MIT Chemical Engineering Department
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Antigen-Glycopolymer Conjugates: Engineering Immunity and Tolerance

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66-110

Abstract: Since Edward Jenner first used puss from a milkmaid's cowpox lesions to inoculate children against smallpox in the late 1700's, scientist have sought to develop antigen-specific immunotherapies (ASI)s that bias the immune response towards immunity (*i.e.,* vaccines), and, more recently, tolerance (*i.e.,* inverse vaccines). While considerable progress has been made in the development of vaccines that muster antibody-mediated immunity, clinical success of other ASIs, such as subunit vaccines that elicit T cell-mediated immunity and inverse vaccines capable of curing autoimmunity, have yet to match their pre-clinical promise. Here, I will introduce approaches that utilized synthetic polymeric glycosylations to target antigens and immunostimulatory adjuvants to specific subsets of antigen presenting cells for induction of antigen-specific immunity or tolerance. In the context of immunity, I will present a polymeric glycol-adjuvant that when conjugated to a malaria-specific protein induces a more robust antibody- and T cell-mediated immune response than malaria-specific protein formulated with the adjuvant used in the most clinical advanced malaria vaccine. In addition, I will highlight the development of another class of synthetic glycopolymers that, by targeting autoantigens to the liver's immunosuppressive microenvironment, elicit durable autoantigen-specific immunological tolerance marked by auto-reactive T cell anergy and functional regulatory T cells. Together, these antigen-glycopolymer conjugate platforms represent promising clinically-viable treatments for a variety of complex infections and autoimmune disorders.