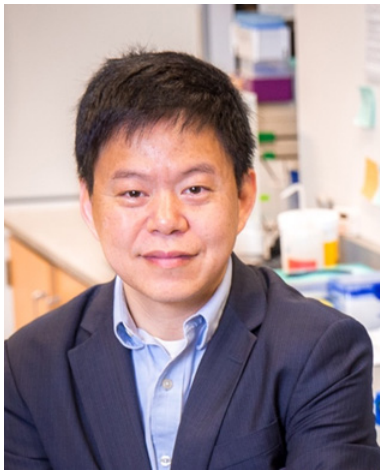
# CARNEGIE MELLON UNIVERSITY
# BME 2025 SPRING SEMINAR SERIES

## Ultrasound Control of Genetics/Epigenetics and Cellular Functions for Cancer Immunotherapy



### PRESENTED BY

**Peter Yingxiao Wang, Ph.D.**
Department Chair
Dwight C. and Hildagarde E. Baum Professor
Alfred E. Mann Dept. of Biomedical Engineering
University of Southern California

### SCHEDULE

**Doherty Hall (DH) 2315**

**Thursday,**
**January 23, 2025**
(11:00-12:00 PM)

Cell-based cancer immunotherapy is quickly emerging as a promising therapeutic intervention for cancer treatment. However, non-specific killing against healthy tissues (e.g. on-target/off-tumor effect) is a major hurdle for solid tumor treatment. Here we show that the genetics and cellular functions of chimaeric antigen receptor T cells (CAR-T cells) within tumors can be remotely controlled by focused ultrasound (FUS) via a CAR cassette under a controllable promoter. In mice with subcutaneous tumors, T cells with the inducible CAR and activated via FUS mitigated on-target off-tumor activity and enhanced the suppression of tumor growth, compared with the performance of standard constitutive CAR-T cells. We have also developed controllable on-switch gene cassettes to reprogram the target cancer cell by FUS. Viral vectors were used to deliver the gene cassettes into the tumor cells, which will be activated by FUS to produce synthetic antigens and then targeted by CAR T for cancer immunotherapy. We applied this system to successfully treat prostate cancer cells whose locally metastasized tumors are confined in space but intermingled with vessels and nerves. This local activation of engineered cells by FUS should allow a high precision and safety in eradicating tumors. Recently, we have integrated FUS and CRISPR technologies to remotely guide the focused genomic editing and regulations in vivo. Hence, this approach for immunotherapy should open new opportunities to integrate engineering physics with genetic medicine and lead to successful translation from fundamental science and engineering to cancer therapy and clinical applications.

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