

Adi Diab, M.D.

Associate Professor Department of Melanoma Medical Oncology



July 27, 2021

Dear SITC Young Investigator Award Committee:

I am delighted to write this letter of support for Jamie S. Lin, M.D. who is submitting a Young Investigator Award abstract titled "Tertiary Lymphoid Structure Signature Detected in Immune Checkpoint Inhibitor Associated Renal Immune Related Adverse Events" for the 2021 Society for Immunotherapy of Cancer conference. Dr. Lin is an Assistant Professor in the Section of Nephrology at the University of Texas MD Anderson Cancer Center (MDACC). Importantly she is an onconephrologist and early career NIH K08 awarded physician-scientist with a translational research focus in immune checkpoint inhibitor (ICI) associated nephrotoxicity.

I am an Associate Professor in the Department of Melanoma Medical Oncology and Co-Chair of Immune Toxicity Task Force for Management of Immune-related Toxicities at MD Anderson. My clinical and research experience is focused on developing new Immunotherapeutic Strategies that will improve clinical outcomes in patients. I currently lead multiple clinical trials involving novel immune modulator agent with Melanoma. In addition, I am leading a program for Interventional Immunotherapy that was established to develop intratumoral therapeutic and tumor vaccination strategies in combination with Systemic therapy; designed to improve clinical outcome and allow better understanding of the dynamics of each patient's immune response to the tumor.

I have known Dr. Lin for more than four years – she is an exceptionally smart and dedicated young physician-scientist. Dr. Lin had previously completed her general nephrology fellowship at the University of Pennsylvania as a NIH T32 and F32 research scholar before coming to MD Anderson as an onco-nephrology fellow. During her training at MD Anderson she developed a clinical interest in caring for patients with ICI-associated renal immune related adverse events (irAEs) and recognized early on that nephrologists would care for an increasingly important patient population with adverse effects from novel immuno-oncology (IO) therapies. After Dr. Lin joined faculty on April 1, 2019, she used her research training and onco-nephrology expertise to initiate a new translational research focus to investigate ICI-associated nephritis. To those of us who have seen the emergence of ICI-associated immunotoxicites over the last several years, ICI-nephritis is a largely under-recognized complication of immunotherapy associated with significant morbidity and mortality in our patients. This current project is just one of many ICI-nephritis endeavors that Dr. Lin is currently leading.

While the conception of this project was an idea that I had initially formulated with the support of Dr. Ala Abudayyeh (onco-nephrologist and corresponding author), it is Dr. Lin who has led the execution of this project from start to finish; including data collection and assembly, data analysis and interpretation, and abstract writing. I merely provided her with the raw data. From the beginning I was impressed by Dr. Lin's work ethics and thoroughness. She reviewed all the cases, designed the comparisons, and ensured the samples met quality control metrics before analyzing any data. Although Dr. Lin is not an oncologist, immunologist, or expert in gene expression data analysis, in a short period



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of time she mastered the data sets and made a critical observation which led to the fundamental premise of this groundbreaking abstract. Dr. Lin astutely noted that there was an abundance of T and B cell associated genes in ICI-AIN and several differentially expressed genes associated with cytotoxicity and inflammation. After thoughtful contextualization of the data and thorough review of the literature, she hypothesized that these observations might be associated with tertiary lymphoid structures (TLSs) and confirmed the presence of TLS signatures in the ICI-AIN group. Interestingly, this signature was not present in the drug-AIN group. The depth of Dr. Lin's data analysis and interpretation is a clear example of her intellectual bandwidth and natural talent for research. Her abstract presents several new findings in ICI-AIN that have not been previously reported including: 1) presence of TLS signatures in irAEs, 2) absence of Th17 associated genes in ICI-AIN, 3) detection of TNF signaling in ICI-AIN, and 4) distinct mechanistic differences in ICI-AIN compared with drug-AIN. We believe the findings of this work are exciting and will lead to several additional investigations into understanding irAEs.

In summary, Dr. Lin is an extremely talented young investigator and an exceptional onco-nephrologist who has the rare ability to translate clinical observations to basic research focused on improving the quality of patient care. I believe we need more innovative thinkers like Dr. Lin to help us as oncologist cure cancer in our patients. I hope this letter indicates my sincere enthusiasm for Dr. Jamie S. Lin's Young Investigator Award SITC abstract application.

Sincerely,

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