Research Highlights

International Research
Hydroxyurea is the only medication that can reduce the acute and chronic pain and suffering of persons affected by sickle cell anemia (SCA). Unfortunately, the use of hydroxyurea has mostly been limited to the United States and Europe, which represent less than 2% of the global burden of SCA. There are some concerns that hydroxyurea may not be as safe or effective in countries where problems like malaria and malnutrition are common. Dr. Russell Ware, Dr. Patrick McGann, and the Cincinnati Children's Division of Hematology have developed a prospective clinical trial to evaluate the safety, feasibility, and benefits of hydroxyurea in sub-Saharan Africa. Realizing Effectiveness Across Continents with Hydroxyurea (REACH) is a prospective pilot study that aims to demonstrate that hydroxyurea is indeed both safe and effective for children with SCA living in sub-Saharan Africa. The study, which will treat up to 600 children from three countries (Democratic Republic of Congo, Kenya, and Angola) over four years, has recently enrolled its first patients.

Red Blood Cell Disorders Diagnostic Core
Dr. Theodosia Kalfa and Dr. Charles Quinn have launched a collaboration with Molecular Genetics for the Cincinnati Children's Red Blood Cell (RBC) Disorders Diagnostic Core for the diagnosis of hemolytic anemias due to hemoglobin, RBC membrane and enzyme disorders, as well as for congenital dyserythropoietic anemias. The RBC Disorder Diagnostic Core offers a comprehensive evaluation with a clinical consultation, CLIA-certified genetic testing, and research-based functional assays including ektacytometry, erythrocyte cation content, and RBC membrane protein analysis, serving patients in Cincinnati Children's and outside
institutions from California to Montreal. In the past twelve months, the RBC Core has analyzed over 100 samples.

Division Publications

Faculty, Staff, and Trainees

Faculty Members

Russell E. Ware, MD, PhD, Professor
  Leadership Director, Division of Hematology; Co-Executive Director, Cancer and Blood Diseases Institute
  Research Interests Sickle cell disease; hemolytic anemia; immune-mediated cytopenia; PNH

Ralph A. Gruppo, MD, Professor
  Leadership Director, Comprehensive Hemophilia and Thrombosis Center
  Research Interests Coagulation; hemophilia; thrombosis

Karen Ann Kalinyak, MD, Professor
  Research Interests Hematology; bone marrow failure; sickle cell anemia; hemoglobinopathies

Theodosia Kalfa, MD, PhD, Associate Professor
  Research Interests Study of erythropoiesis, red blood cell structural membrane biology, and of reactive oxygen species in sickle cell disease

Patrick T. McGann, MD, MS, Assistant Professor
  Research Interests Global Hematology, Hydroxyurea for Sickle Cell Anemia

Eric Mullins, MD, Assistant Professor
  Leadership Research Director, Hemophilia Treatment Center
  Research Interests Interactions between hemostatic factors and the immune system in inflammatory disease; hemophilia

Joseph S. Palumbo, MD, Associate Professor
  Leadership Director, Comprehensive Thrombophilia Center
  Research Interests Dissecting the mechanisms coupling the hemostatic and innate immune systems to cancer progression

Charles Quinn, MD, Associate Professor
  Leadership Director, Hematology Clinical and Translational Research
  Research Interests Sickle cell disease: causes and treatment of stroke in sickle cell disease; pathophysiologic role of hemoglobin desaturation; acute sickle cell pain; survival and long-term follow-up of children with sickle cell disease

Lisa Shook, MA, MCHES, Instructor
  Leadership Director, Ohio Department of Health Regional Sickle Cell Newborn Screening Program
  Research Interests Sickle cell disease and trait, newborn screening, transition, chronic disease self-management, health education, quality improvement outcomes

Cristina Tarango, MD, Assistant Professor
Leadership  
Clinical Director, Hematology Division; Medical Director, Hemophilia Treatment Center

Research Interests  
Thrombosis and hemostasis, medical education

Joint Appointment Faculty Members

Punam Malik, MD, Professor (Experimental Hematology and Cancer Biology)

Ahna Pai, PhD, Associate Professor (Behavioral Medicine and Clinical Psychology)

Clinical Staff Members

- Viia Anderson, MSN, CNP-PC
- Margaret Kaiser, MSN, CPNP
- Darice Morgan, MSN, CPNP, FNP, BC, APN Program Lead for Hematology
- Kelly Porter, MSN, CPNP
- Kathy Schibler, MSN, CPNP
- Stephanie Lenahan, PA

Trainees

- Nihal Bakeer, MD, PL-V, Cincinnati Children’s Hospital Medical Center
- Shanmuganathan Chandrakasan, MD, MBBS, PL-VI, Children’s Hospital of Michigan
- Satheesh Chonat, MD, PL-V, Michigan State University-Sparrow Hospital
- Omar Niss, MD, PL-VII, University of Nebraska Medical Center/Creighton University

Division Collaboration

Improving sickle cell transition of care through health information technology. (K. Kalinyak, MD)

Adolescent Medicine  » Maria Britto, MD and Lori Crosby, PsyD

Improving Sickle Cell Disease Outcomes. (K. Kalinyak, MD)

James M. Anderson Center for Health Systems Excellence  » Devesh Dahale

Improving Hemophilia Outcomes. (C. Tarango, MD)

James M. Anderson Center for Health Systems Excellence  » Devesh Dahale

Collaboration of HRSA Sickle Cell Newborn Screening Program grant, including quality improvement, transition and self management. (L. Shook, MA, MCHES)

Behavioral Medicine and Clinical Psychology  » Lori Crosby, PsyD

Evaluating antithrombin infusions in ECMO patients. (R. Ware, MD, PhD & P. McGann, MD)

Cardiology  » Dave Cooper, MD and Jason Frischer, MD

Forming an anticoagulation team for the cardiac intensive care unit. (C. Tarango, MD and J. Palumbo, MD)

Cardiology  » David Nelson, MD, PhD, Dave Cooper, MD, Angela Lorts, MD, and David Morales, MD

Clinical study of sickle cell disease-related cardiomyopathy. (C. Quinn, MD)

Cardiology  » Michael Taylor, MD and Jeffrey Towbin, MD
Management of thrombotic complications in patients with single ventricular physiology. (J. Palumbo, MD)

**Cardiology** » Gruschen Veldtman, MD

The measurement of hydroxyurea to improve dosing and safety of drug therapy. (R. Ware, MD, PhD & P. McGann, MD)

**Clinical Pharmacology** » Sander Vinks, PharmD, PhD

Collaboration on Studies involving patients with Sickle Cell Disease. Losartan Study, Zileuton Study, Placenta Growth Factor Study, Sibling Methacholine Study and Gene Therapy Study. (K. Kalinyak, MD)

**Experimental Hematology and Cancer Biology** » Punam Malik, MD

Collaboration on studies to determine the signaling pathway that regulates ROS production in sickle RBC and assess its contribution to hemolysis, sickle nephropathy and cardiac pathology. (T. Kalfa, MD, PhD)

**Experimental Hematology and Cancer Biology** » Punam Malik, MD

Studies on the role of Rho GTPases in erythropoiesis. (T. Kalfa, MD, PhD)

**Experimental Hematology and Cancer Biology** » Yi Zheng, PhD

Combined hematology and gynecology clinic for young women with bleeding disorders. (E. Mullins, MD and C. Tarango, MD)

**Pediatric and Adolescent Gynecology** » Lesley Breech, MD

Development of a core service, with CCTST funding, for patients with hemolytic anemias due to erythrocyte cytoskeleton disorders, RBC enzyme deficiencies, or congenital dyserythropoietic anemias, that will offer diagnostic evaluation with ektacytometry, high-throughout gene chip analysis, and membrane protein analysis. This core will offer unique-phenotype correlation and understanding of the risk associated with splenectomy for some of these patients regarding thrombophilia and pulmonary hypertension. (T Kalfa, MD, PhD.)

**Human Genetics** » Amber Hogart Begtrup, PhD, Mehdi Keddache, PhD, and Kejian Zhang, MD

Hemoglobinopathy genetic diagnosis laboratory. (C. Quinn, MD)

**Human Genetics** » Amber Begtrup, PhD, Yaping Qian, PhD, and Kejian Zhang, MD

Development of special assays and genetic tests that will aid in the diagnosis and management of children with atypical hemolytic syndrome (aHUS). (R. Gruppo, MD)

**Human Genetics** » Kejian Zhang, MD

**Nephrology** » Bradley Dixon, MD

Studies on the immunosuppressive role of neonatal splenic erythroid cells. (T. Kalfa, MD, PhD)

**Infectious Diseases** » Sing Sing Way, MD, PhD

Evaluating post thrombotic syndrome in patients who have received thrombolysis. (C. Tarango, MD; R. Gruppo, MD and J. Palumbo, MD)

**Interventional Radiology** » Manish Patel, DO and John Racadio, MD

Identify novel urine biomarkers of hydroxyurea adherence for patients with sickle cell anemia. (R. Ware, MD, PhD
Clinical trial of losartan in patients with sickle cell disease. (C. Quinn, MD)

Collaboration in national study of splenectomy in congenital hemolytic anemia. (T. Kalfa, MD, PhD)

Collaboration on clinical trial exploring the role of Placenta Growth Facot in Sickle Acute Chest Syndrome. (K. Kalinyak, MD)

Evaluation of MRI-based methods for quantitation of hepatic iron overload in transfusion-dependent patients. (C. Quinn, MD)

Anticoagulant Sulfated Polymers in Biomaterials. (E. Mullins, MD)

Grants, Contracts, and Industry Agreements

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<tr>
<th>Grant and Contract Awards</th>
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<tr>
<td>Thrombin Promotes Prostate Cancer Progression</td>
<td>$41,634</td>
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<td>The Ohio State University Research Foundation</td>
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<td>07/01/13-06/30/15</td>
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<td>Hemophilia And Thrombosis Center</td>
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<td>Cascade Hemophilia Consortium(Hemophilia Foundation of Michigan)</td>
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<td>Hemophilia Comprehensive Care</td>
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<td>My Life, Our Future: A Hemophilia Genotyping Initiative</td>
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<tr>
<td>Hemophilia Inhibitor Pup Study (per capita)</td>
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<td>Rho GTPases in Terminal Erythroid Maturation</td>
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<td>Cincinnati Center of Excellence in Hemoglobinopathies Research - Research Project 1: Signaling Pathways that Regulate ROS Production in Sickle RBCs and Contribution to Hemolysis, SN and Cardiac Pathology</td>
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<td>Cincinnati Center of Excellence in Hemoglobinopathies Research - Summer Students</td>
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<td>Mechanisms Linking Hemostatic Factors to Neuroinflammatory Disease</td>
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<td>A Controlled Clinical Trial of Regadenoson in Sickle Cell Anemia</td>
<td>National Institutes of Health (Dana Farber Cancer Institute)</td>
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<td>PFAST: Patent Foramen Ovale and Stroke in Sickle Cell Disease (per capita)</td>
<td>Doris Duke Charitable Foundation (The University of Texas Southwestern Medical Center)</td>
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<td>Cincinnati Center of Excellence in Hemoglobinopathies Research - Translational Research Skills Development Core</td>
<td>National Institutes of Health</td>
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<td>Cincinnati Center of Excellence in Hemoglobinopathies Research - Research Project 3 - Novel Cardiac Magnetic Resonance Imaging to Define a Unique Restrictive Cardiomyopathy in Sickle Cell Disease</td>
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<td>Cincinnati Sickle Cell Newborn Screening Network</td>
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<td>Cincinnati Sickle Cell Project</td>
<td>Ohio Department of Health</td>
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WARE, R

**Accurate and Inexpensive Point-of-Care Diagnosis of Sickle Cell Anemia**
Doris Duke Charitable Foundation (Rice University)
09/01/13-08/31/16 $45,305

**Baby Hug Follow-up Study II Core Laboratory**
National Institutes of Health (Clinical Trials & Surveys Corp)
HHSN268201200023C 07/01/13-12/31/16 $2,101

**Genetic Predictors of Cerebrovascular Disease in Sickle Cell Anemia**
Doris Duke Charitable Foundation
08/01/13-07/31/14 $178,722

**RH Genotyping of Patient with Sickle Cell Anemia from a Multi-Center Study (SWiTCH Trial) and Correlation with Alloimmunization Following Blood Transfusion**
Doris Duke Charitable Foundation (New York University School of Medicine)
01/01/14-12/31/14 $9,259

**Sparing Conversion to Abnormal TCD Elevation**
National Institutes of Health
R01 HL 098239 12/01/13-11/30/14 $533,037

**TCD with Transfusions Changing to Hydroxyurea**
National Institutes of Health
R01 HL 095647 08/01/13-07/31/14 $3,033,934

**Endothelialized Microfluidics for Sickle Cell Disease Research & Drug Discovery**
National Institutes of Health (Emory University)
R01 HL 121264 01/01/14-12/31/18 $11,593

**Current Year Direct** $5,559,231

**Industry Contracts**

**GRUPPO, R**

- Alexion Pharmaceuticals, Inc $10,128
- Baxter Healthcare Corporate $98,792
- Bayer Healthcare Pharmaceuticals, Inc $36,723
- Biogen Idec MA Inc. $42,450
- Boehringer Ingelheim Pharmaceuticals $14,650
- Grifols, Inc $1,000
- Novo Nordisk Pharmaceuticals $38,836
- Pfizer, Inc $97,576
- Rho, Inc. $500

**KALFA, T**

- Baxter $750
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<td>WARE, R</td>
<td>Bristol-Myers Squibb</td>
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**Current Year Direct Receipts**  
$490,579

**Total**  
$6,049,810