

2021 Tang Fellowship in Cancer Immunotherapy Progress Report

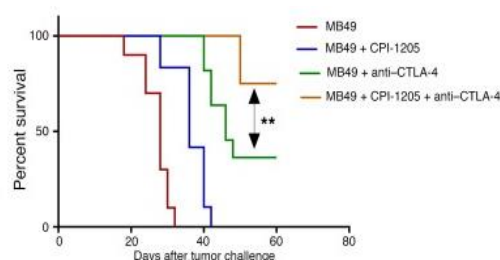
I am pleased to report that the funds for the Tang Fellowship have been used for the recruitment of Sangeeta Goswami, M.D., Ph.D. as the first physician-scientist with a full tenure-track position in the MD Anderson Department of Immunology. Dr. Goswami has very strong background both in fundamental immunology and clinical cancer research. Her recruitment as the Department of Immunology's first physician-scientist (with a clinical appointment in Genitourinary Medical Oncology) is key to the department's strategy and the mission of MD Anderson to end cancer. She was formally hired as a full member of the department in February 2021.



Sangeeta Goswami, MD, PhD
Assistant Professor
Immunology
Genitourinary Medical Oncology

Dr. Goswami received a Bachelor of Medicine and Bachelor of Surgery (M.B.B.S.) degree in 2001 from Gauhati Medical College and then trained as a Junior Resident in Internal Medicine at Sacred Home Hospital and Research Center in India. From 2004 to 2009 she was a student in the Ph.D. program in Immunology at Baylor College of Medicine, where she worked in the laboratory of Dr. Farrah Kheradmand. She showed that autoimmunity to elastin plays a critical role in tobacco-induced emphysema, and further demonstrated that the protease MMP7 regulates T cell function in mouse models of asthma. These findings were published as second- and first-authorships in *Nature Medicine* (Lee, Goswami et al. 2007) and *Nature Immunology* (Goswami, Angkasekwina et al. 2009), respectively, and she received a Ph.D. degree in 2009. Her postdoctoral work in Dr. Jonathan Kurie's laboratory revealed a role of tumor microRNA in tumor evasion and work was published in *Nature Communications* (Chen, Gibbons et al. 2014). Subsequently, she completed her Internal Medicine Residency Program from the

University of Pittsburgh Medical Center and joined MD Anderson Cancer Center for a Medical Oncology Fellowship. She graduated from the Medical Oncology fellowship in June 2016 with the Waun-Ki Hong distinguished award for basic sciences. Dr. Goswami performed outstanding research as an advanced scholar under the mentorship of Dr. Padmanee Sharma. She made an interesting observation that CTLA-4 blockade increases a histone-modifying enzyme (EZH2) in T cells. She subsequently delineated how EZH2 could modulate T cell responses in response to anti-CTLA-4 therapy (Goswami, Apostolou et al. 2018). The pre-clinical study led to a clinical trial where the combination of EZH2 inhibition and anti-CTLA-4 are being tested (NCT04388852, Co-PI: Goswami). She has continued to conduct excellent cancer immunology research resulting in two remarkable first-author publications that identified ARID1A mutation and CXCL13 expression within tumors as predictive markers for response to immune checkpoint therapy (Goswami, Chen et al. 2020) and showed that CD73 is a new drug target for rational glioblastoma combinatorial therapy (Goswami, Walle et al. 2020). Dr. Goswami has demonstrated great creativity in her research, integrating the fields of epigenetics and immunology, a combination crucial in further delineating the mechanisms by which immune cells are activated, exhausted, and repressed. She has recognized the benefit of collaborative science and has set up important collaborations for successful completion of her projects.



Addition of EZH2 inhibitor CPI-1205 significantly increases anti-tumor effect of anti-CTLA4 therapy in tumor-bearing mice (Goswami, Apostolou et al. 2018).

Candidates for the Tang Fellowship were evaluated by a committee consisting of Dr. Jeffrey Mouldrem, Dr. Padmanee Sharma, and me. Dr. Goswami was unanimously selected as the awardee (2-0, with Dr. Sharma abstaining due to conflict). Her strong training background, excellent publication record, and history of developing collaborative relationships were critical factors in her selection.

I will directly mentor Dr. Goswami, whose lab and office are positioned in the same building as my own. During the first two years of her mentoring program, we will meet formally on a monthly basis and as needed. A strong emphasis will be placed on further equipping Dr. Goswami to secure long-term NIH funding to support her research endeavors, drawing upon my experience in over 30 years of continuous NIH funding. It is expected that Dr. Goswami will secure an R01 within the first two years of her appointment. When necessary, I can facilitate development of collaborations with the clinical and basic science partners most relevant to Dr. Goswami's work through the Immunotherapy Platform.

Dr. Goswami has set forth a research plan that will complement existing work in the Immunology department and related basic science and clinical research programs here at MD Anderson. Specifically, she seeks to build upon her previous work that showed that inhibition of the transcription factor EZH2 could increase the anti-tumor efficacy of CTLA-4 blockade, by further characterizing the epigenetic variation that differentiates patients and cancers that respond to immune checkpoint therapy from those that do not. I strongly support Dr. Goswami's research plan and note that it is distinct from continuing work in the lab of her former mentor Dr. Sharma.

I am very proud of our selection of Dr. Goswami to receive the Tang funds. I cannot think of a more worthy recipient as a physician, a scientist, or a person. These funds have been instrumental in starting to set up her laboratory, and I fully expect to see exciting scientific advances coming from that laboratory in the coming years. I want to thank the Tang Prize Foundation for their generous support and let you know that I am confident that you will be proud of our Tang Fellow in Cancer Immunotherapy Dr. Sangeeta Goswami.

REFERENCES

- Chen, L., D. L. Gibbons, S. Goswami, M. A. Cortez, Y. H. Ahn, L. A. Byers, X. Zhang, X. Yi, D. Dwyer, W. Lin, L. Diao, J. Wang, J. Roybal, M. Patel, C. Ungewiss, D. Peng, S. Antonia, M. Mediavilla-Varela, G. Robertson, M. Suraokar, J. W. Welsh, B. Erez, Wistuba, II, L. Chen, D. Peng, S. Wang, S. E. Ullrich, J. V. Heymach, J. M. Kurie and F. X. Qin (2014). "Metastasis is regulated via microRNA-200/ZEB1 axis control of tumour cell PD-L1 expression and intratumoral immunosuppression." *Nat Commun* **5**: 5241.
- Goswami, S., P. Angkasekwinai, M. Shan, K. J. Greenlee, W. T. Barranco, S. Polikepahad, A. Seryshev, L. Z. Song, D. Redding, B. Singh, S. Sur, P. Woodruff, C. Dong, D. B. Corry and F. Kheradmand (2009). "Divergent functions for airway epithelial matrix metalloproteinase 7 and retinoic acid in experimental asthma." *Nat Immunol* **10**(5): 496-503.
- Goswami, S., I. Apostolou, J. Zhang, J. Skepner, S. Anandhan, X. Zhang, L. Xiong, P. Trojer, A. Aparicio, S. K. Subudhi, J. P. Allison, H. Zhao and P. Sharma (2018). "Modulation of EZH2 expression in T cells improves efficacy of anti-CTLA-4 therapy." *J Clin Invest* **128**(9): 3813-3818.
- Goswami, S., Y. Chen, S. Anandhan, P. M. Szabo, S. Basu, J. M. Blando, W. Liu, J. Zhang, S. M. Natarajan, L. Xiong, B. Guan, S. S. Yadav, A. Saci, J. P. Allison, M. D. Galsky and P. Sharma

(2020). "ARID1A mutation plus CXCL13 expression act as combinatorial biomarkers to predict responses to immune checkpoint therapy in mUCC." Sci Transl Med **12**(548).

Goswami, S., T. Walle, A. E. Cornish, S. Basu, S. Anandhan, I. Fernandez, L. Vence, J. Blando, H. Zhao, S. S. Yadav, M. Ott, L. Y. Kong, A. B. Heimberger, J. de Groot, B. Sepesi, M. Overman, S. Kopetz, J. P. Allison, D. Pe'er and P. Sharma (2020). "Immune profiling of human tumors identifies CD73 as a combinatorial target in glioblastoma." Nat Med **26**(1): 39-46.

Lee, S. H., S. Goswami, A. Grudo, L. Z. Song, V. Bandi, S. Goodnight-White, L. Green, J. Hacken-Bitar, J. Huh, F. Bakaeen, H. O. Coxson, S. Cogswell, C. Storness-Bliss, D. B. Corry and F. Kheradmand (2007). "Antielastin autoimmunity in tobacco smoking-induced emphysema." Nat Med **13**(5): 567-569.