OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: TANG, CHIH-HANG Anthony

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-5097-5709

Position Title: Assistant Professor of Oncology

Organization and Location: Houston Methodist Academic Institute, Houston, Texas, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
The Wistar Institute, Philadelphia, Pennsylvania, United States	Postdoctoral Fellow	11/2014	07/2017	Immunology & Biochemistry
H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, United States	Postdoctoral Fellow	02/2012	10/2014	Immunology & Biochemistry
Brandeis University, Waltham, Massachusetts, United States	Doctor of Philosophy (PHD)	08/2005	02/2012	Neuroscience
National Defense Medical Center, Taipei, Not Applicable, N/A, Taiwan	DOCTOR OF MEDICINE	07/1998	07/2005	Medicine

Appointments and Positions

2020 - present	Assistant Professor of Oncology , Houston Methodist Academic Institute, Houston, Texas, United States
2021 - present	Assistant Professor of Cancer Biology in Medicine, Weill Cornell Medical College, Cornell University, New York, New York, United States
2021 - present	Affiliate Assistant Professor, Texas A&M University College of Medicine, Houston, Texas, United States
2017 - 2020	Staff Scientist, Wistar Institute, Philadelphia, Pennsylvania, United States
2014 - 2017	Postdoctoral Fellow, The Wistar Institute, Philadelphia, Pennsylvania, United States
2012 - 2014	Postdoctoral Fellow, H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, United States
2006 - 2012	Graduate Student, Brandeis University, Waltham, Massachusetts, United States
2005 - 2006	Medical Officer, Republic of China Air Force, Hisnchu, Not Applicable, N/A, Taiwan
2003 - 2005	Medical Intern, Taipei Veterans General Hospital, Taipei, Not Applicable, N/A, Taiwan

Products

Products Closely Related to the Proposed Project

1. Lee AC, Pingali SR, Pinilla-Ibarz JA, Atchison ML, Koumenis C, Argon Y, Thomas-Tikhonenko A, De Trez C, Hu CA, Tang CA. Loss of AID exacerbates the malignant progression of CLL. Leukemia. 2022 Oct;36(10):2430-2442. PubMed Central PMCID: PMC9522595.
2. Tang CA, Lee AC, Chang S, Xu Q, Shao A, Lo Y, Spalek WT, Pinilla-Ibarz JA, Del Valle JR, Hu CA. STING regulates BCR signaling in normal and malignant B cells. Cell Mol Immunol. 2021 Apr;18(4):1016-1031. PubMed Central PMCID: PMC8115116.
3. Tang CH, Chang S, Hashimoto A, Chen YJ, Kang CW, Mato AR, Del Valle JR, Gabrilovich DI, Hu CC. Secretory IgM Exacerbates Tumor Progression by Inducing Accumulations of MDSCs in Mice. Cancer Immunol Res. 2018 Jun;6(6):696-710. PubMed Central PMCID: PMC5984713.
4. Tang CH, Ranatunga S, Kriss CL, Cubitt CL, Tao J, Pinilla-Ibarz JA, Del Valle JR, Hu CC. Inhibition of ER stress-associated IRE-1/XBP-1 pathway reduces leukemic cell survival. J Clin Invest. 2014 Jun;124(6):2585-98. PubMed Central PMCID: PMC4038575.
5. Tang CH, Chang S, Paton AW, Paton JC, Gabrilovich DI, Ploegh HL, Del Valle JR, Hu CC. Phosphorylation of IRE1 at S729 regulates RIDD in B cells and antibody production after immunization. J Cell Biol. 2018 May 7;217(5):1739-1755. PubMed Central PMCID: PMC5940306.

Other Significant Products Highlighting Contributions to Science

1. Tang CH, Hu CC, Wei CW, Wang JJ. Synergism of Rana catesbeiana ribonuclease and IFN-gamma triggers distinct death machineries in different human cancer cells. FEBS Lett. 2005 Jan 3;579(1):265-70. PubMed PMID: 15620724.
2. Tang CH, Hinteregger E, Shang Y, Rosbash M. Light-mediated TIM degradation within Drosophila pacemaker neurons (s-LNvs) is neither necessary nor sufficient for delay zone phase shifts. Neuron. 2010 May 13;66(3):378-85. PubMed Central PMCID: PMC3024912.
3. Tang CH, Zundell JA, Ranatunga S, Lin C, Nefedova Y, Del Valle JR, Hu CC. Agonist-Mediated Activation of STING Induces Apoptosis in Malignant B Cells. Cancer Res. 2016 Apr 15;76(8):2137-52. PubMed Central PMCID: PMC4873432.
4. Xie H, Tang CH, Song JH, Mancuso A, Del Valle JR, Cao J, Xiang Y, Dang CV, Lan R, Sanchez DJ, Keith B, Hu CC, Simon MC. IRE1α RNase-dependent lipid homeostasis promotes survival in Myc-transformed cancers. J Clin Invest. 2018 Apr 2;128(4):1300-1316. PubMed Central PMCID: PMC5873889.
5. Shao A, Xu Q, Spalek WT, Cain CF, Kang CW, Tang CA, Del Valle JR, Hu CA. Development of Tumor-Targeting IRE-1 Inhibitors for B-cell Cancer Therapy. Mol Cancer Ther. 2020 Dec;19(12):2432-2444. PubMed Central PMCID: PMC7773214.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

Certified by TANG, CHIH-HANG Anthony in SciENcv on 2026-06-26 12:50:41

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: TANG, CHIH-HANG Anthony

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-5097-5709

Position Title: Assistant Professor of Oncology

Organization and Location: Houston Methodist Academic Institute, Houston, Texas, United States

Personal Statement

I am an Assistant Professor of Cancer Biology at the Houston Methodist Academic Institute. My current research focuses on elucidating the roles of B cells in regulating anti-breast cancer immunity within the tumor microenvironments. After I finished my clinical medical training and military service in Taiwan, I came to the US and have received extensive research training in molecular cell biology, neuroscience, biochemistry, immunology and mouse genetics, as documented in my publications. While I was a medical student, I performed research on the tumor cytotoxicity effect of a ribonuclease (RC-RNase) from the oocytes of local bullfrogs in Taiwan. During my Ph.D. training with Dr. Michael Rosbash at Brandeis University, I studied the Drosophila brain neural circuits that control circadian rhythms using genetic and biochemical approaches. My postdoctoral studies in Dr. Chih-Chi Andrew Hu's laboratory focus on investigating the functions of the IRE-1/XBP-1s pathway of the endoplasmic reticulum (ER) stress response and the IRE-1-associated protein, STING, in normal and malignant B cells. Together with my collaborators in medicinal chemistry, I successfully developed a new small molecule inhibitor, which we named B-I09, to suppress the expression of XBP-1s in B cell-derived leukemia, lymphoma and multiple myeloma in vitro and in vivo. Since becoming independent, I started to investigate how secretory IgM activates the immunosuppressive functions of MDSCs. My studies have led to the hypothesis that activation of STING in B cells can engage SEL1L/HRD1 endoplasmic reticulum associated degradation (ERAD) to downregulate the BCR signaling, contributing to the slow growth of breast cancer. To test this hypothesis, I have successfully generated a novel mouse model in which STING is constitutively activated in B cells only. In this proposal, I aim to firmly establish that STING can indeed engage SEL1L and HRD1 to result in ERAD of the BCR in B cells within the breast cancer microenvironment to slow down breast cancer growth. Based on published data and my preliminary data showing that breast cancer cells express XBP-1s to support their growth, I propose to test whether combining the inhibitor of XBP-1s (B-I09) with 'inhibitors' of the BCR signaling (using a STING agonist or a Bruton's tyrosine kinase inhibitor) can be effective therapeutic strategies for breast cancer. I have the eagerness to become a successful scientist in my research field, and I also have the expertise and leadership necessary to successfully carry out the proposed studies in this grant application.

Honors

2025	NIH Competitiveness Award, Houston Methodist Academic Institute
2018	Poster Award, EACR Conference
2017	Travel Award to EMBO Workshop To-B or not to-B: B-cells in health and disease , EMBO
2016	Travel Award to the Xth International Workshop, German CLL Study Group
2010	Trainee Research Award, Society for Research on Biological Rhythms
2008	Excellent Research Presentation Award, Osaka University
2008 - 2011	Samuel Goldwyn Endowed Fellowship, Brandeis University
2002	Travel Award, Shih-Yuan Foundation, Taiwan
2002	Undergraduate Research Project Award, National Science Council, Taiwan
2001	Undergraduate Research Project Award, National Science Council, Taiwan

Contributions to Science

1. My earliest research works started while I was a medical student working in the laboratory of Dr. Jaang-Jiun Wang, who was then the chairman of the Department of Anatomy and Biology at the National Defense Medical Center in Taiwan. Together with postdocs and graduate students in his lab, I studied death responses and mechanisms of cancer cells in response to an anti-cancer ribonuclease from local bullfrogs (RC-RNase). My work contributed to the understanding of that the anti-tumor activity of RC-RNase is associated with the differentiation status of the tumor cells, and that RC-RNase synergizes with IFN-γ to induce apoptosis in many cancer cell lines.

2. I performed my Ph.D. work in the laboratory of Dr. Michael Rosbash, who is a Howard Hughes Medical Institute investigator known for his discovery of the molecular mechanisms that regulate circadian rhythms in Drosophila. My research at the Rosbash laboratory focuses on the identification of the neural circuits in the fly's brain that underlies the circadian rest-activity cycle as well as the relationship between the pacemaker of Drosophila circadian clock and the light-dark cycle. I challenged the canonical cell-autonomous molecular model of light-induced phase shifting in Drosophila by showing the unique degradation pattern of TIMELESS, a core clock protein, in different clock neurons and its relationship with the photoreceptor CRYPTOCHROME in the fly brain. My research provided the first quantitative assessment of the Drosophila brain clock neuron in response to light stimulation and demonstrated a systems view of light-mediated phase shifting.

3. My postdoctoral work focused on investigating the role of the endoplasmic reticulum (ER) stress response in B cell leukemia. I generated an innovative CLL mouse model to show that deletion of the XBP-1 gene can delay CLL progression in mice, I also developed a novel IRE-1 RNase inhibitor, B-I09, in collaboration with medicinal chemists. This inhibitor successfully induces CLL regression in mice and apoptosis of primary human CLL cells. B-I09 also pharmacologically synergizes with an FDA-approved BTK inhibitor, ibrutinib, to exert strong cytotoxicity on a wide variety of B-cell malignancies, including leukemia, lymphoma and multiple myeloma. Later I contributed to recent development of novel potent IRE-1 inhibitors, in which we modified the functional aldehyde group to allow for the emission of blue fluorescence by the inhibitors, useful for tracking the inhibitors in vitro and in mice. I also discovered that phosphorylation of serine 729 on IRE-1 can lead to activation of the regulated IRE-1-depdent decay (RIDD) of the mRNAs of secretory immunoglobulin μ heavy chains. Based on this important discovery, I can trigger RIDD in B and CLL cells to downregulate the serum levels of secretory IgM in mice, contributing to the inhibition of myeloid-derived suppressor cells (MDSCs) and reactivation of anti-CLL T cell response.

4. By studying the interacting proteins of IRE-1, I discovered that IRE-1 interacts with STING, and demonstrated that activation of STING can induce rapid apoptosis of cancerous B cells in vitro and in vivo. My work showed that STING agonists can be used to treat B cell cancers, such as leukemia, lymphoma and multiple myeloma. Later I also discovered that activated STING can specifically degrade membrane-bound IgM, Igα, and Igβ via SEL1L/HRD1-mediated ER-associated degradation (ERAD), and B cell-specific STING knockout mice showed that STING knockout B cells respond to activation by transducing stronger BCR signals than their STING wild-type counterparts. Since both human and mouse CLL cells downregulated the expression of STING, I generated a STING-deficient CLL mouse model and showed that STING-deficient CLL cells were indeed more responsive to BCR activation than their STING-proficient counterparts. These results revealed a novel B cell-intrinsic role of STING in negatively regulating BCR signaling in both normal and malignant B cells. In collaboration with Dr. Xue-Zhong Yu, we have shown that STING in antigen-presenting cells can dictate T-cell allogeneic responses and validated that STING is a potential therapeutic target for controlling graft-versus-host disease (GVHD) after allogeneic hematopoietic cell transplantation. Recently, we also showed that RIDD promotes host dendritic cell survival and alloreactivity and contributes to GVHD.

5. Importantly, I am a team player and I understand the importance of collaborations in research. (1) I participated in the analysis of the anti-cancer activity of synthetic lucentamycin A, a marine-derived natural product, in collaboration with Dr. Juan Del Valle's group at the University of South Florida. (2) I worked with Dr. Christian Schlieker's group at Yale University to study how TorsinA, an important ER-resident protein, is proteolytic cleaved within the ER membrane in response to ER stress and B cell differentiation, potentially by a site-specific protease. (3) I collaborated with Dr. Xue-Zhong Yu's group at the Medical University of South Carolina to show that genetic deletion of the XBP-1 gene in B cells and pharmacological inhibition of XBP-1 using my B-I09 inhibitor is useful in controlling the development of chronic graft-versus-host disease while preserving the graft-versus-leukemia activity of the grafts. (4) I also worked closely with Dr. M. Celeste Simon's group at the University of Pennsylvania to discover that my B-I09 inhibitor is specifically useful in killing cMyc-overexpressing B cell lymphoma and other types of cancer through suppressing stearoyl-CoA-desaturase 1 (SCD1).

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