

Boosting Chimeric Antigen Receptor T cell therapy via a synthetic vaccine

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Date: 16 October 2023 (Monday)

Time: 10:00 a.m.

Venue: B5-211, 5/F, YEUNG

Abstract

Chimeric Antigen Receptor T cells (CAR T) are effective in hematologic malignancies, but strategies to augment their therapeutic impact especially in solid tumors are still needed. Here we demonstrate an approach to enhance CAR T function by vaccine-boosting donor cells through their chimeric receptor directly in vivo. Amphiphile CAR T ligand vaccine (amph-vax) were designed, which on injection trafficked to lymph nodes, decorated the surfaces of antigen presenting cells, and primed CAR T cells in the native lymph node microenvironment. Amph-vax boosting triggered massive CAR T expansion, increased donor cell polyfunctionality, and enhanced anti-tumor efficacy in multiple immunocompetent tumor models. Unexpectedly, in vivo vaccine boosting of CAR T cells triggered engagement of the endogenous immune system to circumvent antigen-negative tumor escape and more effectively treat established tumors with pre-existing antigenic heterogeneity. This process was accompanied by shifts in CAR T metabolism toward oxidative phosphorylation in CAR T cells and was critically dependent on CAR T-derived IFN- γ . Thus, vaccine boosting provides a clinically-translatable strategy to enhance CAR T cell therapy against solid tumors.

Biography

Dr. Ma obtained his PhD degree in biomedical sciences from Dr. Michael Green's lab at the University of Massachusetts Medical School in 2016. Following graduation, Dr. Ma continued his postdoctoral fellowship in Immunotherapy and Immune Engineering at Massachusetts Institute of Technology and Howard Hughes Medical Institute under the guidance of Dr. Darrell Irvine. During his fellowship, Dr. Ma developed a synthetic booster vaccine to enhance the Chimeric Antigen Receptor T cell therapy for solid tumors, and he was supported by American Cancer Society postdoctoral fellowship from 2019-2021. In 2022, Dr. Ma was appointed as an assistant professor in the department of Pathology and Laboratory Medicine at the University of Pennsylvania. Dr. Ma is also a member of the Raymond G. Perelman Center for Cellular and Molecular Therapeutics (CCMT) at the Children's Hospital of Philadelphia. Dr. Ma was awarded the NIAID new innovators award (DP2), W.W. Smith Charitable Trust award, Melanoma Research Alliance young investigator award, and Ivy foundation Translational Adult Glioma Award.