Targeting tumor sialylation in combination with checkpoint inhibitors for cancer immunotherapy

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Abstract. Immunotherapy with immune checkpoint inhibitors (ICI) targeting PD-(L)1 and CTLA-4 has been successfully introduced into routine oncological practice. Despite the success of ICI, most patients derive no benefit from ICI therapy and new approaches are needed including combinations of ICI with new immunotherapeutics. Recent evidence demonstrated that hypersialylation of tumor cells and the extracellular tumor matrix is a targetable pathway of adaptive immune escape in cancer. Our current work shows that targeting hypersialylation in combination with PD-1 or CTLA-4 inhibition induces tumor control in different preclinical mouse models and T cell activation in primary patient tumor samples. While binding of hypersialylated ligands to inhibitory Siglecs that targeting hypersialylation in combination with PD-1 or CTLA-4 inhibition induces tumor control in different preclinical mouse models and T cell activation in primary patient tumor samples. However, the combined approach of targeting sialylation may represent a new immunotherapeutic modality and can be combined with PD-(L)1 and/or CTLA-4 inhibition for further clinical development.

References