Exploring the chemical composition of immune modulators and their conjugates: how targeted delivery creates anti-tumor immunity.

Immune-stimulating antibody conjugates (ISACs) represent a promising new therapeutic option for oncology. By harnessing mechanisms of the innate immune response, treatment with ISACs can lead to prolonged adaptive immune responses, effectively "teaching" the immune system to recognize and eliminate cancer cells. The innate immune system, which is governed by the interaction of chemical agonists with Toll-like receptors (TLRs) helps distinguish self from non-self. Antigen presenting cells (APCs), serve as the bridge between the innate and adaptive immune system. Activation of TLRs leads to activation of APCs, which in turn stimulate T cells, part of the adaptive immune response. By conjugating powerful TLR 7/8 small molecule agonists to tumor targeted antibodies, ISACs activate tumor resident APCs, driving uptake, processing and presentation of tumor neoantigens to T cells that mediate anti-tumor immunity. In this presentation, we will present structure activity relationships (SAR) for the chemical components of ISACs, such as conjugation chemistry, linker, and small molecule TLR agonist. We shall demonstrate how the use of ISACs leads to tumor clearance and the development of anti-tumor immunologic memory, providing strong rationale for this technology as a platform for cancer immunotherapy.