DISCOVERY AND DEVELOPMENT OF COM701, A THERAPEUTIC ANTIBODY TARGETING THE NOVEL IMMUNE CHECKPOINT PVRIG

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BACKGROUND, METHODS

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MATERIALS AND METHODS: The binding of PVRIG, DNM1, TIGIT to PVRL2 and PVRIG was assessed by ELISA. Antibody discovery was performed using phage display and hybridoma platforms and antibodies against human PVRIG were screened by binding to PVRIG, disrupting PVRIG-PVRL2 interactions, and enhancing T cell activity in vitro. Expression of PVRIG was evaluated in healthy donor PBMCs and from dissociated human tumors by flow cytometry.

CONCLUSIONS:

PVRIG is a novel inhibitory T cell receptor that is expressed in the TME.

- Human phage display and human phage display.
- Antibodies screened for:
  - High affinity (KD < 1nM)
  - Ability to block PVRIG/PVRL2 binding
- In vitro enhancement of T cell activation
- COM701 selected as therapeutic lead

INDUCTION OF PVRL2 IN MELANOMA, LUNG, OVARIAN, COLON CANCER

Use of "Functional Homology" in absence of sequence similarity based on exon size, phase, and functional elements within exons.

COMBINED PVRIG AND TIGHT BLOCKADE INCREASES TIL ACTIVATION

INCREASED T CELL ACTIVATION AND REDUCED TUMOR GROWTH OBSERVED WITH PVRIG - MICE

PVRIG BLOCKING ANTIBODIES REDUCE TUMOR GROWTH AND INCREASE SURVIVAL IN COMBINATION WITH PD1 PATHWAY BLOCKADE

CONCLUSIONS:

- PVRIG is a novel inhibitory T cell receptor that is expressed in the TME.
- COM701 is a high affinity antagonistic antibody that is currently in preclinical development.
- COM701 increased T cell activation of resting and effector human T cells
- PVRIG mice display increased T cell function and reduced MC38 tumor growth
- A surrogate Ab to PVRIG reduced tumor growth in combination with PD-L1 antibody
- Antibody blockade of the PVRIG-PVRL2 interaction has the potential to be efficiently combined with PD1 or TIGIT blockade for enhancing anti-tumor immunity.