**Introduction**

- TGFβ production by tumor cells and their microenvironment is a major mechanism used by tumors to evade immune recognition.

- Blockade of TGFβ has shown promise to promote anti-tumor activity, however, systemic blockade of TGFβ has also been associated with toxicity.

- We hypothesized that a targeted TGFβ2 bispecific antibody could selectively block the suppressive activity of TGFβ on specific cell populations and enhance their anti-tumor activity while avoiding the toxicity associated with systemic blockade.

1. XmAβ® heterodimeric Fc platform allows for well-behaved and easily manufactured bispecific antibodies

2. PDI x TGFβR2 selectively inhibits pSMA\(\text{D}\) induction in PD1-positive T cells

3. PDI x TGFβR2 promotes human T cell engraftment in mice

4. Using higher density CDS as the targeting anchor is predicted to increase avidity factor

5. CDS x TGFβR2 selectively and more potently inhibits pSMA\(\text{D}\) induction in a broader T cell population

6. PDI x TGFβR2 and CDS x TGFβR2 promote anti-tumor responses in solid tumor models

**Summary**

- PDI x TGFβR2 and CDS x TGFβR2 bispecific antibodies were engineered to selectively block TGFβ signaling on targeted cell populations and evaluated in vitro and in vivo.

- PDI x TGFβR2 and CDS x TGFβR2 showed high specificity blocking of TGFβ1/PD1 in high and CDS-TGFβ T cell populations, respectively.

- PDI x TGFβR2 and CDS x TGFβR2 were active in immune models, promoting T cell engagement and anti-tumor response while exhibiting additivity with PD1 blockade.

**PD1 x TGFβR2 and CDS x TGFβR2**

- 2. PD1 x TGFβR2 selectively inhibits pSMA\(\text{D}\) induction in PD1-positive T cells
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- 4. Using higher density CDS as the targeting anchor is predicted to increase avidity factor
- 5. CDS x TGFβR2 selectively and more potently inhibits pSMA\(\text{D}\) induction in a broader T cell population
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**PD1 x TGFβR2 and CDS x TGFβR2**

- PD1 x TGFβR2 and CDS x TGFβR2 bispecifics selectively block TGFβR2 on target-positive T cells, promote T cell activation, and elicit an anti-tumor response in solid tumors

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