Investigating the role of galectins and poly-LacNAc in cancer therapy

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Galectins are a family of immune checkpoint soluble proteins that bind β-galactoside-containing glycans on and within cells. These proteins are widely expressed in tumor microenvironments and have been shown to promote cancer growth and metastasis. Thus, galectins interaction with cancer cells is a new pathway for immune checkpoint regulation, equivalent to PD-1/PD-L1. While each member of the galectin family shares the ability to interact with poly N-acetyllactosamine [poly-LacNAc; $(Gal\beta1–4GlcNac)_n$], a tumor-associated carbohydrate antigen (TACA), the modes of interaction can vary significantly due to glycan modifications, such as the presence of terminal sialic acids. Understanding the binding specificities of human and mouse galectins to diverse poly-LacNAc glycans is essential for advancing cancer research, as it could provide insights into new therapeutic approaches.

Here, we demonstrate a broad screening of human and mouse galectins on glycan microarray in different conditions, illustrating great variability in binding between galectins. Moreover, removal of sialic acids by sialidase from a sialoglycan array increased galectin-glycan recognition for most of the galectins. Additionally, we examined the effect of sialic acid on binding in vitro. Altogether, these results may open new opportunities for immune checkpoint regulation, leading to novel cancer therapies.