Docket #: S19-168

Alternative Immunotherapy for MYC-Driven Cancers by Targeting Glycans and Sialyltransferases

Technology summary

Tumor cells are decorated with glycans that inhibit immune function by binding to a family of receptors on immune cells known as Siglecs. The Siglecs are analogous to checkpoint proteins, such as PD1 and SIRPa, however their ligands are carbohydrates instead of proteins. The Siglecs are rapidly emerging as targets for immunotherapy given that patients routinely develop resistance to checkpoint inhibitors such as anti-PD1/anti-PD-L1. We identified a glycoprotein displayed by tumors that inhibits NK cell and macrophage activity by engaging a Siglec. We further defined a genetic signature comprising high MYC oncogene activity and accompanying expression of glycan biosynthetic machinery characteristic of highly malignant cancers that are amenable to glycan-targeted therapies. Targeting these glycans confers the ability to modulate the anti-cancer immune response. Additionally, inactivation of MYC-controlled glycans has demonstrated anti-tumor activity against leukemia in mouse models.

Applications

- Targeting sugars as novel immune checkpoints for cancer therapy
- Source of compounds which inhibit Siglec-ligand expression
- MYC-controlled sialosides as cancer biomarkers
- Inhibition of macrophage Siglec-glycan interactions by small molecules

Advantages

- Alternative to existing immune checkpoint targets by targeting glycans rather than proteins (e.g. PD1/PDL1)
- Activation of innate immunity and promoting anticancer defenses
- New approach for drug development of small molecules targeting enzyme activity

Patents

- Published Application: WO2021011377
- Published Application: 20220283165

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