

Bone Marrow Transplantation and Immune Deficiency

Division Summary

RESEARCH AND TRAINING DETAILS

Number of Faculty	16
Number of Joint Appointment Faculty	3
Number of Research Fellows	2
Number of Support Personnel	28
Direct Annual Grant Support	\$726,676
Direct Annual Industry Support	\$106,294
Peer Reviewed Publications	41

CLINICAL ACTIVITIES AND TRAINING

Number of Clinical Staff	7
Number of Staff Physicians	7
Number of Clinical Fellows	5
Number of Other Students	1
Inpatient Encounters	9,674
Outpatient Encounters	5,258

Division Photo



Row 1: P Khandelwal, P Mehta, K Myers, S Davies, R Marsh
Row 2: S Chandra, J Bleesing, J Sumegi, M Jordan, M Grimley

Division Publications

1. Bitan M, He W, Zhang MJ, Abdel-Azim H, Ayas MF, Bielei B, Carpenter PA, Cairo MS, Diaz MA, Horan JT, Jodele S, Kitko CL, Schultz KR, Kletzel M, Kasow KA, Lehmann LE, Mehta PA, Shah N, Pulsipher MA, Prestidge T, Seber A, Shenoy S, Woolfrey AE, Yu LC, Davies SM. **Transplantation for children with acute myeloid leukemia: a comparison of outcomes with reduced intensity and myeloablative regimens.** *Blood.* 2014; 123:1615-20.
2. Buchbinder D, Nugent DJ, Filipovich AH. **Wiskott-Aldrich syndrome: diagnosis, current management, and emerging treatments.** *Appl Clin Genet.* 2014; 7:55-66.
3. Cai CX, Siringo FS, Odel JG, Lignelli-Dipple A, Lanzman BA, Gindin T, Filipovich AH. **Downbeat nystagmus secondary to familial hemophagocytic lymphohistiocytosis.** *J Neuroophthalmol.* 2014; 34:57-60.
4. Chaigne-Delalande B, Li FY, O'Connor GM, Lukacs MJ, Jiang P, Zheng L, Shatzer A, Biancalana M, Pittaluga S, Matthews HF, Jancel TJ, Bleesing JJ, Marsh RA, Kuijpers TW, Nichols KE, Lucas CL, Nagpal S, Mehmet H, Su HC, Cohen JI, Uzel G, Lenardo MJ. **Mg2+ regulates cytotoxic functions of NK and CD8 T cells in chronic EBV infection through NKG2D.** *Science.* 2013; 341:186-91.
5. Chandrakasan S, Filipovich AH. **Hemophagocytic lymphohistiocytosis: advances in pathophysiology, diagnosis, and treatment.** *J Pediatr.* 2013; 163:1253-9.
6. Chellapandian D, Das R, Zelle K, Wiener SJ, Zhao H, Teachey DT, Nichols KE, Group E-HRS. **Treatment of Epstein Barr virus-induced haemophagocytic lymphohistiocytosis with rituximab-**

- containing chemo-immunotherapeutic regimens. *Br J Haematol*. 2013; 162:376-82.
7. Dandoy CE, Hirsch R, Chima R, Davies SM, Jodele S. **Pulmonary hypertension after hematopoietic stem cell transplantation.** *Biol Blood Marrow Transplant*. 2013; 19:1546-56.
 8. DiPaola F, Grimley M, Bucuvalas J. **Pediatric acute liver failure and immune dysregulation.** *J Pediatr*. 2014; 164:407-9.
 9. Du W, Erden O, Wilson A, Sipple JM, Schick J, Mehta P, Myers KC, Steinbrecher KA, Davies SM, Pang Q. **Deletion of Fanca or Fancd2 dysregulates Treg in mice.** *Blood*. 2014; 123:1938-47.
 10. Dvorak CC, Cowan MJ, Logan BR, Notarangelo LD, Griffith LM, Puck JM, Kohn DB, Shearer WT, O'Reilly RJ, Fleisher TA, Pai SY, Hanson IC, Pulsipher MA, Fuleihan R, Filipovich A, Goldman F, Kapoor N, Small T, Smith A, Chan KW, Cuvelier G, Heimall J, Knutsen A, Loechelt B, Moore T, Buckley RH. **The natural history of children with severe combined immunodeficiency: baseline features of the first fifty patients of the primary immune deficiency treatment consortium prospective study 6901.** *J Clin Immunol*. 2013; 33:1156-64.
 11. Gadalla SM, Sales-Bonfim C, Carreras J, Alter BP, Antin JH, Ayas M, Bodhi P, Davis J, Davies SM, Deconinck E, Deeg HJ, Duerst RE, Fasth A, Ghavamzadeh A, Giri N, Goldman FD, Kolb EA, Krance R, Kurtzberg J, Leung WH, Srivastava A, Or R, Richman CM, Rosenberg PS, Toledo Codina JS, Shenoy S, Socie G, Tolar J, Williams KM, Eapen M, Savage SA. **Outcomes of allogeneic hematopoietic cell transplantation in patients with dyskeratosis congenita.** *Biol Blood Marrow Transplant*. 2013; 19:1238-43.
 12. Gonsalves CS, Crable S, Chandra S, Li W, Kalra VK, Joiner CH. **Angiogenic growth factors augment K-Cl cotransporter expression in erythroid cells via hypoxia-inducible factor-1alpha.** *Am J Hematol*. 2014; 89:273-81.
 13. Griffith LM, Cowan MJ, Notarangelo LD, Kohn DB, Puck JM, Pai SY, Ballard B, Bauer SC, Bleesing JJ, Boyle M, Brower A, Buckley RH, van der Burg M, Burroughs LM, Candotti F, Cant AJ, Chatila T, Cunningham-Rundles C, Dinanuer MC, Dvorak CC, Filipovich AH, Fleisher TA, Bobby Gaspar H, Gungor T, Haddad E, Hovermale E, Huang F, Hurley A, Hurley M, Iyengar S, Kang EM, Logan BR, Long-Boyle JR, Malech HL, McGhee SA, Modell F, Modell V, Ochs HD, O'Reilly RJ, Parkman R, Rawlings DJ, Routes JM, Shearer WT, Small TN, Smith H, Sullivan KE, Szabolcs P, Thrasher A, Torgerson TR, Veys P, Weinberg K, Zuniga-Pflucker JC, workshop p. **Primary Immune Deficiency Treatment Consortium (PIDTC) report.** *J Allergy Clin Immunol*. 2014; 133:335-47.
 14. Gupta M, Khalequzzaman M, Jodele S, Mortensen J, Mueller MA, Gupta A. **Cruled scabies in a 15-year-old boy with congenital neutropenia and myelodysplastic syndrome.** *J Clin Oncol*. 2014; 32:e49-51.
 15. Hale GA, Arora M, Ahn KW, He W, Camitta B, Bishop MR, Bitan M, Cairo MS, Chan K, Childs RW, Copelan E, Davies SM, Perez MA, Doyle JJ, Gale RP, Vicent MG, Horn BN, Hussein AA, Jodele S, Kamani NR, Kasow KA, Kletzel M, Lazarus HM, Lewis VA, Myers KC, Olsson R, Pulsipher M, Qayed M, Sanders JE, Shaw PJ, Soni S, Stiff PJ, Stadtmayer EA, Ueno NT, Wall DA, Grupp SA. **Allogeneic hematopoietic cell transplantation for neuroblastoma: the CIBMTR experience.** *Bone Marrow Transplant*. 2013; 48:1056-64.
 16. Jing H, Zhang Q, Zhang Y, Hill BJ, Dove CG, Gelfand EW, Atkinson TP, Uzel G, Matthews HF, Mustillo PJ, Lewis DB, Kavadas FD, Hanson IC, Kumar AR, Geha RS, Douek DC, Holland SM, Freeman AF, Su HC. **Somatic reversion in dedicator of cytokinesis 8 immunodeficiency modulates disease phenotype.** *J Allergy Clin Immunol*. 2014; 133:1667-75.
 17. Jodele S, Fukuda T, Vinks A, Mizuno K, Laskin BL, Goebel J, Dixon BP, Teusink A, Pluthero FG, Lu L, Licht C, Davies SM. **Ecilizumab therapy in children with severe hematopoietic stem cell transplantation-associated thrombotic microangiopathy.** *Biol Blood Marrow Transplant*. 2014; 20:518-25.
 18. Jodele S, Licht C, Goebel J, Dixon BP, Zhang K, Sivakumaran TA, Davies SM, Pluthero FG, Lu L, Laskin

- BL. **Abnormalities in the alternative pathway of complement in children with hematopoietic stem cell transplant-associated thrombotic microangiopathy.** *Blood*. 2013; 122:2003-7.
19. Johnson TS, Terrell CE, Millen SH, Katz JD, Hildeman DA, Jordan MB. **Etoposide selectively ablates activated T cells to control the immunoregulatory disorder hemophagocytic lymphohistiocytosis.** *J Immunol*. 2014; 192:84-91.
20. Kachapati K, Bednar KJ, Adams DE, Wu Y, Mittler RS, Jordan MB, Hinerman JM, Herr AB, Ridgway WM. **Recombinant soluble CD137 prevents type one diabetes in nonobese diabetic mice.** *J Autoimmun*. 2013; 47:94-103.
21. Karkare S, Chhipa RR, Anderson J, Liu X, Henry H, Gasilina A, Nassar N, Roychoudhury J, Clark JP, Kumar A, Pauletti GM, Ghosh PK, Dasgupta B. **Direct inhibition of retinoblastoma phosphorylation by nimbolide causes cell-cycle arrest and suppresses glioblastoma growth.** *Clin Cancer Res*. 2014; 20:199-212.
22. Khandelwal P, Brewer AJ, Minevich E, Miles L, Geller JI. **High-grade transitional cell carcinoma of the bladder in a 5-year-old boy successfully treated with partial cystectomy and intravesical bacillus Calmette-Guerin.** *J Pediatr Hematol Oncol*. 2014; 36:e234-6.
23. Khandelwal P, Lawrence J, Filipovich AH, Davies SM, Bleesing JJ, Jordan MB, Mehta P, Jodele S, Grimley MS, Kumar A, Myers K, Marsh RA. **The successful use of alemtuzumab for treatment of steroid-refractory acute graft-versus-host disease in pediatric patients.** *Pediatr Transplant*. 2014; 18:94-102.
24. Khandelwal P, Marsha R, Schmid DS, Folster J, Radford KW, Davies SM, Filipovich A. **Non dermatomal rash and pancytopenia in a 5 year old child.** *J Clin Virol*. 2014; 60:81-3.
25. Khodoun MV, Kucuk ZY, Strait RT, Krishnamurthy D, Janek K, Lewkowich I, Morris SC, Finkelman FD. **Rapid polyclonal desensitization with antibodies to IgE and FcepsilonR1alpha.** *J Allergy Clin Immunol*. 2013; 131:1555-64.
26. Laskin BL, Denburg M, Furth S, Diorio D, Goebel J, Davies SM, Jodele S. **BK viremia precedes hemorrhagic cystitis in children undergoing allogeneic hematopoietic stem cell transplantation.** *Biol Blood Marrow Transplant*. 2013; 19:1175-82.
27. Laskin BL, Maisel J, Goebel J, Yin HJ, Luo G, Khoury JC, Davies SM, Jodele S. **Renal arteriolar C4d deposition: a novel characteristic of hematopoietic stem cell transplantation-associated thrombotic microangiopathy.** *Transplantation*. 2013; 96:217-23.
28. Lee YN, Frugoni F, Dobbs K, Walter JE, Giliani S, Gennery AR, Al-Herz W, Haddad E, LeDeist F, Bleesing JH, Henderson LA, Pai SY, Nelson RP, El-Ghoneimy DH, El-Feky RA, Reda SM, Hossny E, Soler-Palacin P, Fuleihan RL, Patel NC, Massaad MJ, Geha RS, Puck JM, Palma P, Cancrini C, Chen K, Vihinen M, Alt FW, Notarangelo LD. **A systematic analysis of recombination activity and genotype-phenotype correlation in human recombination-activating gene 1 deficiency.** *J Allergy Clin Immunol*. 2014; 133:1099-108.
29. Lerner D, Dandoy C, Hirsch R, Laskin B, Davies SM, Jodele S. **Pericardial effusion in pediatric SCT recipients with thrombotic microangiopathy.** *Bone Marrow Transplant*. 2014; 49:862-3.
30. Linabery AM, Blommer CN, Spector LG, Davies SM, Robison LL, Ross JA. **ARID5B and IKZF1 variants, selected demographic factors, and childhood acute lymphoblastic leukemia: a report from the Children's Oncology Group.** *Leuk Res*. 2013; 37:936-42.
31. Liu X, Chhipa RR, Pooya S, Wortman M, Yachyshin S, Chow LM, Kumar A, Zhou X, Sun Y, Quinn B, McPherson C, Warnick RE, Kendler A, Giri S, Poels J, Norga K, Viollet B, Grabowski GA, Dasgupta B. **Discrete mechanisms of mTOR and cell cycle regulation by AMPK agonists independent of AMPK.** *Proc Natl Acad Sci U S A*. 2014; 111:E435-44.
32. Majhail NS, Tao L, Bredeson C, Davies S, Dehn J, Gajewski JL, Hahn T, Jakubowski A, Joffe S, Lazarus

- HM, Parsons SK, Robien K, Lee SJ, Kuntz KM. **Prevalence of hematopoietic cell transplant survivors in the United States.** *Biol Blood Marrow Transplant.* 2013; 19:1498-501.
33. Marsh RA, Kim MO, Liu C, Bellman D, Hart L, Grimley M, Kumar A, Jodele S, Myers KC, Chandra S, Leemhuis T, Mehta PA, Bleesing JJ, Davies SM, Jordan MB, Filipovich AH. **An intermediate alemtuzumab schedule reduces the incidence of mixed chimerism following reduced-intensity conditioning hematopoietic cell transplantation for hemophagocytic lymphohistiocytosis.** *Biol Blood Marrow Transplant.* 2013; 19:1625-31.
34. McNally JP, Elfers EE, Terrell CE, Grunblatt E, Hildeman DA, Jordan MB, Katz JD. **Eliminating encephalitogenic T cells without undermining protective immunity.** *J Immunol.* 2014; 192:73-83.
35. Medical Advisory Committee of the Immune Deficiency F, Shearer WT, Fleisher TA, Buckley RH, Ballas Z, Ballow M, Blaese RM, Bonilla FA, Conley ME, Cunningham-Rundles C, Filipovich AH, Fuleihan R, Gelfand EW, Hernandez-Trujillo V, Holland SM, Hong R, Lederman HM, Malech HL, Miles S, Notarangelo LD, Ochs HD, Orange JS, Puck JM, Routes JM, Stiehm ER, Sullivan K, Torgerson T, Winkelstein J. **Recommendations for live viral and bacterial vaccines in immunodeficient patients and their close contacts.** *J Allergy Clin Immunol.* 2014; 133:961-6.
36. Myers KC, Bolyard AA, Otto B, Wong TE, Jones AT, Harris RE, Davies SM, Dale DC, Shimamura A. **Variable clinical presentation of Shwachman-Diamond syndrome: update from the North American Shwachman-Diamond Syndrome Registry.** *J Pediatr.* 2014; 164:866-70.
37. Nestheide S, Bridge JA, Barnes M, Frayer R, Sumegi J. **Pharmacologic inhibition of epigenetic modification reveals targets of aberrant promoter methylation in Ewing sarcoma.** *Pediatr Blood Cancer.* 2013; 60:1437-46.
38. Parvaneh N, Filipovich AH, Borkhardt A. **Primary immunodeficiencies predisposed to Epstein-Barr virus-driven haematological diseases.** *Br J Haematol.* 2013; 162:573-86.
39. Qian Y, Johnson JA, Connor JA, Valencia CA, Barasa N, Schubert J, Husami A, Kissell D, Zhang G, Weirauch MT, Filipovich AH, Zhang K. **The 253-kb inversion and deep intronic mutations in UNC13D are present in North American patients with familial hemophagocytic lymphohistiocytosis 3.** *Pediatr Blood Cancer.* 2014; 61:1034-40.
40. Terrell CE, Jordan MB. **Mixed hematopoietic or T-cell chimerism above a minimal threshold restores perforin-dependent immune regulation in perforin-deficient mice.** *Blood.* 2013; 122:2618-21.
41. Wada T, Kanegane H, Ohta K, Katoh F, Imamura T, Nakazawa Y, Miyashita R, Hara J, Hamamoto K, Yang X, Filipovich AH, Marsh RA, Yachie A. **Sustained elevation of serum interleukin-18 and its association with hemophagocytic lymphohistiocytosis in XIAP deficiency.** *Cytokine.* 2014; 65:74-8.

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.

Javier El-Bietar, MD, Instructor

Research Interests Bone marrow transplantation for malignant and nonmalignant diseases of childhood, transplant-associated complications and infections involving the gut.

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.

Pooja Khandelwal, MD, Instructor

Research Interests Acute Graft Versus Host Disease, Refractory autoimmune cytopenias post transplant, Biology of engraftment syndrome.

Zeynep Kucuk, MD, Instructor

Research Interests Characterization and clinical investigation of Primary Immunodeficiency Disorders including immune dysregulation disorders, autoimmune gastroenteropathy and epidemiology of HLH.

Ashish Kumar, MD, PhD, Associate Professor

Research Interests Etiology of childhood leukemia, transplantation of children with malignancy and primary immune deficiencies.

Adam Lane, PhD, Instructor

Research Interests Adaptive designs for phase I/II clinical trials, survival analysis and structural equation modeling.

Rebecca Marsh, MD, Assistant Professor

Research Interests Pathogenesis of HLH with XIAP 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

- **Stephanie Benoit, MD**
- **Paulina Daniels, MD**
- **Michael Huang, MD**
- **Ernest Lawhorn, MD**
- **Lisa Petiniot, 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

- **Christopher Dandoy, MD**, PL-VII, Miami Children's Hospital
- **Aharon Gefen, MD**, PL-VII, Rambam Medical Center, Israel
- **Adam Nelson, MD**, PL-VII, Centre for Children's Cancer & Blood Disorders, Sydney Children's Hospital
- **Ahmad Rayes, MD**, PL-V, SUNY Upstate Medical University
- **Beverly Schaefer, MD**, PL-IV, Thomas Jefferson University/Dupont Hospital for Children

Division Collaboration

Gene therapy for Hemophagocytic Lymphohistiocytosis (Michael Jordan, MD)

Allergy and Immunology » Kimberly Risma, MD, PhD

The biology of cytotoxicity: Genotype/phenotype correlations (Michael Jordan, MD)

Allergy and Immunology » Kimberly Risma, MD, PhD

Immune profiling in Hemophagocytic Lymphohistiocytosis (Michael Jordan, MD)

Allergy and Immunology » Kimberly Risma, MD, PhD

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

Asthma Research » Melinda Butsch-Kovacic, MD, MPH

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. (Parinda Mehta, MD)

Asthma Research » Melinda Butsch-Kovacic, MD, MPH

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 Sonata Jodele, MD for this project. (*Dandoy, et al, Bio. Blood Marrow Transplant 2013, Jul 23*) (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Cardiology » John L. Jefferies, MD, MPH, FAAP, FACC and Russel Hirsch, MD

Critical Care » Ranjit Chima, MD and Hector Wong, MD

Pathology » David Witte, MD

Hematology/Oncology » Christopher Dandoy, MD

"Echocardiographic screening for pulmonary hypertension in HSCT patients". I am mentoring Dr. Christopher Dandoy for this project. This project was completed, data analyzed and manuscript is in under review in BBMT journal. Project was awarded oral presentation at ASBMT 2013 and plenary session at ASPHO 2013 meetings. (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Cardiology » John L. Jefferies, MD, MPH, FAAP, FACC and Russel Hirsch, MD

Critical Care » Ranjit Chima, MD and Hector Wong, MD

Pathology » David Witte, MD

Hematology/Oncology » Christopher Dandoy, MD

Pulmonary Hypertension in HSCT patients: biomarker pilot study". I am mentoring Dr. Christopher Dandoy for this project. Study samples are being analyzed based on preliminary data.

(Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Cardiology » John L. Jefferies, MD, MPH, FAAP, FACC and Russel Hirsch, MD

Critical Care » Ranjit Chima, MD and Hector Wong, MD

Bone Marrow Transplantation and Immune Deficiency » Christopher Dandoy, MD

Pathology » David Witte, MD

Selective ablation of undesirable T cell responses (Michael Jordan, MD)

Immunobiology » David Hildeman, PhD

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.

(Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP, Adam Lane, PhD)

Critical Care Medicine » Ranjit Chima, MD and Derek Wheeler, MD

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 (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Critical Care Medicine » Ranjit Chima, MD, Derek Wheeler, MD, and Hector Wong, MD

PRES working group. To identify patients at risk for PRES, outline uniform evaluation and therapy guidelines. (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Critical Care Medicine » Hector Wong, MD

Radiology » William Ball, MD, James Leach, MD, and Sue Poynter, MD

Nephrology and Hypertension » Jens Goebel, MD and Mark Mitsnefes, MD

Endocrine phenotype of children and adults with Fanconi anemia. (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP, Kasiani Myers, MD, Richard Harris, MD)

Endocrinology » Deborah Elder, MD and Susan Rose, MD

Quercetin in patients with Fanconi Anemia: A pilot study. (Parinda Mehta, MD)

Endocrinology » Deborah Elder, MD and Susan Rose, MD

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

Endocrinology » Susan Rose, MD

Gene correction strategies for Hemophagocytic lymphohistiocytosis. (Michael Jordan, MD)

Experimental Hematology and Cancer Biology » Punam Malik, MD

Allergy and Immunology » Kimberly Risma, MD, PhD

Novel methods to promote stem cell engraftment. (Michael Jordan, MD)

Experimental Hematology and Cancer Biology » Punam Malik, MD

Animal models of human leukemia: Research project aimed at developing xenograft mouse models of human leukemia using primary patient derived material. (Ashish Kumar, MD, PhD)

Experimental Hematology and Cancer Biology » James Mulloy, PhD

The molecular origin of monosomy 7 in very young children. Translational research project exploring the causes of monosomy 7. (Parinda Mehta, MD, S. Davies, MB BS, PhD, MRCP)

Experimental Hematology and Cancer Biology » Jose Cancelas, MD, PhD and James Mulloy, PhD

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

Experimental Hematology and Cancer Biology » Nancy Ratner, PhD

The Fanconi Anemia Pathway Limits Human Papillomavirus Replication. (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Experimental Hematology and Cancer Biology » Susanne Wells, PhD

Fanconi Anemia Links Reactive Oxygen Species to Insulin Resistance and Obesity. (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Experimental Hematology and Cancer Biology » Qishen Pang, PhD

The FA pathway counteracts oxidative stress through selective protection of antioxidant defense gene promoters. (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Experimental Hematology and Cancer Biology » Qishen Pang, PhD

Ongoing collaboration on a translational study: Quercetin in patients with Fanconi anemia, a Pilot study (Parinda Mehta, MD)

Experimental Hematology and Cancer Biology » Qishen Pang, PhD

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). (Parinda Mehta, MD)

Experimental Hematology and Cancer Biology » Jose Cancelas, MD, PhD and James Mulloy, PhD

Gene therapy for Hemophagocytic Lymphohistiocytosis. (Michael Jordan, MD)

Experimental Hematology and Cancer Biology » Punam Malik, MD

Novel methods to promote stem cell engraftment. (Michael Jordan, MD)

Experimental Hematology and Cancer Biology » Punam Malik, MD

Biology of MAP2K1 mutations in histiocytoses. (Ashish Kumar, MD, PhD)

Experimental Hematology and Cancer Biology » Nicolas Nassar, PhD

Novel immune-dysregulatory diseases presenting as IBD. (Ashish Kumar, MD, PhD)

Gastroenterology, Hepatology and Nutrition » Lee Denson, MD

Discovering biomarkers and pathogenesis of hepatitis associated aplastic anemia. (Ashish Kumar, MD, PhD)

Gastroenterology, Hepatology and Nutrition » Alexander Miethke, MD

The clinical phenotype of children with Fanconi anemia caused by biallelic FANCD1/BRCA2 mutations. *Pediatr Blood Cancer*. 2011 (Kasiani Myers, MD, Stella Davies, MB BS, PhD, MRCP, Richard Harris, MD, Parinda Mehta, MD)

Human Genetics » Teresa Smolarek, PhD and S. Zimmerman, PhD

Pathology » Richard McMasters, MD

Project: Abnormalities in the alternative pathway of complement in children with hematopoietic stem cell transplant-associated thrombotic microangiopathy. Manuscript is published in *Blood* (Jodele et al, *Blood*. 2013 Jun 27. [Epub ahead of print]) (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Human Genetics » Kejian Zhang, MD, MBA

Nephrology » Bradley Dixon, MD and Jens Goebel, MD

Project: "Complement gene testing in patients with hematopoietic stem cell transplant-associated thrombotic

microangiopathy”

Project support: The Investigator Initiated Trial Grant from Alexion Therapeutics. (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Human Genetics » Kejian Zhang, MD, MBA

Hematology » Ralph Gruppo, MD

Genotyping for PID and HLH (Alexandra Filipovich, MD, Jacob Bleesing, MD, PhD)

Human Genetics » Kejian Zhang, MD, MBA

Genetics of hepatitis-associated aplastic anemia (Ashish Kumar, MD, PhD)

Human Genetics » Kejian Zhang, MD, MBA

Identification of novel mutations in CVID (Ashish Kumar, MD, PhD)

Human Genetics » Kejian Zhang, MD, MBA

Development of molecular diagnostic assays for LCH (Ashish Kumar, MD, PhD)

Human Genetics » Kejian Zhang, MD, MBA

Discovery and characterization of new primary immune deficiencies (Michael Jordan, MD, Rebecca Marsh, MD)

Human Genetics » Kejian Zhang, MD, MBA

Abnormalities in the alternative pathway of complement in children with hematopoietic stem cell transplant-associated thrombotic microangiopathy. Manuscript is published in *Blood* journal (Jodele, et al, 2013. Jun 27. [epub ahead of print] (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Human Genetics » Kejian Zhang, MD, MBA

Nephrology » Bradley Dixon, MD and Jens Goebel, MD

Role of Pharmacogenetics and Therapeutic Drug Monitoring in BMT Patients (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP

Human Genetics » Kejian Zhang, MD, MBA

Assessment of minimal residual disease in ewing sarcoma. (Janos Sumegi, PhD)

Human Genetics » Teresa Smolarek, PhD

Exploiting the DNA damage response for selective immunomodulation (Michael Jordan, MD)

Immunobiology » David Hildeman, PhD and Jonathan Katz, PhD

Severe Congenital Neutropenia: Research project investigating novel genetic etiologies and molecular and cellular phenotypes of severe congenital neutropenia (Kasiani Myers, MD, Parinda Mehta, MD)

Immunobiology » H. Leighton Grimes, PhD

Incidence and Outcomes of Fungal Infections in Children after Bone Marrow Transplant: CCHMC Experience. (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Infectious Diseases » Beverly Connelly, MD

Incidence and outcomes of RSV infections in pediatric bone marrow transplant center. (Javier El-Bietar, MD, Stella Davies, MB BS, PhD, MRCP)

Infectious Diseases » Lara Danziger-Isakov, MD, MPH

“A Prospective Analysis of Clinical and Biochemical Markers for Pediatric Stem Cell Transplant-Associated Thrombotic Microangiopathy (TA-TMA)”

Project support:

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

(Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP, Adam Lane, PhD, All BMT Faculty)

Biostatistics and Epidemiology » Jane Khoury, PhD

Nephrology and Hypertension » Prasad Devarajan, MD and Jens Goebel, MD

Project: “Retrospective analysis of BK virus infections in an existing cohort of pediatric hematopoietic cell transplant recipients at Cincinnati Children’s Hospital Medical Center” Manuscript published in Biology of Bone Marrow Transplantation journal. (*Laskin, et al, Biol Blood Marrow Transplant. 2013 Aug;19(8):1175-82*) (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Nephrology and Hypertension » Jens Goebel, MD

Project: “Cystatin C to Estimate Renal Function in Bone Marrow Transplant and Oncology Patients” Publication: Biol Blood Marrow Transplantation (*Laskin, et al, Biol Blood Marrow Transplant 2012 Nov; 18(11):1745-52*) (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Nephrology and Hypertension » Jens Goebel, MD

Biostatistics and Epidemiology » Jane Khoury, PhD

Project: " Complement C4d staining in tissue samples of patients with stem cell transplant associated thrombotic microangiopathy (SCT-TMA)" Manuscript is published in Transplantation journal (*Laskin, et al, Transplantation. 2013 Jul 27;96(2):217-223*) (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Nephrology and Hypertension » Jens Goebel, MD

Project: Estimated versus measured glomerular filtration rate in children prior to hematopoietic cell transplantation. Manuscript is print in Biology of Bone Marrow Transplantation journal. (*Laskin et al, Biol Blood Marrow Transplant. 2014*) (Sonata Jodele, MD)

Nephrology and Hypertension » Jens Goebel, MD and Edward Nehus, MD, MS

Clinical assay for Eculizumab measurements in serum (Sonata Jodele, MD)

Nephrology and Hypertension » Bradley Dixon, MD

Novel therapeutic approaches for EVI1+ leukemias (Ashish Kumar, MD, PhD)

Oncology » John Perentesis, MD, FAAP

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

Ophthalmology » Terry Schwartz, MD

Pharmacokinetics of Quercetin in patients with Fanconi anemia (Parinda Mehta, MD, Stella Davies, MB BS, PhD, MRCP)

Pathology and Laboratory Medicine » Kenneth Setchell, PhD

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP

Intestinal transplant-associated microangiopathy (iTMA) Project. Retrospective review of intestinal biopsy samples to explore the incidence, risk factors and outcomes of patients with iTMA. (Javier El-Bietar, MD, Stella Davies, MB BS, PhD, MRCP)

Pathology and Laboratory Medicine » Mikako Warren, MD

Therapeutic Drug Monitoring of Voriconazole in pediatric BMT patients. (Parinda Mehta, MD)

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP

Pharmacokinetics of every 4th day Micafungin in high risk pediatric BMT patients. (Parinda Mehta, MD)

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP

The Impact of Alemtuzumab Levels on Donor Chimerism and Graft Versus Host Disease Following Allogeneic Hematopoietic Cell Transplantation: A Prospective Study. (Parinda Mehta, MD, Rebecca Marsh, MD)

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP

Gene expression profiling of peripheral blood mononuclear cells from children with active hemophagocytic lymphohistiocytosis. (Janos Sumegi, PhD, Alexandra Filipovich, MD)

Allergy and Immunology » Kimberly Risma, MD, PhD

Human Genetics » Kejian Zhang, MD, MBA

Rheumatology » Alexi Grom, MD

Preparation of a stem cell transplant protocol for children with epidermolysis bullosa. (Sonata Jodele, MD, Stella Davies, MB BS, PhD, MRCP)

Pediatric Dermatology » Anne Lucky, MD

Pediatric General and Thoracic Surgery » Richard Azizkhan, MD

"Intersection of PI3K and DNA damage signaling for immune modulation" (Michael Jordan, MD)

UC, Department of Cancer Biology » D. Plas

Grants, Contracts, and Industry Agreements

Grant and Contract Awards			Annual Direct
DAVIES, S			
Childhood Cancer Survivor Study			
National Institutes of Health(St Jude's Children's Hospital)			
U24 CA 055727	12/01/11-11/30/16		\$178,628
COG Group Chair Award - Scientific Leadership			
National Institutes of Health(Children's Hospital of Philadelphia)			

U10 CA 098543	03/01/12-02/28/17	\$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	\$11,370
Children's Oncology Group Chair - WorkLoad Intensity		
National Institutes of Health(Children's Hospital of Philadelphia)		
U10 CA 098543	04/13/12-02/28/15	\$5,775

FILIPOVICH, 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	\$54,140
Rare Diseases Clinical Consortia for the Rare Diseases		
National Institutes of Health(The Regents of the University of California)		
U54 AI 082973	09/12/09-08/31/14	\$1,000

KUMAR, A

The Role of MEIS1 in Hematopoiesis and Hematopoietic Transformation		
National Institutes of Health		
R01 HL 111192	05/01/13-04/30/17	\$271,032

MEHTA, P

Phase I Study of Quercetin for the Treatment of Fanconi Anemia		
U.S Food and Drug Administration		
R01 FD 004383	09/16/13-07/31/16	\$130,719

MYERS, K

Chemoprevention of Leukemia in a Genetically Susceptible Population		
Conquer Cancer Foundation		
	07/01/12-06/30/15	\$62,466

Current Year Direct	\$726,676
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Industry Contracts

GRIMLEY, M

Baxter Healthcare Corporation	\$1,143
Chimerix Inc	\$58,769

HARRIS, R

Alexion Pharmaceuticals, Inc	\$1,155
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JODELE, S

Alexion Pharmaceuticals, Inc.		\$30,800
MEHTA, P		
Astellas Scientific and Medical Affairs, Inc		\$14,427
	Current Year Direct Receipts	\$106,294
	Total	\$832,970