### **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.** 

NAME: Megan S. Lim

### eRA COMMONS USER NAME: MEGANLIM

POSITION TITLE: Attending Hematopathologist, Director of Lymphoma Translational Research Program

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<br>(if<br>applicable) | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY        |
|---|------------------------------|-------------------------------|-----------------------|
| University of Calgary, Calgary, Alberta, Canada | BSc                          | 1983                          | Cell and Microbiology |
| University of Calgary, Calgary, AB              | MD                           | 1983                          | Medicine              |
| University of Calgary, Calgary, AB              | Residency                    | 1993                          | Anatomic Pathology    |
| National Cancer Institute, NIH, Bethesda, MD    | Fellowship                   | 1995-1998                     | Hematopathology       |
| University of Calgary, Calgary, AB              | PhD                          | 1995-2000                     | Molecular Oncology    |

### **A. Personal Statement**

I am a physician-scientist with subspecialty board certification in Hematopathology and Molecular Genetic Pathology. I am an attending pathologist in the Hematopathology Service, 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 at MSKCC. My research interests are focused on elucidating mechanisms involved in lymphoma pathogenesis. We utilize unbiased genomic and mass spectrometry-based proteomic strategies to identify novel genetic events and pathobiologic insights in lymphoma. As the former Director of the Division of Hematopathology at the Hospital of the University of Pennsylvania, I oversaw the clinical and administrative operations of the Hematopathology laboratory. I have significant experience in working in multi-disciplinary settings within the Children's Oncology Group as a pathology reviewer and *designing correlative biologic studies for clinical trials* which have led to successful identification of prognostic biomarkers that provide opportunities for risk stratification in patients with ALK+ anaplastic large cell lymphoma. I have contributed to the field of molecular hematopathology by characterizing novel genetic events in many forms of lymphoma including NOTCH2 mutations in splenic marginal zone lymphoma, MAP2K1 mutations in Langerhans cell histiocytosis and the NPM::TYK2 fusion gene in cutaneous anaplastic large cell lymphoma. I am passionate about teaching and have served as Director of the ACGMEaccredited Hematopathology Fellowship training program at the University of Michigan (2006-2015) and the University of Pennsylvania (2016-2022) and mentor to numerous junior colleagues.

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

| R01 CA255350-01<br>"Circulating biomarkers     | Lim MS (PI)<br>s of ALK+ anaplastic large cell lymphoma"   | 08/16/2021-07/31/2025 |
|--|--|-----------------------|
| R01 CA238552-01A1<br>"Genomic biomarkers f     | Lim MS (PI)<br>for cutaneous T-cell lymphoma"              | 02/15/2020-01/31/2025 |
| <b>R01HL141408-01</b><br>"Castleman disease pa | Lim MS (Co-investigator) Fajgenbaum D (PI)<br>athogenesis" | 04/01/2018-06/30/2023 |

**R01 CA255655-01** Lim MS, (Co-investigator) Elenitoba-Johnson KSJ (PI) 12/01/2020-11/30/2025 "Genomic biomarkers of splenic lymphoma"

**R01 CA251764-01** Lim MS, (Co-investigator) Elenitoba-Johnson KSJ (PI) 06/01/2020-05/31/2025 "Epiproteomic Profiling of Sézary Syndrome"

**R01 CA231021-01A1** Lim MS, (Co-investigator) Elenitoba-Johnson KSJ (PI) 7/03/2019-06/30/2024 "Role of FBXO45 in Diffuse Large B Cell Lymphoma Pathogenesis"

**R01FD007262-01A1** Lim MS, (Co-investigator) Kim Ellen (PI) 09/01/2022-5/31/2026 "Assessment of Treatment with Visible Light Activated Synthetic Hypericin ointment in Mycosis Fungoides Patients"

**R01FD007632-01** Lim MS, (Co-investigator) David Fajgenbaum (PI) 09/01/2022-8/31/2026 "ACCELERATE: An Efficient and Innovative Natural History Study Addressing Unmet Needs in Castleman Disease"

### B. Positions, Scientific Appointments, and Honors

### **Positions and Scientific Appointments**

| 2022-      | Attending Hematopathologist, Department of Pathology and Laboratory Medicine, Memorial      |
|------------|---|
|            | Sloan Kettering Cancer Center   |
| 2022-      | Director, Lymphoma Translational Research Program, Center for Hematologic Malignancies,     |
|            | Memorial Sloan Kettering Cancer Center  |
| 2022-      | Director, Hem/Onc Tissue Bank, Center for Hematologic Malignancies, Memorial Sloan          |
|            | Kettering Cancer Center   |
| 2022-      | Clinical Director, Multispectral Imaging Laboratory, Department of Pathology and Laboratory |
|            | Medicine, Memorial Sloan Kettering Cancer Center  |
| 2023- 2027 | Member, Scientific Advisory Board, FANTOM, EU Training Network                              |
| 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,     |
|            | Hospital of the University of Pennsylvania, Philadelphia, PA                                |
| 2015-2022  | Co-Leader, Lymphoma Translational Center of Excellence, Abramson Cancer Center,             |
|            | University of Pennsylvania, Philadelphia, PA  |
| 07/2021-   | Chartered Member, Grant Review Panel – NIH Cancer Biomarkers Study Section                  |
| 06/2025    |   |
| 07/2020-   | Member, Graduate Group in Cell and Molecular Biology, Biomedical Graduate Studies,          |
| 07/2023    | Perelman School of Medicine at the University of Pennsylvania (Philadelphia, Pennsylvania)  |
| 07/2017    | Review of NCI Intramural Research Programs – Lymphoid Malignancies Branch, Bethesda,        |
|            | MD  |
| 2016–      | Member, Scientific Advisory Board, Castleman Disease Collaborative Network, Philadelphia,   |
|            | PA  |
| 2016-2019  | Lymphoma Peer Review Cancer Research Program (PRCRP), DOD, Scientist Reviewer,              |
|            | Washington, DC.   |
| 2015- 2019 | Member, Scientific Advisory Board, ALKATRAS EU Training Network                             |
| 2013- 2017 | Member, Editorial Board, American Journal of Pathology                                      |
| 2012, 2022 | Member, Organizing Committee, International Pediatric and Young Adult NHL Meeting           |
| 06/2012    | Chair, National Institutes of Health Ad Hoc Member in Special Emphasis Study Section        |
|            | "Small Business Innovation Research"  |
| 2010-2020  | Vice Chair, Children's Oncology Group Non-Hodgkin Lymphoma Disease Committee                |
|            |   |
| Honors     |   |

2005-2013 Best Doctors of America

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

## **C.** Contribution to Science

## 1. Identification of novel genomic alterations in hematopoietic neoplasms

Using integrated next generation sequencing and proteomic studies in some instances, our research laboratory has identified novel genetic alterations in T cell lymphoma/leukemias and Langerhans cell histiocytosis. These are notable discoveries that will impact the delivery of precision medicine for patients with these disorders.

- a. 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\*, and Elenitoba-Johnson KSJ. Integrated genomic sequencing reveals mutational landscape of T-cell prolymphocytic leukemia. *Blood* 2014 Aug 28;124(9):1460-72. PMID: 24825865 PMCID: PMC4148768 \*(co-corresponding author)
- b. 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\*(co-corresponding author)
- c. 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, Lim MS\*, and Elenitoba-Johnson KSJ. *TYK2* translocations in cutaneous CD30-positive lymphoproliferative disorders. *Blood* December 2014. PMID: 25349176 [PubMed in process] \*(co-corresponding author)
- d. Kiel M, Sahasrabuddhe A, Rolland D, Velusamy T, Chung F, Schaller M, Bailey N, Betz B, Miranda R, Porcu P, Byrd, JL, Medeiros J, Kunkel S, Bahler D, **Lim MS**\*, and Elenitoba-Johnson KSJ. Genomic Analyses Reveal Recurrent Mutations in Epigenetic Modifiers and JAK-STAT Pathway in Sézary Syndrome. *Nature Communications* 2015 Sep 29;6:8470. PMID: 26415585 [PubMed in process] PMCID: PMC4598843\*(co-corresponding author)

# 2. 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 interactome map of proteins that interact with 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 by 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. Crockett DK, Lin Z, Elenitoba-Johnson KS, Lim MS. Identification of NPM-ALK interacting proteins by tandem mass spectrometry. *Oncogene* 2004; 23:2617-2629. PMID: 14968112
- b. 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; 103:7402-7407. PMID: 16651537/PMCID: PMC1464352
- c. Nie Z, Du M, McAllister-Lucas LM, Lucas PC, Bailey NG, Hogaboam CM, Lim MS, and Elenitoba-Johnson KSJ. Conversion of the LIMA1 tumor suppressor into an oncogenic LMO-like protein by API2-MALT1 paracaspase cleavage in MALT lymphoma. *Nat Comms*, January 2015. PMID: 25569716
- d. Rolland DCM, Basrur V, Jeon YK, McNeil-Schwalm C, Fermin D, Conlon KP, Zhou Y, Ng SY, Tsou C-C, Brown NA, Thomas DG, Bailey NG, Omenn GS, Nesvizhskii AI, Weinstock DM, Faryabi RB, Lim MS\*, and Elenitoba-Johnson KSJ. Functional proteogenomics reveals biomarkers and therapeutic targets in lymphomas. *Proc Natl Acad Sci USA*. 2017 Jun 20;114(25):6581-86. doi: 10.1073/pmas. Epub 2017 Jun 12. PMID: 28607076 \*(co-corresponding author)

# 3. 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.

- Murga-Zamalloa CA, Mendoza-Reinoso V, Sahasrabuddhe AA, Rolland DCM, Hwang SR, McDonnell SR, Scialis AP, Wilcox RA, Bashur V, Elenitoba-Johnson KSJ, Lim MS. NPM-ALK phosphorylates WASp Y102 and contributes to oncogenesis of anaplastic large cell lymphoma. *Oncogene*. 2016 Oct 3. doi: 10.1038/onc.2016.366. PMID: 27694894. [Epub ahead of print]
- McDonnell SRP, Hwang SR, Rolland D, Murga-Zamalloa C, Basrur V, Conlon KP, Fermin D, Wolfe T, Raskind A, Ruan C, Jiang J, Thomas CJ, Hogaboam CM, Burant CF, Elenitoba-Johnson KSJ, 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. PMID: 23814019 PMCID: PMC3739039
- c. 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; 114:1585-95. PMID: 19531656
- d. McDonnell S, Hwang SR, Basrur V, Conlon KP, Fermin D, Wey E, Murga-Zamalloa C, Zeng Z, Zu Y, Elenitoba-Johnson KSJ, Lim MS. NPM-ALK signals through glycogen synthase kinase 3β to promote oncogenesis. Oncogene 2012 ;31:3733-40. PMID: 22179823 PMCID: PMC4244868

# 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. Lui C, Iqbal J, Teruya-Feldstein J, Shen Y, Dabrowska MJ, Dybkaer K, Lim MS, Piva R, Barreca A, Pellegrino E, Spaccarotella E, Lachel CM, Kucuk C, Jiang CS, Hu X, Bhagvari S, Greiner TC, Weisenburger DD, Aoun P, Mckeithan TW, Inghirami G, Chan WC. MicroRNA expression profiling identifies molecular diagnostic signatures for anaplastic large cell lymphoma. *Blood* 2013 June 25. PMID: 23801630/PMCID: PMC3779551
- b. Deffenbacher K, Iqbal J, Sanger W, Shen Y, Lachel C, Liu Z, Liu YY, Lim MS, Perkins S, Fu K, Smith L, Lynch J, Staudt L, Rimsza L, Jaffe E, Rosenwald A, Ott G, Delabie J, Campo E, Gascoyne R, Cairo M, Weisenburger D, Greiner T, Gross T, Chan W. Molecular distinctions between pediatric and adult mature B-cell non-Hodgkin lymphomas identified through genomic profiling. *Blood* 2012; Apr 19;119(16):3757-66 PMID: 22374697 PMCID: 3335381
- c. Mosse 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. *The Lancet Oncology*. 2013 May:14(6):472-80. doi: 10.1016/s1470-2045(13)70095-01 [Epub 2013 Apr16]. PMID: 23598171/PMCID: PMC3730818; NIHMS: 476957
- d. Mossé YP, Voss SD, Lim MS, Rolland D, Minard CG, Fox E, Blaney SM, Weigel BJ. Targeting ALK with Crizotinib in Pediatric Anaplastic Large Cell Lymphoma: A Children's Oncology Group Study (ADVL0912). *J Clin Oncol* 2017 Aug 8:JCO2017734830. doi: 10.1200/JCO.2017.73.4830 [Epub ahead of print]. PMID: 28787259

# 5. Characterization of clinical, pathologic and immunologic aspects of Castleman disease

I have worked closely with Dr. Fajgenbaum over the last 7 years during which time we have had the unique opportunity to delineate the diagnostic criteria for patients with iMCD as well as investigate various aspects of the clinical, pathologic and immunologic aspects of Castleman disease.

- a. Fajgenbaum DC, Uldrick TS, Bagg A, Frank D, Wu D, Srkalovic G, Simpson D, Liu AY, Menke D, Shanmuganathan C, Lechowicz MJ, Wong RSM, Paessler M, Rossi JF, Ide M, Ruth J, Croglio M, Suarez A, Krymskaya V, Chadburn A, Colleoni G, Nasta S, Jayanthan R, Nabel C, Casper C, Dispenzieri A, Fossa A, Kelleher D, Kurzrock R, Voorhees P, Dogan A, Yoshizaki K, van Rhee F, Oksenhendler E, Jaffe ES, Elenitoba-Johnson KSJ, Lim MS. International, evidence-based consensus diagnostic criteria for HHV-8-negative/idiopathic multicentric Castleman disease. *Blood* 2017; Jan 13. PMID: 28087540.
- b. Van Rhee F, Öksendhendler E, Casper C, Uldrick, T, Kurzrock R, Yoshizaki K, Nasta S, Rossi JF, Wong

R, Simpson D, Sato Y, Terriou L, Ferrero S, Zinzani PL, Hoffman C, Goodman A, Krymskaya V, Elenitoba-Johnson KSJ, **Lim MS**, Chadburn A, Penmaraju N, Leitch H, Jaffe ES, Jayanthan R, Chandrasakan S, Lechowicz MJ, Ruth J, Greenway A, Stone K, Shilling D, Mukherjee S, Partridge HL, Pierson SK, Streetly M, Schey S, Munshi N, Ide M, Srkalovic G, Fossa A, Dispenzieri A, Voorhees P, Fajgenbaum DC. International, evidence-based consensus treatment guidelines for the management of idiopathic multicentric Castleman disease. *Blood*, 2018; Sep 4. PMID: 30181172.

- c. Fajgenbaum DC, Wu D, Goodman A, Wong R, Chadburn A, Nasta S, Srkalovic G, Mukherjee S, Leitch H, Jayanthan R, Ferrero S, Sato Y, Schey S, Dispenzieri A, Oksenhendler E, Zinzani PL, Lechowicz MJ, Hoffman C, Pemmaraju N, Bagg A, Fossa A, Lim MS, van Rhee F on behalf of the Castleman Disease Collaborative Network Scientific Advisory Board diagnostic criteria international working group and treatment guidelines international working group. Insufficient evidence exists to use histopathologic subtype to guide treatment of idiopathic Castleman Disease. *Am J Hematol.*2020 Sep 7. PMID: 32894785.
- d. van Rhee F, Oksenhendler E, Srkalovic G, Voorhees P, Lim MS, Dispenzieri A, Ide M, Parente S, Schey S, Streetly M, Wong R, Wu D, Maillard I, Brandstadter J, Munshi N, Bowne W, Elenitoba-Johnson KSJ, Fossä A, Lechowicz MJ, Chandrakasan S, Pierson SK, Greenway A, Nasta S, Yoshizaki K, Kurzrock R, Uldrick TS, Casper C, Chadburn A, Fajgenbaum DC. International evidence-based consensus diagnostic and treatment guidelines for unicentric Castleman disease. *Blood* Adv. 2020 Dec 8;4(23):6039-50. Pubmed: 33284946.

# Complete List of Published Work in MyBibliography: https://www.ncbi.nlm.nih.gov/myncbi/megan.lim.1/bibliography/public/