Targeting Glycosylated PD-L1 in Triple-Negative Breast Cancer

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Triple negative breast cancer (TNBC) and immunotherapy

- **TNBC** accounts for approximately 15-20% of breast cancers in the United States, and is associated with reduced patient survival compared with other breast cancer subtypes.

- **Cancer immunotherapy** utilizes the patient’s immune system to treat cancer.

- **Immune checkpoint blockade**, one of the most promising cancer immunotherapies, has demonstrated success in other cancers such as melanoma and lung cancer, but remains limited in TNBC treatment.

- Therefore, there is an **unmet clinical need** for new immunotherapeutic strategies to treat the TNBC patients.
Checkpoint blockade activates anti-tumor immunity

(Wolchok and Chan, *Nature* 2014)
PD-L1 is glycosylated in cancer cells

(Nature Commune. 2016)
Glycosylation of PD-L1 is required for PD-1 interaction

(Cancer Cell 2018)
Targeting PD-L1 glycosylation enhances anti-tumor immunity

(A) gPD-L1-ADC

(B) Viability (%)

(C) Tumor volume (mm^2)

(D) Percent survival

(E) Immunofluorescence images of PD-L1 expression

(F) Color heatmaps with x-axis labels: IgG-ADC, gPD-L1, gPD-L1-ADC

(Cancer Cell 2018)
Glycosylated PD-L1 antibody-drug conjugate
To overcome PD-1/PD-L1 blockade resistance
1. PD-L1 is glycosylated in cancer cells.

2. Our glycosylated PD-L1 (gPD-L1) antibody induced internalization of PD-L1.

3. gPD-L1 antibody-drug conjugate (ADC) eradicated breast cancer with triple impact.

4. gPD-L1-ADC eradicated PD-1/PD-L1 therapy resistant breast cancer cells.
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Thank you for your attention!