1989BIOGRAPHICAL SKETCH

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NAME: Kim, Youn H.

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

POSITION TITLE: Professor of Dermatology, Director of Multidisciplinary Cutaneous Lymphoma 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 (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Wellesley College, Wellesley, MA	B.A.	06/80	Chemistry
Stanford U School of Medicine, Stanford, CA	M.D.	06/84	Medicine
Kaiser Foundation Hospital, San Francisco, CA		06/85	Internal Medicine
Stanford U School of Medicine, Stanford, CA		06/87	Dermatology (Fellow)
Stanford U Hospital & Clinics, Stanford, CA		06/89	Dermatology (Residency)

A. Personal Statement

I am the Joanne and Peter Haas Jr. Professor for Cutaneous Lymphoma Research at Stanford University School of Medicine and member of Stanford Cancer Institute. I have served as the Director of the Multidisciplinary Cutaneous Lymphoma Program at Stanford, an interdisciplinary clinical and research program with members in dermatology, oncology, and pathology, for more than 30 years. We have made major contributions in furthering knowledge, establishing improved diagnostic/prognostic methods, identifying new actionable targets and developing newer therapies in cutaneous lymphoma. As the key regional, national, and international referral center for this group of rare malignancy, we have continued to build our tissue/blood bank of patient samples and are able to lead enrollments in clinical and translational investigative studies. I have a successful record of leading multidisciplinary and multicenter teams and have led and authored key consensus projects that have served to advance the clinical practice in cutaneous lymphoma management. I am the global co-leader for the Cutaneous Lymphoma International Consortium (CLIC) and am committed to building an international platform for sharing patient data and biosamples for translational research. My background and institutional support makes me well suited to be a principal investigator for this proposed study.

B. Positions and Honors

Positions

1993-1996 1998-2004 1992-Present 2004-Present	Assistant Professor, Department of Dermatology, Stanford University, Stanford, CA Associate Professor, Department of Dermatology, Stanford University, Stanford, CA Director, Multidisciplinary Cutaneous Lymphoma Program, Stanford University, Stanford, CA Professor, Department of Dermatology, Stanford University, Stanford, CA
2004-Present	Professor, Department of Medicine/Oncology (by Courtesy) Member, Stanford Cancer institute Co-Leader, Lymphoma Clinical Research Group, Stanford Cancer Institute, Stanford, CA
2013-Present	Co-Leader, Lymphoma Clinical Research Group, Stanford Cancer Institute, Stanford, CA

<u>Honors</u>

1984	Research Honors Award, Stanford University School of Medicine
1986	Katharine McCormick Award, Stanford University School of Medicine
1991	Physician Scientist Award, National Institutes of Health (NIAMS)

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C. Contributions to Science

1. Improvement in clinical staging and prognostic models in cutaneous lymphoma

Mycosis fungoides (MF) and Sézary syndrome (SS) comprise 60% of cutaneous lymphomas (CL) with very heterogeneous clinical presentation and outcome. The clinical stage primarily directs the clinical management and guide the design of clinical trials. However our clinical staging system needs to be updated using current data and tools. I have partnered with other international experts to gather prospective data to revise our TNMB and clinical staging systems. Furthermore, I have led the establishment of the CL International Consortium, CLIC, which will be the conduit for large-scale collaborative research. An international platform of clinical data repository has been established and being expanded, linked with a federated Biobank and digitized pathology databank, to incorporate new biomarkers in the prognostic modeling and for future translational projects.

- a. Scarisbrick JJ, Prince HM, Vermeer MH, Quaglino P, Horwitz S, Porcu P, Stadler R, Wood G, Beylot-Barry M, Pham-Ledard A, Foss F, Girardi M, Bagot M, Michel L, Battistella M, Guitart J, Kuzel TM, Martinez-Escala M, Estrach T, Papadavid E, Antoniou C, Rigopoulos D, Nikolaou V, Sugaya M, Miyagaki T, Gniadecki R, Saches J, Cury-Martins J, Miyashiro D, Servitje O, Muniesa C, Berti E, Onida F, Corti L, Hodak E, Amitay-Laish I, Ortiz-Romero P, Rodriguez-Peralto J, Knobler R, Porkert S, Bauer W, Pimpinelli N, Grandi V, Cowan R, Rook A, Kim E, Pileri A, Patrizi A, Pujol R, Wong H, Tyler K, Stranzenbach R, Querfeld C, Fava P, Maule M, Willemze R, Evison F, Morris S, Twigger R, Talpur R, Kim J, Ognibene G, Li S, Tavallaee M, Hoppe RT, Duvic M, Whittaker SJ, Kim YH. Cutaneous Lymphoma International Consortium (CLIC) Study of Outcome in Advanced Stages of Mycosis Fungoides & Sézary Syndrome: Effect of Specific Prognostic Markers on Survival and Development of a Prognostic Model. J Clin Oncol 33:3766-73, 2015.
- b. Quaglino P, Maule M, Prince HM, Porcu P, Horwitz S, Duvic M, Vermeer M, Bagot M, Guitart J, Papadavid L, Sanches JA, Hodak E, Sugaya M, Berti E, Ortiz-Romero P, Pimpinelli N, Octavio S, Pileri A, Zinzani PL, Estrach T, Knobler R, Stadler R, Rook AH, Geskin LJ, Willemze R, Whittaker S, Hoppe R, Scarisbrick J, **Kim YH.** Global patterns of care in advanced stage MF/SS: a multicenter retrospective follow-up study from the Cutaneous Lymphoma International Consortium (CLIC). Ann Oncol 28:2517-25, 2017.
- c. Gru AA, Kim J, Pulitzer M, Guitart J, Battistella M, Wood GS, Cerroni L, Kempf W, Willemze R, Pawade J, Querfeld C, Schaffer A, Pincus L, Tetzlaff M, Duvic M, Scarisbrick J, Porcu P, Mangold AR, DiCaudo DJ, Shinohara M, Hong EK, Horton B, **Kim YH**. The use of central pathology review with digital slide scanning in advanced stage mycosis fungoides and Sezary syndrome: a multi-institutional and international pathology study. Am J Surg Pathol 42:726-34, 2018.

2. Deciphering the molecular pathogenesis in MF/SS and identification of actionable alterations

Molecular pathogenesis of cutaneous lymphomas remains largely unknown including MF and SS. I have partnered with Khavari and Chang laboratories (Department of Dermatology, Program in Epithelial Biology) and Khodadoust laboratory (Medical Oncology/Medicine) at Stanford to apply next generation sequencing tools to decipher the molecular drivers in MF and SS. We have one of the largest referral clinics for these rare disorders and have an established Biobank with thorough clinical annotation. These clinical samples were used to identify novel and/or recurrent pathogenic variants in the T-cell signaling, activation and survival pathways involved in CTCL. These aberrant findings will be targeted for potential therapeutic relevance.

- a. Ungewickell A, Bhuduri A, Rios E, Reuter J, Lee CS, Mah A, Zehnder A, Ohgami R, Kulkarni S, Armstrong R, Gratzinger D, Tavallaee M, Rook A, Snyder M, Kim Y, Khavari P. Genomic analysis of mycosis fungoides and Sézary syndrome identifies recurrent alterations in TNFR2. Nat Genet 47:1057-1060, 2015.
- b. Qu K, Zaba LC, Satpathy AT, Giresi PG, Jin Y, Armstrong R, Jin C, Schmitt N, Rahbar Z, Ueno H, Greenleaf WJ, **Kim YH**, Chang HY. Chromatin accessibility landscape of cutaneous T cell lymphoma and dynamic response to HDAC inhibitors. Cancer Cell 32:27-41, 2017.
- c. Satpathy AT, Saligrama N, Buenrostro JD, Wei Y, Wu B, Rubin AJ, Granja JM, Lareau CA, Li R, Qi Y, Parker KR, Mumbach MR, Serratelli WS, Gennert DG, Schep AN, Corces MR, Khodadoust MS, Kim YH, Khavari PA, Greenleaf WJ, Davis MM, Chang HY. Transcript-indexed ATAC-seq for precision immune profiling. Nat Med 24:580-90, 2018.
- d. Beygi S, Fernandez-Pol S, Duran G, Wang EB, Stehr H, Zehnder JL, Nirasha R, Fling SP, Cheever MA, Weng W-K, **Kim YH**, Khodadoust MS. Pembrolizumab in mycosis fungoides with PD-L1 structural variants. Blood Adv. 5(3):771-4, 2021.

3. Advancing novel therapeutics and biomarker-based clinical management

I have led the clinical development of novel or new therapies and strategies to improve our management approach or options in CL. I have played critical roles in the design and conduct of clinical trials, which led to successful FDA approval of new agents in CTCL, including romidepsin, brentuximab, and mogamulizumab. In a rare disease group with heterogeneous clinical, path/lab, and molecular features, it is critical to explore biomarkers to better align the patient's disease profile with new therapies.

- a. Kim YH, Tavallaee MT, Sundram U, Salva KA, Wood GS, Li S, Rozati S, Nagpal S, Krathen M, Reddy S, Hoppe RT, Nguyen-Lin A, Weng WK, Armstrong R, Pulitzer M, Advani RA, Horwitz SM. Phase II investigator-initiated study of brentuximab vedotin in mycosis fungoides and Sézary syndrome with variable Cd30 expression level: a multi-institution collaborative project. J Clin Oncol 33:3750-8, 2015
- b. Prince HM^{*}, Kim YH^{*}, Horwitz SM, Dummer R, Scarisbrick J, Quaglino P, Zinzani PL, Wolter P, Sanches JA, Ortiz-Romero PL, Akilov OE, Geskin L, Trotman J, Taylor K, Dalle S, Weichenthal M, Walewski J, Fisher D, Dreno B, Stadler R, Feldman T, Kuzel TM, Wang Y, Palanca-Wessels MC, Zagadailov E, Trepicchio WL, Zhang W, Lin H-M, Huebner D, Little M, Whittaker S, Duvic M. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma: an open-label, multicenter, randomized phase 3 trial. Lancet 390:555-66, 2017, *equal contribution.
- c. Kim YH, Bagot M, Pinter-Brown L, Rook AH, Horwitz SM, Whittaker S, Tokura Y, Vermeer M, Zinzani PL, Sokol L, Morris S, Kim EJ, Ortiz-Romero PL, Eradat H, Scarisbrick J, Tsianakas A, Elmets C, Dalle S, Halwani A, Poligone B, Greer J, Fierro MT, Khot A, Moskowitz AJ, Musiek A, Shustov A, Pro B, Geskin LJ, Dwyer K, Moriya J, Leoni M, Humphrey JS, Hudgens S, Grebennik DO, Tobinai K, Duvic M; MAVORIC Investigators. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomized, controlled phase 3 trial. Lancet Oncol 19:1192-1204, 2018.
- d. Beygi S, Duran GE, Fernandez-Pol S, Rook AH, Kim YH, Khodadoust MS. Resistance to mogamulizumab is associated with loss of CCR4 in cutaneous T-cell lymphoma. Blood 139:3732-3736, 2022.
- e. Khodadoust MS, Rook AH, Porcu P, Foss F, Moskowitz AJ, Shustov A, Shanbhag S, Sokol L, Fling SP, Ramchurren N, Pierce R, Davis A, Shine R, Li S, Fong S, Kim J, Yang Y, Blumenschein WM, Yearley JH, Karlovich C, Williams PM, Subrahmanyam PB, Maecker HT, Horwitz SM, Sharon E, Kohrt HE, Cheever MA, Kim YH. Pembrolizumab in relapsed and refractory mycosis fungoides and Sézary syndrome: a multicenter phase II study. J Clin Oncol 38:20-28, 2020.
- f. Su T, Duran GE, Kwang AC, Ramchurren N, Fling SP, **Kim YH,** Khodadoust MS. Single-cell RNAsequencing reveals predictive features of response to pembrolizumab in Sezary syndrome. Oncoimmunol 11:e2115197, 2022.

4. New tools for identifying and monitoring residual disease in MF and SS (CTCL)

In close collaboration with Stanford BMT/Weng group, we have been conducting NMA allogeneic hematopoietic stem cell transplantation (HSCT) in advanced MF and SS using a novel preparatory regimen of total skin electron beam therapy, total lymphoid irradiation and anti-thymocyte globulin. As part of this transplant project, we have effectively applied high-throughput sequencing (HTS) of tumor-specific rearranged

TCR CDR3 to monitor molecular residual disease (MRD) in patients treated with allogeneic HSCT. Molecular cure or relapse assessed by HTS tool is likely to allow improved clinical management and outcome. We have begun to explore the utility of TCR HTS method in monitoring MRD in patients treated with standard therapies as well as characterizing patient's TCR profile with new immune therapies.

- a. Weng W-K, Armstrong R, Arai S, Desmarais C, Hoppe R, Kim YH. Minimal residual disease monitoring with high-throughput sequencing of T cell receptors in cutaneous T cell lymphoma. Sci Transl Med 5(214):214ra171, 2013
- b. Weng W-K, Arai S, Rezani A, Johnston L, Lowsky R, Miklos D, Shizuru J, Muffly L, Meyer E, Negrin RS, Wang E, Almazan T, Million L, Khodadoust M, Li S, Hoppe RT, Kim YH. Nonmyeloablative allogeneic transplantation achieves clinical and molecular remission in cutaneous T-cell lymphoma. Blood Advances 4:4474-4482, 2020.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1LY6anLyVxW5g/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Drs. Martin and Dorothy Spatz Charitable Foundation 05/01/15-7/31/37 CLIC Prognostic and Treatment Outcome Studies in Advanced Mycosis Fungoides and Sézarv Syndrome: Biobank Establishment for Biomarkers and Translational Research Role: Y Kim, PI (Stanford led multi-center, international project; global co-leader, led to 2.5M endowment)

E7777-G000-302: Eisai, Inc.

07/01/13-5/31/22

Phase III Study to Demonstrate Safety and Efficacy of E7777 (Denileukin Diftitox) in Persistent or Recurrent Cutaneous T Cell Lymphoma

Role: Y Kim, Stanford PI (Scientific Steering Committee member to ensure proper conduct)

LYMNHL0155: Kyowa Kirin and Haas Family Foundation 03/16/20-11/30/23 A Phase 2 Single-Center, Single-Arm, Open-Label Mogamulizumab Combined Upfront with Low-dose Total Skin Electron Beam Therapy (LD-TSEBT) in Patients with Mycosis Fungoides and Sezary Syndrome Role: Y Kim, Stanford PI (Investigator-initiated trial)

IPH4102: Innate Pharmaceuticals, Inc.

04/23/2019-6/30/23 TELLOMAK: An Open Label, Multi-Cohort, Multi-Center Phase II Study Evaluating the Efficacy and Safety of IPH4102 Alone or in Combination with Chemotherapy in patients with Advanced T-cell Lymphoma. Role: Y Kim, Stanford PI (Key role in study design)

MSK 16-042: Memorial Sloan Kettering Cancer Center 09/19/16-08/30/22 A Phase I Trial of Duvelisib (IPI-145) in Combination with Either Romidepsin or Bortezomib in Relapsed/Refractory T-cell Lymphomas Protocol Director: S Horwitz (MKSCC) Role: Y Kim, Stanford PI (Role in study design and correlative science; study is based on Stanford genomics)

CITN-13: Fred Hutchinson Cancer Center and Horizon Pharma 12/22/17-12/31/22 A Phase II Trial of MK-3475 (pembrolizumab) and Interferon Gamma 1-b Combination Immunotherapy in Patients with Previously Treated Mycosis Fungoides and Sézary Syndrome Role: Y Kim, Stanford PI (Role in study design and correlative science)

TTI-621: Trillium

10/03/18-6/31/22

A Phase 1a/1b Dose Escalation and Expansion Trial of TTI-621, a Novel Biologic Targeting CD47, in Subjects with Relapsed or Refractory Hematologic Malignancies in Selected Solid Tumors Role: Y Kim, Stanford PI

A Phase 1/1b Dose-Escalation Trial Evaluating CPI-818, an Oral Interleukin-2-Inducible T-Cell Kinase Inhibitor, in Subjects With Relapsed/Refractory T-Cell Lymphoma Role: Y Kim, Stanford PI

CRSP-ONC-004: CRISPR Therapeutics 11/21/20-11/20/24 A phase 1. Open-Label, Multicenter, Dose Escalation and Cohort Expansion Study of the Safety and Efficacy of Anti-CD70 Allogeneic CRISPR-Cas9-Engineered T-cells (CTX130) in Adult Subjects with R/R T or B-cell Malignancies

Role: Sub-Investigator, Stanford site (Wen-Kai Weng, PI)

Completed Research Support

PRT 062070-13-601: Portola Pharmaceuticals, Inc. 08/17/17-2/28/21 A Phase 1/2A Open-Label, Multi-Dose, Multi-Center Escalation and Exploratory Study of Cerdulatinib (PRT062070) in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) OR B-Cell or T-Cell Non-Hodgkin Lymphoma (NHL)

KW0761-010: Kyowa Hakko Kirin Pharma, Inc. 12/01/12-11/30/19 Phase III Study of Open-Label, Multi-Center, Randomized Study of Anti-CCR4 Monoclonal Antibody KW-0761 (Mogamulizumab) Versus Vorinostat in Subjects with Previously Treated Cutaneous T-cell Lymphoma Role: Y Kim, Stanford PI (Lead PI for multicenter phase III study, key role in study design, protocol director, data led to FDA-approval)

C25001: Millennium Pharmaceuticals, Inc. 07/01/12-05/03/19 A Randomized, Open-Label, Phase 3 Trial of Brentuximab Vedotin (SGN 35) Versus Physician's Choice (Methotrexate or Bexarotene) in Patients with CD30-Positive Cutaneous T-Cell Lymphoma Role: Y Kim, Stanford PI (Key role in study design, based on data from our phase 2 trial, led to FDA-approval)

CITN-10: Fred Hutchinson Cancer Center & Merck Co. 04/02/15-08/31/17 A Phase 2 Investigator-Initiated Study of MK-3475 for the Treatment of Relapsed/Refractory Mycosis Fungoides/Sézary Syndrome

Role: Y Kim, Multicenter PI, Stanford PI (key role in study design and correlative science)

Drs. Martin and Dorothy Spatz Charitable Foundation 04/1/14-03/31/15 International Consortium (CLIC), an International Collaborative Alliance towards Large-Scale Prospective Investigations in Cutaneous Lymphoma: A Pilot Study to Demonstrate the Feasibility and Effectiveness of CLIC Machinery and to Establish the Foundation for Prospective Projects Role: Y Kim, PI

Drs. Martin and Dorothy Spatz Charitable Foundation 09/1/12-08/31/13 Identification and Functional Characterization of Novel Biomarkers and Therapeutic Targets in Cutaneous Tcell Lymphomas by Whole Transcriptome and Exome Sequencing Role: Y Kim, PI