Final Report on the Salk Institute Tang Foundation Prize Fellowship Program (2020-2021)

Program Director: Tony Hunter

The 2018 Tang Prize Foundation Grant to Tony Hunter was used to establish two one-year postdoctoral fellowships at the Salk Institute from January 1, 2020 - December 31, 2021. The Tang Prize Foundation Fellowships were advertised and selected through the annual Salk Institute internal postdoctoral fellowship competition run by the Fellowship Committee. The Tang Prize Foundation Fellowship competition was open to fellows of any nationality who were between years 1 and 3 of starting their position at the Salk Institute and working on cancer signaling mechanisms. The fellowship application was limited to two pages plus a CV, a letter of support from the fellow's mentor, and letters from two outside references. Two members of the Fellowship Committee reviewed each application scoring on a 1-5 scale. The candidate with the best score was selected as the Tang Prize Foundation Fellow in the 2020 and 2021 competitions. Each one-year fellowship provided $50,000 in salary support and a $5,000 laboratory allowance.

Year 1: Eight excellent applications were received, and Annelise Snyder in Susan Kaech's group was appointed to pursue a project to test the role of prostaglandin D2 (PGD2) receptor signaling in regulating cytotoxic T cell function in tumor immunity in pancreatic cancer. She showed that overexpression or global deletion of the PGD2-producing enzyme HPGDSTG in host cells, or pharmacological inhibition of the PGD2 receptors DP1 and DP2 had no effect on either tumor burden or immune infiltration into the tumor. She concluded that the generation of PGD2 in host cells does not change tumor outgrowth or tumor immune responses in the orthotopic PDAC models used in her studies. Unfortunately, her progress was limited since she suffered from COVID soon after she was appointed, and because her results were disappointingly negative, she did not publish a paper. However, she has stayed in science and after a short second postdoctoral fellowship at the Fred Hutchinson Cancer Center, she obtained a teaching position at Western Washington University, where she is now an Assistant Professor, running a small lab, teaching immunology and inspiring the next generation..

Year 2: Nine strong applications were received, and Helen McRae in Diana Hargreaves' group was appointed to investigate the molecular and functional role of the BAF SWI/SNF chromatin-remodeling complex in tumor-associated macrophages (TAMs), focusing on the role of the ARID1A subunit, which is one of the most commonly mutated genes in a variety of cancers. Using *Arid1a* knockout mouse bone marrow-derived macrophages, she found that deleting ARID1A leads to remodeling of the chromatin landscape in TAMs, and reprograms TAM transcription and cell surface protein expression to a more inflammatory state, including upregulated expression of interferon (IFN) α and IFN-γ inflammatory signatures. These changes may underly the improved response tumor-bearing $Arid1a^{f/f};LysM^{Cre}$ mice, which specifically lack Arid1a expression in macrophages, to immunotherapy. On the strength of her findings funded by the Tang Fellowship, she received a very prestigious external Cancer Research Institute (CRI) postdoctoral fellowship and is now in the process of writing up a nice story that will be submitted to a leading journal in 2025. The Tang Prize Foundation Fellowship will be acknowledged in this paper. Her ambition is to obtain an academic position and run a research laboratory.

Summary: In my view, this was a successful endeavor, and the Institute is very grateful to the Tang Prize Foundation for providing this much needed support for postdoctoral fellows, who represent the next generation of scientists. I am particularly pleased that two women were supported by this grant. In conclusion. I would recommend that other Tang Prize winners use their laboratory allowance in this manner.