Abstract 2884

Optimized CD28 bispecific antibodies for targeted activation of T cells within the tumor microenvironment

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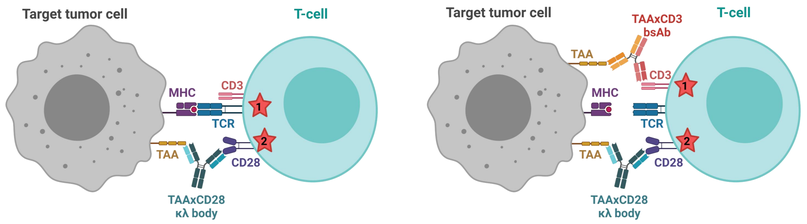
A brand of Novimmune SA

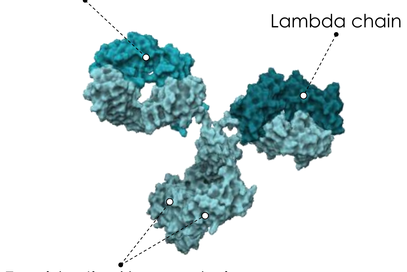
Background

- Tumor-targeted CD28 bispecific antibodies (bsAbs) are designed to co-stimulate T cells specifically within the tumor microenvironment



- Costimulatory CD28 bsAbs can reinvigorate an existing anti-tumoral response, boost the efficacy of bispecific T cell engagers (CD3 bsAbs) or enhance PD-(L)1 checkpoint inhibitors

The κλ body platform – Truly native bispecific IgGs

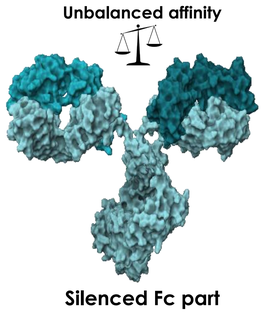


- Unmodified native human antibody sequence and structure
- Indistinguishable from natural human IgGs
- Light chain CDRs drive specific binding to selected antigen
- Favorable CMC properties
  - Platform purification process
  - Multiple GMP runs performed
- 2 clinical stage programs and several other κλ bodies in development, including various partnered programs

Human bsAbs for targeted delivery of "Signal 2"

anti-TAA arm

- Binds specifically to **TAA positive cells**
- High affinity, **drives the specificity**

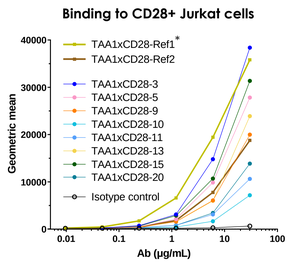


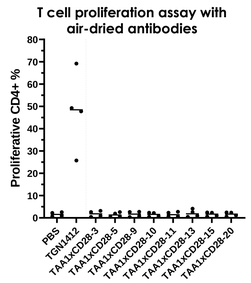
anti-CD28 arm

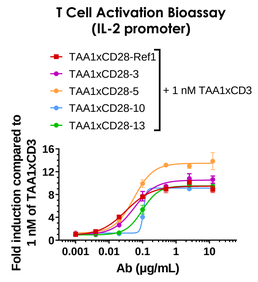
- Binds specifically to CD28 on **T cells**
- **Agonist arm:** delivers T cell activation Signal 2 in the TME
- Can be **paired** with no effort **to existing κλ body compatible anti-TAA arms**

Evaluating κλ body compatible anti-CD28 arms

- **A panel of agonist (and non superagonist) anti-CD28 arms with different binding affinity was identified ‡**

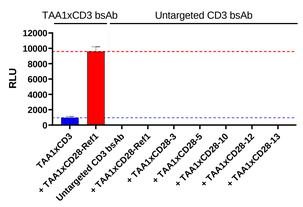


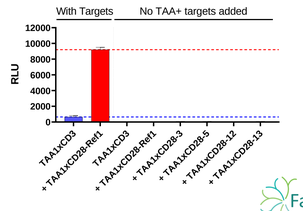




* *CD28-Ref1: 14226P2 anti-CD28 arm*
CD28-Ref2: V8 anti-CD28 arm

- **CD28 bispecifics are unable to activate T cells in the absence of either T cell activation signal 1 or TAA-expressing cancer cells**



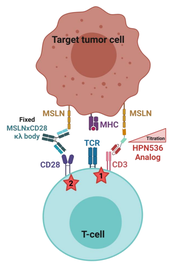


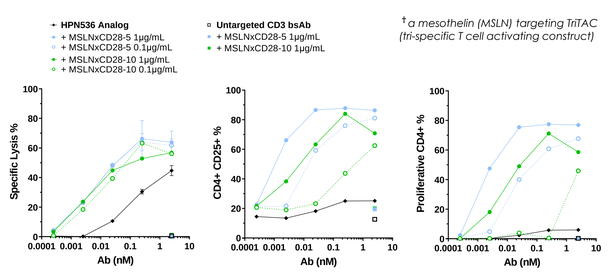
FairJourney Biologics

‡ **in collaboration with FairJourney Biologics [www.fjb.pt]**

in vitro functional characterization of CD28 κλ bodies

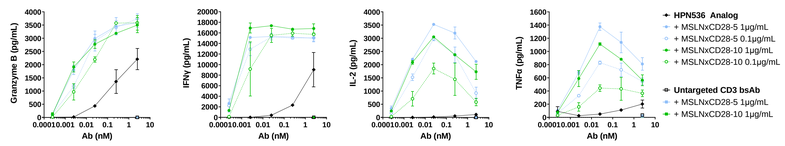
- **Various internal and partnered TAAxCD28 κλ body programs are in development**
- **MSLNxCD28 κλ bodies synergize with a HPN536 analog† to kill mesothelin-positive target cells and to induce T cell activation and proliferation**
- **The potency of the CD28 arm affects how T cells are activated and proliferate**



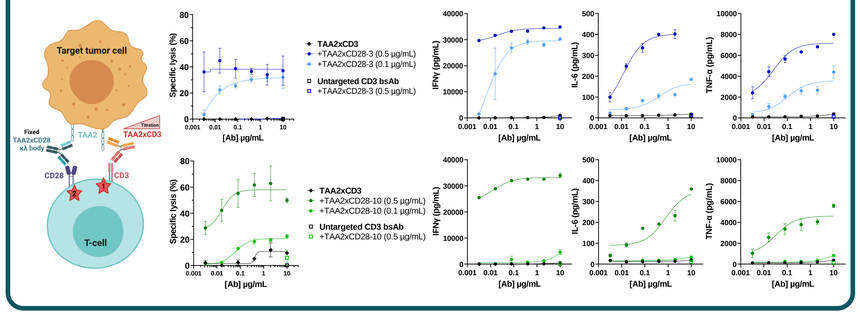


† *a mesothelin (MSLN) targeting TriTAC (tri-specific T cell activating construct)*

- **Combinations of CD3- and CD28 bsAbs enhance T cell-mediated cytokine release**

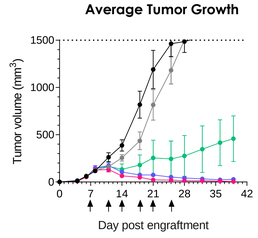


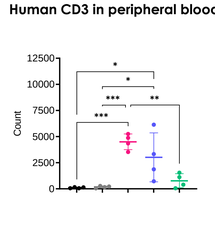
CD28 κλ bodies are active in the context of other TAAs

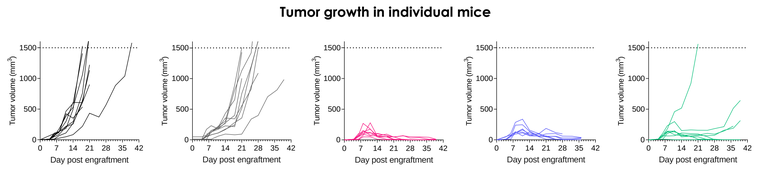


CD28 κλ bodies enhance the *in vivo* activity of T cell engagers

- **Combination of CD3 and CD28 leads to tumor control or eradication, and to an increase of circulating human T cells**







Conclusions and Perspectives

- Using a panel of agonist anti-CD28 arms, CD28 bsAbs targeting multiple TAAs were designed for tumor-specific activation of the immune system
- The resulting TAA-CD28 κλ bodies enhance the antitumor response induced by CD3-retargeting bsAbs via the induction of T cell proliferation and activation, increased cytokine secretion and enhanced anti-tumoral cytotoxicity
- Other anti-TAA arms are being explored, to expand the panel of TAAs that could be easily paired with Light Chain Bio's anti-CD28 platform arms
- Contact bd@lightchainbio.com for partnering opportunities

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