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: Betof Warner, Allison

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

POSITION TITLE: Assistant Attending Physician

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	BA (Honors)	05/2005	Biology, Physiology
Duke University School of Medicine, Durham, NC	PhD	05/2012	Pathology, Cancer Biology
Duke University School of Medicine, Durham, NC	MD	05/2013	Medicine
Massachusetts General Hospital, Boston, MA		06/2016	Internal Medicine (Residency)
Memorial Sloan Kettering Cancer Center, New York, NY		06/2019	Medical Oncology (Fellow)

A. Personal Statement

I am a translational clinician-investigator with both laboratory and clinical trial expertise in tumor immunology and microenvironment. My research focuses on improving the efficacy immunotherapy treatment by leading clinical trials of immunotherapy in difficult-to-treat subsets of melanoma, including those patients whose disease is refractory to standard immune checkpoint inhibitors and patients with central nervous system metastases. As a junior faculty member, I have built the foundation for a strong clinical trial portfolio and deep collaborations with laboratory-based investigators. I have been integrally involved in clinical trial design and management of melanoma patients on clinical studies. At Memorial Sloan Kettering, I took leadership of the Melanoma Service's research on central nervous system (CNS) metastasis and developed a cellular therapy program for melanoma. My involvement with these projects has enabled me to establish strong collaborative relationships with investigators around the world in surgery, neuro-oncology, neurosurgery, radiation oncology, pathology and several translational laboratories and facilitated my recent appointment as Director of the Melanoma Program and Director of Solid Tumor Cellular Therapy within the Division of Oncology at Stanford University School of Medicine. I am also the Principal Investigator of the Betof Laboratory, which is funded to pursue translational research on melanoma central nervous system metastases and immunotherapy therapy-refractory malignancies.

B. Positions and Honors

Positions and Employment

2013-2016 Internal Medicine Resident, Massachusetts General Hospital, Boston, MA

2016-2019 Medical Oncology Fellow, Melanoma and Immunotherapeutics Service, Memorial Sloan Kettering Cancer Center, New York, NY

2017-2019 Postdoctoral Fellow, Laboratory of Jedd Wolchok, MD, PhD, Chief of Melanoma and Immunotherapeutics Service, Associate Director of Ludwig Center for Cancer Immunotherapy, Memorial Sloan Kettering Cancer Center, New York, NY

2019-2023 Assistant Attending Physician, Melanoma Service and Cellular Therapy Service, Memorial Sloan Kettering Cancer Center, New York, NY

2023- Clinical Instructor (pending academic appointment as Assistant Professor), Director of Melanoma Medical Oncology, Leader of the Melanoma Clinical Research Group, Director of Solid Tumor Cellular Therapy, Stanford Cancer Institute, Stanford University, Palo Alto, CA

Other Experience

2009 Chairperson, Duke University Medical Scientist Training Program Student Council
2016-2020 AACR Associate Member Council; Chairperson in 2018
2017 AACR Molecular Biology in Clinical Oncology Workshop, Snowmass, CO
2018 AACR/ASCO Methods in Clinical Cancer Research Workshop
2018 Selected to represent early career researchers for AACR Early Career Hill Day
2018 Faculty, ASCO University Immuno-Oncology Program Update
2019-2020 Program Committee, ASCO-SITC Immuno-Oncology Symposium
2020-2022 Memorial Sloan Kettering Cancer Center Junior Faculty Council
2020- Project Member, Parker Institute for Cancer Immunotherapy
2020- Memorial Sloan Kettering Cancer Center Melanoma representative to ECOG-ACRIN
2020-2022 Course Director, Memorial Sloan Kettering Cancer Center Department of Medicine Grand Rounds
2020-2021 Neurologic Immune-Related Adverse Event Disease Definition Panel
2021- Member, Society for Immunotherapy of Cancer Early Career Scientist Committee
2021- ASCO Plenary Series Scientific Review Committee- Melanoma/Skin Cancers Track

Honors and Awards

2002-2005 NACGC Academic All-American
2003 Phi Beta Kappa
2004 Cornell University Sphinx Head Senior Honorary
2004 Cornell University Richie Moran Award, awarded to the senior student-athlete who has distinguished herself through academics, athletics and ambassadorship
2004, 2005 Eastern College Athletic Conference Scholar-Athlete of the Year, Women's Gymnastics
2005 Magna cum laude in Biology with Distinction in all subjects, Cornell University
2009 Gertrude Elion Mentored Medical Student Research Award, Triangle Community Foundation/ Burroughs Wellcome Fund
2010 Department of Defense Breast Cancer Predoctoral Traineeship Grant
2016 Newton-Wellesley Hospital Department of Medicine Teaching Commendation
2017 Society for Translational Oncology Fellows Award
2018 Finalist, *The Oncologist* Young Investigator Award
2018 Conquer Cancer Foundation of ASCO/Amgen Young Investigator Award
2019, 2021 Memorial Sloan Kettering Cancer Center Housestaff Didactic Teaching Award
2022 Conquer Cancer Foundation of ASCO Career Development Award
2022 40 Under 40 in Cancer Award

Professional Memberships

American Association for Cancer Research, American Society of Clinical Oncology, Society for Melanoma Research, Society for Immunotherapy in Cancer, European Society of Medical Oncology

C. Contributions to Science

1. Optimizing the tumor microenvironment to improve response to anti-cancer therapy: Tumor microenvironmental factors are key mechanisms of resistance to systemic therapy for solid tumors. As a PhD student, I demonstrated that reversal of hypoxia, therapeutic hyperthermia, liposomes, and exercise can improve delivery and efficacy of chemotherapy (Betof 2012, Betof 2015). As an oncology trainee and junior faculty member, my focus shifted to microenvironment-targeted interventions to optimize anti-tumor immunity. Using murine models and clinical data, we demonstrated that corticosteroids decreased low- but not high-affinity memory T cells by suppressing fatty acid metabolism essential for memory T cells (Tokunga 2019). My co-first author work demonstrated that microenvironment modification with cyclophosphamide enhances the anti-tumor potency of GITR engagement by increasing oligoclonal cytotoxic T cell fitness (Hirschhorn/Betof Warner 2021). Cellular therapy is now becoming a feasible means to manipulate the immune microenvironment for solid tumors

including melanoma. I am the co-PI and one of the lead accruers to the immunotherapy-refractory melanoma cohort of the basket study of lifileucel in solid tumors (NCT03645928).

a) **Betof AS**, Rabbani ZN, Hardee ME, Kim SJ, Broadwater G, Bentley RC, Snyder SA, Vujaskovic Z, Oosterwijk E, Harris LN, Horton JK, Dewhirst MW, Blackwell KL. Carbonic anhydrase IX is a predictive marker of doxorubicin resistance in early-stage breast cancer independent of HER2 and TOP2A amplification. British journal of cancer. 2012 Feb; 106(5): 916-922. PMCID: PMC3305967.
b) **Betof AS**, Lascola CD, Weitzel, D, Landon C, Scarbrough PM, Devi GR, Palmer G, Jones LW, Dewhirst MW. Modulation of murine breast tumor vascularity, hypoxia and chemotherapeutic response by exercise. Journal of the national cancer institute. 2015 Mar; 107(5). PMCID: PMC4822524.
c) Hirschhorn D*, **Betof Warner A***, Maniyar R, Chow A, Mangarin LMB, Cohen AD, Hamadene L, Rizzuto GA, Budhu S, Suek N, Liu C, Houghton AN, Merghoub T, Wolchok JD. Cyclophosphamide enhances the antitumor potency of GITR engagement by increasing oligoclonal cytotoxic T cell fitness. JCI Insight. 2021 Oct 22;6(20). PMCID: PMC8564916.
***Denotes co-first authorship**

2. Long-term responses and adverse events from immune checkpoint inhibition: I co-directed a project that was the first to analyze the clinical safety of rechallenging with PD-1 blockade as monotherapy in patients who had to discontinue combined nivolumab plus ipilimumab (Pollack/ Betof Warner 2017). I led an analysis of long-term outcomes in melanoma patients after discontinuation of anti-PD-1 therapy and efficacy of retreatment (Betof Warner 2020) and was the senior author on a manuscript analyzing the safety and efficacy of re-induction with ipilimumab plus nivolumab in melanoma patients previously treated with these agents (Chapman 2021).

a) Pollack MH*, **Betof Warner A*,** Dearden H, Rapazzo K, Valentine I, Brohl AS, Ancell KK, Long GV, Menzies AM, Eroglu Z, Johnson DB, Shoushtari A. Safety of resuming anti-PD-1 in patients with immune related adverse events (irAEs) during combined anti-CTLA-4 and anti-PD1 in metastatic melanoma. Annals of oncology. 2017 Oct; 29(1):250-255. PMCID: PMC5834131.
*Denotes equal contribution
b) **Betof Warner A**, Palmer JS, Shoushtari AS, Goldman DA, Panageas KS, Hayes SA, Bajwa R, Callahan MK, Wolchok JD, Postow MA, Chapman PB. Long-term outcomes and responses to retreatment in melanoma patients treated with PD-1 blockade. Journal of Clinical Oncology. 2020 May 38(15): 1655-1663. PMID: 32053428, PMCID: PMC7238490.
c) Chapman P, Jayaprakasa VS, Panageas K, Callahan M, Postow M, Shoushtari A, Wolchok JD, **Betof Warner A**. Risks and benefits of re-induction ipilimumab/nivolumab in melanoma patients previously treated with ipilimumab/nivolumab. Journal for ImmunoTherapy of Cancer. 2021 Oct;9(10). PMCID: PMC8549669.

3. Novel treatments for CNS metastasis from melanoma: The blood-brain and blood-CSF barriers pose unique obstacles to the treatment of CNS metastases. My research expertise in drug delivery, tumor angiogenesis, and resistance to immunotherapy makes me uniquely suited to tackle this challenge. I am the PI of a pilot trial of lifileucel (tumor infiltrating lymphocytes) for patients with active melanoma brain metastases (NCT05640193) and was a key collaborator on a recent trial demonstrating efficacy of proton craniospinal radiation for leptomeningeal metastatsis.

a) Wjetunga NA, Boire A, Young RJ, Yamada Y, Wolden S, Yu H, Kris M, Seidman A, **Betof Warner A^**, Diaz M, Reiner A, Malani R, Pentsova E, Yang JT. Quantitative Cerebrospinal Fluid Circulating Tumor Cells are a Potential Biomarker of Response for Proton Craniospinal Irradiation for Leptomeningeal Metastasis. Neuro-Oncology Advances. 2021 Dec; 3(1):vdab181. PMCID: PMC8717892.
b) Yang JT, Wijetunga NA, Pentsova E, Wolden S, Young RJ, Correa D, Zhang Z, Zheng J, Steckler A, Bucwinska W, Bernstein A, **Betof Warner A**, Yu H, Kris MG, Seidman AD, Wilcox JA, Malani R, Lin A, DeAngelis LM, Lee NY, Powell SN, Boire A. Randomized phase II trial of proton craniospinal irradiation versus photon involved-field radiotherapy for patients with solid tumor leptomeningeal metastasis. Journal of Clinical Oncology. 2022 Jul; epub ahead of print. PMID: 35802849.

Complete List of Published Work in My Bibliography
https://www.ncbi.nlm.nih.gov/myncbi/allison.betof%20warner.1/bibliography/public/

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

Ongoing Research Support

Award Source:(funding agency - federal, foundation, industry; type of grant)*	Conquer Cancer Foundation of ASCO
Project title:	A Pilot Trial of Autologous Tumor Infiltrating Lymphocytes (Lifileucel) for Patients with Asymptomatic Melanoma Brain Metastases
Duration of support:	07/2022 – 06/2025
Name of Principal Investigator:	Betof Warner
The major goals of this project are:	Complete a pilot study to rigorously define the feasibility of manufacturing and successfully treating patients with melanoma brain metastases (MBM) with lifileucel. This will be the first study to specifically evaluate lifileucel for active MBM. My lab is performing extensive correlative analyses on blood and cerebrospinal fluid to enhance mechanistic understanding of the baseline tumor microenvironment of MBM and immunologic and genomic changes during the course of TIL therapy.

Award Source:(funding agency - federal, foundation, industry; type of grant)*	Melanoma Research Foundation Career Development Award
Project title:	A Pilot Trial of Autologous Tumor Infiltrating Lymphocytes (Lifileucel) for Patients with Asymptomatic Melanoma Brain Metastases
Duration of support:	09/2022 – 08/2024
Name of Principal Investigator:	Betof Warner
The major goals of this project are:	Complete a pilot study to rigorously define the feasibility of manufacturing and successfully treating patients with melanoma brain metastases (MBM) with lifileucel. This will be the first study to specifically evaluate lifileucel for active MBM. My lab is performing extensive correlative analyses on blood and cerebrospinal fluid to enhance mechanistic understanding of the baseline tumor microenvironment of MBM and immunologic and genomic changes during the course of TIL therapy.

Award Source:(funding agency - federal, foundation, industry; type of grant)*	Imaging and Radiation Sciences Program Seed Grant
Project title:	Imaging and Radiation Sciences Program (IMRAS)
Duration of support:	09/2021 - 08/2023
Name of Principal Investigator:	Betof Warner
The major goals of this project are:	The efficacy of proton craniospinal irradiation plus immune checkpoint blockade in melanoma leptomeningeal disease (LMD)- identifying genomic, immune, and microenvironmental biomarkers predictive of clinical benefit

Award Source:(funding agency - federal, foundation, industry; type of grant)*	Iovance Biotherapeutics
Project title:	A Pilot Trial of Autologous Tumor Infiltrating Lymphocytes (Lifileucel) for Patients with Asymptomatic Melanoma Brain Metastases
Duration of support:	11/2022– 11/2025
Name of Principal Investigator:	Betof Warner
The major goals of this project are:	The goal of this project is to complete a pilot study to rigorously define the feasibility of manufacturing and successfully treating patients with melanoma brain metastases (MBM) with lifileucel. This will be the first study to specifically evaluate lifileucel for active MBM. Establishing feasibility and safety of this approach could rapidly lead to larger phase II efficacy and combination trials, which have the potential to change treatment paradigms and improve outcomes from this dreaded complication of melanoma.

Completed Research Support

NIH- K12 Paul Calabresi Career Development Award for Clinical Oncology 9/2022-2/2023

Project Title: A Pilot Trial of Autologous Tumor Infiltrating Lymphocytes (Lifileucel) for Patients with Asymptomatic Melanoma Brain Metastases
PI: Allison Betof Warner, MD, PhD
Description: First study to specifically evaluate lifileucel for active melanoma brain metastases.

MSK MIND

Project Title: Defining immunologic factors associated with response or toxicity after checkpoint blockade
PI: Margaret Callahan, MD, PhD
Role: co-Investigator
Sponsor: MSK MIND
Description: AIM 1. Use pre-treatment peripheral blood markers to predict toxicity to ICB. AIM 2. Test the validity of our novel response biomarker in a pan cancer population . AIM 3. Characterize the pharmacodynamic effects of ICB and relationship to toxicity and response

MSKCC IRB #19-234 2019-2020

Project Title: A Dose Escalation and Expansion Study of TRX518 in Combination with Cyclophosphamide Plus Avelumab in Advanced Solid Tumors
PI: Allison Betof Warner, MD, PhD
Sponsor: Leap Therapeutics
Description: Funding to support clinical trial costs of phase 1b/2a clinical trial and correlative analyses

Young Investigator Award, Conquer Cancer Foundation of ASCO 7/1/2018-6/30/2019

Project Title: Exercise Regulation of Immune Activation and Response in Cancer: Implications for Immunotherapy
PI: Allison Betof Warner, MD, PhD
Source: Conquer Cancer Foundation of ASCO
Description: Funding primarily for salary support for pre-clinical investigations as a Medical Oncology fellow