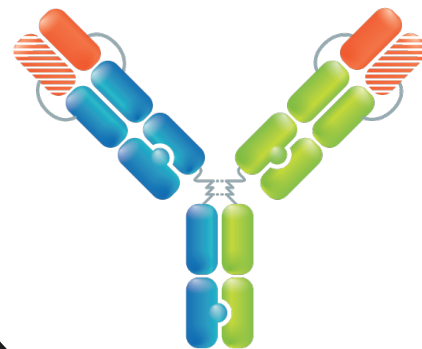




PROgrammed Tumor Engagement & Checkpoint/Co-stimulation Targeting (ProTECT™)



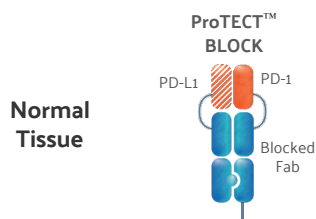
Tumor-Specific Immune Co-Stimulation in a single, transferable, conditionally-active design

With PROgrammed Tumor Engagement & Checkpoint/Co-stimulation Targeting, the ProTECT™ platform delivers multifunctional tumor-specific activity while simultaneously enhancing immune modulation through the conditional activity of a natural immunomodulatory pair such as PD-1/PD-L1.

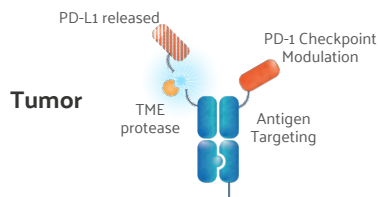
Therapeutics utilizing ProTECT™ have limited exposure and activity in normal healthy tissue, avoiding on-target, off-tumor toxicities. Once in the tumor microenvironment, proteases cleave and release one half of the functional block. This activates both the targeting antibody and the immunomodulatory function when and where it is needed.

How It Works

- Therapeutic activity is blocked in normal tissue to avoid on-target, off-tumor toxicities and improve pharmacokinetics
- Antibody is localized to the tumor through tumor associated antigen targeting
- Tumor-specific proteases cleave and release the blocking half of the immunomodulatory pair
- Both the targeting antibody and the remaining immunomodulatory checkpoint/co-stimulator become active
- The resulting activated multifunctional therapeutic enables immune modulation in concert with antigen binding to enhance potency
- Overall increase in therapeutic window through selective tumor activity and enhanced potency



- Antibody activity is masked to enhance tolerability by avoiding on-target, off-tumor toxicities
- Target mediated drug disposition is avoided
- Therapeutic window increased by reducing toxicity



- Tumor-specific proteases cleave and release the steric block to activate the biologic
- Multifunctional therapeutic enables immune modulation in concert with antigen binding to enhance potency
- Therapeutic window increased through selective tumor activity and enhanced potency

Right Place at the Right Time

The ProTECT™ platform is the first conditionally-active antibody technology that simultaneously addresses both ends of the therapeutic window, potentially reducing toxicity and increasing efficacy.

Unique features of ProTECT™:

- Tumor-specific activity via conditional blocking to reduce systemic toxicities
- Functional block adds co-stimulation or checkpoint modulation to enhance efficacy in the tumor
- Unique geometry enhances T cell bridging with tumor cells
- Increased avidity and target engagement with multispecific binding
- Beyond PD-1/PD-L1, additional blocking pairs are being used to provide alternative immunomodulatory approaches e.g. CTLA-4/CD80, CD28/CD80, PD-L1/CD80, ICOS/ICOSL, CD47/SIRPα
- Plug-and-play: Blocking approach is transferable with minimal engineering to apply to different antibodies