2013 Research Annual Report

Bone Marrow Transplantation and Immune Deficiency

Division Details

Division Data Summary

<table>
<thead>
<tr>
<th>RESEARCH AND TRAINING DETAILS</th>
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<tr>
<td>Number of Faculty</td>
<td>14</td>
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<td>Number of Joint Appointment Faculty</td>
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<td>Number of Research Fellows</td>
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<td>Number of Support Personnel</td>
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<td>Direct Annual Grant Support</td>
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<td>Direct Annual Industry Support</td>
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<td>Peer Reviewed Publications</td>
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<th>CLINICAL ACTIVITIES AND TRAINING</th>
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<tr>
<td>Number of Clinical Staff</td>
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<td>Number of Clinical Fellows</td>
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<td>Number of Other Students</td>
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<td>Inpatient Encounters</td>
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<td>Outpatient Encounters</td>
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Division Publications


32. Sumegi J, Nestheide SV, Barnes MG, Villanueva J, Zhang K, Grom AA, Filipovich AH. Gene-expression


Faculty, Staff, and Trainees

Faculty Members

Stella Davies, MBBS, PhD, MRCP, Professor

Leadership Jacob G. Schmidlapp Endowed Chair; Director, Bone Marrow Transplantation and Immune Deficiency; Executive Co-Director, Cancer and Blood Diseases Institute; Director, Division of Bone Marrow Transplantation and Immune Deficiency

Research Interests Blood and Marrow Transplant, Fanconi anemia and other marrow failure disorders, Pharmacogenetics and Pharmacokinetics, Survivorship Research, and BMT for Children with Leukemia.

Jacob Bleesing, MD, PhD, Associate Professor

Research Interests Clinical Investigation of Primary Immunodeficiency Disorders, with emphasis on disorders of immunodysregulation and B-cell disorders

Sharat Chandra, MD, Instructor

Research Interests Bone marrow transplantation for children with malignant and primary immune deficiency disorders.

Alexandra Filipovich, MD, Professor

Leadership Ralph J. Stolle Chair in Clinical Immunology; Director, Immunodeficiency and; Medical Director, Diagnostic Laboratory

Research Interests Histiocytic disorders, primary immune deficiency disorders and Immunoreconstitution Following Pediatric Stem Cell Transplantation

Michael Grimley, MD, Associate Professor

Research Interests Bone marrow transplantation for children with malignant and non-malignant disorders and treatment of chronic GVHD.

Richard Harris, MD, Professor

Research Interests Transplantation for children with bone marrow failure syndromes and aplastic anemia

Sonata Jodele, MD, Associate Professor

Research Interests Phase I clinical trials; stem cell transplantation; high risk pediatric malignancies; childhood neuroblastoma, Ewing's sarcoma, renal complications of transplantation.

Ashish Kumar, MD, PhD, Assistant Professor
Research Interests  Etiology of childhood leukemia, transplantation of children with malignancy and primary immune deficiencies.

Rebecca Marsh, MD, Assistant Professor
  Research Interests  Pathogenesis of HLH with XAP deficiency, diagnostic laboratory assays, improving outcomes of allogeneic BMT in primary immune deficiencies, use of reduced intensity conditioning regimens.

Parinda Mehta, MD, Associate Professor
  Research Interests  Blood and Marrow Transplant, Fanconi anemia and other failure disorders, Pharmacogenetics and Pharmacokinetics

Kasiani Myers, MD, Assistant Professor
  Research Interests  Blood and Marrow Transplant, Fanconi anemia and other marrow failure disorders, longitudinal studies of hematopoiesis

Janos Sumegi, MD, PhD, Professor
  Research Interests  Lymphoproliferative disease, Hemophagocytic Lymphohistiocytosis, Usher syndrome, etiology of childhood sarcomas.

Joint Appointment Faculty Members

Mark Johnson, MD, Assistant Professor (Child Psychiatry)
  Research Interests  Psychiatric support of bone marrow transplant patients

Michael Jordan, MD, Associate Professor (Immunobiology)
  Research Interests  Regulation of the immune response; immunotherapy of cancer, animal models of hemophagocytic disorders.

Ahna Pai, PhD, Associate Professor (Adherence Psychology in children receiving bone marrow transplantation)

Clinical Staff Members

Michael Huang, MD
Ernest Lawhorn, MD
Sunil Raiker, MD
Kristen Stefanski, MD
Gregory Wallace, DO
Paula Cuthrell, RN, MSN, CFNP
Jennifer Detzel, RN, MSN, CFNP
Laura Diggs, RN, MSN, CNP
Emily Herman, RN, CNP
Mary Ann Michael, RN, MSN, CPNP
Katie Scholle, RN, CNP
Gretchen Vaughn, RN, MSN, CNP

Trainees

Pooja Khandelwal, MD, PL-VI, University of Arizona College of Medicine
Zeynep (Yesim) Kucuk, MD, PL-VII, North Shore University-Long Island Jewish Medical Center, New Hyde Park, NY
Samantha Michaels, MD, PL-IV, University of Kentucky Children’s Hospital
Omar Niss, MD, PL-VI, University of Nebraska Medical Center/Creighton University
Ahmad Rayes, MD, PL-IV, SUNY Upstate Medical University
Jordan Wright, MD, PL-VI, University of Alabama at Birmingham, Birmingham, AL

Division Collaboration

Immunobiology » L. Grimes
MEIS1 and MLL-fusion leukemia: Research project investigating the role of MEIS1 in MLL-fusion leukemia using transgenic mice. (A. Kumar)

Experimental Hematology and Cancer Biology » J. Mulloy
Animal models of human leukemia: Research project aimed at developing xenograft mouse models of human leukemia using primary patient derived material. (A. Kumar)

Experimental Hematology and Cancer Biology » J. Mulloy and J. Cancelas
The molecular origin of monosomy 7 in very young children. Translational research project exploring the causes of monosomy 7. (P. Mehta, SM Davies)

Experimental Hematology and Cancer Biology » N. Ratner
MEIS1 and MPNSTs: Research project aimed at understanding the role of MEIS1 in malignant peripheral nerve sheath tumors (MPNST). (A. Kumar)

Critical Care; Radiology; Nephrology » H. Wong, S. Poynter, W. Ball, J. Leach, J. Goebel, and M. Mitsnefes
PRES working group
To identify patients at risk for PRES, outline uniform evaluation and therapy guidelines. (S. Jodele, SM Davies)

Nephrology » J. Goebel

Nephrology » J. Goebel
Small vessels, big trouble in the kidneys and beyond: hematopoietic stem cell transplantation-associated thrombotic microangiopathy. (S Jodele, SM Davies).

Critical Care » R. Chima and D. Wheeler
BMT-PICU risk score index working group: To determine outcome predictors for BMT patients that are treated in PICU. To validate BMT-PICU risk score at Cincinnati Children’s and later at collaborating institutions. (S Jodele, SM Davies)

Critical Care » R. Chima and D. Wheeler
Paper describing excellent outcomes for children admitted to PICU post-transplant admitted to PICU. (S Jodele, SM Davies)

Surgery; Gastroenterology » J. Nathan, G. Tiao, M. Alonzo, N. Yazigi, and S. Kocoshis

Surgery; Dermatology » R. Azizkhan and A. Lucky
Preparation of a stem cell transplant protocol for children with epidermolysis bullosa. (S Jodele and SM Davies)

Genetics; Pathology » T. Smoralek, S. Zimmerman, and R. McMasters
Oncology » J. Perentesis
   Novel therapeutic approaches for EVI1+ leukemias (Kumar A)

Genetics » K. Zhang
   Genotyping for PID and HLH (Filipovich, Bleeing)

Experimental Hematology and Cancer Biology » S. Wells
   The Fanconi Anemia Pathway Limits Human Papillomavirus Replication. (P. Mehta, Davies, S.)

Experimental Hematology and Cancer Biology » Q. Pang
   Fanconi Anemia Links Reactive Oxygen Species to Insulin Resistance and Obesity. (P. Mehta, Davies, S.)

Experimental Hematology and Cancer Biology » Q. Pang
   The FA pathway counteracts oxidative stress through selective protection of antioxidant defense gene promoters. (P. Mehta, Davies, S., Myers, K.)

Experimental Hematology and Cancer Biology » Q. Pang
   Etanercept Treatment in Fanconi Anaemia; Combined US and Italian Experience.(P. Mehta, Davies, S., Harris, R)

Experimental Hematology and Cancer Biology » Q. Pang
   Ongoing collaboration on a translational study: Quercetin in patients with Fanconi anemia, a Pilot study (P. Mehta)

Experimental Hematology and Cancer Biology » J. Mulloy and J. Cancelas
   Identify the cell of origin of the monosomy 7 clone in children with MDS arising in children with and without known genetic predisposition syndromes, and establish timing of onset in very young children (in utero vs. ex utero). (P.Mehta)

Endocrinology » S. Rose and D. Elder
   Endocrine phenotype of children and adults with Fanconi anemia. (P. Mehta, S. Davies, Myers, K.,Harris, R.)

Asthma Research » M. Butsch-Kovacic
   HPV and Immune Function in Fanconi anemia: Research project investigating the epidemiology of HPV infection and the role of immune function in Fanconi Anemia. (P. Mehta)

Asthma Research » M. Butsch-Kovacic
   Determination of antibody responses to natural infection with HPV and HPV vaccination in individuals with Fanconi anemia and to evaluate the predictors of effective or ineffective immune responses to HPV in individuals with FA. (P. Mehta)

Pharmacology » S. Vinks
   Therapeutic Drug Monitoring of Voriconazole in pediatric BMT patients. (P. Mehta)

Pharmacology » S. Vinks
   Pharmacokinetics of every 4th day Micafungin in high risk pediatric BMT patients. (P. Mehta)

Pharmacology » S. Vinks
   The Impact of Alemtuzumab Levels on Donor Chimerism and Graft Versus Host Disease Following Allogeneic Hematopoietic Cell Transplantation: A Prospective Study. (P. Mehta)

Immunobiology » L. Grimes
   Severe Congenital Neutropenia: Research project investigating novel genetic etiologies and molecular and cellular phenotypes of severe congenital neutropenia (K,Myers)
**Asthma Research** » M. Butsch Kovacic

HPV and Immune Function in Fanconi anemia: Research project investigating the epidemiology of HPV infection and the role of immune function in Fanconi Anemia. (K. Myers, P. Mehta)

**Endocrinology** » S. Rose

Endocrine function after RIC: Research project investigating endocrine function in pediatric patients after reduced intensity bone marrow transplantation. (K. Myers)

**Ophthalmology** » T. Schwartz

Ophthalmic GHVD: Research project investigating the incidence, severity and treatment of ophthalmic graft versus host disease in patients with systemic GVHD after bone marrow transplant. (K. Myers)

**Experimental Hematology and Cancer Biology** » P. Malik

Gene therapy for Hemophagocytic Lymphohistiocytosis (M. Jordan)

**Experimental Hematology and Cancer Biology** » P. Malik

Novel methods to promote stem cell engraftment (M. Jordan)

**Allergy and Immunology** » K. Risma

Gene therapy for Hemophagocytic Lymphohistiocytosis (M. Jordan)

**Allergy and Immunology** » K. Risma

The biology of cytotoxicity: Genotype/phenotype correlations (M. Jordan)

**Cellular and Molecular Immunology** » D. Hildeman

Selective ablation of undesirable T cell responses (M. Jordan)

**Allergy and Immunology** » M. Jordan

Immune profiling in Hemophagocytic Lymphohistiocytosis

**Nephrology; Biostatistics & Epidemiology; Experimental Hematology and Cancer Biology** » Dr. Prasad, Devarajan, J. Goebel, J. Khoury, and A. Lane

Project: “A Prospective Analysis of Clinical and Biochemical Markers for Pediatric Stem Cell Transplant-Associated Thrombotic Microangiopathy (TA-TMA)” Clinical and biomarker data analysis is ongoing. Project support:

1. P50 Application in response to RFA-DK-11-009 – Pediatric Centers of Excellence in Nephrology
2. Center for Clinical and Translational Science and Training (CCTST), University of Cincinnati Academic Health Center, T1 Pilot Grant (All BMT Faculty)

**Human Genetics; Hematology** » K. Zhang and R. Gruppo

Project: “Complement gene testing in patients with hematopoietic stem cell transplant-associated thrombotic microangiopathy”

Project support: The Investigator Initiated Trial Grant from Alexion Therapeutics (S. Jodele, S. Davies)

**Human Genetics; Nephrology** » K. Zhang, J. Goebel, and B. Dixon


**Cardiology; Critical Care; Pathology** » R. Hirsch, R. Chima, H. Wong, and D. Witte

Project: “Pulmonary Hypertension in Patients with Hematopoietic Stem Cell Transplant -Associated Thrombotic Microangiopathy”

Manuscript is published in Biology of Bone Marrow Transplantation journal *(Jodele, et al, Biol Blood Marrow*
Cardiology; Critical Care; Pathology » R. Hirsch, R. Chima, H. Wong, and D. Witte
Invited Pulmonary Hypertension in HSCT patient's manuscript is published in Biology of Bone Marrow Transplantation journal. First author, C. Dandoy, Hematology/Oncology Fellow and mentee to S. Jodele for this project. (Dandoy, et al, Bio. Blood Marrow Transplant 2013, Jul 23) (S. Jodele)

Cardiology; Critical Care; Pathology » R. Hirsch, R. Chima, H. Wong, and D. Witte
"Echocardiographic screening for pulmonary hypertension in HSCT patients." S. Jodele is mentoring C. Dandoy for this project. This project was completed, data analyzed and manuscript is in preparation. This project was awarded oral presentation at ASBMT 2013, and plenary session at ASPHO 2013 meetings. (S. Jodele, S. Davies)

Cardiology; Critical Care; Pathology » R. Hirsch, R. Chima, H. Wong, and D. Witte
Pulmonary Hypertension in HSCT patients: biomarkers pilot study." S. Jodele is mentoring C. Dandoy for this project. The study has been completed and data is being analyzed. (S. Jodele, S. Davies)

Nephrology » J. Goebel

Nephrology; Pathology » J. Goebel, H. Yin, and J. Khoury
Project: “Cystatin C to Estimate Renal Function in Bone Marrow Transplant and Oncology Patients”

Nephrology; Pathology; Biostatistics and Epidemiology » J. Goebel, H. Yin, and J. Khoury

Critical Care » R. Chima, D. Wheeler, H. Wong, and T. Shanley
Book Chapter: "Pediatric intensive care for patients undergoing hematopoietic stem cell transplantation."
Chapter Authors: Shilpa Sha, Sonata Jodele, Stella Davies and Ranjit Chima. Pediatric Critical Care Medicine: Basic Science and Clinical Evidence, 2nd Edition, Volume 1: "Care of the Critically Ill or Injured Child."
Editor(s) name(s): Derek S. Wheeler, Hector R. Wong, Thomas P. Shanley (S. Jodele, S. Davies)

Critical Care » R. Chima

Nephrology; Hoxworth Cell Therapy Team; Biostatistics & Epidemiology » J. Goebel, J. Khoury, and P. Carey

Critical Care; Biostatistics Epidemiology; Experimental Hematology and Cancer Biology » R. Chima, D. Wheeler, and A. Lane
BMT-PICU risk score index working group. Research is ongoing (S. Jodele, S. Davies)
Critical Care » R. Chima and D. Wheeler

Rheumatology; Human Genetics; Allergy » A. Grom, Barnes, K. Zhang, and K. Risma
Gene expression profiling of peripheral blood mononuclear cells from children with active hemophagocytic lymphohistiocytosis. (J. Sumegi, A. Filipovich)

Oncology; Human Genetics » L. Wagner and T. Smolarek
Assessment of minimal residual disease in ewing sarcoma. (J. Sumegi)

Gastroenterology, Hepatology and Nutrition » L. Denson
Novel immune-dysregulatory diseases presenting as IBD (A. Kumar)

Gastroenterology, Hepatology and Nutrition » A. Miethke
Discovering biomarkers and pathogenesis of hepatitis associated aplastic anemia (A.Kumar)

Neonatology and Pulmonary Biology » J. Bridges
Investigating the connection between HIF-1 and MEIS1 (A. Kumar)

Pediatrics » K. Setchell
Pharmacokinetics of Quercetin in patients with Fanconi anemia (P. Mehta, S. Davies)

Human Genetics » K. Zhang
Role of Pharmacogenetics and Therapeutic Drug Monitoring in BMT Patients (P. Mehta, S. Davies)

Infectious Diseases » B. Connelly
Incidence and Outcomes of Fungal Infections in Children after Bone Marrow Transplant: CCHMC Experience. (P. Mehta, S. Davies)

Immunobiology » D. Hildeman and J. Katz
Exploiting the DNA damage response for selective immunomodulation (M. Jordan)

Allergy and Immunology » K. Risma
The biology of cytotoxicity: Genotype/phenotype correlations (M. Jordan)

Experimental Hematology and Cancer Biology; Allergy and Immunology » P. Malik and K. Risma
Gene correction strategies for Hemophagocytic lymphohistiocytosis (M. Jordan)

Experimental Hematology and Cancer Biology » P. Malik
Novel methods to promote stem cell engraftment (M. Jordan)

Human Genetics » K. Zhang
Discovery and characterization of new primary immune deficiencies. (M. Jordan, R. Marsh)

Grants, Contracts, and Industry Agreements

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<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
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<td><strong>Childhood Cancer Survivor Study</strong></td>
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<td>National Institutes of Health(St Jude's Children's Hospital)</td>
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<td>U24 CA 055727</td>
<td>12/01/11-11/30/16</td>
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<td><strong>Children's Oncology Chair Award - Scientific Leadership</strong></td>
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National Institutes of Health (Children's Hospital of Philadelphia)

**Children's Oncology Chair Award**
National Institutes of Health (Children's Hospital of Philadelphia)

U10 CA 098543 03/01/11-02/28/14 $11,546

**Molecular Epidemiology of Pediatric Germ Cell Tumors**
National Institutes of Health (University of Minnesota)

R01 CA 151284 08/10/11-05/31/16 $11,039

**RLIPOVICH, A**

**Gene Therapy for SCID-X1 Using Self-Inactivating (SIN) Gammaretroviral Vector**
National Institutes of Health (Children's Hospital Boston)

U01 AI 087628 09/01/10-08/31/15 $270,783

**Rare Diseases Clinical Consortia for the Rare Diseases**
National Institutes of Health (The Regents of the Univ of California)

U54 AI 082973 09/12/09-08/31/14 $3,696

**KUMAR, A**

**A New Leukemia Treatment using an Old Drug**
Cancer Free Kids

06/01/13-05/31/14 $25,000

**The Role of MEIS1 in Hematopoiesis and Hematopoietic Transformation**
National Institutes of Health

R01 HL 111192 07/15/15-04/30/17 $238,000

**MEHTA, P**

**Quercetin in Patients with Fanconi Anemia, a Pilot Study**
Aplastic Anemia & MDS International Fdn

07/01/11-06/30/13 $27,273

**Serology as a Biomarker for Immune Response to HPV Vaccination and Exposure in Fanconi Anemia**
Fanconi Anemia Research Fund

07/01/12-06/30/13 $40,000

**MYERS, K**

**Chemoprevention of Leukemia in a Genetically Susceptible Population**
Conquer Cancer Foundation

07/01/12-06/30/15 $62,466

**SUMEGI, J**

**PAX3-NCOA1 and PAX3-NCOA2, Downstream Target Genes in Phabdomyosarcoma**
Bear Necessities Pediatric Cancer Foundation

01/01/13-12/31/13 $20,000
# Identification of PAX3-NCOA1 and PAX3-NCOA2 Target Genes

Cancer Free Kids

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<th>Period</th>
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<td>07/01/12-06/30/13</td>
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| Current Year Direct | $915,563 |

## Industry Contracts

**GRIMLEY, M**

- Chimerix, Inc: $66,400

**HARRIS, R**

- Alexion Pharmaceuticals, Inc: $1,001

**JODELE, S**

- Alexion Pharmaceuticals, Inc: $113,829

| Current Year Direct Receipts | $181,230 |

| Total                       | $1,096,793 |