BIOGRAPHICAL SKETCH

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NAME: Lim, Megan

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

POSITION TITLE: Member, Attending Pathologist

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)	END DATE MM/YYYY	FIELD OF STUDY
University of Calgary, Calgary, Alberta	BS	1983	Cell and Microbiology
University of Calgary, Calgary, Alberta	MD	1983	Medicine
University of Calgary, Calgary, Alberta	PhD	2000	Molecular Oncology
University of Calgary, Calgary, Alberta	Resident	1993	Anatomic Pathology
National Cancer Institute, Bethesda, Maryland	Fellow	1998	Hematopathology

A. Personal Statement

I am a physician-scientist with subspecialty board certification in Hematopathology and Molecular Genetic Pathology. At MSK, I am the Director of the Multispectral Imaging Laboratory and Attending Hematopathologist in the Department of Pathology and Laboratory Medicine and serve as the Director of the Lymphoma Translational Research Program and the Director of the Hem/Onc Tissue Bank within the Center of Hematologic Malignancies. This experience, combined with my previous 7 years directing the Division of Hematopathology and co-leading the Lymphoma Translational Center of Excellence at Penn, demonstrate my capabilities in leading integrated translational research programs.

Over the last 25 years, my research has focused on the study of genomic and proteomic alterations in lymphoid neoplasms. To identify novel mechanisms driving lymphomagenesis and lymphoma progression, we have developed substantial expertise in large-scale mass spectrometry-based proteomics and genomics. Additionally, we have developed significant capabilities in biochemistry, affinity purification of protein complexes, and molecular biology, permitting a unique and deep understanding of the functional consequences, structural derangements, and intricate cellular networks that are perturbed by these aberrations. Our research program has utilized large-scale unbiased mass spectrometry-based proteomics to define the phosphoproteomic signature of tyrosine kinase-driven ALK+ and ALK– anaplastic large cell lymphoma. Using these innovative approaches, we have contributed to the understanding of the oncogenic mechanisms in a variety of T and B cell derived lymphomas. Importantly, we discovered a *NPM1::TYK2* fusion in T cell lymphomas, the first gene fusion found to affect this tyrosine kinase in any human cancer. In subsequent studies, we and others have identified recurrent fusions targeting TYK2 and other JAK kinases in other forms of cutaneous and nodal TCL. We have also generated cell lines and xenograft and transgenic mouse models (*Cd4cre-NPM1::TYK2*) to understand the phenotypic consequences of these genetic alterations. Further elucidation of the mechanisms by which these fusions drive T cell lymphomagenesis and progression will inform improvements to lymphoma classification, which is based on the presence of genetic events.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 - Member, Editorial Board, *Blood Neoplasia*

2022 - Scientific Director, Multispectral Imaging Laboratory, Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center (MSK), New York, NY

2022 - Attending Hematopathologist, Department of Pathology and Laboratory Medicine, MSK

2022 - Director, Lymphoma Translational Research Program, Center for Hematologic Malignancies, MSK

2022 - Director, Hem/Onc Tissue Bank, Center for Hematologic Malignancies, MSK

2022 -	Member, Scientific Advisory Board, FANTOM EU Training Network
2022 - 2022	Member, Organizing Committee, International Pediatric and Young Adult NHL Meeting
2021 - 2025	Chartered Member, Grant Review Panel, NIH Cancer Biomarkers Study Section
2020 - 2023	Member, Graduate Group in Cell and Molecular Biology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
2017	Review of NCI Intramural Research Programs Lymphoid Malignancies Branch, Bethesda, MD
2016 -	Member, Scientific Advisory Board, Castleman Disease Collaborative Network, Philadelphia, PA
2016 -	Scientist Reviewer, Lymphoma Peer Review Cancer Research Program (PRCRP), Department of Defense, Washington, DC
2015 - 2022	Professor, Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA
2015 - 2022	Director, Division of Hematopathology, Department of Pathology and Laboratory Medicine, University of Pennsylvania
2015 - 2022	Co-Leader, Lymphoma Translational Center of Excellence, Abramson Cancer Center, Hospital of the University of Pennsylvania
2015 - 2019	Member, Scientific Advisory Board, ALKATRAS EU Training Network
2013 - 2017	Member, Editorial Board, *American Journal of Pathology*
2012 - 2012	Member, Organizing Committee, International Pediatric and Young Adult NHL Meeting
2012 - 2012	Scientist Reviewer, St. Baldrick's Foundation Career Development Grant Review
2011 - 2012	Scientist Reviewer, Veterans Administration Merit Review Subcommittee for Oncology
2010 -	Vice-Chair, Children's Oncology Group, HEME-ITSC
2010 - 2020	Vice Chair, Children's Oncology Group Non-Hodgkin Lymphoma Disease Committee

Honors

2005 - 2013	Best Doctors of America
1996 - 1998	Fogarty Visiting Fellowship, National Institutes of Health
1993 - 1998	Clinical Research Fellowship, Medical Research Council of Canada
2004	Translational Research Award, Children's Oncology Group
2002	Young Investigator Award, Children's Oncology Group
2000	Junior Scientist Award, Canadian Association of Pathologists

C. Contributions to Science

1. **Identification of novel genomic alterations in hematopoietic neoplasms.** Using integrated next generation sequencing and proteomic studies, our research laboratory has identified novel genetic alterations in T cell lymphoma/leukemias and Langerhans cell histiocytosis. These discoveries will impact the delivery of precision medicine for patients with these disorders.
   a. Kiel MJ, Sahasrabuddhe AA, Rolland DCM, Velusamy T, Chung F, Schaller M, Bailey NG, Betz BL, Miranda RN, Porcu P, Byrd JC, Medeiros LJ, Kunkel SL, Bahler DW, **Lim MS**, Elenitoba-Johnson KSJ. Genomic analyses reveal recurrent mutations in epigenetic modifiers and the JAK-STAT pathway in Sézary syndrome. Nat Commun. 2015 Sep 29;6:8470. PMCID: PMC4598843.
   b. Velusamy T, Kiel MJ, Sahasrabuddhe AA, Rolland D, Dixon CA, Bailey NG, Betz BL, Brown NA, Hristov AC, Wilcox RA, Miranda RN, Medeiros LJ, Jeon YK, Inamdar KV, **Lim MS**, Elenitoba-Johnson KS. A novel recurrent NPM1-TYK2 gene fusion in cutaneous CD30-positive lymphoproliferative disorders. Blood. 2014 Dec 11;124(25):3768-71. PMID: 25349176.
   c. Brown NA, Furtado LV, Betz BL, Kiel MJ, Weigelin HC, **Lim MS**, Elenitoba-Johnson KS. High prevalence of somatic MAP2K1 mutations in BRAF V600E-negative Langerhans cell histiocytosis. Blood. 2014 Sep 4;124(10):1655-8. PMID: 24982505.
   d. Kiel MJ, Velusamy T, Rolland D, Sahasrabuddhe AA, Chung F, Bailey NG, Schrader A, Li B, Li JZ, Ozel AB, Betz BL, Miranda RN, Medeiros LJ, Zhao L, Herling M, **Lim MS**, Elenitoba-Johnson KS. Integrated genomic sequencing reveals mutational landscape of T-cell prolymphocytic leukemia. Blood. 2014 Aug 28;124(9):1460-72. PMCID: PMC4148768.

2. **Elucidation of ALK-mediated oncogenic mechanisms in anaplastic large cell lymphoma.** Our laboratory has contributed to understanding of pathogenetic mechanisms in ALK-driven lymphoma utilizing large-scale unbiased genomic and proteomic strategies.
   a. Murga-Zamalloa CA, Mendoza-Reinoso V, Sahasrabuddhe AA, Rolland D, Hwang SR, McDonnell SR, Sciallis AP, Wilcox RA, Bashur V, Elenitoba-Johnson K, **Lim MS**. NPM-ALK phosphorylates WASp Y102 and contributes to oncogenesis of anaplastic large cell lymphoma. Oncogene. 2017 Apr;36(15):2085-2094. PMID: 27694894.
   b. McDonnell SR, Hwang SR, Rolland D, Murga-Zamalloa C, Basrur V, Conlon KP, Fermin D, Wolfe T, Raskind A, Ruan C, Jiang JK, Thomas CJ, Hogaboam CM, Burant CF, Elenitoba-Johnson KS, **Lim MS**. Integrated phosphoproteomic and metabolomic profiling reveals NPM-ALK-mediated phosphorylation of PKM2 and metabolic reprogramming in anaplastic large cell lymphoma. Blood. 2013 Aug 8;122(6):958-68. PMCID: PMC3739039.
   c. McDonnell SR, Hwang SR, Basrur V, Conlon KP, Fermin D, Wey E, Murga-Zamalloa C, Zeng Z, Zu Y, Elenitoba-Johnson KS, **Lim MS**. NPM-ALK signals through glycogen synthase kinase 3β to promote oncogenesis. Oncogene. 2012 Aug 9;31(32):3733-40. PMCID: PMC4244868.
   d. **Lim MS**, Carlson ML, Crockett DK, Fillmore GC, Abbott DR, Elenitoba-Johnson OF, Tripp SR, Rassidakis GZ, Medeiros LJ, Szankasi P, Elenitoba-Johnson KS. The proteomic signature of NPM/ALK reveals deregulation of multiple cellular pathways. Blood. 2009 Aug 20;114(8):1585-95. PMID: 19531656.

3. **Identification of novel protein biomarkers of lymphoma using mass spectrometry-based proteomics.** We have utilized large-scale mass spectrometry-based proteomic strategies to elucidate pathogenetically relevant signaling pathways implicated in a variety of human lymphomas. Using tandem mass spectrometry we defined the protein interactome of the fusion oncogenic tyrosine kinase NPM::ALK. Over the last 10 years we have elucidated the proteomic consequences of the ectopic expression of NPM::ALK using isotope-coded affinity tags. Recent advances in phosphoproteomic analyses have identified novel signaling mediators implicating metabolic proteins in the pathogenesis of NPM::ALK-positive lymphomas.
   a. Rolland DCM, Basrur V, Jeon YK, McNeil-Schwalm C, Fermin D, Conlon KP, Zhou Y, Ng SY, Tsou CC, Brown NA, Thomas DG, Bailey NG, Omenn GS, Nesvizhskii AI, Root DE, Weinstock DM, Faryabi RB, **Lim MS**, Elenitoba-Johnson KSJ. Functional proteogenomics reveals biomarkers and therapeutic targets in lymphomas. Proc Natl Acad Sci U S A. 2017 Jun 20;114(25):6581-6586. PMCID: PMC5488937.
   b. Nie Z, Du MQ, McAllister-Lucas LM, Lucas PC, Bailey NG, Hogaboam CM, **Lim MS**, Elenitoba-Johnson KS. Conversion of the LIMA1 tumour suppressor into an oncogenic LMO-like protein by API2-MALT1 in MALT lymphoma. Nat Commun. 2015 Jan 8;6:5908. PubMed PMID: 25569716.
   c. Elenitoba-Johnson KS, Crockett DK, Schumacher JA, Jenson SD, Coffin CM, Rockwood AL, **Lim MS**. Proteomic identification of oncogenic chromosomal translocation partners encoding chimeric anaplastic lymphoma kinase fusion proteins. Proc Natl Acad Sci U S A. 2006 May 9;103(19):7402-7. PMCID: PMC1464352.
   d. Crockett DK, Lin Z, Elenitoba-Johnson KS, **Lim MS**. Identification of NPM-ALK interacting proteins by tandem mass spectrometry. Oncogene. 2004 Apr 8;23(15):2617-29. PMID: 14968112.

4. **Correlative biology studies utilizing patient specimens from the Children's Oncology Group.** As Vice-Chair of the COG non-Hodgkin Lymphoma Disease Committee since 2010, I have provided scientific direction to the design of clinical trials and prioritization of correlative biology studies of patients with non-Hodgkin lymphoma including anaplastic large cell lymphomas that are NPM-ALK+. Our laboratory has carried out correlative studies utilizing plasma samples of patients to evaluate for molecular evidence of disease using RT-PCR.
   a. Lowe EJ, Reilly AF, **Lim MS**, Gross TG, Saguilig L, Barkauskas DA, Wu R, Alexander S, Bollard CM. Crizotinib in Combination With Chemotherapy for Pediatric Patients With ALK+ Anaplastic Large-Cell

Lymphoma: The Results of Children's Oncology Group Trial ANHL12P1. J Clin Oncol. 2023 Apr 10;41(11):2043-2053. PMCID: PMC10082271.

b. Lowe EJ, Reilly AF, **Lim MS**, Gross TG, Saguilig L, Barkauskas DA, Wu R, Alexander S, Bollard CM. Brentuximab vedotin in combination with chemotherapy for pediatric patients with ALK+ ALCL: results of COG trial ANHL12P1. Blood. 2021 Jul 1;137(26):3595-3603. PMCID: PMC8462406.

c. Mossé YP, Voss SD, **Lim MS**, Rolland D, Minard CG, Fox E, Adamson P, Wilner K, Blaney SM, Weigel BJ. Targeting ALK With Crizotinib in Pediatric Anaplastic Large Cell Lymphoma and Inflammatory Myofibroblastic Tumor: A Children's Oncology Group Study. J Clin Oncol. 2017 Oct 1;35(28):3215-3221. PMCID: PMC5617123.

d. Mossé YP, **Lim MS**, Voss SD, Wilner K, Ruffner K, Laliberte J, Rolland D, Balis FM, Maris JM, Weigel BJ, Ingle AM, Ahern C, Adamson PC, Blaney SM. Safety and activity of crizotinib for paediatric patients with refractory solid tumours or anaplastic large-cell lymphoma: a Children's Oncology Group phase 1 consortium study. Lancet Oncol. 2013 May;14(6):472-80. PMCID: PMC3730818.

Complete List of Published Work in My Bibliography:
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