae KR, Palumbo JS, Raskob GE, Chan AT, Sood AK. Thrombosis in Cancer: Research Priorities Identified by a National Cancer Institute/National Heart, Lung, and Blood Institute Strategic Working Group. *Cancer Res.* 2016 Jul 1;76(13):3671-5. PMID: 27527638

Jieqing Zhu, PhD

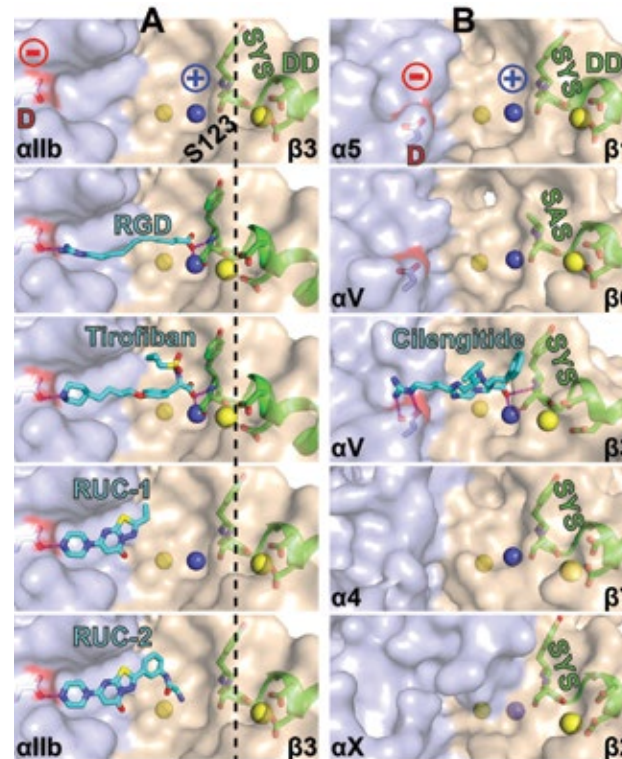
Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Department of Biochemistry, Medical College of Wisconsin
PhD, Institute of Microbiology, Chinese Academy of Sciences, Beijing 2003
Immune Disease Institute, Harvard Medical School, Boston 2009
Employed at BloodCenter of Wisconsin: 2011



Research Interests

Membrane protein complexes designated “integrins” function as cell surface receptors to regulate cell-cell and cell-matrix interactions critical for organ development, hemostasis, antigen recognition, cellular homing to specific body sites and inflammation. Dr. Zhu is using structural biology, biochemistry, and cell biology techniques to investigate how particular structural domains of integrins function in integrin activation and in transmembrane signaling, and how integrin-binding molecules (ligands) trigger integrin activation. These studies will guide the development of small molecule inhibitors of integrin function that can be useful in the treatment and prevention of thrombosis and a range

of other conditions. Recent studies have revealed the previously unappreciated function of α integrin cytoplasmic domain in integrin activation and signaling, and the structural basis of integrin ligand-mimic inhibitors induced integrin structural changes, which provides new information of structure-based drug design.



Awards and Honors

- Member, American Society of Hematology (ASH) 2016
- Member American Heart Association (AHA) 2016

Funding

R56 HL122985 “Conformational Regulation in Integrin Bidirectional Transmembrane Signaling”
R01 HL131836 “Structural Transition of Cellular Integrins and Applications Thereof”

Publications

1. Lertkiatmongkol P, Paddock C, Newman DK, Zhu J, Thomas MJ, Newman PJ. The role of sialylated glycans in human PECAM-1-mediated trans-homophilic interactions and endothelial cell barrier function. *J Biol Chem.* 2016 Dec 9;291(50):26216-26225. PMID: 27793989
2. Paddock C, Zhou D, Lertkiatmongkol P, Newman PJ, Zhu J. Structural basis for PECAM-1 homophilic binding. *Blood.* 2016 Feb 25;127(8):1052-61. PMID: 26702061
3. Santoso S, Wihadmadyatami H, Bakchoul T, Werth S, Al-Fakhri N, Bein G, Kiefel V, Zhu J, Newman PJ, Bayat B, Sachs UJ. Antiendothelial $\alpha\beta3$ Antibodies Are a Major Cause of Intracranial Bleeding in Fetal/Neonatal Alloimmune Thrombocytopenia. *Arterioscler Thromb Vasc Biol.* 2016 Aug;36(8):1517-24. PMID: 27283740



Immunology

Immunobiology has been a cornerstone of research at BloodCenter of Wisconsin since 1947, going back to the early days of immunohematology. Studies by BCW investigators led to the identification of some of the first antigen systems specific to red blood cells.

BloodCenter investigators facilitated the first bone marrow transplant from an unrelated donor to successfully treat bone marrow failure (aplastic anemia) and played key roles in creation of the National Marrow Donor Program.

As knowledge of the immune system has grown, BCW's research activities in immunology have kept pace. Current research interests include fundamental aspects of the immune response as well as immunological memory, host responses to pathogens and tumors, and autoimmune responses. BCW immunologists also engage in the development of new therapies for cancer and autoimmunity.

Matthew Anderson, MD, PhD

Medical Director, Diagnostic Laboratories
Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Pathology, Medical College of Wisconsin
Member, Human and Molecular Genetics Center, Medical College of Wisconsin
MD, Medical College of Wisconsin, 2006
PhD, Medical College of Wisconsin, 2004
Employed at BloodCenter of Wisconsin: 2013



Research Interests

Dr. Anderson's research interests include the use of high-throughput sequencing technologies for clinical diagnostics and biomarker discovery, with a focus on transplantation. Human leukocyte antigens (HLA) are key molecular determinants of the adaptive immune response, and also control the host immune response to hematopoietic and solid-organ transplants. Clinically, the success of a transplant critically depends on a high degree of similarity between the HLA molecules of the donor and recipient. However, HLA genes are among the most polymorphic in the human genome, complicating our efforts to genotype patients using standard DNA sequencing techniques. Next-generation

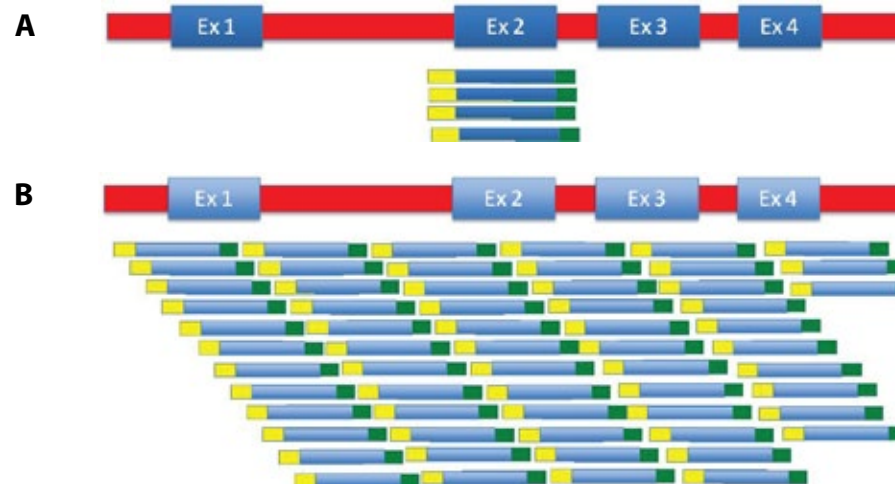
sequencing technologies can improve the accuracy of HLA genotyping by virtue of clonal template amplification and sequencing, and we currently utilize this approach for routine clinical testing. Dr. Anderson also is partnering with FMLH and CIBMTR to investigate the impact of full-gene HLA sequencing on the outcome of hematopoietic cell transplantation. In the future, he plans to develop next-generation sequencing assays to analyze other genes important for the immune response to transplants and to monitor patients for rejection.

Awards and Honors

- Member, Association of Molecular Pathology 2016
- Fellow, College of American Pathologists 2016
- Member, Government Affairs Committee, BioForward of Wisconsin 2016

Publications

1. Churchill JL, Puca KE, Meyer ES, Carleton MC, Truchan SL, Anderson MJ. Comparison of ϵ -Aminocaproic Acid and Tranexamic Acid in Reducing Postoperative Transfusions in Total Hip Arthroplasty. *J Arthroplasty*. 2016 Dec;31(12):2795-2799.PMID: 27286909



Strategies for HLA genotyping

A: Standard methods for HLA genotyping typically sequence only 1-3 exons of the HLA gene (exon 2 in this example).

B: Next-generation sequencing methods utilize overlapping DNA fragments to sequence the entire HLA gene.

Weiguo Cui, MD, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Department of Microbiology and Molecular Genetics, Medical College of Wisconsin
MD/PHD, Tianjin Medical University, China, 2004
Dept. of Immunobiology, Yale University School of Medicine, 2012
Employed at BloodCenter of Wisconsin: 2012



Awards and Honors

- Member, American Association of Immunologists 2016
- Member, American Association of Hematologists 2016
- Member, American Association for the Advancement of Science 2016

Funding

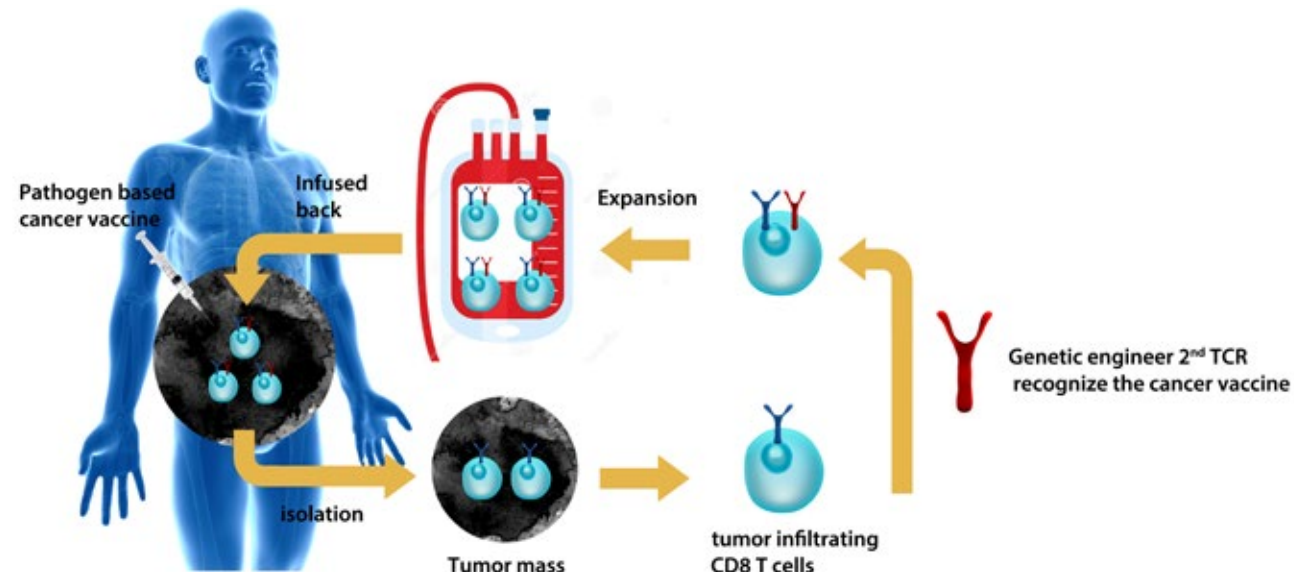
R01 AI125741 "The Cellular and Transcriptional Control of CD8 T Cell Functional Adaptation to Chronic Viruses"

Publications

1. Kutty RG, Xin G, Schauder DM, Cossette SM, Bordas M, Cui W, Ramchandran R. Dual Specificity Phosphatase 5 Is Essential for T Cell Survival. PLoS One. 2016 Dec 9;11(12):e0167246. doi: 10.1371/journal.pone.0167246. PMID: 27936095
2. Newman DK, Fu G, Adams T, Cui W, Arumugam V, Bluemn T, Riese MJ. The adhesion molecule PECAM-1 enhances the TGF- β -mediated inhibition of T cell function. Sci Signal. 2016 Mar 8;9(418):ra27. PMID: 26956486

Research Interests

Following infection, induction of a subset of lymphocytes designated memory T cells is critical for achieving protection against exposure to bacteria and viruses. Dr Cui's studies are aimed at improving the understanding of memory T cell development. His current work is focused on the study of epigenetic changes that take place in lymphocytes during the response to an acute infection. An immediate goal is to identify specific chromosomal structures that influence T cell memory. Findings made will improve basic understanding of the immune response and have implications for the treatment and prevention of infectious diseases.



Bonnie Dittel, PhD

Senior Investigator, BloodCenter of Wisconsin, Blood Research Institute
Medical College of Wisconsin, Department of Microbiology and Immunology
PhD, University of Minnesota
Postdoctoral Training, Yale University
Employed at BloodCenter of Wisconsin: 2000



Research Interests

Autoimmunity occurs when the immune system mounts an inappropriate attack on one's own body tissues. Dr. Dittel's laboratory is concerned with immune regulation that occurs during multiple sclerosis (MS), the most prevalent autoimmune disorder affecting the central nervous system (CNS). For this work, she is utilizing a mouse model of MS designated experimental autoimmune encephalomyelitis (EAE). Current studies are aimed at understanding how key cells of the immune system (T and B lymphocytes) interact to influence the autoimmune process that causes damage to CNS tissue. Recent studies have shown that B lymphocytes influence a critical subset of T lymphocytes designated T regulatory

cells (Treg) that are essential for controlling autoimmunity. Dr. Dittel also is investigating how T lymphocytes propagate EAE by studying the mechanisms whereby they open the blood-brain-barrier and induce neuronal damage. Findings made are expected to suggest new approaches for treating MS and other immune disorders affecting the nervous system.

Awards and Honors

- Stephen C. Reingold Award, National Multiple Sclerosis Society 2016
- Member, American Association of Immunologists 2016
- Member, American Society for Neurochemistry 2016

Funding

R56AI122655 "Mechanisms of a Novel Regulatory B Cell Subset"

Publications

1. Ray, A. and B.N. Dittel. B cells to the rescue: regulatory B cells are a promising therapeutic target for autoimmune disease. Atlas of Science. Feb. 1, 2016. <http://atlasofscience.org/b-cells-to-the-rescue-regulatory-b-cells-are-a-promising-therapeutic-target-for-autoimmune-disease/#more-7195>

Jack Gorski, PhD

Senior Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Microbiology and Immunology, Medical College of Wisconsin
PhD, University of Cincinnati, 1976
Employed at BloodCenter of Wisconsin: 1986



Research Interests

The immune response is a complicated process involving direct and indirect communication between many specialized types of cells. Dr. Gorski studies this process at a molecular level. Recent studies have provided new insights into how the immune system recognizes and generates a response against protein fragments (peptides) from germs or viruses. He is the inventor of innovative methods to characterize genetic differences between individuals that determine which protein fragments can be recognized, and how to measure the range of unique immune cells that recognize these protein fragments. Dr. Gorski currently studies how immune responses are affected by aging, how T cell

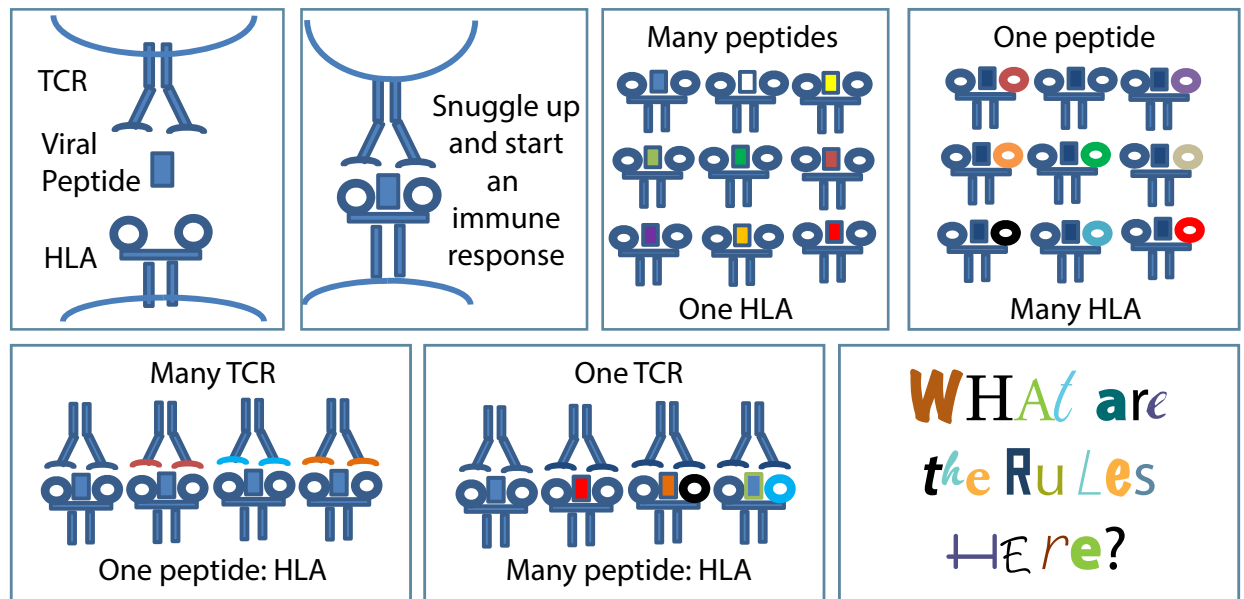
responses differ between healthy children and children with an autoimmune disease, and how the spread of influenza among older persons in the US can be tracked utilizing the tools of molecular biology. Findings made in this work will advance basic understanding of the human immune response and its relation to autoimmunity, tissue transplantation and infectious disease.

Awards and Honors

- Director, Center for Human Immunology, Blood Research Institute 2016
- Ad hoc reviewer – National Institutes of Health special study sections 2016

Publications

1. Yassai MB, Demos W, Gorski J. CDR3 motif generation and selection in the BV19-utilizing subset of the human CD8 T cell repertoire. *Mol Immunol.* 2016 Apr;72:57-64. PMID: 26963408
2. Yassai MB, Demos W, Janczak T, Naumova EN, Gorski J. CDR3 clonotype and amino acid motif diversity of BV19 expressing circulating human CD8 T cells. *Hum Immunol.* 2016 Jan;77(1):137-45. PMID: 26593155



Subramaniam Malarkannan, PhD

Investigator Garetto Chair for Immunology and Immunotherapy, Blood Research Institute
Professor of Medicine, Divisions of Hematology/Oncology, Microbiology & Molecular Genetics, and Pediatrics,
Medical College of Wisconsin
PhD, Madurai Kamaraj University, Madurai, TN, India, 1991
Employed at BloodCenter of Wisconsin: 2000



Research Interests

Natural Killer (NK) cells are a type of white blood cells that specialize in killing virus-infected and malignant cells. Due to this specialty, there is a great deal of interest in using NK cells for therapeutic purposes. Dr. Malarkannan's group studies basic, translational, and clinical aspects of NK cells. The group's studies have identified pathways that influence target cell killing and associated inflammatory changes. This work may show how these pathways can be manipulated to maximize the killing effect and minimize the adverse effects of NK cell therapy. This constitutes a new form of transfusion therapy for treatment of malignant conditions.

Awards and Honors

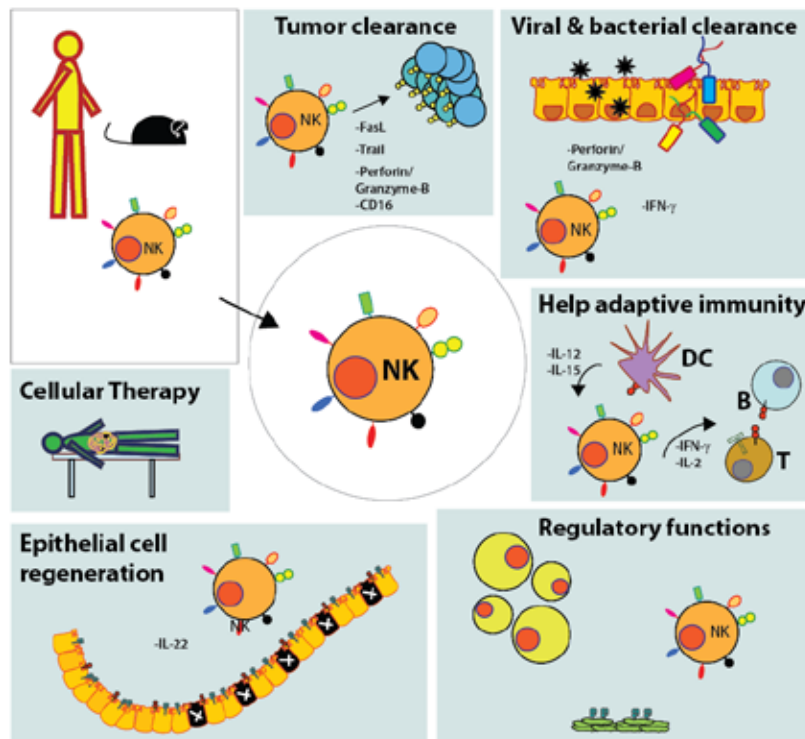
- External Reviewer, Swiss Cancer League, Bern Switzerland 2016
- Ad hoc Member, Innate Immunity and Inflammation Study Section, NIAID, NIH 2016

Funding

RO1 AI102893 "Molecular Mechanisms of Signaling Co-Ordination in Innate Lymphocytes"

Publications

1. Rajasekaran K, Riese MJ, Rao S, Wang L, Thakar MS, Sentman CL, Malarkannan S. Signaling in Effector Lymphocytes: Insights toward Safer Immunotherapy. *Front Immunol.* 2016 May 12;7:176. Review. PMID: 27242783

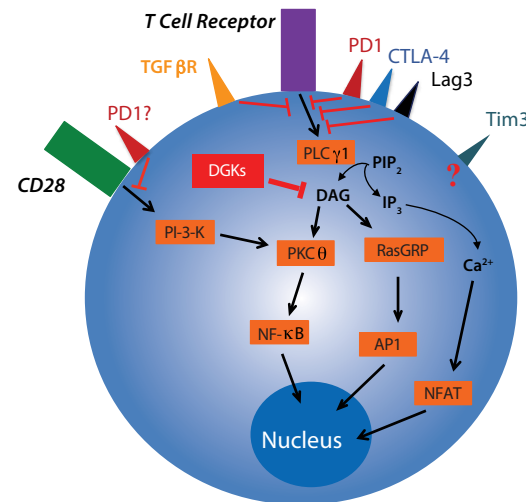


Matthew Riese, MD, PhD

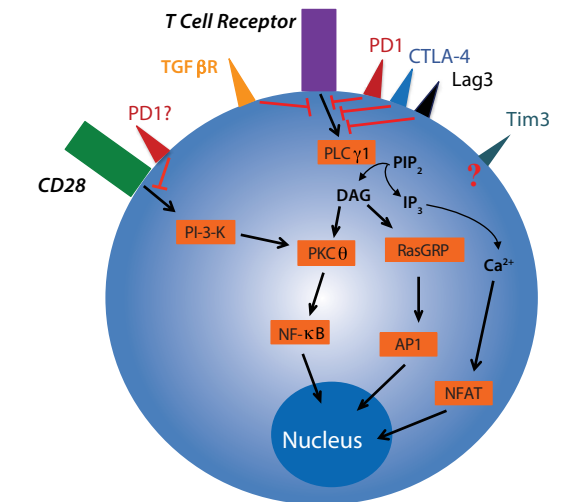
Assistant Professor, Department of Medicine, Division of Hematology/Oncology, Medical College of Wisconsin
Associate Investigator, Blood Research Institute, Blood Center of Wisconsin
PhD, Medical College of Wisconsin, 2002
MD, Medical College of Wisconsin, 2004
Employed at BloodCenter of Wisconsin: 2012



Normal T Cell



DGK-Deficient Effector T Cell



Research Interests

Immunotherapies for the treatment of malignancy have recently begun to demonstrate impressive success in achieving long-term disease control and eradication, however, the therapies work in a minority of patients. The Riese lab is investigating ways to improve upon existing cancer immunotherapies by targeting “off” switches inside T cells, the cells responsible for killing cancer cells. His studies have incorporated both oncology and chemistry and have allowed him to blend medicine and research throughout his career.

Awards and Honors

- Member, American Society for Hematology 2016
- Member, American Association for Cancer Research 2016
- Member Society for Leukocyte Biology 2016

Publications

1. Newman DK, Fu G, Adams T, Cui W, Arumugam V, Bluemn T, Riese MJ. The adhesion molecule PECAM-1 enhances the TGF-β-mediated inhibition of T cell function. *Sci Signal*. 2016 Mar 8;9(418):ra27. PMID: 26956486

2. Rajasekaran K, Riese MJ, Rao S, Wang L, Thakar MS, Sentman CL, Malarkannan S. Signaling in Effector Lymphocytes: Insights toward Safer Immunotherapy. *Front Immunol*. 2016 May 12;7:176. Review. PMID: 27242783
3. Riese MJ, Moon EK, Johnson BD, Albelda SM. Diacylglycerol Kinases (DGKs): Novel Targets for Improving T Cell Activity in Cancer. *Front Cell Dev Biol*. 2016 Oct 17;4:108. Review. PMID: 27800476

Demin Wang, PhD

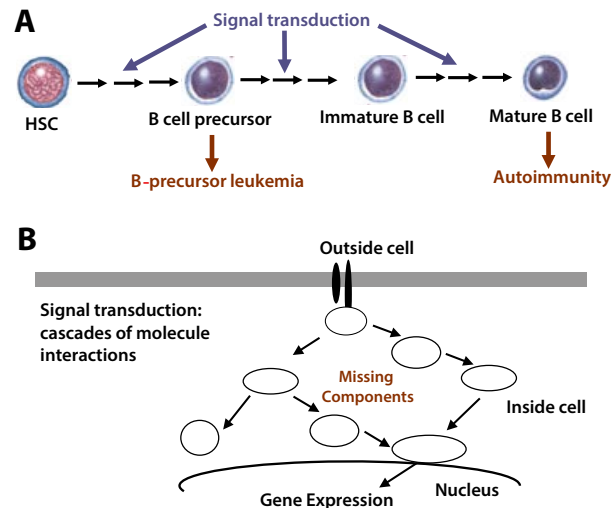
Senior Investigator, and John B. and Judith A. Gardetto Chair for Cancer Research
Blood Research Institute, BloodCenter of Wisconsin
Adjunct Faculty, Department of Microbiology and Immunology, Medical College of Wisconsin
PhD, University of Tennessee, 1995
Employed at BloodCenter of Wisconsin: 2000



Research Interests

Dr. Wang is concerned with self-renewal and differentiation of cells (hematopoietic stem cells, HSCs) that give rise to blood cells and to the subset of white blood cells (B lymphocytes) that produce antibodies. His studies are designed to identify and functionally characterize signaling molecules and pathways that are critical to HSC and B cell biology. Recent studies have identified a novel and critical signal transduction pathway that controls the development of normal early B cells and the formation of B-precursor acute lymphoblastic leukemia. These findings further our understanding of B cell development and transformation, and suggest new approaches to the treatment of

leukemia. Furthermore, recent studies have identified new mechanisms that regulate induction of tolerance in B cells, thereby limiting the possibility of autoantibody production and have led to the findings that antibodies causing heparin-induced thrombocytopenia and thrombosis (HIT) are produced by a subset of B lymphocytes designated marginal zone B cells when self-tolerance is broken. Work in these fields is expected to provide an improved understanding of autoantibody formation in human disease and suggest new approaches to prevention and treatment of autoimmunity.



Awards and Honors

- Associate Editor, Journal of Immunology 2016
- Chair, Stem Cell Faculty Recruitment Committee, Blood Research Institute 2016
- Member, American Association of Hematology 2016

Funding

R01 AI079087 "PLCGammas in B Cell Biology and Immunity"

P01 HL044612 "Molecular & Cellular Mechanisms in Transfusion Medicine; Project 3: Cell Responses in Heparin-Induced Thrombocytopenia"

Publications

1. Chen Y, Zheng Y, You X, Yu M, Fu G, Su X, Zhou F, Zhu W, Wu Z, Zhang J, Wen R, Wang D. Kras Is Critical for B Cell Lymphopoiesis. *J Immunol.* 2016 Feb 15;196(4):1678-85. PMID: 26773157
2. Chang YI, Damnernsawad A, Kong G, You X, Wang D, Zhang J. The mystery of oncogenic KRAS: lessons from studying its wild-type counterpart. *Small GTPases.* 2016 Jul 22:1-4. PMID:27449543
3. Padmanabhan A, Jones CG, Curtis BR, Bougie DW, Sullivan MJ, Peswani N, McFarland JG, Eastwood D, Wang D, Aster RH. A novel PF4-dependent platelet activation assay identifies patients likely to have heparin-induced thrombocytopenia/thrombosis (HIT). *Chest.* 2016 Sep;150(3):506-15. PMID: 26905366

Renren Wen, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
PhD, University of Tennessee Medical School, Memphis 1996
St. Jude Children's Research Hospital, Memphis 1996-2000
Employed at BloodCenter of Wisconsin: 2000



to maturity and defining pathways that are critical for T cell functions. This work will potentially lead to a better understanding of the molecular pathogenesis of immune deficiency, autoimmunity, or cancer development. Dr. Wen also works on heparin induced thrombocytopenia (HIT), a serious disease that sometimes causes thrombocytopenia/thrombosis following clinical administration of heparin. It is believed that heparin complexed with a self-protein PF4 induces PF4/heparin antibodies, some of which causes HIT. Dr. Wen is trying to understand the cellular and molecular mechanisms underlying this condition. Her work on understanding the antibody in HIT at a clonal level would potentially lead to novel and improved diagnosis and HIT treatment.

Awards and Honors

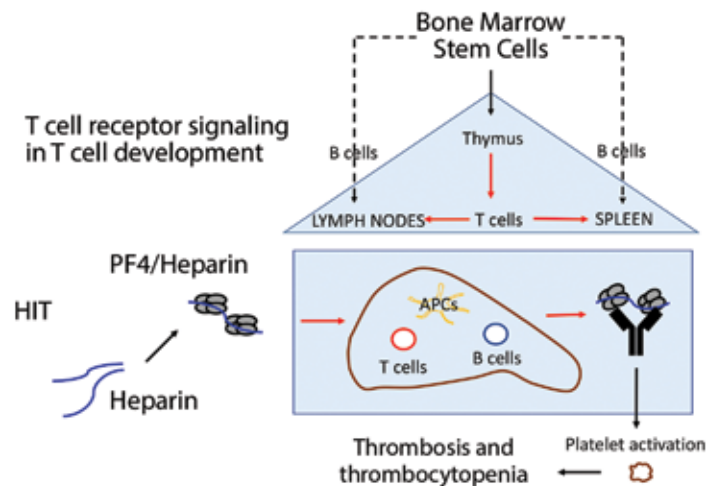
- Member, American Society of Microbiology 2016
- Member, American Association for the Advancement of Science 2016

Publications

1. Chen Y, Zheng Y, You X, Yu M, Fu G, Su X, Zhou F, Zhu W, Wu Z, Zhang J, Wen R, Wang D. Kras Is Critical for B Cell Lymphopoiesis. *J Immunol*. 2016 Feb 15;196(4):1678-85. PMID: 26773157
2. Su X, Yu M, Qiu G, Zheng Y, Chen Y, Wen R, Fu G, Zhu W, Chen J, Wu N, Ma P, Chen W, Wu Z, Wang D. Evaluation of nestin or osterix promoter-driven cre/loxp system in studying the biological functions of murine osteoblastic cells. *Am J Transl Res*. 2016 Mar 15;8(3):1447-59. PMID: 27186271

Research Interests

T and B lymphocytes are two important cell types in our adaptive immune system. B cells secrete antibodies that are essential for protection against extracellular pathogens. T cells are critical for the control of infection by intracellular pathogens, and for enabling B lymphocytes to efficiently produce antibodies. However, aberrant signaling in B and T cells can lead to abnormal development and activation of B and T cells, resulting in immune deficiency, autoimmunity, or cancer development. Dr. Wen's work is aimed at more fully understanding the molecular events, particularly in the T cell receptor signaling pathways that govern development of T cells from their earliest precursors



Stem Cells

Research in Stem Cell Biology and Hematopoiesis is aimed at understanding the many factors that regulate the normal process of how blood cells are formed (hematopoiesis), as well as understanding disease mechanisms that lead to abnormal hematopoiesis, which either could lead to a failure of healthy blood cell production or cause leukemia.

Studies in this area are bringing the BloodCenter into the fields of regenerative medicine, and cancer biology. These studies reflect an ongoing commitment to expanding foundational research into areas that will fundamentally improve the understanding and treatment of currently incurable blood diseases.

Housed in a new wing of the Blood Research Institute, Stem Cell Biology investigators are using cutting-edge technology to characterize molecular mechanisms involved in regulation of hematopoietic stem cells and their maturation into mature red cells, white cells and platelets.



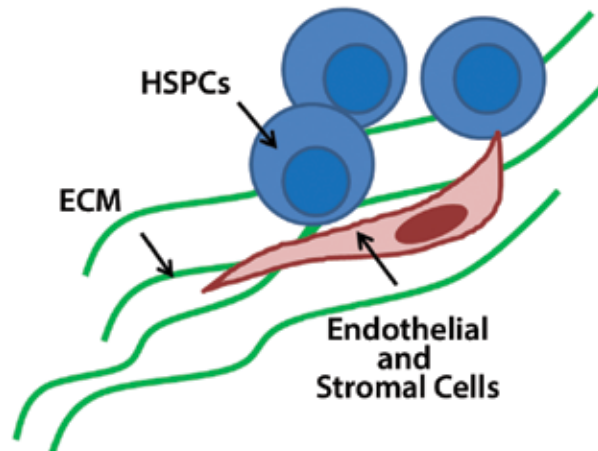
Karen Carlson, MD PhD

Assistant Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Department of Internal Medicine, Division of Hematology and Oncology, Medical College of Wisconsin
MD/PhD University of Wisconsin-Madison, 2004
Hematology/Oncology Fellowship: New York Presbyterian, Weill-Cornell Medical Center, 2011
Employed at BloodCenter of Wisconsin, 2016



Using murine model systems, Dr. Carlson studies how hematopoietic and stromal cells contribute to the bone marrow extracellular matrix, and how this in turn promotes development and production of mature blood cells. She has identified active synthesis of laminin- γ 1 to be necessary to maintain the structure of the perivascular bone marrow hematopoietic niche. She also is working to understand how production of laminin- γ 1 contributes to megakaryocyte development and platelet production and function.

Dr. Carlson's long-term goal is to apply what she learns about the basic biology of the hematopoietic extracellular matrix in order to develop niche-targeted therapies that will help her patients with hematopoietic diseases.



Research Interests

Dr. Karen-Sue Carlson is a board certified clinical hematologist. She joined the faculty at the Medical College of Wisconsin as an Assistant Professor of Medicine in the Division of Hematology and Oncology in 2013, and was appointed Assistant Investigator at the Blood Research Institute in 2016.

She maintains an active clinical focus on diseases of disordered hematopoiesis including aplastic anemia, acute and chronic leukemias, and myelodysplastic and myeloproliferative syndromes at the Medical College of Wisconsin. At the Blood Research Institute, her research focuses on the bone marrow extracellular matrix and its regulation of normal blood cell development.

Awards and Honors

- Best Doctors® designation 2016
- Member, American Society of Matrix Biology 2016
- Member, American Society of Biochemistry and Molecular Biology 2016

Funding

K08 HL127187 "One Marrow Failure in Mice Deficient for the Extracellular Matrix Component, Laminin-Gamma1"

Publications

1. Carlson KS, Nguyen LT, Schwartz K, Lawrence DA, Schwartz B. Neuroserpin Differentiates Between Forms of Tissue Type plasminogen Activator via pH Dependent Deacylation. *Frontiers in Cellular Neuroscience*; 10(154). eCollection June, 2016. (PMID: 27378851)
2. Michaelis L, Hanif A, Hari P, Atallah E, Carlson KS, and Pasquini M. Safety of Ruxolitinib Therapy Prior to Allogeneic Hematopoietic Stem Cell Transplantation for Myeloproliferative Neoplasms. *Bone Marrow Transplantation*; 51(4):617-8. April, 2016. (PMID: 26726940)

Alex C. Minella, MD

Associate Investigator, Blood Research Institute
Hematology/Oncology & Cell Biology Medical College of Wisconsin
MD, Vanderbilt University School of Medicine, 1998
Employed at BloodCenter of Wisconsin: 2014



in the molecular pathogenesis of hematopoietic diseases.

Awards and Honors

- Chair, Red Cell Biology Scientific Committee, American Society of Hematology 2016
- Editorial Board Member, Leukemia and Lymphoma 2016
- Ad hoc service on NIH CSRS study section 2016

Funding

RO1 HL098608 "Cyclin E Regulation in Normal and Neoplastic Hematopoiesis"

Publications

1. Mitzelfelt KA, Limphong P, Choi MJ, Kondrat FD, Lai S, Kolander KD, Kwok WM, Dai Q, Grzybowski MN, Zhang H, Taylor GM, Lui Q, Thao MT, Hudson JA, Barresi R, Bushby K, Jungbluth H, Wraige E, Geurts AM, Benesch JL, Riedel M, Christians ES, Minella AC, Benjamin IJ. The Human 343delT HSPB5 Chaperone Associated with Early-onset Skeletal Myopathy Causes Defects in Protein Solubility. *J Biol Chem.* 2016 Jul 15;291(29):14939-53. PMID: 27226619
2. Swartz KL, Wood SN, Murthy T, Ramirez O, Qin G, Pillai MM, Rao S, Minella AC. E2F-2 promotes nuclear condensation and enucleation of terminally differentiated erythroblasts. *Mol Cell Biol.* 2016 Dec 19;37(1). PMID: 27795297

Research Interests

Dr. Minella's laboratory seeks to understand how the cell division cycle is interconnected with other fundamental pathways that control cell fate and function. Current projects center on mediators of the G1-to-S-phase transition, including transcription factors, ubiquitin ligases, cyclins/cyclin-dependent kinases, and their inhibitors. One major objective is to determine how these maintain hematopoietic stem cell function, preserve normal hematopoietic differentiation programs, and restrain malignant transformation of hematopoietic progenitor cells. Another objective is to identify pathways within which the cyclin-dependent kinases have non-redundant functions in regulating protein substrates that are drivers

Sridhar Rao, MD, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
MD, University of Chicago, Pritzker School of Medicine, 2001
PhD, University of Chicago, 1999
Employed at BloodCenter of Wisconsin: 2010



Research Interests

Acute Myelogenous Leukemia (AML) is a common malignancy, but despite modern chemotherapy, the majority of patients relapse. One reason for this may be that chemotherapy targets rapidly dividing tumor cells but not a small pool of quiescent stem cells (leukemia stem cells, LSCs). Dr. Rao is attempting to define novel pathways that are specific for LSCs in the hope of developing improved tools that will target LSCs and improve the effectiveness of therapy. In related studies, he is investigating the role of a newly identified type of ribonucleic acid (RNA) designated non-coding RNA in regulating stem cell development.

Awards and Honors

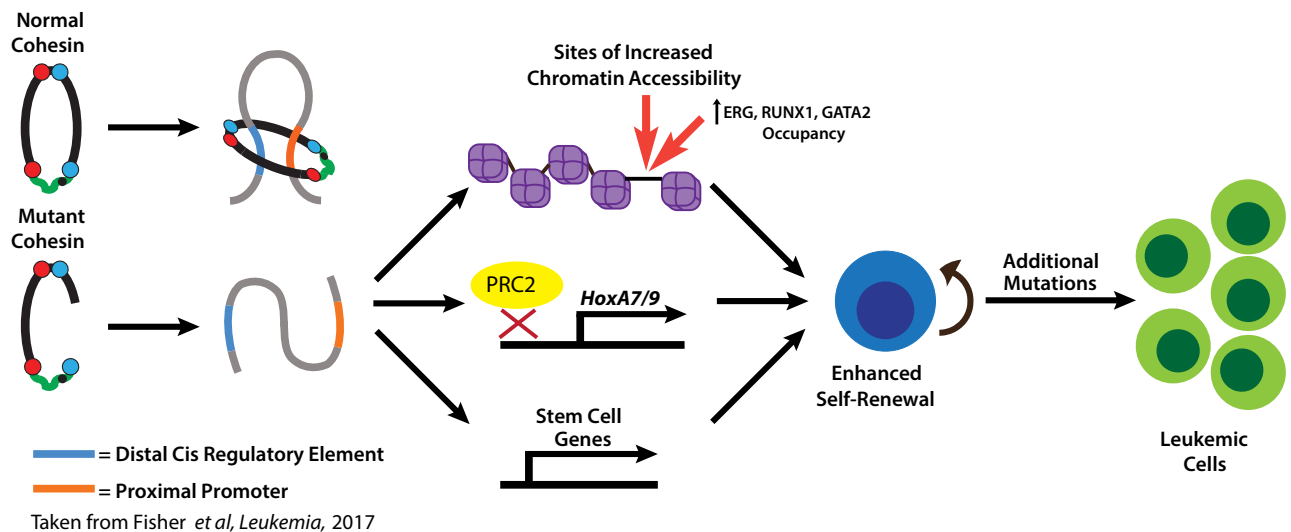
- Ad hoc Reviewer, N.I.H., New York Stem 2016
- Member, American Society for Blood & Marrow Transplantation (ASBMT) 2016
- Member, International Society for Stem Cell Research (ISSCR) 2016

Funding

R01 DK102716 "Molecular Basis of Human Hepatic Progenitor Cell Formation"

Publications

1. Blinka S, Reimer MH Jr, Pulakanti K, Rao S. Super-Enhancers at the Nanog Locus Differentially Regulate Neighboring Pluripotency-Associated Genes. *Cell Rep.* 2016 Sep 27;17(1):19-28. PMID: 27681417
2. Stelloh C, Reimer MH, Pulakanti K, Blinka S, Peterson J, Pinello L, Jia S, Roumiantsev S, Hessner MJ, Milanovich S, Yuan GC, Rao S. The cohesin-associated protein Wapal is required for proper Polycomb-mediated gene silencing. *Epigenetics Chromatin.* 2016 Apr 15;9:14. PMID: 27087855
3. Zhang N, Zhi H, Curtis BR, Rao S, Jobaliya C, Poncz M, French DL, Newman PJ. CRISPR/Cas9-mediated conversion of human platelet alloantigen allotypes. *Blood.* 2016 Feb 11;127(6):675-80. PMID: 26634302



Dove Twins

Lily and Bailey Dove share a special bond: they are identical twins. They also are connected by the disease they are battling.

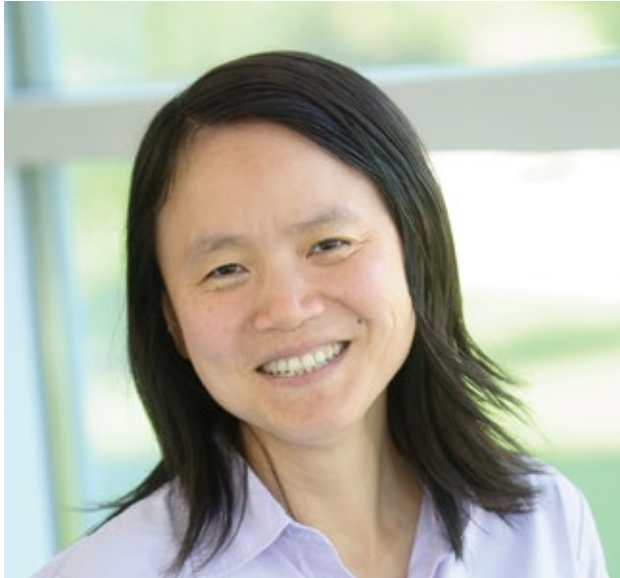
Lily and Bailey both have leukemia. Lily completed two years of treatment in August 2015. Her sister Bailey ended her high-risk treatment in June 2017. Both girls have received numerous blood and platelet transfusions while BloodCenter investigators research new treatments for leukemia and other cancers.

“Not only does BloodCenter help girls like mine with cancer, there’s a wider range of people that they’re helping,” said the girls’ mom, Erin. “I just want my daughters to have a normal future and enjoy a long and healthy life.”



Nan Zhu, PhD

Associate Investigator, Blood Research Institute, BloodCenter of Wisconsin
Assistant Professor, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin
PhD, Boston University, Boston, MA, 2007
Employed at BloodCenter of Wisconsin: 2015



epigenetic regulators as important for the maintenance of acute myeloid leukemia (AML). Currently we are working on elucidating their role in normal and malignant stem cell function and understanding the precise underlying molecular mechanism. In 2015, our study on JMJD1C, an epigenetic regulator, demonstrated that it is important for LSC function but dispensable for HSC function, thus a potential therapeutic target. The ultimate goal of our research is to identify therapeutic targets and develop targeted therapy in AML based on knowledge gained from our research.

Awards and Honors

- Member American Society for Hematology 2016

Funding

R00 CA168996 "The Role of JMJD1C in Normal and Leukemic Hematopoiesis"

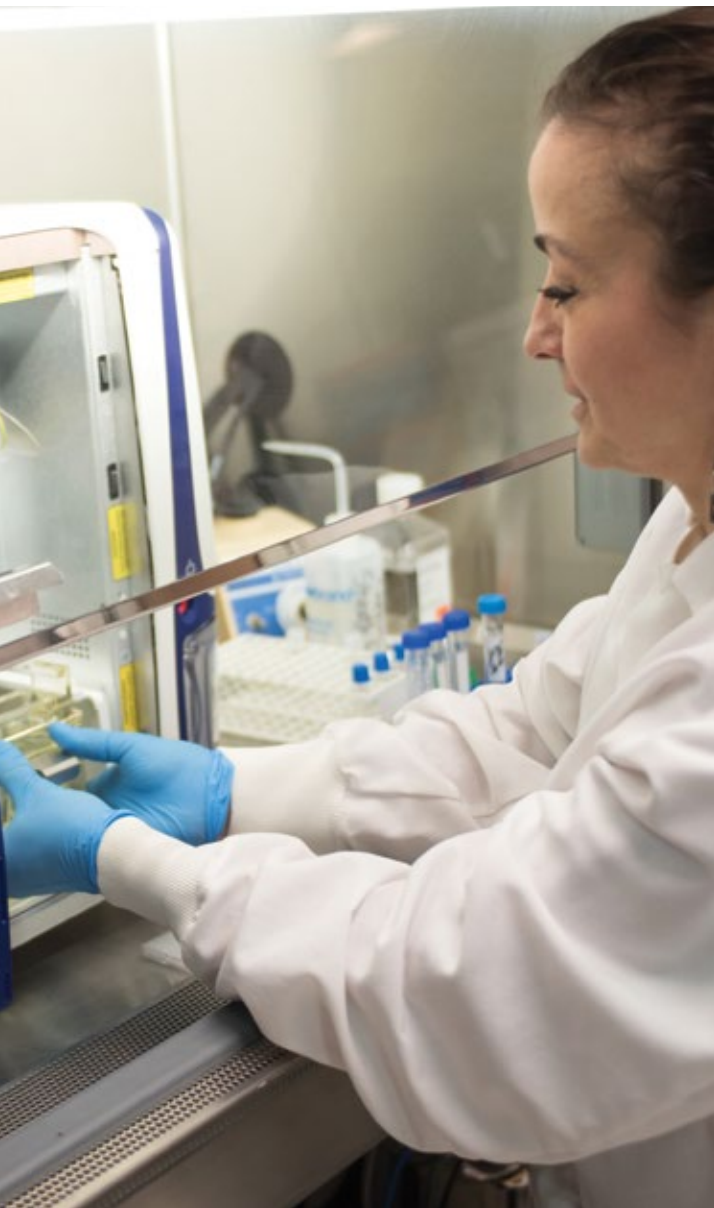
Publications

1. Danis E, Yamauchi T, Echanique K, Zhang X, Haladyna JN, Riedel SS, Zhu N, Xie H, Orkin SH, Armstrong SA, Bernt KM, Neff T. Ezh2 Controls an Early Hematopoietic Program and Growth and Survival Signaling in Early T Cell Precursor Acute Lymphoblastic Leukemia. *Cell Rep.* 2016 Mar 1;14(8):1953-65. PMID: 2690494
2. Zhu N, Chen M, Eng R, DeJong J, Sinha AU, Rahnamay NF, Koche R, Al-Shahrour F, Minehart JC, Chen CW, Deshpande AJ, Xu H, Chu SH, Ebert BL, Roeder RG, Armstrong SA. MLL-AF9- and HOXA9-mediated acute myeloid leukemia stem cell self-renewal requires JMJD1C. *J Clin Invest.* 2016 Mar 1;126(3):997-1011. PMID: 26878175

Research Interests

Research in Dr. Zhu's laboratory focuses on understanding epigenetic regulation in normal and malignant hematopoiesis with an emphasis on the role of such regulation in hematopoietic stem cell (HSC) as well as leukemia stem cell (LSC). Epigenetic regulation refers to changes in gene activities that are independent of the underlying gene sequences. Epigenetic regulators play an important role in normal development and differentiation. More recently, they emerge as important players in the development of cancer as evident by recurrent mutations across a spectrum of cancers. We have previously screened and identified several

Core Laboratories



Modern biomedical research requires access to a wide range of specialized technologies. The Blood Research Institute maintains cutting-edge technology platforms that give researchers from the BRI, and its affiliates on the Medical College of Wisconsin (MCW) campus, access to state-of-the-art equipment and expertise. These centralized core laboratories are a shared resource and are staffed by technical specialists that support individual research projects. Currently, the BRI is home to 11 different core laboratories:

The **Molecular Cell Biology Core** offers DNA sequencing using both capillary-based and Next-generation platforms and quantitative assays for DNA and RNA utilizing several different instrument platforms, such as a QuantStudio 6 Flex Real-time PCR system for rapid measurement of gene activity.

The **Protein Chemistry Core** synthesizes peptides using a microwave-enhanced Liberty 1 synthesizer and offers peptide purification and a variety of post synthesis peptide modifications. The Core aids investigators with protein purifications using AKTA and Agilent chromatography systems.

The **Hybridoma Core** produces murine monoclonal antibodies for research and diagnostic purposes.

The **Flow Cytometry Core** utilizes two Becton Dickinson LSR II multicolor cytometers, one BD Accuri cytometer, a BD FACSAria high-speed cell sorter, and a BD FACS Melody cell sorter.

The **Microscopic Imaging Core** includes the confocal/multiphoton laboratory featuring an Olympus FV1000-MPEconfocal, multiphoton microscope as well as an inverted Nikon TE200, a Zeiss Axioscope and a Zeiss Lumar

V12 stereo microscope with fluorescence capabilities. A PhD Imaging Specialist manages the Microscopic Imaging Core.

The **Biophysics Core** is equipped with a BIAcore 3000 Plasmon Resonance Spectrometer that enables scientists to study protein-protein interactions in real time.

The **Viral Vector Core** is shared between the BRI and the MCW and specializes in vectors based on lentivirus, adenovirus and adeno-associated virus needed for research in the field of gene therapy and other experimental applications.

The **Thrombosis Core** maintains a spinning disk confocal microscope system for in vivo studies on thrombosis. This core also features an in vitro flow system designed to recapitulate the in vivo conditions of flowing blood in the vasculature (VenaFlux system from Cellix Ltd; Zeiss inverted microscope with phase contrast, fluorescence and incubation capabilities).

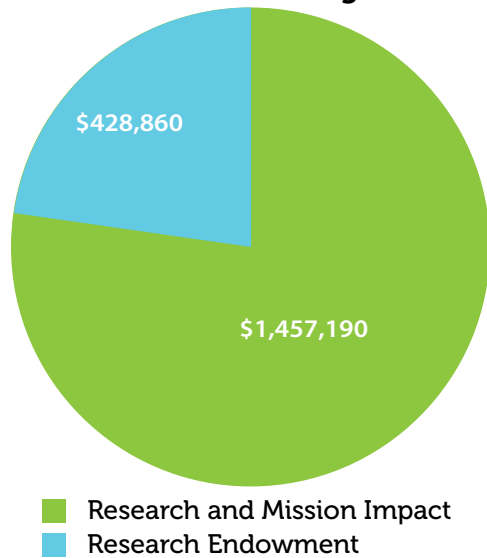
The **Histology Core** specializes in tissue preparation, cutting of fixed and frozen sections and various staining techniques. This core is staffed by a histology technician with 30 years of experience in experimental and clinical histology.

The **Gene Editing Core** is available as a resource for researchers that want to make targeted mutations in cells using recently developed CRISPR technology.

The joint BRI/MCW **Transgenic Core** aids in the generation of genetically altered animal models for the study of human disease.

BloodCenter Research Foundation

Gifts and Pledge



Thank you to the more than 750 people who supported us through a charitable gift this year. These gifts have been invested in life-enhancing research, technology that accelerates new discoveries, and in helping families make important decisions about organ and tissue donations that can save another person's life.

Your gifts matter because one American dies every 40 seconds as a result of a heart disease, stroke, or other cardiovascular diseases. This number is projected to increase. Additionally, 1 out of every 4 people who die today will succumb to a disease for which we actively are seeking a cure. The need for our work is clear. At the Blood Research Institute, our mission is to seek treatments and cures for all diseases of the blood.

Our highest priority is increasing our capacity to close the knowledge gap between what is known and what is yet to be discovered about diseases of the blood, to develop better medical tests and to discover new treatments that may possibly lead to new cures. Solving society's urgent health problems is the function of foundational scientific inquiry. Science needs curiosity, serendipity, and collaboration-driven research to fill the reservoirs of knowledge that will be drawn upon for clinical application. Foundational discoveries become the bedrock on which clinical diagnosis and treatment are built.

Your Charitable Gifts to the BloodCenter Research Foundation make all this possible

And, we have more to do. Every day our research and physician teams work together to find answers to questions such as:

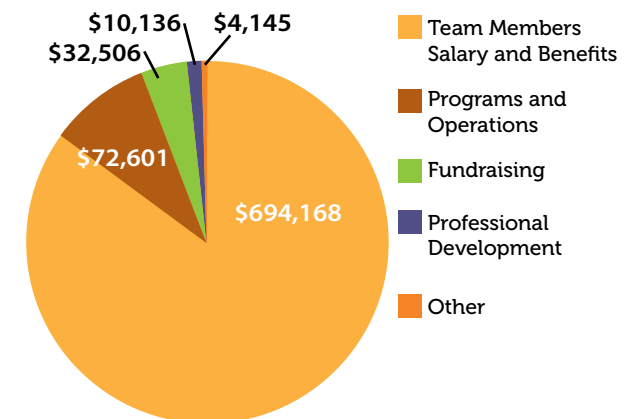
- What role do platelets have in causing heart attack and stroke?
- What causes clots to form in the deep veins of the body, such as those found in the legs, and what new treatments are required to solve this problem?
- How do cells recover from radiation and chemotherapy given during cancer treatments?
- How can we harness the power of the immune system to combat cancer?
- How can we make blood transfusions safer and more effective?

The answers to these questions and many others will lead to a better understanding of how to treat and cure diseases of the blood; leading to fewer deaths caused by heart disease, stroke, other cardiovascular diseases and cancer.

Improving Lives: Our Aspiration and Impact Areas

Our newest initiative, Research 2025, is a nine-year plan focused on closing the gap between what is known and what is still to be learned about blood diseases. During this time, we will grow and innovate more than ever before. We look ahead to this new phase with anticipation, buoyed by the success of our last 70 years. We are doing more research, establishing more partnerships and collaborations, and consistently achieving more positive outcomes. Above all, we are guided by the profound impact that an integrated research program—both foundational and clinical—can have on healthcare, our clarity of purpose, and our commitment to improving lives.

Philanthropy and Operation Expenses



Intellectual Property

Novel Approaches to Help Patients

Basic and applied biomedical research studies are aimed primarily at understanding disease and improving diagnosis, treatment and prevention. Research findings impact patients and patient care when companies develop products and services out of the discovery process. Intellectual property and patents help them differentiate and protect these new markets. Federal guidelines encourage protection of grant-supported discoveries through patents and other mechanisms that have the potential to transform research findings into products and services that benefit the health of the public. The Technology Transfer Office of BloodCenter of Wisconsin helps to identify, protect, and commercially partner discoveries to serve patient needs. Net revenues generated support further research. In 2016, four new patents were filed, and royalty revenue totaled

approximately \$647,444. BloodCenter technologies are licensed to more than 20 companies.

Intellectual Property Revenue

Patents and licensing agreements shown below for the years 2000-2016. Figures in bubble indicate number of individual patent filings for that year.

Mission Statement

Technology Transfer Office supports BloodCenter of Wisconsin's (BCW's) organizational mission of bringing life-saving solutions to the patient through a departmental focus on placing innovations into the hands of customers and colleagues.

Background

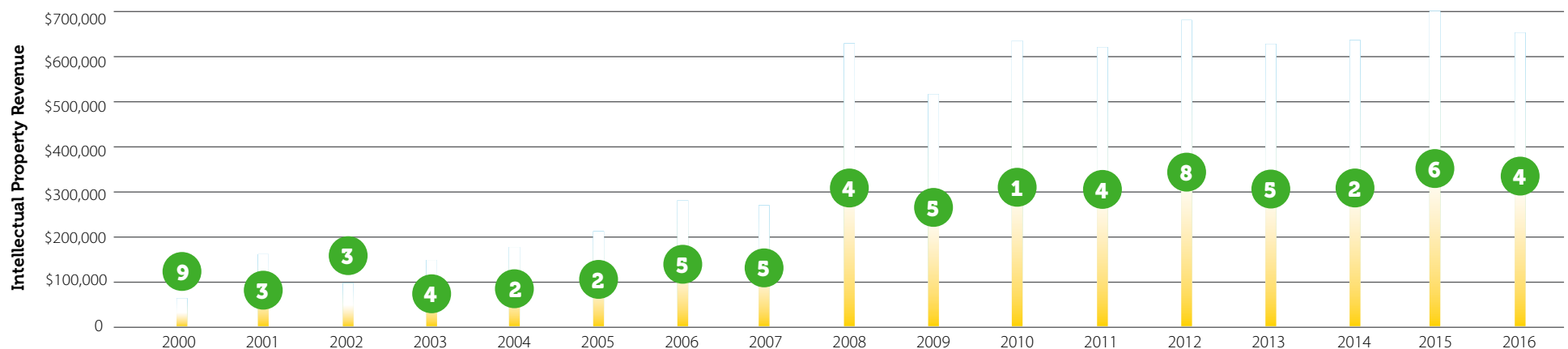
Inventor Tibor Greenwalt and colleagues discovered a white cell filtration method for blood in the 1960s. Patent activity increased in the 1980s with the discovery

of the human platelet antigen system. Currently, BCW's Technology Transfer Office provides intellectual property, contract management, and business development administrative services for the organization. A cross functional team called the Technology Transfer and Intellectual Property Review Group provides executive oversight for this function.

Performance Metrics

Metrics for BCW are from Jan. to Dec. 2016 as compared to the Association of University Technology Managers (AUTM) 2015 survey data, the latest available. Data for the AUTM survey respondents and for BCW are normalized for each \$10 million in total research expenditures (federal plus industry sponsored research as reported by AUTM respondents). BCW's total research expenditures were up 1.9% to \$7.92 million for 2016.

PATENT APPLICATIONS FILED PER YEAR



Patents 2016



Method of Manufacturing Dual Specific T Cells for Use in Cancer Immunotherapy

Researcher Weiguo Cui has filed a Patent Cooperative Treaty application this year, for protection around a method of manufacturing dual-specific T cells for use in cancer immunotherapy.

At its heart, this method seeks to take functionally “exhausted” T cells that react to tumor antigens and genetically-engineer them to have renewed strength. To make this happen, Dr. Cui has developed a process to remove T cells from cancerous tumors, and genetically alter them to add a second T cell receptor that recognizes an antigen in a cancer vaccine. The cancer vaccine is injected directly into the tumor and the modified T cells are then transfused. Effectiveness of the T cells against the cancer is increased by having a second receptor specific for the cancer vaccine. In mouse experiments, the new approach has led to tumor eradication without relapse in 70% of cases.

PEA Descriptor for the Research 2016 Publication in the section describing patent applications for the year

Dr. Richard Aster; Dr. Anand Padmanabhan; Dan Bougie, Ph.D.; and research technologist Curtis Jones filed for a patent in Japan, Canada, and Europe in 2016. Their patent is for an improved method to diagnose Heparin-Induced Thrombocytopenia (HIT), a life-and-limb threatening disorder that develops in some patients who receive heparin, a commonly-used blood thinner.

Currently, there are two basic assays (tests) that are commonly used to diagnose HIT. The first assay, Heparin/PF4-ELISA, is plagued by frequent “false” positives due to detection of non-pathogenic antibodies by this test. While the results for this assay come in quickly, positive results are often obtained in patients who don’t have HIT. The second assay, the Serotonin Release Assay (SRA), generally considered the “gold standard” HIT test, utilizes radioactive reagents and is technically complex. Thus, it is performed only by a few specialized laboratories.

A new assay developed on the basis of research findings made at BCW, the subject of this patent application, is known as the Platelet Factor 4-dependent p-selectin expression assay (PEA). This assay is favorable from multiple standpoints: enhanced speed, highly accurate results, and technical simplicity so that it can be offered by a variety of laboratories, both large and small. It is hoped that this technology will greatly improve the diagnosis and treatment of this dangerous condition by providing early, accurate diagnosis thereby facilitating immediate effective therapy.

Leadership 2016

Versiti Board of Directors

Richard Fotsch, Chair
Jacquelyn Fredrick
Fred Geilfuss
Thomas Hauske
Dale Kent
Maureen Kwiecinski
Gregory Larkin, MD
Robert H. Manegold
Jeff McDonald
John Oliverio
John Perras
James Rauh
Mitch Watt
L. Alan (Skip) Whaley
E. Randall Wright
Peter D. Ziegler

BloodCenter of Wisconsin Board of Directors 2016 (through September)

James M. Rauh, Chair
Andy Anderson, MD
Richard Anderson, MD
Cathy Buck
Susan Edwards
Jacquelyn Fredrick
Marc Gorelick, MD
Emery K. Harlan
Dale Kent
Robert H. Manegold
John Oliverio
Larry Rambo
Corey Rubenstein
Johan C.R. Segerdahl
Paul Skalecki
Gilbert C. White, II, MD
Peter D. Ziegler

BloodCenter Research Foundation Board 2016

Robert H. Manegold, Chair
Kristin Severson, Vice Chair
Julia Syburg, Secretary
Jacquelyn Fredrick
Maureen Kwiecinski
Richard Gallagher, Treasurer
Andy Anderson
Guy Crane
Brenda Garbo
Emery Harlan
Sarah Joerres, MD
John R. Raymond, Sr., MD
Johan C.R. Segerdahl
Paul Skalecki
John J. Stollenwerk
Rob Wawrzyn
Gilbert C. White, II, MD
Michael H. White
Peter D. Ziegler

BCW Leadership 2016

Thomas Abshire, MD, Executive Vice President, Medical Sciences Institute & Chief Medical Officer
Barbara Bryant, MD, Vice President, Transfusion Medicine
Lynne Briggs, Vice President & Chief Information Officer
Jacquelyn Fredrick, President & Chief Executive Officer
Michael Frohna, CFRE, Vice President & Chief Philanthropy Officer
Maureen Kwiecinski, Executive Vice President, Corporate Counsel
Sandi Lemons, Vice President and Chief Human Resources Officer
Colleen McCarthy, Vice President, Organ Procurement Organization & Tissue Bank

Meg McElligott, Vice President and Chief Quality Officer

Jim Mitchell, Senior Vice President, Blood Services

Peter Newman, PhD, Vice President, Research & Associate Director, BRI

Ilke Panzer, Executive Vice President and Chief Innovation Officer

Janet Slater, Vice President, Corporate Marketing & Chief Marketing Officer

Tony Watkins, Executive Vice President and Chief Financial Officer

Gilbert White, II, MD, Executive Vice President and Chief Scientific Officer, Blood Research Institute

Research Administration 2016

Andrea S. Brown, MBA, Director of Research Administration, Blood Research Institute

William Cashdollar, PhD, Director Research Core Lab, Blood Research Institute

Tina Johnson, Grants & Contracts Program Supervisor

Susan Knight, MBA, CNMT, Administrative Director, Medical Sciences Institute

Laura Savatski, MBA, CLP, RTTP, Technology Transfer Officer, Blood Research Institute

Advisory Boards 2016

2016 Scientific Advisory Board Members

Gail A. Bishop, PhD
Holden Chair of Cancer Biology
Professor of Microbiology and Internal Medicine
Assoc. Director for Basic Science Research
Holden Comprehensive Cancer Center
Director, Center for Immunology & Immune-Based Diseases
The University of Iowa

David Bodine, PhD
Chief and Senior Investigator
National Human Genome Research Institute
Genetics and Molecular Biology Branch
National Institutes of Health

Lawrence Brass, MD, PhD
Professor of Medicine and Pharmacology
Hematology-Oncology Div.
Associate Dean and Director, Combined Degree and Physician
Scholars Program
University of Pennsylvania School of Medicine

John L. Cleveland, PhD
Associate Center Director, Division of Basic Science
H. Lee Moffitt Cancer Center and Research Institute

Charles T. Esmon, PhD
Member and Head of Coagulation Biology
Oklahoma Medical Research Foundation
Professor of Pathology and Biochemistry & Molecular Biology

Margaret A. Goodell, PhD
Vivian L. Smith Chair of Regenerative Medicine
Director, Stem Cells and Regenerative Medicine Center
Baylor College of Medicine

Susan K. Pierce, PhD
Chief, Laboratory of Immunogenetics
Chief, Lymphocyte Activation Section
NIAID, NIH
Brad Schwartz
Chief Executive Officer
Morgridge Institute for Research
Professor of Medicine and Biomolecular Chemistry
University of Wisconsin

Leslie E. Silberstein, MD
Director, Joint Program in Transfusion Medicine
Professor, Harvard Medical School

Denisa D. Wagner, PhD
Edwin Cohn Professor of Pediatrics Program in Cellular and
Molecular Medicine
Division of Hematology/Oncology
Boston Children's Hospital
Harvard Medical School
External Advisory Board Medical Sciences Institute 2016

External Advisory Board Medical Sciences Institute 2016

Paul M. Ness, MD
Director, Transfusion Medicine, Department of Pathology
Johns Hopkins School of Medicine

Ellis Neufeld, MD, PhD
Associate Chief, Division of Hematology/Oncology
Boston Children's Hospital
Egan Family Foundation Professor of Translational Medicine,
Department of Pediatrics
Harvard Medical School

Barbara A. Konkle, MD
Director, Clinical and Translational Research and Medical Director,
Hemostasis Reference Laboratory
Puget Sound Blood Center
Professor of Medicine
University of Washington School of Medicine

Publications 2016

- Abbott DW, Friedman KD, Karafin MS. Differentiation of pernicious anemia from thrombotic thrombocytopenic purpura: The clinical value of subtle pathologic findings. *Transfus Apher Sci.* 2016 Dec;55(3):318-322. PMID: 27765664
- Anani WQ, Zeevi A, Lunz JG. EDTA Treatment of Serum Unmasks Complement-Mediated Prozone Inhibition in Human Leukocyte Antigen Antibody Testing. *Am J Clin Pathol.* 2016 Sep;146(3):346-52. PMID: 27543980
- Bercovitz RS, Brenner MK, Newman DK. A whole blood model of thrombocytopenia that controls platelet count and hematocrit. *Ann Hematol* 2016 Oct; 95(11):1887-94. PMID: 27515424
- Bercovitz RS, Josephson CD. Transfusion Considerations in Pediatric Hematology and Oncology Patients. *Hematol Oncol Clin North Am.* 2016 Jun;30(3):695-709. Review. PMID: 27113005
- Blinka S, Reimer MH Jr, Pulakanti K, Rao S. Super-Enhancers at the Nanog Locus Differentially Regulate Neighboring Pluripotency-Associated Genes. *Cell Rep.* 2016 Sep 27;17(1):19-28. PMID: 27681417
- Bougie DW, Nayak D, Aster RH. Immune destruction of human platelets in the NOD/scid mouse. *Transfusion.* 2016 Oct;56(10):2648-2649. PMID: 27739154
- Boylan B, Rice AS, Neff AT, Manco-Johnson MJ, Kempton CL, Miller CH; Hemophilia Inhibitor Research Study Investigators. . . Abshire TC. Survey of the anti-factor IX immunoglobulin profiles in patients with hemophilia B using a fluorescence-based immunoassay. *J Thromb Haemost.* 2016 Oct;14(10):1931-1940. PMID: 27501440
- Brandow AM, Wandersee NJ, Dasgupta M, Hoffmann RG, Hillery CA, Stucky CL, Panepinto JA. Substance P is increased in patients with sickle cell disease and associated with haemolysis and hydroxycarbamide use. *Br J Haematol.* 2016 Oct;175(2):237-245. doi: 10.1111/bjh.14300. PMID: 27539682
- Brenner MK, Clarke S, Mahnke DK, Simpson P, Bercovitz RS, Tomita-Mitchell A, Mitchell ME, Newman DK. Effect of 22q11.2 deletion on bleeding and transfusion utilization in children with congenital heart disease undergoing cardiac surgery. *Pediatr Res.* 2016 Mar;79(2):318-24 PMID: 26492284
- Cable RG, Brambilla D, Glynn SA, Kleinman S, Mast AE, Spencer BR, Stone M, Kiss JE; National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study-III (REDS-III). Effect of iron supplementation on iron stores and total body iron after whole blood donation. *Transfusion.* 2016 Aug;56(8):2005-12. PMID: 27232535
- Cancelas JA, Padmanabhan A, Le T, Ambruso DR, Rugg N, Worsham DN, Pinkard SL, Graminske S, Buck J, Goldberg J, Bill J. Spectra Optia granulocyte apheresis collections result in higher collection efficiency of viable, functional neutrophils in a randomized, crossover, multicenter trial. *Transfusion.* 2015 Apr;55(4):748-55. PMID: 25382805
- Chang YI, Damnernasawad A, Kong G, You X, Wang D, Zhang J. The mystery of oncogenic KRAS: lessons from studying its wild-type counter part. *Small GTPases.* 2016 Jul 22:1-4. PMID:27449543
- Chen Y, Schroeder JA, Chen J, Luo X, Baumgartner CK, Montgomery RR, Hu J, Shi Q. The immunogenicity of platelet-derived FVIII in hemophilia A mice with or without pre-existing anti-FVIII immunity. *Blood.* 2016 Mar 10;127(10):1346-54P. PMID: 26668132
- Chen Y, Zheng Y, You X, Yu M, Fu G, Su X, Zhou F, Zhu W, Wu Z, Zhang J, Wen R, Wang D. Kras Is Critical for B Cell Lymphopoiesis. *J Immunol.* 2016 Feb 15;196(4):1678-85. PMID: 26773157
- Churchill JL, Puca KE, Meyer ES, Carleton MC, Truchan SL, Anderson MJ. Comparison of ϵ -Aminocaproic Acid and Tranexamic Acid in Reducing Postoperative Transfusions in Total Hip Arthroplasty. *J Arthroplasty.* 2016 Dec;31(12):2795-2799.PMID: 27286909
- Cooper S, Sell S, Nelson L, Hawes J, Benrud JA, Kohlnhofer BM, Burmeister BR, Flood VH. Von Willebrand factor is reversibly decreased during torpor in 13-lined ground squirrels. *J Comp Physiol B.* 2016 Jan;186(1):131-9. PMID: 26481634
- Crescente M, Pluthero FG, Li L, Lo RW, Walsh TG, Schenk MP, Holbrook LM, Louriero S, Ali MS, Vaiyapuri S, Falet H, Jones IM, Poole AW, Kahr WH, Gibbins JM. Intracellular Trafficking, Localization, and Mobilization of Platelet-Borne Thiol Isomerases. *Arterioscler Thromb Vasc Biol.* 2016 Jun;36(6):1164-73. PMID: 27079884
- Curtis BR, Roman AS, Sullivan MJ, Raven CS, Larison J, Weitekamp LA. Two cases of maternal alloimmunization against human neutrophil alloantigen-4b, one causing severe alloimmune neonatal neutropenia. *Transfusion.* 2016 Jan;56(1):101-6.PMID: 26332036
- Dai B, Wu P, Xue F, Yang R, Yu Z, Dai K, Ruan C, Liu G, Newman PJ, Gao C. Integrin- α IIb β 3-mediated outside-in signalling activates a negative feedback pathway to suppress platelet activation. *Thromb Haemost.* 2016 Jul 28;116(5). PMID: 27465472
- Danis E, Yamauchi T, Echanique K, Zhang X, Haladyna JN, Riedel SS, Zhu N, Xie H, Orkin SH, Armstrong SA, Bernt KM, Neff T. Ezh2 Controls an Early Hematopoietic Program and Growth and Survival Signaling in Early T Cell Precursor Acute Lymphoblastic Leukemia. *Cell Rep.* 2016 Mar 1;14(8):1953-65. PMID: 2690494
- Delaney M, Wendel S, Bercovitz RS, Cid J, Cohn C, Dunbar NM, Apolseth TO, Popovsky M, Stanworth SJ, Tinmouth A, Van De Watering L, Waters JH, Yazer M, Ziman A; Biomedical Excellence for Safer Transfusion (BEST) Collaborative. Transfusion reactions: prevention, diagnosis, and treatment. *Lancet.* 2016 Dec 3;388(10061):2825-2836. Review. PMID: 27083327
- Englum BR, Rothman J, Leonard S, Reiter A, Thornburg C, Brindle M, Wright N, Heeney MM, Jason Smithers C, Brown RL, Kalfa T, Langer JC, Cada M, Oldham KT, Scott JP, St Peter SD, Sharma M, Davidoff AM, Nottage K, Bernabe K, Wilson DB, Dutta S, Glader B, Cray SE, Dassinger MS, Dunbar L, Islam S, Kumar M, Rescorla F, Bruch S, Campbell A, Austin M, Sidonio R, Blakely ML, Rice HE; Splenectomy in Congenital Hemolytic Anemia (SICHA) Consortium. Hematologic outcomes after total splenectomy and partial splenectomy for congenital hemolytic anemia. *J Pediatr Surg.* 2016 Jan;51(1):122-7. PMID: 26613837
- Epperla N, Hemauer K, Friedman KD, George JN, Foy P. Congenital Thrombotic Thrombocytopenic Purpura related to a Novel Mutation in ADAMTS13 Gene and Management during Pregnancy. *Am J Hematol.* 2016 Jun;91(6):644-6. PMID: 26822222
- Epperla N, Kapke JT, Karafin M, Friedman KD, Foy P. Effect of Systemic Bevacizumab in Severe Hereditary Hemorrhagic Telangiectasia (HHT) associated with Bleeding. *Am J Hematol.* 2016 Jun;91(6):E313-4. PMID: 26994402
- Falk G, Winans CG, Bowens K, Bougie DW, Curtis BR, Aster RH. An unexpected development after surgery-post-transfusion purpura! *Am J Hematol.* 2016 Aug;91(8):848-51. PMID: 27159228
- Flegel WA, Castilho L, Heaton WA, Keller MA, Klapper EB, Lane WJ, Pirenne F, Shehata N, Stack G, St-Louis M, Tormey CA, Wagner FF, Waxman DA, Denomme GA. Molecular immunohaematology round table discussions at the AABB Annual Meeting, Anaheim 2015. *Blood Transfus.* 2016 Jul 29:1-9. PMID: 27483480
- Flegel WA, De Castilho SL, Keller MA, Klapper EB, Moulds JM, Noizat-Pirenne F, Shehata N, Stack G, St-Louis M, Tormey CA, Waxman DA, Weinstock C, Wendel S, Denomme GA. Molecular immunohaematology round table discussions at the AABB Annual Meeting, Philadelphia 2014. *Blood Transfus.* 2016 Sep;14(5):425-33. PMID: 26710354
- Flesch BK, Curtis BR, de Haas M, Lucas G, Sachs UJ. Update on the nomenclature of human neutrophil antigens and alleles. *Transfusion.* 2016 June; 56(6):1477-9. PMID: 27039828

29. Flood VH, Christopherson PA, Gill JC, Friedman KD, Haberichter SL, Bellissimo DB, Udani RA, Dasgupta M, Hoffmann RG, Ragni MV, Shapiro AD, Lusher JM, Lentz SR, Abshire TC, Leissing C, Hoots WK, Manco-Johnson MJ, Gruppo RA, Boggio LN, Montgomery KT, Goodeve AC, James PD, Lillicrap D, Peake IR, Montgomery RR. Clinical and laboratory variability in a cohort of patients diagnosed with type 1 VWD in the United States. *Blood*. 2016 May 19;127(20):2481-8. PMID: 26862110
30. Fuentes RE, Zaitsev S, Ahn HS, Hayes V, Kowalska MA, Lambert MP, Wang Y, Siegel DL, Bougie DW, Aster RH, Myers DD, Stepanova V, Cines DB, Muzykantov VR, Poncz M. A chimeric platelet-targeted urokinase prodrug selectively blocks new thrombus formation. *J Clin Invest*. 2016 Feb;126(2):483-94. PMID: 26690701
31. Hendrickson JE, Roubinian NH, Chowdhury D, Brambilla D, Murphy EL, Wu Y, Ness PM, Gehrie EA, Snyder EL, George Hauser R, Gottschall JL, Kleinman S, Kakaiya R, Strauss RG; National Heart, Lung, and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study (REDS-III). Incidence of transfusion reactions: a multicenter study utilizing systematic active surveillance and expert adjudication. *Transfusion*. 2016 Oct;56(10):2587-2596. PMID: 27460200
32. Hoffmeister KM, Falet H. Platelet clearance by the hepatic Ashwell-Morrell receptor: mechanisms and biological significance. *Thromb Res*. 2016 May;141 Suppl 2:S68-72. PMID: 27207430
33. Hu W, Zhang W, Chen Y, Rana U, Teng RJ, Duan Y, Liu Z, Zhao B, Foeckler J, Weiler H, Kallinger RE, Thomas MJ, Zhang K, Han J, Miao QR. Nogo-B receptor deficiency increases liver X receptor alpha nuclear translocation and hepatic lipogenesis through an adenosine monophosphate-activated protein kinase alpha-dependent pathway. *Hepatology*. 2016 Nov;64(5):1559-1576. PMID: 27480224
34. Johnson CP, Schiller JJ, Zhu YR, Hariharan S, Roza AM, Cronin DC, Shames BD, Ellis TM. Renal Transplantation with Final Allocation Based on the Virtual Crossmatch. *Am J Transplant*. 2016 May;16(5):1503-1515. PMID: 26602886
35. Karafin MS, Dogra S, Rodeghier M, Burdick M, Mehrad B, Rose CE, Strieter RM, DeBaun MR, Strunk RC, Field JJ. Increased circulating fibrocytes are associated with higher reticulocyte percent in children with sickle cell anemia. *Pediatr Pulmonol*. 2016 Mar;51(3):295-9. PMID: 26130026
36. Karafin MS, Sachais BS, Connelly-Smith L, Field JJ, Linenberger ML, Padmanabhan A. NHLBI state of the science symposium in therapeutic apheresis: Knowledge gaps and research opportunities in the area of hematology-oncology. *J Clin Apher*. 2016 Feb;31(1):38-47. PMID: 25940408
37. Karafin MS, Singavi AK, Irani MS, Puca KE, Baumann Kreuziger L, Simpson P, Field JJ. Red cell storage age policy for patients with sickle cell disease: A survey of transfusion service directors in the United States. *Transfus Apher Sci*. 2016 Feb;54(1):158-62. PMID: 26775259
38. Key NS, Khorana AA, Mackman N, McCarty OJ, White GC, Francis CW, McCrae KR, Palumbo JS, Raskob GE, Chan AT, Sood AK. Thrombosis in Cancer: Research Priorities Identified by a National Cancer Institute/National Heart, Lung, and Blood Institute Strategic Working Group. *Cancer Res*. 2016 Jul 1;76(13):3671-5. PMID: 27527638
39. Kreuziger LB, Streiff M. Anti-Xa monitoring of low-molecular-weight heparin in adult patients with cancer. *Hematology Am Soc Hematol Educ Program*. 2016 Dec 2;2016(1):206-207. PMID: 27913481
40. Kutty RG, Xin G, Schauder DM, Cossette SM, Bordas M, Cui W, Ramchandran R. Dual Specificity Phosphatase 5 Is Essential for T Cell Survival. *PLoS One*. 2016 Dec 9;11(12):e0167246. doi: 10.1371/journal.pone.0167246. PMID: 27936095
41. Laiosa MD, Tate ER, Ahrenhoerster LS, Chen Y, Wang D. Effects of Developmental Activation of the Aryl Hydrocarbon Receptor by 2,3,7,8-Tetrachlorodibenzo-p-dioxin on Long-Term Self-Renewal of Murine Hematopoietic Stem Cells. *Environ Health Perspect*. 2016 Jul;124(7):957-65. PMID: 26495820
42. Lertkiatmongkol P, Liao D, Mei H, Hu Y, Newman PJ. Endothelial functions of platelet/endothelial cell adhesion molecule-1 (CD31). *Curr Opin Hematol*. 2016 May;23(3):253-259. PMID: 27055047
43. Lertkiatmongkol P, Paddock C, Newman DK, Zhu J, Thomas MJ, Newman PJ. The role of sialylated glycans in human PECAM-1-mediated trans-homophilic interactions and endothelial cell barrier function. *J Biol Chem*. 2016 Dec 9;291(50):26216-26225. PMID: 27793989
44. Li R, Hoffmeister KM, Falet H. Glycans and the platelet life cycle. *Platelets*. 2016 Sep;27(6):505-11. PMID: 27135356
45. Lin C, von der Thüsen J, Isermann B, Weiler H, van der Poll T, Borensztajn K, Spek CA. High endogenous activated protein C levels attenuates bleomycin-induced pulmonary fibrosis. *J Cell Mol Med*. 2016 Nov;20(11):2029-2035. PMID: 27295971
46. Mahlangu J, Kuliczkowski K, Karim FA, Stasyshyn O, Kosinova MV, Lepatan LM, Skotnicki A, Boggio LN, Klamroth R, Oldenburg J, Hellmann A, Santagostino E, Baker RI, Fischer K, Gill JC, P'Ng S, Chowdary P, Escobar MA, Khayat CD, Rusen L, Bensen-Kennedy D, Blackman N, Limsakun T, Veldman A, St Ledger K, Pabinger I; AFFINITY Investigators.. Efficacy and safety of rVIII-SingleChain: results of a phase 1/3 multicenter clinical trial in severe hemophilia A. *Blood*. 2016 Aug 4;128(5):630-7. PMID: 27330001
47. Marek E, Momper JD, Hines RN, Takao CM, Gill JC, Pravica V, Gaedigk A, Burckart GJ, Neville KA. Prediction of Warfarin Dose in Pediatric Patients: An Evaluation of the Predictive Performance of Several Models. *J Pediatr Pharmacol Ther*. 2016 May-Jun;21(3):224-32. PMID: 27453700
48. Mast AE. Tissue Factor Pathway Inhibitor: Multiple Anticoagulant Activities for a Single Protein. *Arterioscler Thromb Vasc Biol*. 2016 Jan;36(1):9-14. Review. PMID: 26603155
49. Mast AE, Bialkowski W, Bryant BJ, Wright DJ, Birch R, Kiss JE, D'Andrea P, Cable RG, Spencer BR. A randomized, blinded, placebo-controlled trial of education and iron supplementation for mitigation of iron deficiency in regular blood donors. *Transfusion*. 2016 Jun;56(6 Pt 2):1588-97. PMID: 26813849
50. Mitzelfelt KA, Limphong P, Choi MJ, Kondrat FD, Lai S, Kolander KD, Kwok WM, Dai Q, Grzybowski MN, Zhang H, Taylor GM, Lui Q, Thao MT, Hudson JA, Barresi R, Bushby K, Jungbluth H, Wraige E, Geurts AM, Benesch JL, Riedel M, Christians ES, Minella AC, Benjamin JJ. The Human 343delT HSPB5 Chaperone Associated with Early-onset Skeletal Myopathy Causes Defects in Protein Solubility. *J Biol Chem*. 2016 Jul 15;291(29):14939-53. PMID: 27226619
51. Montgomery RR. The heads and the tails of malaria and VWF. *Blood*. 2016 Mar 3;127(9):1081-2. PMID: 26941390
52. Montgomery RR, Flood VH. What have we learned from large population studies of von Willebrand disease? *Hematology Am Soc Hematol Educ Program*. 2016 Dec 2;2016(1):670-677. PMID: 27913545
53. Newman DK, Fu G, Adams T, Cui W, Arumugam V, Bluemn T, Riese MJ. The adhesion molecule PECAM-1 enhances the TGF-beta-mediated inhibition of T cell function. *Sci Signal*. 2016 Mar 8;9(418):ra27. PMID: 26956486
54. Niebler RA, Woods KJ, Murkowski K, Ghanayem NS, Hoffman G, Mitchell ME, Punzalan RC, Scott JP, Simpson P, Tweddell JS. A Pilot Study of Antithrombin Replacement Prior to Cardiopulmonary Bypass in Neonates. *Artif Organs*. 2016 Jan;40(1):80-5. PMID: 26620919
55. Olonisakin TF, Li H, Xiong Z, Kochman EJ, Yu M, Qu Y, Hulver M, Kolls JK, St Croix C, Doi Y, Nguyen MH, Shanks RM, Mallampalli RK, Kagan VE, Ray A, Silverstein RL, Ray P, Lee JS. CD36 provides host protection against Klebsiella pneumoniae intrapulmonary infection by enhancing LPS responsiveness and macrophage phagocytosis. *J Infect Dis*. 2016 Dec 15;214(12):1865-1875. PMID: 27683817
56. Paddock C, Zhou D, Lertkiatmongkol P, Newman PJ, Zhu J. Structural basis for PECAM-1 homophilic binding. *Blood*. 2016 Feb 25;127(8):1052-61. PMID: 26702061
57. Padmanabhan A, Jones CG, Curtis BR, Bougie DW, Sullivan MJ, Peswani N, McFarland JG, Eastwood D, Wang D, Aster RH. A novel PF4-dependent platelet activation assay identifies patients likely to have heparin-induced thrombocytopenia/thrombosis (HIT). *Chest*. 2016 Sep;150(3):506-15. PMID: 26905366
58. Peterson JA, Maroney SA, Mast AE. Targeting TFPI for hemophilia treatment. *Thromb Res*. 2016 May;141 Suppl 2:S28-30. PMID: 27207418
59. Peyvandi F, Oldenburg J, Friedman KD. A critical appraisal of one-stage and chromogenic assays of factor VIII activity. *J Thromb Haemost*. 2016 Feb;14(2):248-61. Review. PMID: 26663865
60. Pipe SW, Montgomery RR, Pratt KP, Lenting PJ, Lillicrap D. Life in the shadow of a dominant partner: the FVIII-VWF association and its clinical implications for hemophilia A. *Blood*. 2016 Oct 20;128(16):2007-2016. PMID: 27587878
61. Pollard RD, Fulp B, Sorci-Thomas MG, Thomas MJ. High-Density Lipoprotein Biogenesis: Defining the Domains Involved in Human Apolipoprotein A-I Lipidation. *Biochemistry*. 2016 Sep 6;55(35):4971-81. PMID: 27501467
62. Punzalan RC, Gottschall JL. Use and Future Investigations of Recombinant and Plasma-Derived Coagulation and Anticoagulant Products in the Neonate. *Transfus Med Rev*. 2016 Oct;30(4):189-96. Review. PMID: 27576087

64. Quon D, Chitlur M, Rajpurkar M, Simpson M, O'Brien S, Flood V, Hsieh L, Acharya S, Kruse-Jarres R, Sood S, Maahs J. Women leaders in hematology: Inspirations & insights. *Am J Hematol*. 2016 Apr;91 Suppl 1:S6-S34. PMID: 26851875
65. Rajasekaran K, Riese MJ, Rao S, Wang L, Thakar MS, Sentman CL, Malarkannan S. Signaling in Effector Lymphocytes: Insights toward Safer Immunotherapy. *Front Immunol*. 2016 May 12;7:176. Review. PMID: 27242783
66. Ramakrishnan DP, Hajji-Ali RA, Chen Y, Silverstein RL. Extracellular Vesicles Activate a CD36-Dependent Signaling Pathway to Inhibit Microvascular Endothelial Cell Migration and Tube Formation. *Arterioscler Thromb Vasc Biol*. 2016 Mar;36(3):534-44. PMID: 26821945
67. Rana U, Liu Z, Kumar SN, Zhao B, Hu W, Bordas M, Cossette S, Szabo S, Foeckler J, Weiler H, Chrzanowska-Wodnicka M, Holtz ML, Misra RP, Salato V, North PE, Ramchandran R, Miao QR. Nogo-B receptor deficiency causes cerebral vasculature defects during embryonic development in mice. *Dev Biol*. 2016 Feb 15;410(2):190-201. PMID: 26746789
68. Rangrez AY, Eden M, Poyanmehr R, Kuhn C, Stiebeling K, Dierck F, Bernt A, Lüllmann-Rauch R, Weiler H, Kirchof P, Frank D, Frey N. Myozap Deficiency Promotes Adverse Cardiac Remodeling via Differential Regulation of Mitogen-activated Protein Kinase/Serum-response Factor and β -Catenin/GSK-3 β Protein Signaling. *J Biol Chem*. 2016 Feb 19;291(8):4128-43. PMID: 26719331
69. Ren B, Best B, Ramakrishnan DP, Walcott B, Storz P, Silverstein RL. LPA/PKD-1-FoxO1 Signaling Axis Mediates Endothelial Cell CD36 Transcriptional Repression and Proangiogenic and Proarteriogenic Reprogramming. *Arterioscler Thromb Vasc Biol*. 2016 Jun;36(6):1197-208. PMID: 27013613
70. Riese MJ, Moon EK, Johnson BD, Albelda SM. Diacylglycerol Kinases (DGKs): Novel Targets for Improving T Cell Activity in Cancer. *Front Cell Dev Biol*. 2016 Oct 17;4:108. Review. PMID: 27800476
71. Roberts JC, Morateck PA, Christopherson PA, Yan K, Hoffmann RG, Gill JC, Montgomery RR, Program Investigators TZ. Rapid discrimination of the phenotypic variants of von Willebrand disease. *Blood*. 2016 May 19;127(20):2472-80. PMID: 26917779
72. Santagostino E, Martinowitz U, Lissitchkov T, Pan-Petesich B, Hanabusa H, Oldenburg J, Boggio L, Negrier C, Pabinger I, von Depka Prondzinski M, Altisent C, Castaman G, Yamamoto K, Álvarez-Roman MT, Voigt C, Blackman N, Jacobs I; PROLONG-9FP Investigators Study Group. Gill, JC. Long-acting recombinant coagulation factor IX albumin fusion protein (rIX-FP) in hemophilia B: results of a phase 3 trial. *Blood*. 2016 Apr 7;127(14):1761-9. PMID: 26755710
73. Santoso S, Wihadmadyatami H, Bakchoul T, Werth S, Al-Fakhri N, Bein G, Kiefel V, Zhu J, Newman PJ, Bayat B, Sachs UJ. Antiendothelial α v β 3 Antibodies Are a Major Cause of Intracranial Bleeding in Fetal/Neonatal Alloimmune Thrombocytopenia. *Arterioscler Thromb Vasc Biol*. 2016 Aug;36(8):1517-24. PMID: 27283740
74. Schwartz J, Padmanabhan A, Aqai N, Balogun RA, Connelly-Smith L, Delaney M, Dunbar NM, Witt V, Wu Y, Shaz BH. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. *J Clin Apher*. 2016 Jun;31(3):149-62. PMID: 27322218
75. Shirel T, Hubler CP, Shah R, Rankin AB, Koch KL, Sheth D, Uhing MR, Jones CW, Field JJ. Maternal opioid dose is associated with neonatal abstinence syndrome in children born to women with sickle cell disease. *Am J Hematol*. 2016 Jun;91(4):416-9. PMID: 26799428
76. Silverstein RL. Metabolic Manipulation to Put the Brakes on Platelet Activation: A Potential Novel Pharmacologic Approach to Atherothrombosis. *Arterioscler Thromb Vasc Biol*. 2016 Oct;36(10):2031-2. PMID: 27655777
77. Sola-Visner M, Bercovitz RS. Neonatal Platelet Transfusions and Future Areas of Research. *Transfus Med Rev*. 2016 Oct;30(4):183-8. Review. PMID: 27282660
78. Sorci-Thomas MG, Thomas MJ. Microdomains, Inflammation, and Atherosclerosis. *Circ Res*. 2016 Feb 19;118(4):679-91. PMID: 26892966
79. Srivastava K, Polin H, Sheldon SL, Wagner FF, Grabmer C, Gabriel C, Denomme GA, Flegel WA. The DAU cluster: a comparative analysis of 18 RHD alleles, some forming partial D antigens. *Transfusion*. 2016 Oct;56(10):2520-2531. PMID: 27480171
80. Stelloh C, Reimer MH, Pulakanti K, Blinka S, Peterson J, Pinello L, Jia S, Roumiantsev S, Hessner MJ, Milanovich S, Yuan GC, Rao S. The cohesin-associated protein Wapal is required for proper Polycomb-mediated gene silencing. *Epigenetics Chromatin*. 2016 Apr 15;9:14. PMID: 27087855
81. Su X, Yu M, Qiu G, Zheng Y, Chen Y, Wen R, Fu G, Zhu W, Chen J, Wu N, Ma P, Chen W, Wu Z, Wang D. Evaluation of nestin or osterix promoter-driven cre/lox system in studying the biological functions of murine osteoblastic cells. *Am J Transl Res*. 2016 Mar 15;8(3):1447-59. PMID: 27186271
82. Swartz KL, Wood SN, Murthy T, Ramirez O, Qin G, Pillai MM, Rao S, Minella AC. E2F-2 promotes nuclear condensation and enucleation of terminally differentiated erythroblasts. *Mol Cell Biol*. 2016 Dec 19;37(1). PMID: 27795297
83. Wang H, Han X, Bretz CA, Becker S, Gambhir D, Smith GW, Samulski RJ, Wittchen ES, Quilliam LA, Chrzanowska-Wodnicka M, Hartnett ME. Retinal pigment epithelial cell expression of active Rap 1a by scAAV2 inhibits choroidal neovascularization. *Mol Ther Methods Clin Dev*. 2016 Aug 24;3:16056. PMID: 27606349
84. White-Adams TC, Ng CJ, Jacobi PM, Haberichter SL, Di Paola JA. Mutations in the D'D3 region of VWF traditionally associated with type 1 VWD lead to quantitative and qualitative deficiencies of VWF. *Thromb Res*. 2016 Sep;145:112-8. PMID: 27533707
85. Wilcox DA. Megakaryocyte- and megakaryocyte precursor-related gene therapies. *Blood*. 2016 Mar 10;127(10):1260-8. PMID: 26787735
86. Wood JP, Baumann Kreuziger LM, Desai UR, Mast AE. Blocking inhibition of prothrombinase by tissue factor pathway inhibitor alpha: a procoagulant property of heparins. *Br J Haematol*. 2016 Oct;175(1):123-32. PMID:27301751
87. Yassai MB, Demos W, Gorski J. CDR3 motif generation and selection in the BV19-utilizing subset of the human CD8 T cell repertoire. *Mol Immunol*. 2016 Apr;72:57-64. PMID: 26963408
88. Yassai MB, Demos W, Janczak T, Naumova EN, Gorski J. CDR3 clonotype and amino acid motif diversity of BV19 expressing circulating human CD8 T cells. *Hum Immunol*. 2016 Jan;77(1):137-45. PMID: 26593155
89. Yu C, Yang Q, Chen Y, Wang D, Levine R, Crispino J, Wen Q, Huang Z. Tyrosine 625 plays a key role and cooperates with tyrosine 630 in MPL W515L-induced signaling and myeloproliferative neoplasms. *Cell Biosci*. 2016 May 23;6:34. PMID: 27222706
90. Zhang N, Zhi H, Curtis BR, Rao S, Jobaliya C, Poncz M, French DL, Newman PJ. CRISPR/Cas9-mediated conversion of human platelet alloantigen allotypes. *Blood*. 2016 Feb 11;127(6):675-80. PMID: 26634302
91. Zhu N, Chen M, Eng R, DeJong J, Sinha AU, Rahnamay NF, Koche R, Al-Shahrour F, Minehart JC, Chen CW, Deshpande AJ, Xu H, Chu SH, Ebert BL, Roeder RG, Armstrong SA. MLL-AF9- and HOXA9-mediated acute myeloid leukemia stem cell self-renewal requires JMJD1C. *J Clin Invest*. 2016 Mar 1;126(3):997-1011. PMID: 26878175
92. Zhu W, Gregory JC, Org E, Buffa JA, Gupta N, Wang Z, Li L, Fu X, Wu Y, Mehrabian M, Sartor RB, McIntyre TM, Silverstein RL, Tang WH, DiDonato JA, Brown JM, Lusic AJ, Hazen SL. Gut Microbial Metabolite TMAO Enhances Platelet Hyperreactivity and Thrombosis Risk. *Cell*. 2016 Mar 24;165(1):111-24. PMID: 26972052
93. Zimmerman MA, Schiller J, Kim J, Martin A, Selim M, Nydam TL, Cronin D 2nd, Hong JC. Pathologic sequelae of allosensitization in liver transplantation. *J Surg Res*. 2016 Jan;200(1):195-9. Review. PMID: 26253457

A Brief History

For 70 years, BloodCenter of Wisconsin has been dedicated to research as a vital part of our mission. Our researchers have made numerous medical breakthroughs that have helped people in our community, across the nation, and around the world. We are extremely proud of our reputation as one of the world's premier blood research centers.

The Blood Research Institute (BRI) is home to more than 150 physicians, scientists, and technologists who work in 36 investigative laboratories. They seek knowledge that will lead to faster diagnosis, improved treatments, and ultimately cures for many diseases that threaten our communities.

The majority of our work is foundational research in the areas of:

Vascular Biology, Thrombosis, and Hemostasis – studies of bleeding and clotting disorders, coagulation, sickle cell disease, and vascular events such as: inflammation, platelet interactions, and the integrity of the blood vessel wall

Immunobiology – studies of B cells, T cells, NK cells, autoimmunity, immune system development, and neuroimmunology

Stem Cell Biology/Hematopoiesis – studies of stem cells, the formation of blood, and malignant conditions involving blood cells

Transfusion Medicine – studies of immune diseases of the blood, transfusion therapy, and donor safety

