BIOGRAPHICAL SKETCH

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NAME: Margaret Ann Shipp

eRA COMMONS USERNAME (credential, e.g., agency login): MSHIPP

POSITION TITLE: Professor of Medicine and Chief, Division of Hematologic Neoplasia

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Southern Methodist University, Dallas, TX	BA	05/1975	English and Biology
Washington University School of Medicine, St. Louis, MO	MD	05/1979	Medicine

A. Personal Statement

Our research interests include the characterization of comprehensive molecular signatures, survival pathways and associated rational therapeutic targets in aggressive B-cell malignancies including diffuse large B-cell lymphoma (DLBCL), additional large B-cell lymphoma subtypes and classical Hodgkin lymphoma (cHL). We have identified genetic bases of immune evasion in specific lymphoid malignancies and targeted these pathways in associated clinical trials. In particular, we have defined recurrent 9p24.1 copy number alterations and associated overexpression of the PD-1 ligands as a genetic basis for sensitivity of cHL and primary mediastinal large B-cell lymphoma (PMBL) to PD-1 blockade. Additionally, we have elucidated mechanisms of action of PD-1 blockade in cHL and PMBL which are largely MHC class I-negative tumors. Our group has also developed a widely accepted genetic taxonomy of diffuse large B-cell lymphoma which includes five discrete subtypes with associated targets for therapy. I serve as Chief of the Division of Hematologic Neoplasia in the Department of Medical Oncology at DFCI and Director of the DFCI Lymphoma Research Center.

Ongoing and recently completed projects that I would like to highlight include:

Ongoing Projects

NIH/NCI R01 CA161026 Shipp (PI) 08/22/11 – 06/30/22
Complementary Signaling Pathways in Hodgkin Lymphoma and Related Malignancies

LLS Translational Research Program Shipp (PI) 07/01/19 – 06/30/22
Matching Genetic Signatures and Targeted Combination Therapy in High-Risk DLBCL

LLS Blood Cancer Discovery Program Shipp (PI), Rodig (Co-PI) 07/01/20 – 06/30/23
Discovery and Characterization of an Immunosuppressive Tumor Microenvironmental (TME) Niche in Classic Hodgkin Lymphoma (cHL)

Bristol-Myers Squibb Company Shipp (PI), Rodig (Co-PI) 10/21/15 – 10/20/22
Analyses of tissue biopsy specimens for LAG3 expression in hematological malignancies

Bristol-Myers Squibb Company Shipp (PI), Rodig (Co-PI) 06/01/21 – 05/30/23
Mechanisms of action of single-agent nivolumab in relapsed cHL

Bristol-Myers Squibb Company Shipp (PI), Rodig (Co-PI) 06/01/21 – 05/30/23
Analysis of Biomarkers in relapsed /refractory primary mediastinal large B-cell lymphoma treated with combined nivolumab and brentuximab

AstraZeneca Shipp (PI) 08/01/21 – 07/31/23
Perturbed Co-stimulation and Immune Evasion in Diffuse Large B-cell Lymphoma

Completed Projects

NIH/NCI P30 CA06516 Benz (PI) / Shipp (Program Leader) 12/01/05 – 11/30/20
DF/Harvard Comprehensive Cancer Center Grant – Lymphoma and Myeloma Program

RTFCCR/LLS Shipp (PI) 10/01/16 – 09/30/19
Patient-focused Immunotherapy Research Grant: Targetable Bases of Immune Evasion in Lymphomas of the Primary Central Nervous System and Testes

Bristol-Myers Squibb Company Shipp and Rodig (Co-PIs) 10/29/14 – 10/28/20
Correlative Studies for Nivolumab Lymphoma Trials

Merck Sharp & Dohme Shipp and Rodig (Co-PIs) 12/07/17 – 12/06/20
9p24.1 amplification in primary mediastinal B-cell lymphoma from PN-013 and PN-170 Clinical Trials

Citations

a. Roemer MG, Advani RH, Ligon AH, Natkunam Y, Redd RA, Homer H, Connelly CF, Sun HH, Daadi SE, Freeman GJ, Armand P, Chapuy B, de Jong D, Hoppe RT, Neuberg DS, Rodig SJ, **Shipp MA**. PD-L1 and PD-L2 Genetic Alterations Define Classical Hodgkin Lymphoma and Predict Outcome. J Clin Oncol. 2016;34(23):2690-7. PMID: 27069084; PMC5019753 Selected as "Rapid Communication" (top 5% of JCO published papers)
b. Roemer MGM, Redd RA, Cader FZ, Pak CJ, Abdelrahman S, Ouyang J, Sasse S, Younes A, Fanale M, Santoro A, Zinzani PL, Timmerman J, Collins GP, Ramchandren R, Cohen JB, De Boer JP, Kuruvilla J, Savage KJ, Trneny M, Ansell S, Kato K, Farsaci B, Sumbul A, Armand P, Neuberg DS, Pinkus GS, Ligon AH, Rodig SJ, **Shipp MA**. Major Histocompatibility Complex Class II and Programmed Death Ligand 1 Expression Predict Outcome After Programmed Death 1 Blockade in Classic Hodgkin Lymphoma. J Clin Oncol. 2018;36(10):942-950. PMID: 29394125; PMC5877802 Selected as "Rapid Communication" (top 5% of JCO published papers)
c. Cader FZ, Schackmann RCJ, Hu X, Wienand K, Redd R, Chapuy B, Ouyang J, Paul N, Gjini E, Lipschitz M, Armand P, Wu D, Fromm JR, Neuberg D, Liu XS, Rodig SJ, **Shipp MA**. Mass cytometry of Hodgkin lymphoma reveals a CD4+ regulatory T-cell-rich and exhausted T-effector microenvironment. Blood. 2018;132(8):825-836. PMID: 29880615; PMC6107878. Accompanying Blood Commentary. Timmerman J. The run-down immunologic neighborhood in Hodgkin lymphoma. Blood. 2018;132:770-771. PMID: 30139828
d. Cader FZ, Hu X, Goh WL, Wienand K, Ouyang J, Mandato E, Redd R, Lawton LN, Chen PH, Weirather JL, Schackmann RCJ, Li B, Ma W, Armand P, Rodig SJ, Neuberg D, Liu XS, **Shipp MA**. A peripheral immune signature of responsiveness to PD-1 blockade in patients with classical Hodgkin lymphoma. Nat Med. 2020;26(9):1468-1479. PMID: 32778827

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

1979 – 1982	Intern and Resident in Internal Medicine, Barnes Hospital, St. Louis, MO
1982 – 1983	Research Fellow in Immunology, Washington University School of Medicine, St. Louis, MO
1983 – 1986	Fellow in Medical Oncology, HMS; DFCI, Boston, MA
1986 – 1988	Instructor in Medicine, HMS; DFCI, Boston, MA
1986 –	Associate Physician, Medicine, Brigham and Women's Hospital, Boston, MA
1988 – 1994	Assistant Professor of Medicine, HMS; DFCI, Boston, MA
1988 –	Attending Physician, Medical Oncology, DFCI, Boston, MA
1994 – 2007	Associate Professor of Medicine, HMS; DFCI, Boston, MA
1996 – 1999	Chairperson, National Cancer Center Network, Lymphoma Committee, Plymouth Meeting, PA

1997 –	Attending Physician Bone Marrow Transplant Service, DFCI/BWH, Boston, MA
1999 – 2010	Medical and Scientific Affairs Committee, Leukemia and Lymphoma Society of America, Rye Brook, NY
1999 – 2020	Director, Lymphoma Program, Dana-Farber/Harvard Comprehensive Cancer Center, Boston, MA
1999 –	Scientific Advisory Committee, International Conference on Malignant Lymphoma, Lugano, Switzerland
2001 – 2007	Scientific Advisory Board, Lymphoma Research Foundation, New York, NY
2002 – 2012	Editorial Board, Blood
2007 –	Professor, Harvard Medical School (HMS); DFCI, Boston, MA
2008 – 2011	Board of Directors, American Association for Cancer Research, Philadelphia, PA
2009 –	Steering Committee, International Symposium on Hodgkin Lymphoma, Cologne, Germany
2010 –	Chief, Division of Hematologic Neoplasia, DFCI, Boston, MA
2011 –	Editorial Board, Cancer Discovery
2012 – 2016	Councilor, American Society of Hematology, Washington, DC
2013 –	Associate Member, Broad Institute, Cambridge, MA
2016 –	Director, Lymphoma Research Center, Dana-Farber Cancer Institute (DFCI), Boston, MA
2017 –	Scientific Advisory Board, Lymphoma Research Foundation, New York, NY
2017 –	Scientific Advisory Board, Mayo-Iowa Lymphoma SPORE, Rochester, MN
2019 –	Editorial Board, Blood Cancer Discovery

Honors

1979	Alpha Omega Alpha
1985	NIH Clinical Investigator Award
1991	American Cancer Society Junior Faculty Award
1995	Leukemia Society Scholar Award
1996	American Society of Clinical Investigation
2000	Leukemia and Lymphoma Society Stohlman Scholar
2001	Doris Duke Distinguished Clinical Scientist Award
2005	Association of American Physicians
2007	Distinguished Woman in Medicine and Science, Northwestern University School of Medicine
2010	Leloir Prize of International Cooperation in Science, Technology and Innovation, Nacional de Relaciones Internacionales, Argentina
2011	Claire W. and Richard P. Morse Research Award, Dana-Farber Cancer Institute
2014	Institute of Medicine (National Academy of Medicine)
2017	Distinguished Woman in Medicine, City of Hope Comprehensive Cancer Center
2017	Designee, Gianni Bonnadonna Memorial Lecture, Fourteenth International Conference on Malignant Lymphoma, Lugano, Switzerland
2018	Douglas F. Miller Chair, Dana-Farber Cancer Institute
2018	John Ultmann Award for Contributions to Lymphoma, SASS Foundation for Medical Research
2019	Medical Oncology Discovery Award, Department of Medical Oncology, Dana-Farber Cancer Institute
2020	James D. Griffin, MD Team Science Award (co-recipients, Philippe Armand, Scott Rodig and Gordon Freeman), Department of Medical Oncology, Dana-Farber Cancer Institute
2021	Ernest Beutler Lecture and Prize, American Society of Hematology

C. Contributions to Science

1. We have defined chromosome 9p24.1 copy number alterations and associated dependency on PD-1 signaling as a genetic basis for immune evasion in cHL and PMBL and targeted the pathway in practice-changing clinical trials.

    a. Green MR, Monti S, Rodig SJ, Juszczynski P, Currie T, O'Donnell E, Chapuy B, Takeyama K, Neuberg D, Golub TR, Kutok JL, **Shipp MA**. Integrative analysis reveals selective 9p24.1 amplification, increased

PD-1 ligand expression, and further induction via JAK2 in nodular sclerosing Hodgkin lymphoma and primary mediastinal large B-cell lymphoma. Blood. 2010;116(17):3268-77. PMID: 20628145; PMC2995356

b. Ansell SM, Lesokhin AM, Borrello I, Halwani A, Scott EC, Gutierrez M, Schuster SJ, Millenson MM, Cattry D, Freeman GJ, Rodig SJ, Chapuy B, Ligon AH, Zhu L, Grosso JF, Kim SY, Timmerman JM, **Shipp MA***, Armand P*. PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. N Engl J Med. 2015;372(4):311-9. PMID: 25482239; PMC4348009. *Contributed equally

c. Carey CD, Gusenleitner D, Lipschitz M, Roemer MGM, Stack EC, Gjini E, Hu X, Redd R, Freeman GJ, Neuberg D, Hodi FS, Liu XS, **Shipp MA**, Rodig SJ. Topological analysis reveals a PD-L1-associated microenvironmental niche for Reed-Sternberg cells in Hodgkin lymphoma. Blood. 2017;130(22):2420-2430. 28893733; PMC5766840

d. Armand P, Rodig S, Melnichenko V, Thieblemont C, Bouabdallah K, Tumyan G, Özcan M, Portino S, Fogliatto L, Caballero MD, Walewski J, Gulbas Z, Ribrag V, Christian B, Perini GF, Salles G, Svoboda J, Zain J, Patel S, Chen PH, Ligon AH, Ouyang J, Neuberg D, Redd R, Chatterjee A, Balakumaran A, Orlowski R, **Shipp M**, Zinzani PL. Pembrolizumab in Relapsed or Refractory Primary Mediastinal Large B-Cell Lymphoma. J Clin Oncol. 2019;37(34):3291-3299. PMID: 31609651; PMC6881098

2. We have also characterized the comprehensive genetic signatures of cHL and PMBL and defined additional genetic bases of immune evasion in these diseases.

a. Roemer MG, Advani RH, Redd RA, Pinkus GS, Natkunam Y, Ligon AH, Connelly CF, Pak CJ, Carey CD, Daadi SE, Chapuy B, de Jong D, Hoppe RT, Neuberg DS, **Shipp MA***, Rodig SJ*. Classical Hodgkin Lymphoma with Reduced β2M/MHC Class I Expression Is Associated with Inferior Outcome Independent of 9p24.1 Status. Cancer Immunol Res. 2016;4(11):910-916. PMID: 27737878; PMC5210180 *Contributed equally

b. Patel SS, Weirather JL, Lipschitz M, Lako A, Chen PH, Griffin GK, Armand P, **Shipp MA**, Rodig SJ. The microenvironmental niche in classic Hodgkin lymphoma is enriched for CTLA-4-positive T cells that are PD-1-negative. Blood. 2019;134(23):2059-2069. PMID: 31697809; PMC7218752

c. Wienand K*, Chapuy B*, Stewart C*, Dunford AJ*, Wu D, Kim J, Kamburov A, Wood TR, Cader FZ, Ducar MD, Thorner AR, Nag A, Heubeck AT, Buonopane MJ, Redd RA, Bojarczuk K, Lawton LN, Armand P, Rodig SJ, Fromm JR**, Getz G**, **Shipp MA****. Genomic analyses of flow-sorted Hodgkin Reed-Sternberg cells reveal complementary mechanisms of immune evasion. Blood Adv. 2019;3(23):4065-4080. PMID: 31816062; PMC6963251 *contributed equally, **supervised jointly

d. Chapuy B*, Stewart C*, Dunford AJ*, Kim J, Wienand K, Kamburov A, Griffin GK, Chen PH, Lako A, Redd RA, Cote CM, Ducar MD, Thorner AR, Rodig SJ, Getz G**, **Shipp MA****. Genomic analyses of PMBL reveal new drivers and mechanisms of sensitivity to PD-1 blockade. Blood. 2019;134(26):2369-2382. PMID: 31697821; PMC6933293 *contributed equally, **supervised jointly

3. We have characterized the genetic signatures and associated survival pathways in diffuse large B-cell lymphoma and large B-cell lymphoma subtypes.

a. Monti S, Chapuy B, Takeyama K, Rodig SJ, Hao Y, Yeda KT, Inguilizian H, Mermel C, Currie T, Dogan A, Kutok JL, Beroukhim R, Neuberg D, Habermann TM, Getz G, Kung AL, Golub TR, **Shipp MA**. Integrative analysis reveals an outcome-associated and targetable pattern of p53 and cell cycle deregulation in diffuse large B cell lymphoma. Cancer Cell. 2012;22(3):359-72. PMID: 22975378; PMC3778921

b. Chapuy B, Roemer MG, Stewart C, Tan Y, Abo RP, Zhang L, Dunford AJ, Meredith DM, Thorner AR, Jordanova ES, Liu G, Feuerhake F, Ducar MD, Illerhaus G, Gusenleitner D, Linden EA, Sun HH, Homer H, Aono M, Pinkus GS, Ligon AH, Ligon KL, Ferry JA, Freeman GJ, van Hummelen P, Golub TR, Getz G, Rodig SJ, de Jong D, Monti S, **Shipp MA**. Targetable genetic features of primary testicular and primary central nervous system lymphomas. Blood. 2016;127(7):869-81. PMID: 26702065; PMC4760091

c. Chapuy B, Stewart C, Dunford AJ, Kim J, Kamburov A, Redd RA, Lawrence MS, Roemer MGM, Li AJ, Ziepert M, Staiger AM, Wala JA, Ducar MD, Leshchiner I, Rheinbay E, Taylor-Weiner A, Coughlin CA, Hess JM, Pedamallu CS, Livitz D, Rosebrock D, Rosenberg M, Tracy AA, Horn H, van Hummelen P, Feldman AL, Link BK, Novak AJ, Cerhan JR, Habermann TM, Siebert R, Rosenwald A, Thorner AR, Meyerson ML, Golub TR, Beroukhim R, Wulf GG, Ott G, Rodig SJ, Monti S, Neuberg DS, Loeffler M,

Pfreundschuh M, Trümper L, Getz G, **Shipp MA**. Molecular subtypes of diffuse large B cell lymphoma are associated with distinct pathogenic mechanisms and outcomes. Nat Med. 2018;24(5):679-690. Erratum in: Nat Med. 2018 Aug;24(8):1292. Erratum in: Nat Med. 2018;24(8):1290-1291. PMID: 29713087; PMC6613387

d. Griffin GK, Weirather JL, Roemer MGM, Lipschitz M, Kelley A, Chen PH, Gusenleitner D, Jeter E, Pak C, Gjini E, Chapuy B, Rosenthal MH, Xu J, Chen BJ, Sohani AR, Lovitch SB, Abramson JS, Ishizuka JJ, Kim AI, Jacobson CA, LaCasce AS, Fletcher CD, Neuberg D, Freeman GJ, Hodi FS, Wright K, Ligon AH, Jacobsen ED, Armand P, **Shipp MA**, Rodig SJ. Spatial signatures identify immune escape via PD-1 as a defining feature of T-cell/histiocyte-rich large B-cell lymphoma. Blood. 2021;137(10):1353-1364. PMID: 32871584

4. We have characterized and targeted the BCR signaling pathway and associated metabolic vulnerabilities in large B-cell lymphomas.

   a. Caro P, Kishan AU, Norberg E, Stanley IA, Chapuy B, Ficarro SB, Polak K, Tondera D, Gounarides J, Yin H, Zhou F, Green MR, Chen L, Monti S, Marto JA, **Shipp MA**, Danial NN. Metabolic signatures uncover distinct targets in molecular subsets of diffuse large B cell lymphoma. Cancer Cell. 2012;22(4):547-60. PMID: 23079663; PMC3479446
   b. Chen L, Monti S, Juszczynski P, Ouyang J, Chapuy B, Neuberg D, Doench JG, Bogusz AM, Habermann TM, Dogan A, Witzig TE, Kutok JL, Rodig SJ, Golub T, **Shipp MA**. SYK inhibition modulates distinct PI3K/AKT- dependent survival pathways and cholesterol biosynthesis in diffuse large B cell lymphomas. Cancer Cell. 2013;23(6):826-38. PMID: 23764004; PMC3700321
   c. Bojarczuk K, Wienand K, Ryan JA, Chen L, Villalobos-Ortiz M, Mandato E, Stachura J, Letai A, Lawton LN, Chapuy B, **Shipp MA**. Targeted inhibition of PI3Kα/δ is synergistic with BCL-2 blockade in genetically defined subtypes of DLBCL. Blood. 2019;133(1):70-80. PMID: 30322870; PMC6318426
   d. Chen L, Ouyang J, Wienand K, Bojarczuk K, Hao Y, Chapuy B, Neuberg D, Juszczynski P, Lawton LN, Rodig SJ, Monti S, **Shipp MA**. CXCR4 upregulation is an indicator of sensitivity to B-cell receptor/PI3K blockade and a potential resistance mechanism in B-cell receptor-dependent diffuse large B-cell lymphomas. Haematologica. 2020;105(5):1361-1368. PMID: 31471373; PMC7193488

5. We have identified additional targetable pathways and inhibitors in large B-cell lymphomas and Hodgkin lymphoma and developed model systems to explore therapeutic inhibition.

   a. Ouyang J, Juszczynski P, Rodig SJ, Green MR, O'Donnell E, Currie T, Armant M, Takeyama K, Monti S, Rabinovich GA, Ritz J, Kutok JL, **Shipp MA**. Viral induction and targeted inhibition of galectin-1 in EBV+ posttransplant lymphoproliferative disorders. Blood. 2011;117(16):4315-22. PMID: 21300977
   b. Chapuy B*, McKeown MR*, Lin CY, Monti S, Roemer MG, Qi J, Rahl PB, Sun HH, Yeda KT, Doench JG, Reichert E, Kung AL, Rodig SJ, Young RA, **Shipp MA****, Bradner JE**. Discovery and characterization of super-enhancer-associated dependencies in diffuse large B cell lymphoma. Cancer Cell. 2013;24(6):777-90. Erratum in: Cancer Cell. 2014;25(4):545-6. PMID: 24332044; PMC4018722 *Contributed equally; **Contributed equally
   c. Hao Y, Chapuy B, Monti S, Sun HH, Rodig SJ, **Shipp MA**. Selective JAK2 inhibition specifically decreases Hodgkin lymphoma and mediastinal large B-cell lymphoma growth in vitro and in vivo. Clin Cancer Res. 2014;20(10):2674-83. PMID: 24610827; PMC4084704
   d. Chapuy B, Cheng H, Watahiki A, Ducar MD, Tan Y, Chen L, Roemer MG, Ouyang J, Christie AL, Zhang L, Gusenleitner D, Abo RP, Farinha P, von Bonin F, Thorner AR, Sun HH, Gascoyne RD, Pinkus GS, van Hummelen P, Wulf GG, Aster JC, Weinstock DM, Monti S, Rodig SJ, Wang Y, **Shipp MA**. Diffuse large B-cell lymphoma patient-derived xenograft models capture the molecular and biological heterogeneity of the disease. Blood. 2016;127(18):2203-13. PMID: 26773040; PMC4859195

Complete List of Published Work in My Bibliography:
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