

Name: Kenneth L. McClain M.D. Ph.D.

Affiliation/Current Position: Professor of Pediatrics, Baylor College of Medicine, Texas Children's Hematology/Oncology Center

Country: United States of America

ICKSH2022 Presentation Title: Histiocytic Disorders: recent insights into pathophysiology and practical guidelines

Educational Background:

- 9/63 - 6/67 B.A. (cum laude) - Augustana College, Sioux Falls, South Dakota
- 9/67 - 6/73 M.D. - University of Chicago School of Medicine, Chicago, Illinois
- 7/69 - 12/71 Predoctoral Trainee, Department of Pathology, University of Chicago School of Medicine, Chicago, Illinois (Dr. Werner Kirsten, Advisor)
- 9/72 Ph.D. - University of Chicago School of Medicine, Chicago, Illinois

Postdoctoral Training:

- 7/73 - 6/76 Pediatric Intern and Resident, The Johns Hopkins Hospital, Baltimore, Maryland
- 7/76 - 6/79 Research Associate, NICHD; Laboratory of Molecular Genetics (Dr. J.V. Maizel, Jr., Advisor)
- 7/79 - 7/81 Hematology/Oncology Fellowship, Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota, Minnesota

Professional Experiences:

- 7/80 - 6/81 Instructor, Department of Pediatrics, University of Minnesota
- 7/81 - 6/86 Assistant Professor, Department of Pediatrics, University of Minnesota
- 7/86 - 7/91 Assistant Professor, Department of Pediatrics, Baylor College of Medicine, Houston, Texas
- 7/91 - 6/03 Associate Professor, Department of Pediatrics, Baylor College of Medicine, Houston, Texas
- 6/03 to Present Professor, Department of Pediatrics, Baylor College of Medicine, Houston, Texas

Professional Organizations:

American Society for Hematology
American Society of Pediatric Hematology/Oncology
Harris County Medical Society
Histiocyte Society, President 1998-2001
Children's Oncology Group
Society for Pediatric Research
Texas Medical Association
Erdheim Chester Interest Group

Main Scientific Publications:

1. Willman CL, Busque L, Griffith MS, Favara BE, **McClain KL**, Duncan MH, Gilliland DG: Langerhans cell histiocytosis (histiocytosis x)--A clonal proliferative disease. *New England J Med* 331:154-160, 1994.
2. Palazzi DL, **McClain KL**, Kaplan SL. Hemophagocytic Syndrome in Children: An Important Diagnostic Consideration in Fever of Unknown Origin. *Clinical Infectious Diseases* 36: 306-12, 2003.
3. Rolland A, Guyon L, Cai Y-H, Banchereau J, Palucka K, **McClain KL**. Increased blood myeloid dendritic cells and DC-poietins in Langerhans cell histiocytosis. *J Immunology* 2005; 174:3067-71.
4. Henter J-I, Horne AC, Arico M, Egeler M, Filipovich AH, Imashuku S, Ladisch S, **McClain K**, Nanduri V, Winiarski J, Janka G. HLH-2004: Diagnostic and Therapeutic Guidelines for Hemohagocytic Lymphohistiocytosis. *Pedatric Blood and Cancer* 2007;48:124-131.
5. Allen CE, Yu X, Kozinetz CA, **McClain KL**. Highly elevated ferritin levels are specific for hemophagocytic lymphohistiocytosis. *Pediatric Blood and Cancer*. 2008;50: 1227-35.
6. Phillips M, Allen CE, Gerson CP, **McClain KL**. Comparison of FDG-PET scans to conventional radiography and bone scans in management of Langerhans cell histiocytosis. *Pediatric Blood and Cancer*.2009;52:97-101.
7. Allen CE, Flores R, Rauch R, Dauser R, Murray JC, Puccetti D, Hsu D, Hetherington M, Goldman S, Sondel P, **McClain KL**. Neurodegenerative Central Nervous System Langerhans Cell Histiocytosis and Coincident Hydrocephalus: Treated with Vincristine Cytosine Arabinoside Treatment. *Pediatr Blood Cancer* 2010; 54:416-23.
8. Allen CE, Leung HCE, Yu A, Man TK, Gurusiddappa S, Peters TL, Phillips M, Hicks MJ, Merad M, and **McClain KL**. Cell-Specific Gene Expression in Langerhans Cell Histiocytosis Lesions Reveals a distinct profile compared to epidermal Langerhans cells. *Journal of Immunology*. 2010 184:4557-67.

9. Grois N, Fahrner B, Prayer D, Arceci RJ, Henter J-I, **McClain KL**, Lassmann H, Nanduri V, Prosch H. Central Nervous System Disease in Langerhans Cell Histiocytosis. *Pediatrics*. 2010J;156(6):873-81.
10. Marsh RA, Allen CE, **McClain KL**, Weinstein JL, Washko JK, Skiles J, Lee ND, Khan SP, Lawrence J, Mo J, Bleesing JJ, Filipovich AH, Jordayn MB. Alemtuzumab is an Effective Salvage Therapy for Refractory Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer* 2013 60:101-9.
11. Jordan M, Allen CE, Weitzman S, Filipovich A, **McClain KL**. How We Treat HLH. *Blood* 2011; 118:4041-52.
12. Cantu MA, Lupo PJ, Bigi M, Hicks MJ, Allen CE. **McClain KL**. Optimal Therapy for Adults with Langerhans Cell Histiocytosis Bone Lesions. *PloS One* 2012; 7(8): e43257.
13. Gadner H, Minkov M, Grois N, Pötschger U, Thiem E, Aricò M, Astigarraga I, Braier J, Donadieu J, Henter JI, Janka-Schaub G, **McClain KL**, Weitzman S, Windebank K, Ladisch S. Therapy prolongation improves outcome in multi-system Langerhans cell histiocytosis. *Blood*. 2013;121(25):5006-5014.
14. Simko S, Tran Huy, Jones J, Bilgi M, Beaupin LK, Coulter D, Garrington T, McCavit TL, Moore C, Rivera-Ortegón F, Shaffer L, Stork L, Turcotte L, Welsh EC, Hicks MJ, **McClain KL**, Allen CE Clofarabine salvage therapy in refractory multifocal histiocytic disorders, including Langerhans cell histiocytosis, juvenile xanthogranuloma and Rosai-Dorfman disease. *Pediatr Blood Cancer*. 2014 ;61(3):479-87.
15. Marie-Luise Berres, Karen Phaik-Har Lim, Tricia Peters, Jeremy Price, Hitoshi Takizawa, Helene Salmon, Juliana Idoyaga, Albert Ruzo, Philip J. Lupo⁴, M. John Hicks, Albert Shih, Stephen J. Simko, Harshal Abhyankar, Rikhia Chakraborty, Kenneth M. Heym, Venetia Bigley, Matthew Collin, Markus G. Manz, **Kenneth McClain**, Miriam Merad, Carl E. Allen. *BRAF-V600E* Expression in Precursor Versus Differentiated Dendritic Cells Defines Clinically Distinct LCH Risk-Groups. *J. Exp. Med.* 2014;211: 669-683.
16. Eli Diamond, Lorenzo Dagna, David Hyman, Giulio Cavalli, Filip Janku, Juvianee Estrada-Veras, Marina Ferrarini, Omar Abdel-Wahab, Mark Heaney, Paul Scheel, Nancy Feeley, Elisabetta Ferrero, **Kenneth McClain**, Augusto Vaglio, Thomas Colby, Laurent Arnaud, Julien Haroche. Consensus Guidelines for the Diagnosis and Clinical Management of Erdheim-Chester Disease. *BLOOD* 2014 ;124(4):483-92.
17. Simko SJ, Garmezey B, Abhyankar H, Lupo PJ, Chakraborty R, Phaik Har Lim K, Shih A, Hicks MJ, Wright TS, Levy ML, **McClain KL**, and Allen CE. Differentiating skin-limited and multisystem Langerhans cell histiocytosis. *J Peds*. 2014;165(5):990-6.
18. Simko S, **McClain KL**, Allen CE. Up-front therapy for LCH: is it time to test an alternative to vinblastine/prednisone? *Brit J Hematol*. 2015;169(2):299-301.

19. Allen CE, Ladish S, **McClain KL**. How We Treat Langerhans Cell Histiocytosis. *Blood*. 2015 Jul 2;126(1):26-35.
20. Zinn DJ, Grimes AB, Lin H, Eckstein O, Allen CE, **McClain KL**. Hydroxyurea: a new old therapy for Langerhans cell histiocytosis. *BLOOD* 2016;128:2462-2465.
21. Peckham-Gregory EC, **McClain KL**, Allen CE, Scheurer ME, Lupo PJ. The role of parental and perinatal characteristics on Langerhans cell histiocytosis: characterizing increased risk among Hispanics. *Ann Epidemiol*. 2018;28:521-528.
22. Ballester LY, Cantu MD, Lim KP, Sarabia SF, Ferguson LS, Renee Webb C, Allen CE, **McClain KL**, Mohila CA, Punia JN, Roy A, López-Terrada DH, John Hicks M, Fisher KE. The use of BRAF V600E mutation-specific immunohistochemistry in pediatric Langerhans cell histiocytosis. *Hematol Oncol*. 2018;36:307-315.
23. Paul Milne, Venetia Bigley, Chris M Bacon, Antoine Néel, Naomi McGovern, Simon Bomken, Muzlifah Haniffa, Eli Diamond, Benjamin H Durham, Johann Visser, David Hunt, Harsha Gunawardena, Mac Machete, **Kenneth L McClain**, Carl Allen, Omar Abdel-Wahab, and Matthew Collin. Hematopoietic origin of Langerhans cell histiocytosis and Erdheim Chester disease in adults. *Blood* 2017;130(2):167-175.
24. Daver N, **McClain K**, Allen CE, Parikh SA, Otroock Z, Rojas-Hernandez C, Blechacz B, Wang S, Minkov M, Jordan MB, La Rosée P, Kantarjian HM. A consensus review on malignancy-associated hemophagocytic lymphohistiocytosis in adults. *Cancer*. 2017; 123(17):3229-3240.
25. Peckham-Gregory EC, Chakraborty R, Scheurer ME, Belmont JW, Abhyankar H, Sengal AG, Scull BP, Eckstein O, Zinn DJ, Mayer L, Shih A, Merad M, Parsons DW, **McClain KL**, Lupo PJ, Allen CE. A genome-wide association study of LCH identifies a variant in *SMAD6* associated with susceptibility. *Blood*. 2017; 130(20): 2229-2232.
26. Chakraborty R, Hampton OA, Abhyankar H, Zinn DJ, Grimes A, Skull B, Eckstein O, Mahmood N, Wheeler DA, Lopez-Terrada D, Peters TL, Hicks JM, Elghetany T, Krance R, Poulikakos PI, Merad M, **McClain KL**, Allen CE, Parsons DW Activating MAPK1 (ERK2) mutation in an aggressive case of disseminated juvenile xanthogranuloma. *Oncotarget*. 2017;8(28):46065-46070.
27. Brandon Hogstad, Marie-Luise Berres, Rikhia Chakraborty, Jun Tang, Camille Bigenwald, Madhavika Serasinghe, Karen Phaik Har Lim, Howard Lin, Tsz-Kwong Man, Romain Remark, Samantha Baxter, Veronika Kana, Stefan Jordan, Zoi Karoulia, Wing-hong Kwan, Marylene Leboeuf, Elisa Brandt, Helene Salmon, **Kenneth McClain**, Poulikos Poulikakos, Jerry Chipuk, Willem Mulder, Carl Allen, and Miriam Merad. RAF/MEK/ERK pathway suppresses dendritic cell migration and traps dendritic cells in LCH lesions. *J Exp Med* 2018; 215:319-336.

28. Elisabet Bergsten, Anna Carin Horne, Maurizio Arico, Itziar Astigarraga, Maarten R. Egeler, Alexandra H. Filipovich, EIICHI ISHII, Gritta E. Janka, Stephan Ladisch, Kai Lehmborg, **Kenneth L. McClain**, Milen Minkov, Scott Montgomery, Vasanta Nanduri, Diego Alfredo Rosso, and Jan-Inge Henter. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: Long term results of the cooperative HLH-2004 study. *Blood* 2017; 130:2728-2738.
29. Chinn IK, Eckstein OS, Peckham-Gregory EC, Goldberg BR, Forbes LR, Nicholas SK, Mace EM, Vogel TP, Abhyankar HA, Diaz MI, Heslop HE, Krance RA, Martinez CA, Nguyen TC, Bashir DA, Goldman JR, Stray-Pedersen A, Pedroza LA, Poli MC, Aldave Becerra JC, McGhee SA, Al-Herz W, Chamdin A, Coban-Akdemir ZH, Jhangiani SN, Muzny DM, Cao TN, Hong DN, Gibbs RA, Lupski JR, Orange JS, **McClain KL**, Allen CE. Genetic and mechanistic diversity in pediatric hemophagocytic lymphohistiocytosis. *Blood* 2018;132(1):89-100.
30. **McClain KL**, Picarsic J, Chakraborty R, Zinn D, Lin H, Abhyankar H, Scull B, Shih A, Lim KPH, Eckstein O, Lubega J, Peters TL, Olea W, Burke T, Ahmed N, Hicks MJ, Tran B, Jones J, Dauser R, Jeng M, Baiocchi R, Schiff D, Goldman S, Heym KM, Wilson H, Carcamo B, Kumar A, Rodriguez-Galindo C, Whipple NS, Campbell P, Murdoch G, Kofler J, Heales S, Malone M, Woltjer R, Quinn JF, Orchard P, Kruer MC, Jaffe R, Manz MG, Lira SA, Parsons DW, Merad M, Man TK, Allen CE. CNS Langerhans cell histiocytosis: Common hematopoietic origin for LCH-associated neurodegeneration and mass lesions. *Cancer*. 2018;124: 2607-2620.
31. Oussama Abla, Eric Jacobsen, Jennifer L Picarsic, Zdenka Krenova, Ronald Jaffe, Jean-Francois Emile, Benjamin H Durham, Jorge Luis Braier, Frédéric Charlotte, Jean Donadieu, Fleur Cohen Aubart, Carlos Rodriguez-Galindo, Carl E Allen, James Whitlock, Sheila Weitzman, **Kenneth L McClain**, Julien Haroche, and Eli Diamond. Consensus recommendations for the diagnosis and clinical management of Rosai-Dorfman-Destombes Disease. *Blood* 2018; 131(26):2877-2890.
32. Peckham-Gregory EC, **McClain KL**, Allen CE, Scheurer ME, Lupo PJ. The role of parental and perinatal characteristics on Langerhans cell histiocytosis: characterizing increased risk among Hispanics. *Ann Epidemiol.* 2018;28(8):521-528
33. Goldman J, Desai MS, **McClain KL**, Tcharmtchi MH, Kennedy CE, Thompson K, Lam F, Bashir DA, Chinn IK, Goldberg BR, Allen CE, Nguyen TC. Hepatobiliary Dysfunction and Disseminated Intravascular Coagulation Increase Risk of Mortality in Pediatric Hemophagocytic Lymphohistiocytosis. *Pediatr Crit Care Med.* 2018; (10):e522-e530.
34. Allen CE, Merad M, **McClain KL**. Langerhans-Cell Histiocytosis. *N Engl J Med.* 2018 Aug 30;379(9):856-868.
35. Eckstein O, McAtee CL, Greenberg J, Kumar A, Fein-Levy C, Smith T, Tran B, **McClain KL**. Rituximab therapy for patients with Langerhans cell histiocytosis-associated neurologic dysfunction. *Pediatr Hematol Oncol.* 2018;35(7-8):427-433.

36. Ballester LY, Cantu MD, Lim KP, Sarabia SF, Ferguson LS, Renee Webb C, Allen CE, **McClain KL**, Mohila CA, Punia JN, Roy A, López-Terrada DH, John Hicks M, Fisher KE. The use of BRAF V600E mutation-specific immunohistochemistry in pediatric Langerhans cell histiocytosis. *Hematol Oncol*. 2018;36(1):307-315.
37. Eckstein OS, Zinn DJ, Peckham-Gregory EC, Lin H, Visser J, Henry MH, Morland B, Fein-Levy C, Kumar A, Schiff D, Karras N, Chu R, Abla O, Hijjiya N, Kim SY, Campbell PK, Woods-Swofford W, Ramirez LP, Fernandes C, Murray MJ, Abhyankar H, Chakraborty R, Scull B, Sher AC, Hermiston M, Hogarty MD, Jordan MB, Merad M, Rollins BJ, **McClain KL**, Man TK, Rodriguez-Galindo C, Allen CE. Clinical responses and persistent *BRAF* V600E+ blood cells in children with LCH treated with MAPK pathway inhibition. *Blood* 2018; 133:1691-1694.
38. Lim KPH, Milne P, Poidinger M, Duan K, Lin H, McGovern N, Abhyankar H, Zinn D, Burke TM, Eckstein OS, Chakraborty R, Sengal A, Scull B, Newell E, Merad M, **McClain KL**, Man TK, Ginhoux F, Collin M, Allen CE. Circulating CD1c+ myeloid dendritic cells are potential precursors to LCH lesion CD1a+CD207+ cells. *Blood Adv*. 2020;4(1):87-99
39. Jordan MB, Allen CE, Greenberg J, Henry M, Hermiston ML, Kumar A, Hines M, Eckstein O, Ladisch S, Nichols KE, Rodriguez-Galindo C, Wistinghausen B, **McClain KL**. Challenges in the diagnosis of hemophagocytic lymphohistiocytosis: Recommendations from the North American Consortium for Histiocytosis (NACHO). *Pediatr Blood Cancer*. 2019 Nov;66(11):e27929.
40. Mastropolo R, Close A, Allen SW, **McClain KL**, Maurer S, Picarsic J. *BRAF*-V600E-mutated Rosai-Dorfman-Destombes disease and Langerhans cell histiocytosis with response to BRAF inhibitor. *Blood Adv*. 2019 Jun 25;3(12):1848-1853.
41. Goyal G, Heaney ML, Collin M, Cohen Aubart F, Vaglio A, Durham BH, Hershkovitz-Rokah O, Girschikofsky M, Jacobsen ED, Toyama K, Goodman AM, Hendrie P, Cao XX, Estrada-Veras J, Shpilberg O, Abdo A, Kurokawa M, Dagna L, **McClain KL**, Mazor RD, Picarsic J, Janku F, Go RS, Haroche J, Diamond E. Erdheim-Chester disease: Consensus recommendations for the evaluation, diagnosis, and treatment in the molecular era. *Blood*. 2020; 135(22):1929-1945.
42. Eckstein OS, Nuchtern JG, Mallory GB, Guillerman RP, Musick MA, Barclay M, Bhatt JM, Davies P, Grundy RG, Martin A, Hilliard T, Lowis SP, Picton S, Nanduri V, Visser J, Allen CE, **McClain KL**. Management of severe pulmonary Langerhans cell histiocytosis in children. *Pediatr Pulmonol*. 2020;55:2074-2081.
43. Sengal A, Velazquez J, Hahne MV, Burke T, Abhyankar H, Reyes RWI, Olea W, Scull BP, Eckstein OS, Bigenwald C, Bollard CM, Yu W, Merad M, **McClain KL**, Allen CE, Chakraborty R. Overcoming T cell exhaustion in LCH: PD-1 blockade and targeted MAPK inhibition are synergistic in a mouse model of LCH. *Blood* 2021; 137(13):1777-1791.

44. Bergsten E, Horne A, Hed Myrberg I, Aricó M, Astigarraga I, Ishii E, Janka G, Ladisch S, Lehmberg K, **McClain KL**, Minkov M, Nanduri V, Rosso DA, Sieni E, Winiarski J, Henter JI. Stem cell transplantation for children with hemophagocytic lymphohistiocytosis: results from the HLH-2004 study. *Blood Adv* 2020;4(15):3754-3766.
45. Bigenwald C, Le Berichel J, Wilk CM, Chakraborty R, Chen ST, Tabachnikova A, Mancusi R, Abhyankar H, Casanova-Acebes M, Laface I, Akturk G, Jobson J, Karoulia Z, Martin JC, Grout J, Rafiei A, Lin H, Manz MG, Baccharini A, Poulidakos PI, Brown BD, Gnjatic S, Lujambio A, **McClain KL**, Picarsic J, Allen CE, Merad M. BRAFV600E-induced senescence in hematopoietic progenitors drives Langerhans cell histiocytosis pathophysiology. *Nature Medicine*. 2021; 27:851-861.
46. Lin H, Scull BP, Goldberg BR, Abhyankar HA, Eckstein OS, Zinn DJ, Lubega J, Agrusa J, El-Mallawanay NK, Gulati N, Forbes LR, Chinn IK, Chakraborty R, Velazquez J, Goldman J, Bashir DA, Lam FW, Muscal E, Henry MM, Greenberg J, Ladisch S, Hermiston ML, Meyer LK, Jeng MR, Naqvi A, **McClain K**, Nguyen T, Wong HR, Man TK, Jordan MB, Allen CE. IFN- γ Signature in the Plasma Proteome Distinguishes Pediatric Hemophagocytic Lymphohistiocytosis from Sepsis and SIRS. *Blood Adv*. 2021; 5(17):3457-3467.
47. **McClain KL**, Bigenwald C, Collin M, Haroche J, Marsh RA, Merad M, Picarsic J, Ribeiro KB, Allen CE. Histiocytic Disorders. *Nature Reviews Disease Primer*. 2021; 7:73.