

How to drug an un-druggable transcription factor for immunotherapy using trans-omics and preclinical tools?



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Hosted by Dr Andy Tan

Seminar Abstract

The recent advancements in immune checkpoint blockades and chimeric antigen receptor T-cell therapy have made it possible to achieve durable remissions in patients with refractory or seemingly incurable cancers. However, the emergence of drug resistances, the limited coverage of current immunotherapies and the complexity of tumor microenvironment call for additional and more effective therapeutic solutions. One such strategy is combination immunotherapy which may incorporate multiple means of anti-tumor therapies or disparate anti-tumor agents. Here we started from the fundamental regulatory mechanisms of one transcription factor, based on which we identified synergistic anti-tumor effects between a targeted therapy drug and an immune adjuvant. According to the in vitro biochemical and trans-omics findings, the immune adjuvant activated an inhibitory program that was unexpectedly unleashed by the targeted therapy drug, unlocking an immunoregulatory interferon signature response. In a murine model of subcutaneous melanoma, the combination treatment reprogramed the tumor microenvironment and significantly extended the survival of tumor-bearing animals. The therapeutic potentials of the unlocked responses in human patients with cutaneous melanoma were also examined using retrospective studies.

About the Speaker

Lei has recently joined the Immunology group in BTI as a Project Scientist after his Ph.D training and appointment as research assistant in National University of Singapore. His most recent work was on how chemotherapy drugs may modulate immune cell functions in vitro and in vivo during tumorigenesis and flu virus infection. He has been trained in molecular and cell biology disciplines, with hands-on experiences in various laboratory techniques, advanced high-throughput microarrays and animal models. With the platforms established by BTI and A*STAR, he intends to enrich the current pool of strategies and toolkits for cancer immunotherapies.