BIOGRAPHICAL SKETCH – Updated August 31, 2020

NAME: Matthew S. Davids, MD, MMSc

eRA COMMONS USER NAME (credential, e.g., agency login): msdavids

POSITION TITLE: Associate Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Harvard College, Cambridge, MA	BA	06/2000	Chemistry
Yale Medical School, New Haven, CT	MD	05/2005	Medicine
NY Presbyterian – Cornell, New York, NY	-	06/2008	Medicine Residency
Dana-Farber/Partners Cancer Care, Boston, MA	-	06/2011	Heme/Onc Fellowship
Harvard Medical School, Boston, MA	MMSc	05/2014	Clinical Investigation

A. Personal Statement

I am an attending physician in the Division of Hematologic Malignancies at Dana-Farber Cancer Institute (DFCI), Associate Professor of Medicine at Harvard Medical School (HMS), and Director of Clinical Research in the DFCI Division of Lymphoma. I am also the director of the DFCI Lymphoma BioBank. I conduct translational research in chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma, and have received peer-reviewed funding as a Special Fellow in Clinical Research and Scholar in Clinical Research through the Leukemia & Lymphoma Society (LLS), an ASCO Career Development Award, and a DFCI Clinical Investigator Award. I have published original first author laboratory and clinical research in journals such as *New England Journal of Medicine (NEJM), Journal of Clinical Oncology (JCO), Blood, and Lancet Haematology*. I have also published widely cited review articles and commentaries in journals such as *The Lancet, JCO, Blood,* and *Cancer Cell*. I have had a leadership role in international clinical trials of the Bcl-2 antagonist venetoclax, and we published the results of the first-in-human trial of this drug in *NEJM* and *JCO*. I am now running about a dozen clinical trials, the majority of which are investigator-initiated and are studying novel agents in hematologic malignancies, including targets such as BCL-2, BTK, PI3K, CTLA-4, PD-1 and others. A particular area of focus is Richter syndrome, where I now lead 3 different clinical trials. My independent laboratory focuses on the correlative science related to these clinical trials and in developing novel combination approaches to explore in future clinical trials. I previously led a laboratory effort to improve our understanding of the mechanism of the synergy between BTK inhibitors and venetoclax in CLL, published in *Leukemia.* At the 2017 ASH Annual Meeting I chaired and spoke in the Educational Program in CLL. I am a Senior Editor at *Clinical Cancer Research*, serve on the Editorial Board at *Blood,* and am a member of the ASH Foundation Standing Committee.

1. **Davids MS**, Kim HT, Bachireddy, P., Costello C, Liguori R, Savell A, Lukez AP, Avigan D, Chen YB, McSweeney P, LeBoeuf NR, Rooney MS, Bowden M, Zhou DW, Granter SR, Hornick J, Rodig SJ, Hirakawa M, Severgnini M, Hodi FS, Wu CJ, Ho VT, Cutler C, Koreth J, Alyea EP, Antin JH, Armand P, Streicher H, Ball ED, Ritz J, Bashey A, Soiffer RJ. "Immune Checkpoint Blockade with Ipilimumab in Patients who Relapse after Allogeneic Hematopoietic Cell Transplantation" *N Engl J Med.* 2016 July 14;375(2):143-53.

2. **Davids MS**, Roberts AW, Seymour JF, Pagel JM, Kahl BS, Wierda WG, Puvvada S, Kipps TJ, Anderson MA, Salem AH, Dunbar M, Zhu M, Peale F, Ross JA, Gressick L, Desai M, Kim SY, Verdugo M, Humerickhouse RA, Gordon GB, Gerecitano JF. "A Phase I First-in-Human Study of Venetoclax in Patients With Relapsed or Refractory Non-Hodgkin Lymphoma." *J Clin Oncol*. 2017 Mar 10;35(8):826-33.

3. **Davids MS**, Brander DM, Kim HT, Tyekucheva S, Bsat J, Savell A, Hellman JM, Bazemore J, Francoeur K, Alencar A, Shune L, Omaira M, Jacobson CA, Armand P, Ng S, Crombie J, LaCasce AS, Arnason J, Hochberg EP, Takvorian RW, Abramson JS, Fisher DC, Brown JR. Ibrutinib plus fludarabine, cyclophosphamide, and rituximab as initial treatment for younger patients with chronic lymphocytic leukaemia: a single-arm, multicentre, phase 2 trial. *Lancet Haematol.* 2019 Aug;6(8):e419-e428.

B. Positions and Honors

Positions and Employment

Employment

2011-2016	Instructor in Medicine/Attending Physician (full-time, tenure track), HMS/DFCI; Dept of Medical Oncology, Boston, MA (Chairman: J. Griffin, MD, HMS Professor of Medicine)
2016-2020	Assistant Professor of Medicine/Attending Physician (full-time, tenure track), HMS/DFCI; Dept of Medical Oncology, (Chairman: B. Ebert, MD/PhD, HMS Professor of Medicine)
2020-	Associate Professor of Medicine/Attending Physician (full-time, tenure track), HMS/ DFCI; Dept of Medical Oncology, (Chairman: B. Ebert, MD/PhD, HMS Professor of Medicine)

Other Experience and Professional Memberships

2008-	Member, Massachusetts Medical Society
2008-2018	Diplomat, American Board of Internal Medicine (ABIM)
2008-	Member, American Society of Hematology (ASH)
2009-	Member, American Society of Clinical Oncology (ASCO)
2011-	Diplomat, ABIM Hematology and ABIM Medical Oncology
2013-	Member, European Hematology Association
2013-2018	Member, Dana-Farber/Harvard Cancer Center Scientific Review Committee (SRC)
2014-	Co-PI of the Blood Cancer Research Partnership (BCRP) Cooperative Group
2016-	Associate Director, DFCI CLL Center
2017-	Director, DFCI Lymphoma BioBank
2020-	Director of Clinical Research, DFCI Division of Lymphoma

Honors

2010	ASCO Cancer Foundation Merit Award
2010	Graduate of ASCO/AACR Vail Workshop: Methods in Clinical Cancer Research
2011-2012	Graduate of ASH Clinical Research Training Institute
2011-2014	LLS Special Fellow in Clinical Research
2011-2014	National Institutes of Health – Loan Repayment Program Award Recipient
2012-2013	Chronic Lymphocytic Leukemia Foundation Award
2012-2013	Eleanor and Miles Shore Fellowship Award – Harvard Medical School
2012-2013	Young Scientist Award – Lymphoma Foundation of America
2013	European Hematology Association Travel Award
2013	ASH Annual Meeting Abstract Reviewer and Session Moderator: Lymphoma Therapy
2013-2014	Gloria Spivak Faculty Advancement Award
2014-2017	ASCO Career Development Award
2014-2020	Co-Principal Investigator: LLS Therapy Accelerator Program Grant (BCRP)
2016-2021	DFCI Independent Clinical Investigator Award
2016	George Canellos Award for Excellence in Clinical Research and Clinical Care at DFCI
2017	American Society of Clinical Investigation Young Physician Scientist Award
2017	ASH Annual Meeting Abstract Reviewer and Session Moderator: CLL Therapy
2017	Chairman of the 2017 ASH Annual Meeting CLL Education Session
2017-2018	Harvard Scholar in Cancer Experimental Therapeutics (HSCET)
2018	Chairman of the 2018 Highlights of ASH in North America: CLL Program
2018	Graduate of the DFCI Leadership Bootcamp
2018	James O. Armitage Lymphoma Clinical Investigator Award
2018-2020	ASCO Scientific Program Committee Member and Session Co-Chair: CLL/Lymphoma
2018-	Editorial Board, *Blood*
2018-	Senior Editor, *Clinical Cancer Research*
2018-	Member of the ASH Foundation Standing Committee
2018-2023	LLS Scholar in Clinical Research
2019	ASH Annual Meeting Abstract Reviewer and Session Moderator: CLL Therapy

C. Contributions to Science (with selected publications)

1. **Venetoclax as a new therapy for CLL and NHL.** I have been one of the leading principal investigators internationally in the clinical development of the Bcl-2 antagonist venetoclax (formerly ABT-199) in CLL and NHL since the drug entered the clinic in 2011. I made substantial contributions in particular to the early development of this drug, and our site was one of the leading accruers to the first-in-human trial. I was the first person to present clinical data on venetoclax at a major meeting (2012 ASH Annual Meeting), and have given oral presentations on trial data with this drug at numerous international meetings such as European Hematology Association Annual Meetings, International Workshop of CLL, International Conference on Malignant Lymphoma, and others. I am a co-author on over 30 peer-reviewed publications involving venetoclax, including publications in the *New England Journal of Medicine* and the *Journal of Clinical Oncology* article that first demonstrated clinical activity of venetoclax for Richter syndrome. I am also a co-senior author on a translational manuscript in *Blood* which reports on trial correlative studies, author on multiple perspective pieces in *Blood*, senior author on the manuscript in *Blood* on the results of the first clinical trial of venetoclax in patients who progress on idelalisib, as well as first author on the definitive paper on venetoclax safety in *Clinical Cancer Research.*

   a. Roberts AW, **Davids MS**, Pagel JM, Kahl BS, Puvvada S, Gerecitano JF, Kipps TJ, Anderson MA, Brown JR, Gressick L, Wong S, Dunbar M, Zhu M, Desai M, Cerri E, Enschede SH, Humerickhouse RA, Wierda WG, Seymour JF. "Targeting BCL2 with Venetoclax in Relapsed Chronic Lymphocytic Leukemia." *N Engl J Med.* 2016 Jan 28;374(4):311-22.
   b. **Davids MS**, Roberts AW, Seymour JF, Pagel JM, Kahl BS, Wierda WG, Puvvada S, Kipps TJ, Anderson MA, Salem AH, Dunbar M, Zhu M, Peale F, Ross JA, Gressick L, Desai M, Kim SY, Verdugo M, Humerickhouse RA, Gordon GB, Gerecitano JF. "A Phase I First-in-Human Study of Venetoclax in Patients With Relapsed or Refractory Non-Hodgkin Lymphoma." *J Clin Oncol*. 2017 Mar 10;35(8):826-833.
   c. Coutre S, Choi M, Furman RR, Eradat H, Heffner L, Jones JA, Chyla B, Zhou L, Agarwal S, Waskiewicz T, Verdugo M, Humerickhouse RA, Potluri J, Wierda WG, **Davids MS**. "Venetoclax for patients with chronic lymphocytic leukemia who progressed during or after idelalisib therapy.", *Blood*, 2018 Apr 12;131(15):1704-1711.
   d. **Davids MS**, Hallek M, Wierda WG, Roberts AW, Stilgenbauer S, Jones J, Gerecitano J, Kim SY, Potluri J, Busman T, Best A, Verdugo M, Cerri E, Desai M, Hillmen P, Seymour JF. "Comprehensive Safety Analysis of Venetoclax Monotherapy for Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia". *Clin Cancer Res*. 2018 Jun 12. pii: clincanres.3761.2017.

2. **Developing novel combination approaches for BTK inhibitor-based therapy in CLL treatment.** I lead several investigator-initiated clinical trials to evaluate the efficacy and safety of combination therapies with BTK-inhibition for CLL and NHL, and two of my trials were recently published in *Lancet Haematology*. This work has helped me to become a leading authority on small molecule targeted therapy in hematologic malignancies. I recently contributed to *The Lancet* a single-author perspective piece on the BTK inhibitor acalabrutinib as well as a collaborative review article on small molecule therapies in cancer.

   a. **Davids MS**, Brander DM, Kim HT, Tyekucheva S, Bsat J, Savell A, Hellman JM, Bazemore J, Francoeur K, Alencar A, Shune L, Omaira M, Jacobson CA, Armand P, Ng S, Crombie J, LaCasce AS, Arnason J, Hochberg EP, Takvorian RW, Abramson JS, Fisher DC, Brown JR. Ibrutinib plus fludarabine, cyclophosphamide, and rituximab as initial treatment for younger patients with chronic lymphocytic leukaemia: a single-arm, multicentre, phase 2 trial. *Lancet Haematol.* 2019 Aug;6(8):e419-e428.
   b. **Davids MS**, Kim HT, Nicotra A, Savell A, Francoeur K, Hellman JM, Bazemore J, Miskin HP, Sportelli P, Stampleman L, Maegawa R, Rueter J, Boruchov AM, Arnason JE, Jacobson CA, Jacobsen ED, Fisher DC, Brown JR; Umbralisib in combination with ibrutinib in patients with relapsed or refractory chronic lymphocytic leukaemia or mantle cell lymphoma: a multicentre phase 1-1b study. *Lancet Haematol.* 2019 Jan;6(1):e38-e47.
   c. Bedard PL, Hyman DM, **Davids MS**, Siu LL. Small molecules, big impact: 20 years of targeted therapy in oncology. *Lancet.* 2020 Mar 28;395(10229):1078-1088.

d. **Davids MS**. Acalabrutinib for the initial treatment of chronic lymphocytic leukaemia. *Lancet*. 2020 Apr 18;395(10232):1234-1236.

3. **Understanding the effects of the microenvironment on the intrinsic apoptotic pathway in CLL cells.** As a postdoctoral research fellow in the laboratory of Dr. Anthony Letai, I investigated why CLL cells in the microenvironment are resistant to treatment. A technique known as 'BH3 profiling' had previously been developed in the lab as a functional assay to assess the propensity of cells to undergo apoptosis, a property known as mitochondrial priming. I utilized a stromal co-culture system with primary CLL cells and used BH3 profiling to show that mitochondrial priming is decreased in stroma-exposed CLL cells. I went on to demonstrate that blockade of the B cell receptor pathway can partially restore priming and thereby sensitize CLL cells to treatment. The findings of these laboratory studies inspired the development of the trial of ibrutinib plus FCR as upfront treatment for younger patients with CLL. My more recent work has focused on developing CLL novel agent combination therapy regimens such as venetoclax with BTK inhibitors. And in collaboration with Dr. Catherine Wu, my laboratory recently helped to identify the effect of splicing modulation on apoptotic dependences in CLL cells.

   a. **Davids MS**, Deng, J., Wiestner, A., Lannutti, B.J., Wang, L., Wu, C.J., Wilson, W.H., Brown, J.R., Letai, A. "Decreased mitochondrial apoptotic priming underlies stroma-mediated treatment resistance in chronic lymphocytic leukemia", *Blood*, 2012, Oct 25;120(17):3501-9. PMCID: PMC3482860
   b. **Davids MS,** Letai A, Brown JR. Overcoming stroma-mediated treatment resistance in chronic lymphocytic leukemia through BCL-2 inhibition. *Leuk Lymphoma* 2013 Aug;54(8):1823-5. PMID: 23614795
   c. Deng J, Isik E, Fernandes S, Brown JR, Letai A*, and **Davids MS***. "Bruton's tyrosine kinase inhibition increases BCL-2 dependence and enhances sensitivity to venetoclax in chronic lymphocytic leukemia", *Leukemia.* 2017 Oct;31(10):2075-2084. *Co-senior authors who contributed equally to the research
   d. Ten Hacken, E, Valentin, R, Regis, FF, Sun, J, Yin, S, Werner, L, Deng, J, Gruber, M, Wong, J, Zheng, M, Gill, AL, Seiler, M, Smith, P, Thomas, M, Buonamici, S, Ghia, EM, Kim, E, Rassenti, LZ, Burger, JA, Kipps, TJ, Meyerson, ML, Bachireddy, P, Wang, L, Neuberg, D, Carrasco, R, Brooks, AN, Letai, A, **Davids, MS**, and Wu, CJ. "Splicing modulation remodels mitochondrial apoptotic dependencies and sensitizes CLL cells to venetoclax". *JCI Insight*. 2018 Oct 4;3(19). PMID: 30282833.

4. **Checkpoint blockade as a new therapy for patients with recurrent hematologic malignancies after allogeneic hematopoietic cell transplantation**. I developed an investigator-initiated multicenter clinical trial sponsored by the NCI/CTEP (#9204) of the CTLA-4 blocking antibody ipilimumab for patients with CLL and other hematologic malignancies who relapse after allogeneic hematopoietic cell transplantation, a population with few viable treatment options. This trial is a multicenter effort facilitated by the Blood Cancer Research Partnership (BCRP) with a component of our funding from a Leukemia & Lymphoma Study TAP grant. Ipilimumab was well-tolerated in most patients, with striking anti-tumor activity in a variety of hematologic malignancies, particularly AML, and our results were published in *NEJM*. A separate arm subsequently explored PD-1 blockade with nivolumab in this patient population, and although there was some efficacy, significant toxicities also occurred, as we recently published in *Blood*.

   a. **Davids MS**, Kim HT, Bachireddy, P., Costello C, Liguori R, Savell A, Lukez AP, Avigan D, Chen YB, McSweeney P, LeBoeuf NR, Rooney MS, Bowden M, Zhou DW, Granter SR, Hornick J, Rodig SJ, Hirakawa M, Severgnini M, Hodi FS, Wu CJ, Ho VT, Cutler C, Koreth J, Alyea EP, Antin JH, Armand P, Streicher H, Ball ED, Ritz J, Bashey A, Soiffer RJ. "Immune Checkpoint Blockade with Ipilimumab in Patients who Relapse after Allogeneic Hematopoietic Cell Transplantation" *N Engl J Med.* 2016 July 14;375(2):143-53.
   b. Soiffer RJ, **Davids MS**, Chen YB. Tyrosine kinase inhibitors and immune checkpoint blockade in allogeneic hematopoietic cell transplantation. *Blood,* 2018 Mar 8;131(10): 1073-80. (plus cover image)
   c. **Davids MS,** Kim HT, Costello C, Herrera AF, Locke FL, Maegawa RO, Savell A, Mazzeo M, Anderson A, Boardman AP, Weber A, Avigan D, Chen YB, Nikiforow S, Ho VT, Cutler C, Alyea E, Bachireddy P, Wu CJ, Ritz J, Streicher H, Ball ED, Bashey A, Soiffer RJ, Armand P. "A Multicenter, Phase I Study of Nivolumab for Relapsed Hematologic Malignancies After Allogeneic Transplantation" *Blood*. 2020 June 11;135(24):2182-2191.

Complete List of Published Work (103 total) in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/14Q1zmITx8Ek4/bibliography/40923791/public/?sort=date&direction=ascending

D. Research Support

Ongoing:

Leukemia and Lymphoma Society (LLS) Davids (PI) 07/01/2018 – 06/30/2023
Scholar in Clinical Research
This grant supports multiple investigator-initiated clinical trials in both frontline and relapsed/refractory therapy of CLL and the laboratory correlative studies performed on samples from patients on the trials.
Role: PI

DFCI Clinical Investigator Program Davids (PI) 07/01/2016 -- 06/30/2021
This funded, tenure-track faculty position allows protected research time and a laboratory startup funding package with space for my independent laboratory to conduct translational research in CLL and NHL.

DFCI Medical Oncology Research Grant Davids (PI) 07/01/2018 -- 12/31/2020
This grant provides additional funding to conduct correlative laboratory studies on my clinical trials of venetoclax combinations for patients with CLL. Role: PI

DFCI Collaborative Research Award Davids (PI) 07/1/2019 – 6/30/2021
This grant provides support to extend an existing single-center investigator-initiated trial of Acalabrutinib, Venetoclax, and Obinutuzumab for frontline CLL therapy to become a multicenter study and the award supports both study costs as well as provides salary support.

DFCI Clinical Trial Support Award Davids (PI) 12/1/2019 – 11/30/2021
This grant provides support for a novel investigator-initiated clinical trial of venetoclax, and will cover institutional and research costs for the study.

DFCI Lymphoma Pilot Grant Award Davids (PI) 12/1/2019 – 11/20/2020
This award provides salary support and research funding for a postdoctoral fellow in the Davids Lab to investigate novel mechanisms of venetoclax resistance in hematologic malignancies.

Recently completed:

Leukemia and Lymphoma Society (LLS) Davids (Co-PI) 03/19/2013 -- 6/30/2020
Blood Cancer Research Partnership Grant
The goal of this program has been to support a network to accelerate the development of and expand access to well-designed, innovative clinical trials for blood cancer patients being treated at community sites.

Harvard Scholar in Cancer Experimental Therapeutics Shapiro (PI) 06/1/2017 – 5/31/2018
This funding was provided through the DF/HCC UM1 grant (#1226803) from the National Cancer Institute to support the effort of faculty who are PIs Cancer Therapy Evaluation Program (CTEP) trials.

DFCI Medical Oncology Research Grant Davids (PI) 07/01/2016 -- 12/31/2017
This grant provided additional funding to conduct correlative laboratory studies on my clinical trial of ibrutinib plus FCR for younger patients with CLL. Role: PI

ASCO Career Development Award Davids (PI) 07/01/2014 -- 06/30/2017
This grant provided me with salary support to conduct the phase I/II study of duvelisib + FCR as an upfront therapy for CLL, and to perform correlative laboratory studies embedded in the trial. Role: PI

LLS Special Fellow in Clinical Research - Davids (PI) 07/01/2011 – 06/30/2014
The goal of this career development award was to explore strategies to mobilize CLL cells from stroma to more effectively kill these malignant cells in patients. Role: PI