2014 Research Annual Report

Hematology

Division Summary

RESEARCH AND TRAINING DETAILS	
Number of Faculty	**10**
Number of Joint Appointment Faculty	**2**
Number of Research Fellows	**5**
Number of Support Personnel	**40**

CLINICAL ACTIVITIES AND TRAINING	
Number of Clinical Staff	**6**
Number of Clinical Fellows	**4**
Number of Other Students	**3**
Inpatient Encounters	**1,332**
Outpatient Encounters	**4,257**

Division Photo

Row 1: K Kalinyak, C Tarango, T Kalfa, E Mullins, P Malik
Row 2: R Gruppo, R Ware, J Palumbo, C Quinn
Row 3: L Shook, P McGann

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-thoughout 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 hypertention. (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 Keijan 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 » Keijan 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

& P. McGann, MD)

Metabolomics Core Facility » Lindsay Romick-Rosendale, PhD

Clinical trial of losartan in patients with sickle cell disease. (C. Quinn, MD)

Nephrology » Prasad Devarajan, MD

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

Pediatric Surgery » Rebecca Brown, MD

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

Pulmonary Medicine » Raouf Samy Amin, MD

Radiology » Robert Fleck, MD

Collaboration on study: Sibling Methacholine Study. (K. Kalinyak, MD)

Pulmonary Medicine » Raouf Samy Amin, MD

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

Radiology » Robert Fleck, MD and Daniel Podberesky, MD

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

University of Cincinnati, Department of Chemistry » Neil Ayres, PhD

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
ADAMS, G		
Thrombin Promotes Prostate Cancer Progression		
The Ohio State University Research Foundation		
	07/01/13-06/30/15	$41,634
GRUPPO, R		
Hemophilia And Thrombosis Center		
Cascade Hemophilia Consortium(Hemophilia Foundation of Michigan)		
	06/01/13-05/31/15	$114,250
Hemophilia Comprehensive Care		
Maternal and Child Health Bureau(Hemophilia Foundation of Michigan)		
H30 MC 00015	10/01/97-05/31/14	$22,000
Public Health Surveillance for the Prevention of Complications of Bleeding and Clotting Disorders		
Centers for Disease Control & Prevention(Hemophilia Foundation of Michigan)		
U27 DD 000862	10/01/97-09/29/14	$18,900
My Life, Our Future: A Hemophilia Genotyping Initiative		
American Thrombosis & Hemostasis Network		

02/01/14-01/31/15 $3,500

Hemophilia Inhibitor Pup Study (per capita)

The University of Texas Health Science Center at Houston

04/29/13-04/28/147 $8,540

KALFA, T

Rho GTPases in Terminal Erythroid Maturation

National Institutes of Health

R01 HL 116352 09/26/12-06/30/16 $238,000

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

National Institutes of Health

U01 HL 117709 08/15/13-05/31/18 $123,169

Cincinnati Center of Excellence in Hemoglobinopathies Research - Summer Students

National Institutes of Health

U01 HL 117709 08/15/13-05/31/18 $40,542

MULLINS, E

Mechanisms Linking Hemostatic Factors to Neuroinflammatory Disease

National Institutes of Health

K08 HL 105672 08/22/11-07/31/16 $121,375

QUINN, C

A Controlled Clinical Trial of Regadenoson in Sickle Cell Anemia

National Institutes of Health(Dana Farber Cancer Institute)

P50 HL 110790 07/01/13-06/30/17 $78,470

PFAST: Patent Foramen Ovale and Stroke in Sickle Cell Disease (per capita)

Doris Duke Charitable Foundation(The University of Texas Southwestern Medical Center)

DDCF #2009091 02/15/11 -04/30/14 $10,449

Cincinnati Center of Excellence in Hemoglobinopathies Research - Translational Research Skills Development Core

National Institutes of Health

U01 HL 117709 08/15/13-05/31/18 $258,435

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

National Institutes of Health

U01 HL 117709 08/15/13-05/31/18 $222,743

SHOOK, L

Cincinnati Sickle Cell Newborn Screening Network

Health Resources & Services Administration

U38 MC 22218 06/01/11-05/31/15 $319,804

Cincinnati Sickle Cell Project

Ohio Department of Health

	07/01/98-06/30/14	$123,469

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

KALINYAK, K		
	Novartis Pharmaceuticals	$4,505
PALUMBO, J		
	Novo Nordisk Pharmaceuticals	$43,187
QUINN, C		
	Amgen, Inc.	$51,770
	Eli Lilly and Company	$9,500
	GlycoMimetics, Inc	$5,197
	Mast Therapeutics, Inc.	$15,015
WARE, R		
	Bristol-Myers Squibb	$20,000
	Current Year Direct Receipts	**$490,579**
	Total	**$6,049,810**