Crescendo biologics

The T cell enhancing company

Humabody® V_H: A versatile platform for generation of novel therapeutics

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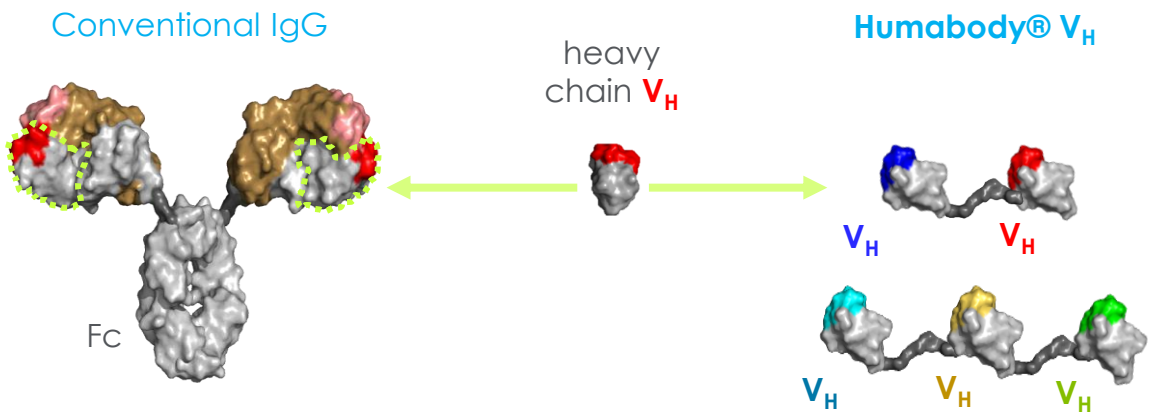
Humabody® V_H are highly versatile molecules, with several key advantages

- Fully human heavy chain antibody fragments (V_H) derived from the Crescendo transgenic mouse[1]
  - Small (~12 KDa per V_H), stable & developable
    - Variety of formats configured with peptide linkers
  - Simple manufacture of multispecific therapeutics
    - Microbial and mammalian expression systems, mAb-like purification processes
  - No Fc region
    - Half-life extension options via panel of serum albumin-binding V_H

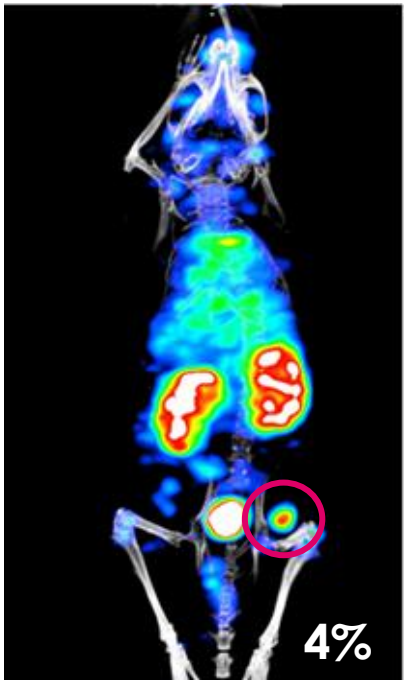


[1]New Biotechnology 2019; 55: 65

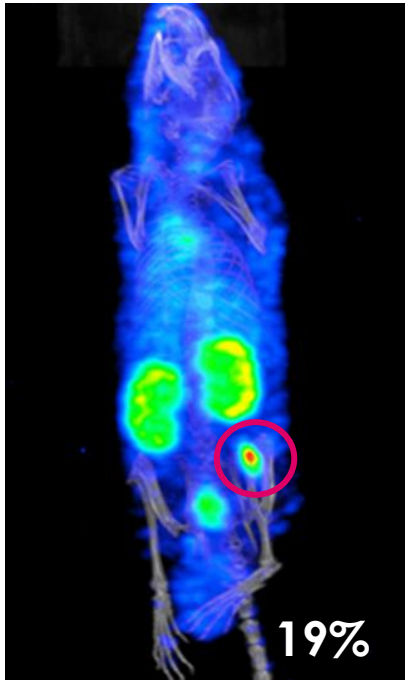
Humabodies® demonstrate superior accumulation in solid tumours *in vivo*

- Comparison of a single dose of radiolabelled anti-PSMA IgG antibody vs radiolabelled half-life extended (HLE) anti-PSMA Humabody® V_H in PSMA positive tumour-bearing mice
- Tumour accumulation (% ID/g) almost five-fold greater in with Humabody vs mAb after 24 hours

PSMA IgG



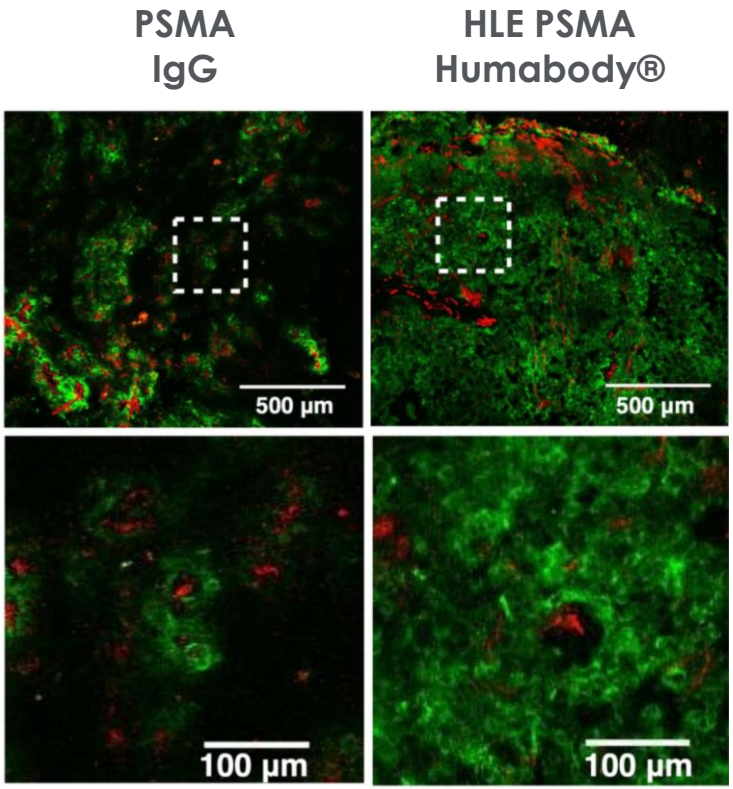
HLE PSMA Humabody®



Tumour accumulation (%ID/g) after 24 hours

Deep tumour penetration demonstrated by Humabody® V_H *in vivo*[2]

- Single dose of fluorescently labelled proteins in PSMA positive tumour-bearing mice
- Half-life extended **PSMA Humabody®** (green, right) shows improved penetration into tumour tissue, away from the vasculature (red) compared with conventional **PSMA IgG** (green, left)[2]



[2]Cancer Research 2020 ; 80 : 1268

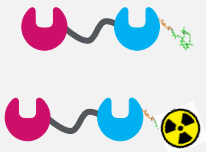
In collaboration with Professor Greg Thurber's Group, University of Michigan

Humabodies® are optimal for addressing novel biology in a range of formats and modalities

- Rapidly configured for a wide range of therapeutic applications using standard molecular biology techniques
- Crescendo Biologics – focus on generation of multispecifics for immuno-oncology

Payload Delivery

- Superior biodistribution
- Tuneable half-life



T cell enhancing multispecifics

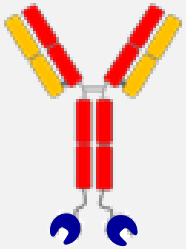
- Potent, tumour-specific costimulation via CD137/4-1BB receptor

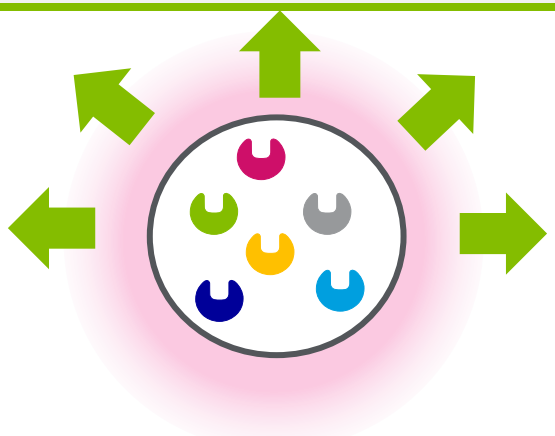
Humabody-armed oncolytic viruses

- Local expression in tumours
- Perfect for multifunctional payloads

Humabody mAb fusions

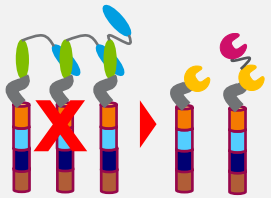
- Enhance existing therapeutic mAbs
- Create bi- or multi-specificity



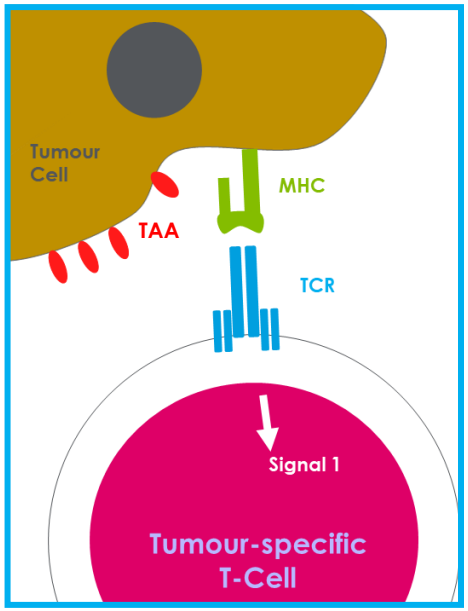


Humabody CAR-T

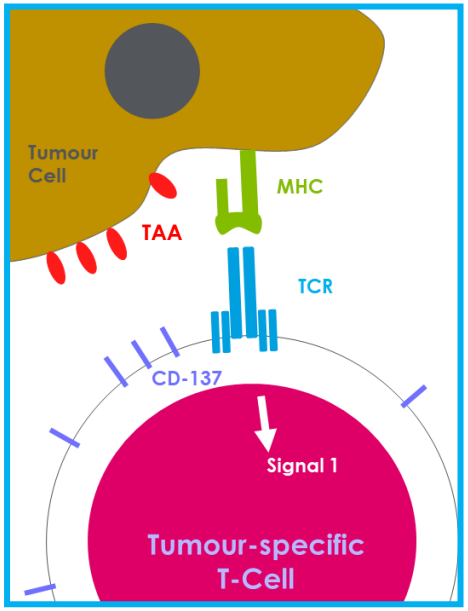
- No V_L required
- Ideal for mono or dual targeting



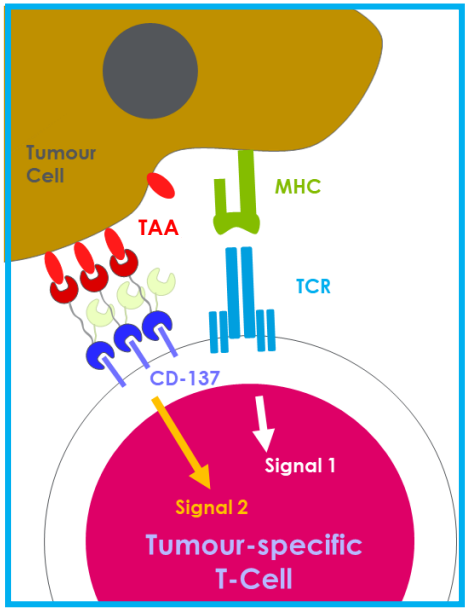
T cell enhancers: Targeted costimulation of T cells



1. T cell recognises tumour antigen



2. CD137 costimulatory receptor is upregulated on T cell



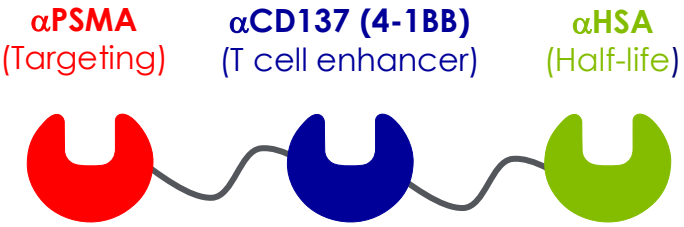
3. CD137x TAA Humabody® binds to TAA on tumour and cross-links CD137 to provide T cell costimulatory signal
   - ✓ Cytotoxicity
   - ✓ Proliferation
   - ✓ Survival

Key mechanistic benefits of T cell enhancers:

- ✓ **Durability** – harnesses the power of natural immunity
- ✓ **Safety** - the right T cells stimulated in the right place

CB307: a half-life extended CD137x PSMA bispecific designed to enhance T cell activity in PSMA expressing solid tumours

- CB307 is a trivalent Humabody® V_H T cell enhancer that binds to CD137, PSMA and human serum albumin (HSA) to increase the activity of tumour-specific T cells
  - sub-nM binding potency to human and cyno PSMA
  - single digit nM binding potency to human and cyno CD137
  - molecular weight <50kDa



- CB307 will be evaluated in patients with PSMA positive advanced and/or metastatic solid tumours in a Phase 1 open-label, dose escalation and expansion trial to investigate safety, pharmacokinetics and pharmacodynamics (POTENTIA)