Using the 23andMe database, novel immuno-oncology (I/O) drug targets are identified as genetic variants with immunomodulatory effects on the risk for cancer and immune diseases, referred to as cell-to-cell signatures (23ME) gene associates with I/O signature (Figure 1).

**UBLP6**

- UL16binding protein (UBLP6) is a member of the stress-induced NKGD ligand (NKG6/ULBP) family that is upregulated on the surface of cancer cells and binds the immune activating NKGD receptor on T and NK cells.
- Cancer cells shed NKG2DLs, including ULBP6, from its surface via proteolytic release to evade immune recognition and killing, and soluble NKG2DLs are elevated in cancer patients.

**Results**

**UBLP6 is upregulated in squamous cell carcinomas and a subset of adenocarcinomas**

- Figure 3. UBLP6/2/5 are present on tumor cells and in circulation in cancer patients.

**Soluble UBLP6 is immunosuppressive even in the presence of membrane-bound NKG2DLs**

- Figure 5. Soluble UBLP6 suppresses immune cell activation and tumor cell growth.

**Fc-attenuated anti-UBLP6/2/5 blocks soluble UBLP6 to restore immune activation and tumor growth control**

- Figure 6. Fc-attenuated anti-UBLP6/2/5 antibody promotes activation of NK and CD8+ T cells.

**Activation of NKGD2 and FcγRIla is synergistic**

- Figure 7. FcγRIla activation is synergistic with NKGD2 activation and promotes ADCC.

**23ME-01473 (Fc-enhanced anti-UBLP6/2/5) induces superior anti-tumor immunity**

- Figure 8. Fc-enhanced anti-UBLP6/2/5 antibody, 23ME-01473, augments NK and T cell activation and tumor cell killing.

**23ME-01473 elicits enhanced tumor cell killing with anti-PD-1**

- Figure 9. 23ME-01473 and anti-PD-1 show increased tumor cell killing.

**Conclusion**


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**References**