

Chemical Engineering Doctoral Defense

Engineering the Immune System using Metabolite-based
Polymers for Cancer Immunotherapy

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Abstract

Drug delivery has made a significant contribution to cancer immunotherapy and can have a tremendous impact on modulating immunometabolism, thereby affecting cancer outcomes. Notably, the science of delivery of cancer vaccines and immunotherapeutics, modulating immune cell functions has inspired development of several successful companies and clinical products. For example, cancer vaccines require activation of Dendritic Cells (DCs) and tumour associated macrophages (TAMs) through modulation of their energy metabolism (e.g., glycolysis, glutaminolysis, Krebs cycle). Similar to activated immune cells, cancer cells also upregulate glucose and glutamine transporters for proliferation and survival. Cancer cells having accelerated energy metabolism, which has been exploited as a target for various therapeutic studies. In the first strategy, an immunometabolism strategy based on sustained release of succinate from biomaterials, which incorporate succinate in the backbone of the polymer was developed. This study demonstrates that succinate-based polymeric MPs act as alarmins by modulating the immunometabolism of DCs and macrophages (M ϕ s) to generate robust pro-inflammatory responses for melanoma treatment in immunocompetent young as well as aging mice. In the second strategy, a biomaterial-based strategy was developed to deliver metabolites one-step downstream of the node where the glycolytic pathway is inhibited, to specifically rescue DCs from glycolysis inhibition. The study successfully demonstrated for the first time that the glycolysis of DCs can be rescued both in vitro and in vivo using a biomaterial strategy of delivering metabolites downstream of the inhibitory node. Overall, it is believed that advanced drug delivery strategies will play an important role in marrying the fields of immunometabolism and immunotherapy to generate translatable anti-cancer treatments.

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Zoom Link: <https://asu.zoom.us/j/3143472193>