invenra platform

THE T-BODY TRISPECIFIC PLATFORM

Invenra's T-Body™ Trispecific Antibody Platform targets three distinct antigens simultaneously, offering a powerful solution for complex diseases by integrating three Fab arms into a single IgG-like structure. This innovative format enhances therapeutic potential through receptor clustering, target-specific engagement, and novel immunomodulatory mechanisms.

WHY TRISPECIFIC ANTIBODIES?

Trispecific antibodies (tsAbs) represent a next-generation modality that addresses the limitations of monospecific and bispecific antibodies by allowing simultaneous engagement with three unique targets.

This approach can:

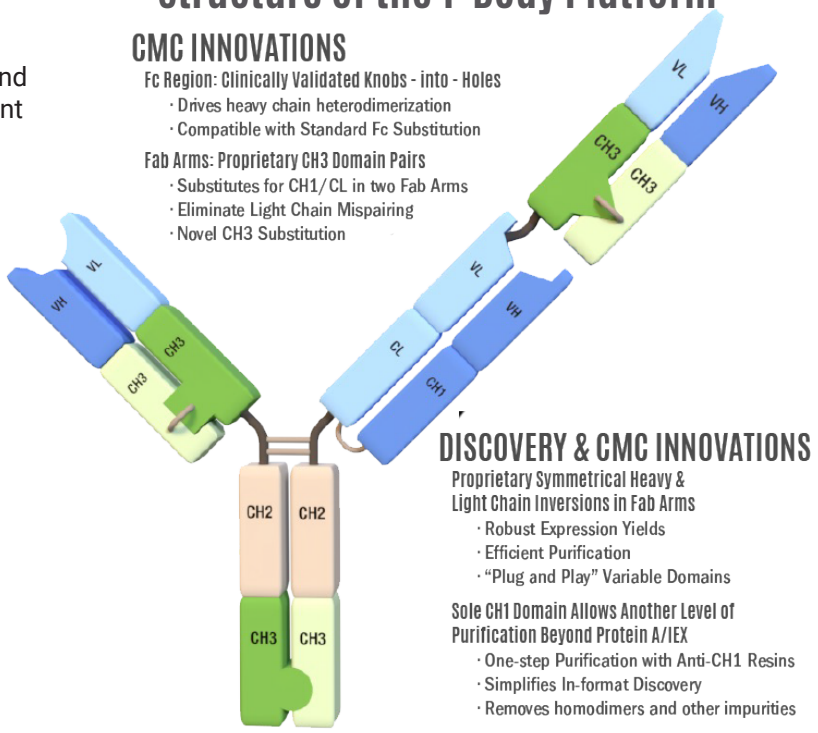
- **Increase target specificity**
- **Reduce antigen escape**
- **Amplify receptor clustering and internalization**
- **Enhance immunostimulatory effects**

ENGINEERED FOR ROBUST EXPRESSION AND PURITY

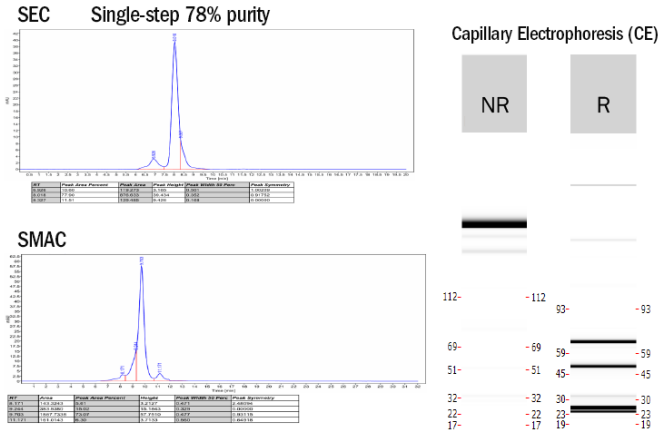
Our T-Body Platform incorporates proprietary CH3 domain pairs engineered for modular, plug-and-play assembly. By substituting CH1/CL with these specialized CH3 domains, we achieve:

- **High expression yields in HEK and CHO cells, consistently exceeding 100 µg/mL**
- **Single-step purification using CH1 resin, delivering >90% purity**
- **Flexible Fab domain pairing with kappa and lambda light chains**
- **Significantly reduced misassembly products**

Structure of the T-Body Platform



Example Trispecific Purification

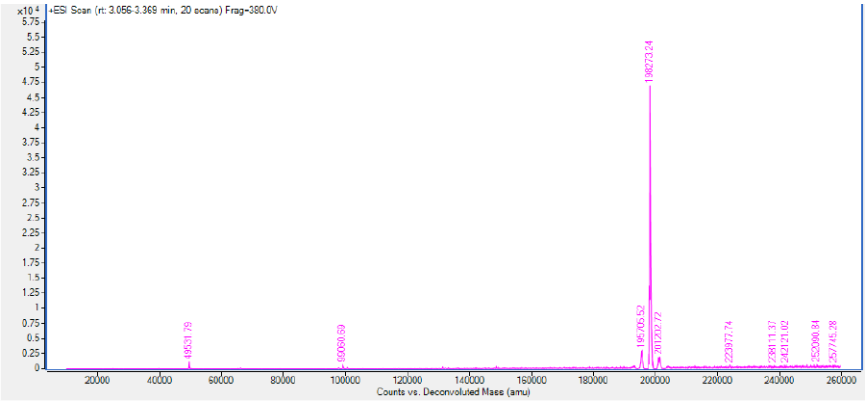


T-Body Trispecific Expression and Purification
T-Body Trispecifics were produced using single CH1 purification from transient CHO cells, resulting in well-resolved chromatograms.

OPTIMIZED MANUFACTURING AND CMC

The T-Body Platform is designed to align with standard antibody manufacturing workflows:

- **Protein A and Ion Exchange polishing**
- **Anti-CH1 resin for one-step purification**
- **Low aggregate formation confirmed by SEC and CE-SDS**



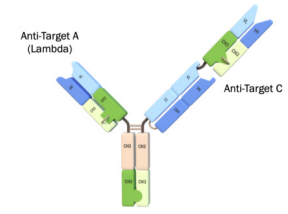
Mass Spec Analysis of a T- Body Trispecific
Assembly of the two-step purified T-Body Trispecific was assessed by LC-MS.

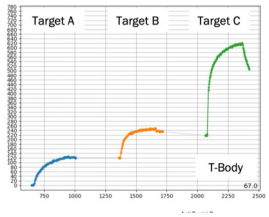
T-BODY BINDING KINETICS

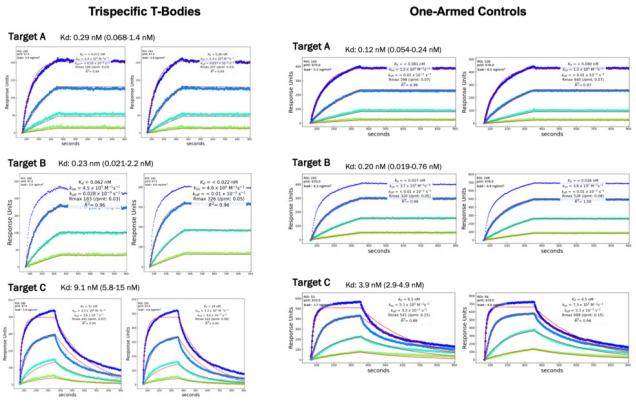
Binding kinetics is crucial in evaluating the therapeutic potential of trispecific antibodies, as it determines the strength, duration, and specificity of antigen-antibody interactions. Our T-Body Platform has been thoroughly investigated with biolayer interferometry (BLI) and surface plasmon resonance (SPR) to assess the simultaneous binding of three distinct antigens. Key kinetic parameters include:

- **Association Rate (ka):** Measures how quickly the antibody binds to the target antigen.
- **Dissociation Rate (kd):** Indicates how rapidly the antibody-antigen complex dissociates.
- **Equilibrium Dissociation Constant (KD):** Reflects the binding affinity, calculated as kd/ka. Lower KD values indicate stronger binding affinity.

In the T-Body Platform, each Fab arm's binding kinetics are independently assessed to ensure optimal affinity and specificity for each target antigen. This approach provides a comprehensive view of multi-target engagement, enhancing therapeutic efficacy.







T-BODY PERFORMANCE: SUPERIOR YIELD WITH CHALLENGING ANTIBODIES

Four clinical antibodies with diverse germlines and developability challenges (Jain et al., PNAS, 2017)—three kappa and one lambda—were combined in a matrixing experiment to generate 24 T-Bodies. The results highlight the platform's robustness, with Expi-CHO expression and one-step CH1 purification delivering strong yields (70–340 mg/L) and high purity (75–95% by non-reducing CE-SDS).

Matrix Analysis of T-Body Performance (Right)
Expression results from a matrix of clinical antibodies (top table) in the T-Body Platform are shown, bottom. Expi-CHO expression followed by one-step CH1 purification resulted in yields ranging from 70-340 mg/L, with 75–95% purity by non-reducing CE-SDS.

Clinical Antibody Targets

Name	hVGene	lVGene	Target	HEK Titer (mg/L)	Fab Tm by DSF (°C)	SGAC-SINS AS100 ($(NH_4)_2SO_4$ mM)	SMAC Retention Time (Min)	Poly-Specificity (PSR) SMP Score (0-1)
Atezolizumab (ATE)	IGHV3-23*04	IGKV1-NL1*01	PD-L1	164.1	73.5	300.0	19.3	0.07
Daclizumab (DAC)	IGHV1-46*01	IGKV1-5*01	CD25	245.1	74.0	900.0	8.8	0.00
Golimumab (GOL)	IGHV3-30*01	IGKV3-11*01	TNFα	163.2	70.0	0.0	12.7	0.23
Guselkumab (GUS)	IGHV5-10-1*04	IGLV1-40*01	IL23	167.3	69.5	700.0	9.2	0.47

Expression Results