Chemical Engineering Thesis Defense

Investigating the Potential of F16BP-poly(I:C) Microparticle Associated CAR Therapies

School for Engineering of Matter, Transport and Energy

Michelle Halim
Advisor: Dr. Abhinav Acharya

Abstract

Adoptive cell therapies such as chimeric antigen receptor (CAR) modified immune cells are revolutionizing cancer treatment. These innovative immunotherapies have a promising outlook for liquid cancers, but lack robustness against solid tumors due to complex variables introduced by the tumor microenvironment (TME). Additionally, existing CAR-T cell treatments are commonly accompanied by toxic side effects. However, by grafting a CAR construct onto macrophages, a professional phagocytic innate cell which are actively recruited by solid tumors, the efficacy of this treatment is hoped to be extended beyond hematological malignancies. Moreover, the introduction of energy metabolite-based polymers (EMPs) to provide a sustained release of activating F16BP-poly(I:C) microparticles could address the toxicity complications that arise from CAR treatments.

It was determined that PLGA-F16BP-poly(I:C) microparticles allow for CAR-macrophage activation in vitro, though not in a sustained manner. Moreover, F16BP-poly(I:C) microparticles were better geared toward reducing cytokine related toxicity in vitro, with in vivo results remaining inconclusive. These findings suggest prioritization between macrophage activation or cytokine storm reduction would be required at this time, though additional future studies to explore variables such as CAR-macrophage sensitivity and the positive control could help refine this immunotherapy.

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