



Conference Proceeding

# New Immunomodulatory Targets and Next Generation Active Immune Checkpoint Control Immunotherapy

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**Presented:** 2018 Chinese Conference on Oncology. Shenyang, China, Aug. 17-19, 2018; **Published:** Oct. 17, 2018.

**Citation:** Jian Ni, New Immunomodulatory Targets and Next Generation Active Immune Checkpoint Control Immunotherapy. *Nano Biomed. Eng.*, 2018, 10(4): 306-307

## Abstract

Despite the success of immunomodulatory antibodies in immuno-oncology, challenges remain in expanding the target space, developing next-generation immune checkpoint inhibitors and active immune checkpoint control immunotherapy with improved efficacy and safety, and addressing innate and acquired resistance to immunotherapy. This presentation focuses the leading immunomodulatory pathways as well as therapeutic targets we have identified in B7 superfamily members: B7-H1 (PD-L1), B7-H2 (ICOSL), B7-H3 and B7-H4, TNF ligands and receptor superfamily: Blys (THANK), DR3 (TNFR25), DR4, DR5, DR6, GITR (AITR, TNFR18), GITRL, TR2, LIGHT, TR6, TL1A, RANK, TNFRSF19, RELT, TR1 (DcR3), DcR1 and DcR2, Siglecs family: Siglec 5, 7, 8, 9, 10, 11, and Galectin family: Galectin 9, 10, 11, 12.

### Next generation active immune checkpoint control immunotherapy

This talk will also discuss the next generation active immune checkpoint control immunotherapy based on a Specific Total Immune Remodeler Platform which have demonstrated the ability to activate and use the full potential of the patient's own immune system to eradicate cancer and is able to induce the killing of tumor target expressing cells by simultaneously activating all possible immunological pathways (humoral and cellular), thus, succeed in controlling all the relevant immune checkpoints that prevent the immune system from attacking and defeating cancer. Whereas current passive checkpoint specific immunotherapy lacks tumor cell specificity with the risk of massive autoimmune reactions, this new active therapy is totally tumor target specific.

### Role of galectins in tumors and immunotherapy

Galectins are glycan-binding proteins that contain one or two carbohydrate domains and mediate multiple biological functions. The abnormal expression of galectins is known to be linked to the development, progression and metastasis of cancers. Galectins also have diverse functions on different immune cells that either promote inflammation or dampen T cell-mediated immune responses, depending on cognate receptors on target cells. Thus, tumor-derived galectins can have bifunctional effects on tumor and immune cells. This talk focuses on the biological effects of galectin-1, galectin-3 and galectin-9 in various cancers and discusses anticancer therapies that target these molecules.

### The role Siglec receptors play in cancer immunity

Siglecs comprise a family of 15 members of sialic acid-binding receptors. Many Siglecs function as inhibitory receptors on innate and adaptive immune cells and may contribute to the attenuation of immune responses to tumors. Recent studies have identified mechanisms for immune evasion based on sialoglycan interactions with immunoregulatory Siglec receptors that are exploited by tumor

cells and microorganisms alike. vSiglecs are mostly inhibitory receptors similar to known immune checkpoints including PD-1 or CTLA-4 that are successfully targeted with blocking antibodies for cancer immunotherapy. Siglec 9 on neutrophils and Siglec 7 on NK cells are prominent examples of inhibitory Siglecs that can potentially dampen anti-tumor immunity. Siglecs have been best studied in the tumor context in animal models of cancer. Modulators of Siglec function are likely to be developed and investigated clinically in a cancer context over the next few years. I will summarize the known changes of sialic acids in cancer and the role Siglec receptors play in cancer immunity and also focus on potential ways to target these Siglec receptors or sialoglycans in order to improve anti-cancer immunity.

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