

Bone Marrow Transplant and Immune Deficiency Annual Report, 2009-10

Division Photo



Left to Right: R. Marsh, K. Myers, S. Jodele, A. Kumar, M. Jordan, A. Filipovich, S. Davies, M. Grimley, P. Mehta, S. Joshi

Division Data Summary

Research and Training Details

Number of Faculty	11
Number of Joint Appointment Faculty	4
Number of Research Fellows	2
Number of Support Personnel	46
Direct Annual Grant Support	\$854,673
Direct Annual Industry Support	\$44,970
Peer Reviewed Publications	17

Clinical Activities and Training

Number of Clinical Staff	4
Number of Clinical Fellows	1
Inpatient Encounters	9,111
Outpatient Encounters	3,850

Significant Publications

Kumar, A. R., A. L. Sarver, B. Wu and J. H. Kersey (2010). "Meis1 maintains stemness signature in MLL-AF9 leukemia." *Blood*115(17): 3642-3643.

Lykens, J. E., C. E. Terrell, E. E. Zoller, S. Divanovic, A. Trompette, C. L. Karp, J. Aliberti, M. J. Flick and M. B. Jordan (2010). "Mice with a selective impairment of IFN-gamma signaling in macrophage lineage cells demonstrate the critical role of IFN-gamma-activated macrophages for the control of protozoan parasitic infections in vivo." *J Immunol*184(2): 877-885.

Marsh, R. A., J. Villanueva, K. Zhang, A. L. Snow, H. C. Su, L. Madden, R. Mody, B. Kitchen, D. Marmer, M. B. Jordan, K. A. Risma, A. H. Filipovich and J. J. Bleesing (2009). "A rapid flow cytometric screening test for X-linked lymphoproliferative disease due to XIAP deficiency." *Cytometry B Clin Cytom*76(5): 334-344.

Mehta, P. A., A. A. Vinks, A. Filipovich, J. Bleesing, S. Jodele, M. B. Jordan, R. Marsh, R. Tarin, S. Edwards, D. Fearing, J. Lawrence and S. M. Davies (2010). "Alternate day Micafungin Anti-fungal Prophylaxis in Pediatric patients undergoing Hematopoietic Stem Cell Transplantation: A Pharmacokinetic study." *Biol Blood Marrow Transplant*.

Verneris, M. R., M. Eapen, R. Duerst, P. A. Carpenter, M. J. Burke, B. V. Afanasyev, M. J. Cowan, W. He, R. Krance, C. K. Li, P. L. Tan, J. E. Wagner and S. M. Davies (2010). "Reduced intensity conditioning regimens for allogeneic transplantation in children with acute lymphoblastic leukemia." *Biol Blood Marrow Transplant*.

Division Collaboration

Collaboration with Immunobiology

Collaborating Faculty: L. Grimes

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

Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: 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)

Collaboration with Experimental Hematology and Cancer Biology

Collaborating Faculty: N. Ratner

MEIS1 and MPNSTs: Research project aimed at understanding the role of MEIS1 in malignant peripheral nerve sheath tumors (MPNST). (A. Kumar)

Collaboration with Nephrology; Biostatistics & Epidemiology; Pathology

Collaborating Faculty: J. Goebel; J. Khoury; Hong J Yin

Early Clinical Indicators of Transplant Associated-Thrombotic Microangiopathy in Pediatric Neuroblastoma Patients Undergoing Autologous Stem Cell Transplantation. *Bone Marrow Transplantation*, **in press** (J. Bleesing, S. Davies, A. Filipovich, S. Jodele, P. Mehta)

Collaboration with Nephrology; Biostatistics & Epidemiology

Collaborating Faculty: J. Goebel; B. Dixon; P. Devarajan; J. Khoury

A Prospective Analysis of Clinical and Biochemical Markers for Pediatric Stem Cell Transplant-Associated Thrombotic Microangiopathy. Study opened and ready to enroll at CCHMC. (J. Bleesing, S. Davies, A. Filipovich, R. Harris, S. Jodele, M. Jordan, S. Joshi, A. Kumar, R. Marsh, P. Mehta)

Collaboration with Hematology/Oncology; Biostatistics & Epidemiology

Collaborating Faculty: J. Perentesis; L. Wagner; R. Nagarajan; M. Kim

Outcomes with High-Dose Chemotherapy and Autologous Stem Cell Transplantation in Comparison to Conventional-Dose Chemotherapy in Pediatric Patients with Relapsed or Refractory Ewing's Family Tumors. *Cancer*, submitted. Awarded Oral presentation at ASBMT 2010. (S. Jodele, S. Davies, P. Mehta, J. Bleesing)

Collaboration with Critical Care; Radiology; Nephrology

Collaborating Faculty: H. Wong; S. Poynter; W. Ball; J. Leach; J. Goebel; M. Mitsnefes

PRES working group: To identify patients at risk for PRES, outline uniform evaluation and therapy guidelines. (S. Jodele, S. Davies)

Collaboration with Critical Care

Collaborating Faculty: R. Chima

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 CCHMC and later at collaborating institutions.

Collaboration with Hoxworth Blood Center

Collaborating Faculty: P. Carey

Plasmapheresis – Early Intervention Produces Positive Outcome For Pediatric Patients with Transplant Associated Thrombotic Microangiopathy. Awarded Poster presentation at American Association of Blood Banks (AABB) Annual Meeting.

Collaboration with Clinical Pharmacology

Collaborating Faculty: S. Vinks

Alternate day Micafungin Anti-fungal Prophylaxis in Immunocompromised Pediatric Patients: A Pharmacokinetic Study.

Biology of Blood and Marrow Transplantation, 2010 May 20 (P. Mehta, S. Davies)

Collaboration with Human Genetics; Biostatistics & Epidemiology

Collaborating Faculty: T. Smolarek; M. Kim

The Clinical significance of Gains in 1q and 3q and Deletions of 7 and 7q as Detected by FISH in Fanconi Anemia Patients followed longitudinally over Time. *Cancer, Genetics and Cytogenetics* In Press (P. Mehta, R. Harris, S. Davies)

Collaboration with Hematology/Oncology

Collaborating Faculty: F. Smith

Bone Marrow Transplantation for Inherited Marrow Failure Syndromes - in an issue of Pediatric Clinics of North America devoted to Bone Marrow Transplantation. *Pediatric Clinics of North Am.* 2010, 57(1):147-70. (P. Mehta)

Collaboration with Hematology/Oncology

Collaborating Faculty: C. Phillips

Computed tomography induced double-stranded DNA breaks as a potential marker of radiation sensitivity in Fanconi anemia. *Pediatric Blood and Cancer* Abstract for 23rd Annual meeting of ASPHO, April 7-10, 2010, Montreal, Quebec, Canada. (P. Mehta, S. Davies)

Faculty Members

Stella Davies, MBBS, PhD, MRCP, Professor ; Division Head

Significant Accomplishments

A record year

The clinical program in bone marrow transplantation and immune deficiency performed a record 108 transplants in 2009. This busy program serves as the backbone of our clinical and research efforts as a Jeffrey Modell Foundation and FOCIS center of excellence in primary immune deficiencies. Our investigators also have obtained significant funding for basic science and translational efforts involving bone marrow failure.

Graft versus host disease

We are working with the Division of Gastroenterology, Hepatology and Nutrition and the Department of Surgical Services to identify important clinical phenomenon of graft versus host disease after transplant, and to prepare clinical guidelines for monitoring and treatment.

Novel parameters for thrombotic microangiopathy

We collaborated with the Division of Nephrology and Hypertension to describe the incidence of thrombotic microangiopathy after transplantation, and we have published novel clinical and biological diagnostic parameters. A prospective study, now IRB-approved, seeks to further clarify the pathophysiology of this disorder.

Testing a severity index

We also are testing a BMT-specific severity index we developed for post-transplant children admitted to the PICU, in collaboration with the Division of Critical Care Medicine. These data will be reported later in the year.

Division Publications

1. :

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct / Project Period Direct

Davies, S

Multicenter Pilot Trial of HSCT Lacking a Genotype Identical Donor

Fanconi Anemia Research Fund

05/01/2010 - 04/30/2013

\$1,920 / \$5,000

Antileukemic Effect of NK Cells in HCT for Pediatric AML

St Jude's Children's Hospital (National Institutes of Health)

R01 CA 120583

08/01/2007 - 06/30/2012

\$8,687 / \$43,521

Childhood Cancer Survivor Study

St Jude's Children's Hospital (National Cancer Institute)

U24 CA 055727

12/01/2005 - 11/30/2010

\$60,000 / \$228,297

Mechanisms of RET/PTC Rearrangement in Thyroid Cancer

University of Pittsburgh (National Institutes of Health)

R01 CA 088041

03/01/2009 - 02/28/2011

\$7,262 / \$14,371

Environmental Exposure: Susceptibility Alleles in a DNA Damage Response Pathway

University of Cincinnati (National Institutes of Health)

R01 ES 016625	12/01/2008 - 11/30/2010	\$4,722 / \$4,722
Prediction Model for Radiation Sensitivity in Children with Cancer		
National Cancer Institute		
U01 CA 139275	07/16/2009 - 06/30/2011	\$150,618 / \$279,136
The Children's Oncology Group Chairs Grant		
National Childhood Cancer Foundation (National Institutes of Health)		
U10 CA 098543	03/01/2008 - 02/28/2011	\$12,294 / \$35,913
HSCT-CHESS to Enhance Hematopoietic Transplant Recovery		
New England Medical Center Hospital, Inc. (National Institutes of Health)		
\$01 CA 120583	06/01/08 - 05/31/11	\$12,321 / \$20,568

Filipovich, A

Primary Immune Deficiency Treatment Consortium		
The Regents of the Univ of California (National Institutes of Health)		
U54 AI 082973	09/12/2009 - 08/31/2010	\$25,000 / \$25,000
Hypoxia and Potassium Channel Activity in T Lymphocytes		
University of Cincinnati (National Institutes of Health)		
R01 CA 095286	06/01/2009 - 04/30/2011	\$19,766 / \$38,956

Kumar, A

Molecular Pathogenesis of MLL-Fusion Gene Leukemia		
National Institutes of Health		
K08 CA 122191	08/19/2009 - 06/30/2012	\$125,250 / \$375,750

Marsh, R

Investigations into XIAP-deficient X-linked Lymphoproliferative Disease		
National Institutes of Health		
R03 AI 079797	09/15/2008 - 08/31/2010	\$50,000 / \$100,000

Myers, K

Leukemogenesis, Genomic Instability and Fanconi Anemia		
Bear Necessities Pediatric Cancer Fdn		
	07/01/2009 - 06/30/2010	\$40,000 / \$40,000

Sumegi, J

Search for Growth Inhibitory Genes in Ewing's Sarcoma by Epigenetic Profiling		
University of Nebraska Medical Center (La Fondation des Gouverneurs de l'espoir)		
	01/01/2008 - 12/31/2010	\$49,500 / \$125,793
Functional Identification of Genes Mutated in FHLH		
National Institutes of Health		
R21 AI 079759	07/15/2008 - 06/30/2011	\$132,333 / \$275,000
Studies of the t(2;2)(p23;q35)(PAX3-NCOA1) and t(2;8)(q35;q13)(PAX3-NCOA2) Translocations in Alveolar Rhabdomyosarcoma		
Joanna McAfee Childhood Cancer Foundation, Inc.		
	01/01/2010 - 12/31/2010	\$5,000 / \$5,000
Identification of Genes Involved in FHLH		
National Institutes of Health		
R21 AI 076746	09/01/2009 - 08/31/2011	\$150,000 / \$275,000

Current Year Direct	\$854,673
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Industry Contracts

Mehta, P		
Astellas Pharma US, Inc		
		\$ 44,970

Current Year Direct Receipts	\$44,970
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Funded Collaborative Efforts

Bleesing, J

Cincinnati Multidisciplinary Clinical Research Center

National Institutes of Health

Glass, D

08/18/08 - 07/31/13

3 %

Total \$899,643
