COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
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Pharmaceutical Sciences Seminar Series

Monday, August 30, 2023
4:00pm
NCRC Building 10 South Atrium
Zoom Meeting

"Boosting Chimeric Antigen Receptor T cell therapy via a synthetic vaccine"

Presented by:

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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.

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