1187 ANTIBODY-LECTIN BISPECIFICS FOR GLYCO-IMMUNE CHECKPOINT BLOCKADE

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Background Despite the curative potential of checkpoint blockade immunotherapy, a majority of patients remain unresponsive to existing treatments. Glyco-immune checkpoints – interactions of cell-surface glycans with lectin, or glycan binding, immunoreceptors – have emerged as prominent mechanisms of immune evasion and therapeutic resistance in cancer.
Methods Here, we describe antibody-lectin chimeras (AbLecs), a modular platform for glyco-immune checkpoint blockade. AbLecs are bispecific antibody-like molecules comprising a tumor-targeting arm as well as a lectin 'decoy receptor' domain that directly binds tumor glycans and blocks their ability to engage lectin receptors on immune cells (figure 1).
Results AbLecs elicited tumor killing *in vitro* via macrophage phagocytosis and NK cell and granulocyte cytotoxicity, matching or outperforming combinations of monospecific antibodies with lectin-blocking or glycan-disrupting therapies. Furthermore, AbLecs synergized with blockade of the 'don't eat me' signal CD47 for enhanced tumor killing.
Conclusions AbLecs can be readily designed to target numerous tumor-associated antigens and glyco-immune checkpoint ligands, and therefore represent a new modality for cancer immune therapy.

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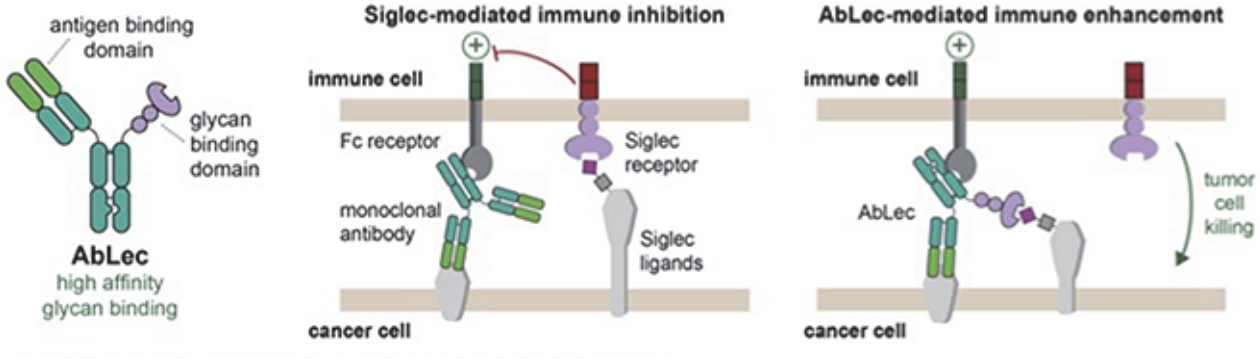

Abstract 1187 Figure 1 Antibody-lectin chimeras for glyco-immune checkpoint blockade

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