

The Problems

In vitro phage-display antibody libraries are a rich source of antibody diversity and are compatible with sophisticated selections that are difficult or impossible to perform with immunization. However, in vitro phage-display libraries can increase downstream risks such as:

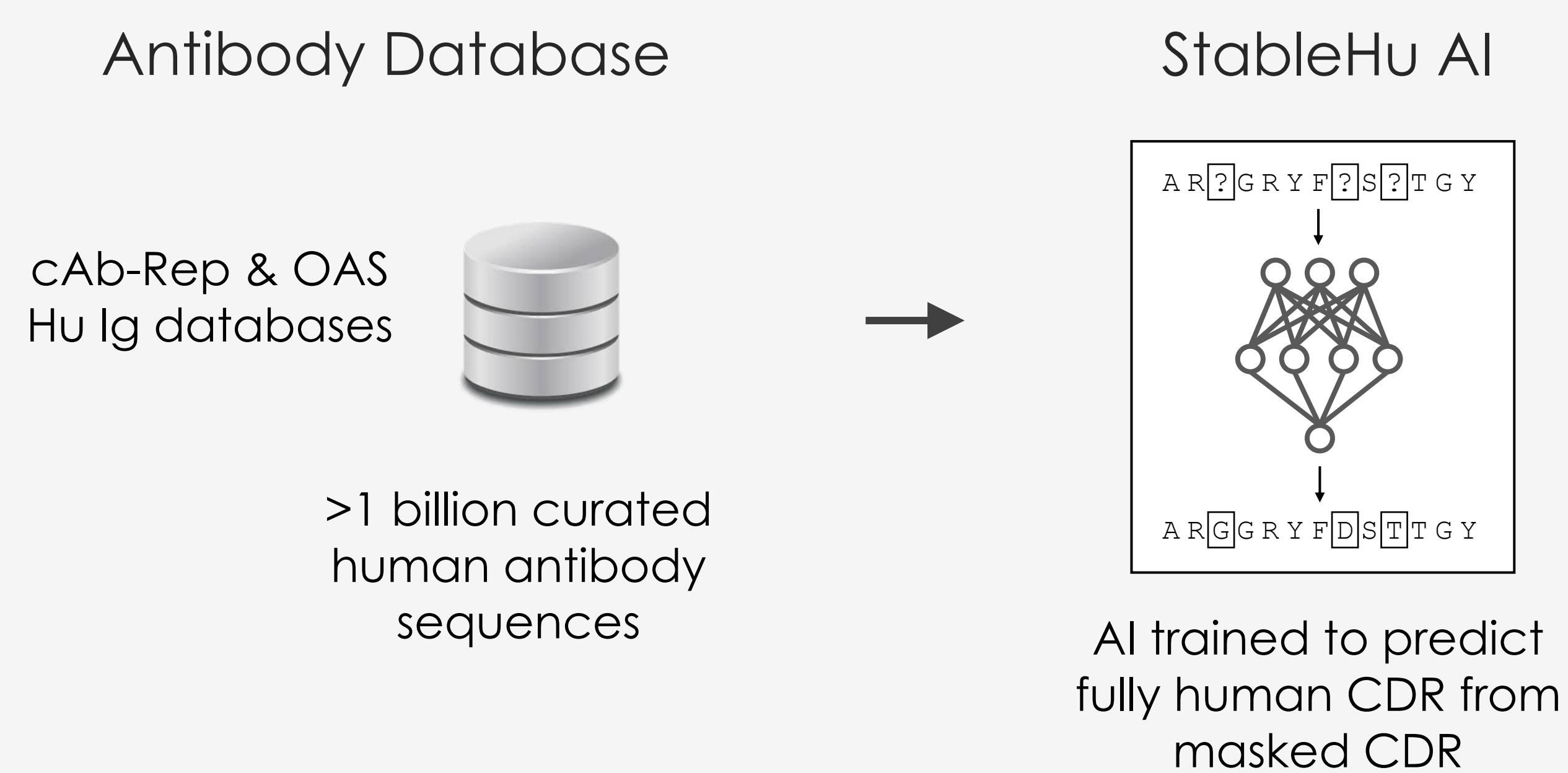
- Low expression in production mammalian cell lines⁽¹⁾
- Instability and aggregation⁽¹⁾
- Immunogenicity due to non-human diversity⁽²⁾

In vitro mammalian-display antibody libraries can minimize the downstream expression and instability risks.⁽³⁾ However, mammalian-display has limited capacity for library diversity.⁽⁴⁾

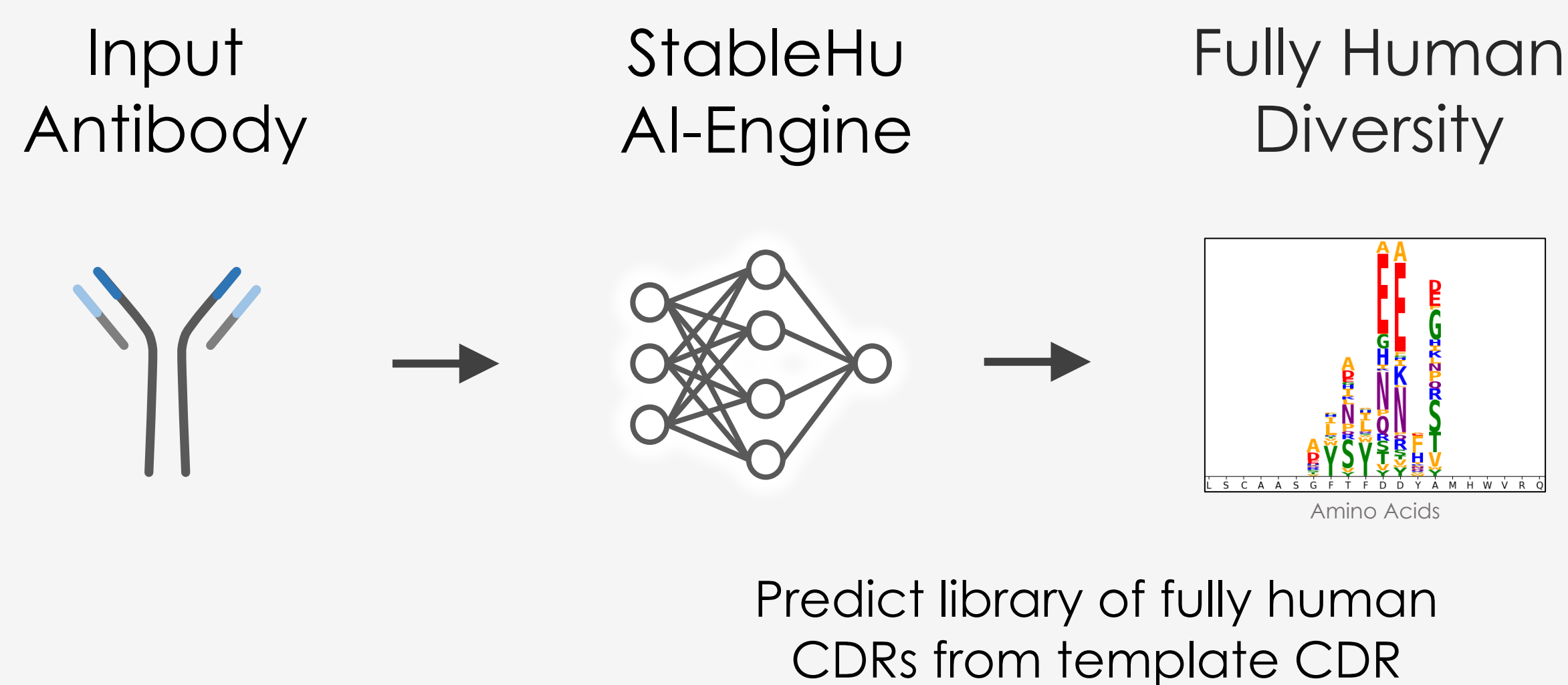
(1) Kaleli et al. *Proteins* (2019) 87 p.607 (3) Dyson et al. *MAbs* (2020) 12(1) p.e1829335
(2) Walsh et al. *MAbs* (2020) 12(0) p.e176482955 (4) Valldorf et al. *Biol. Chem.* (2022) 403(5-6) p.455

Our Solution

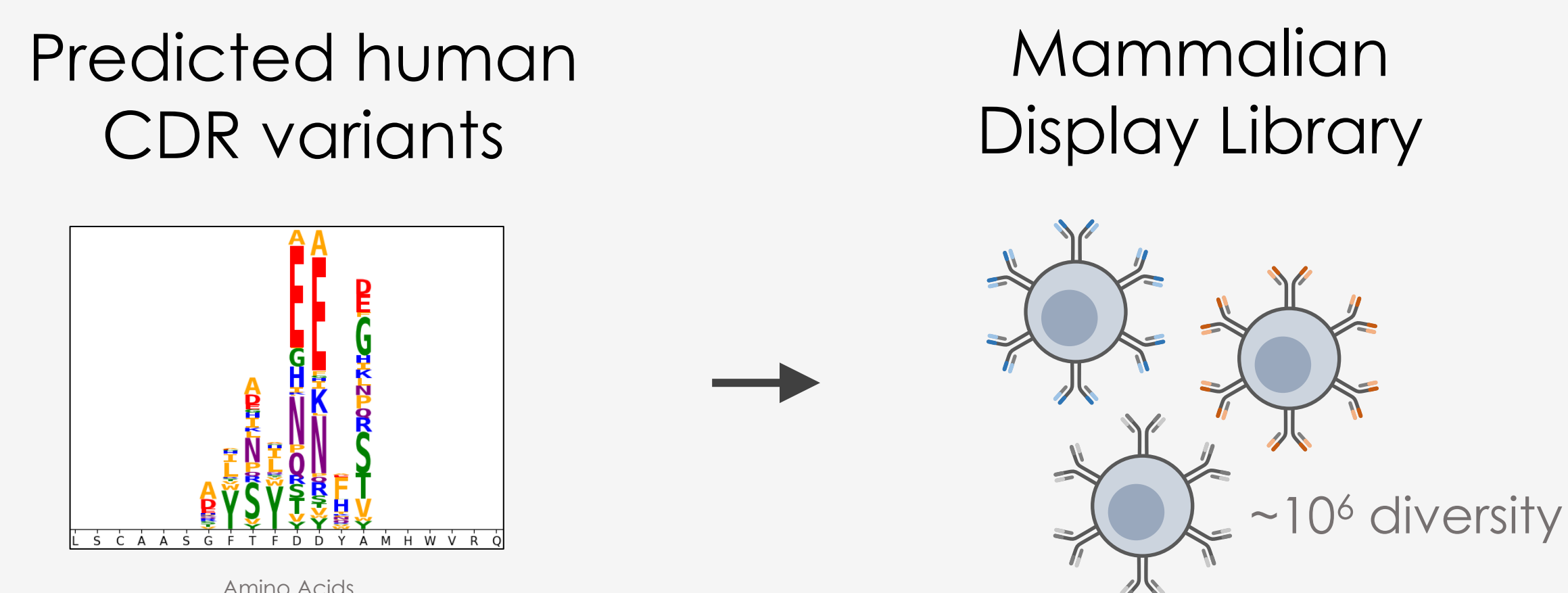
1. Train AI on human antibody sequence space



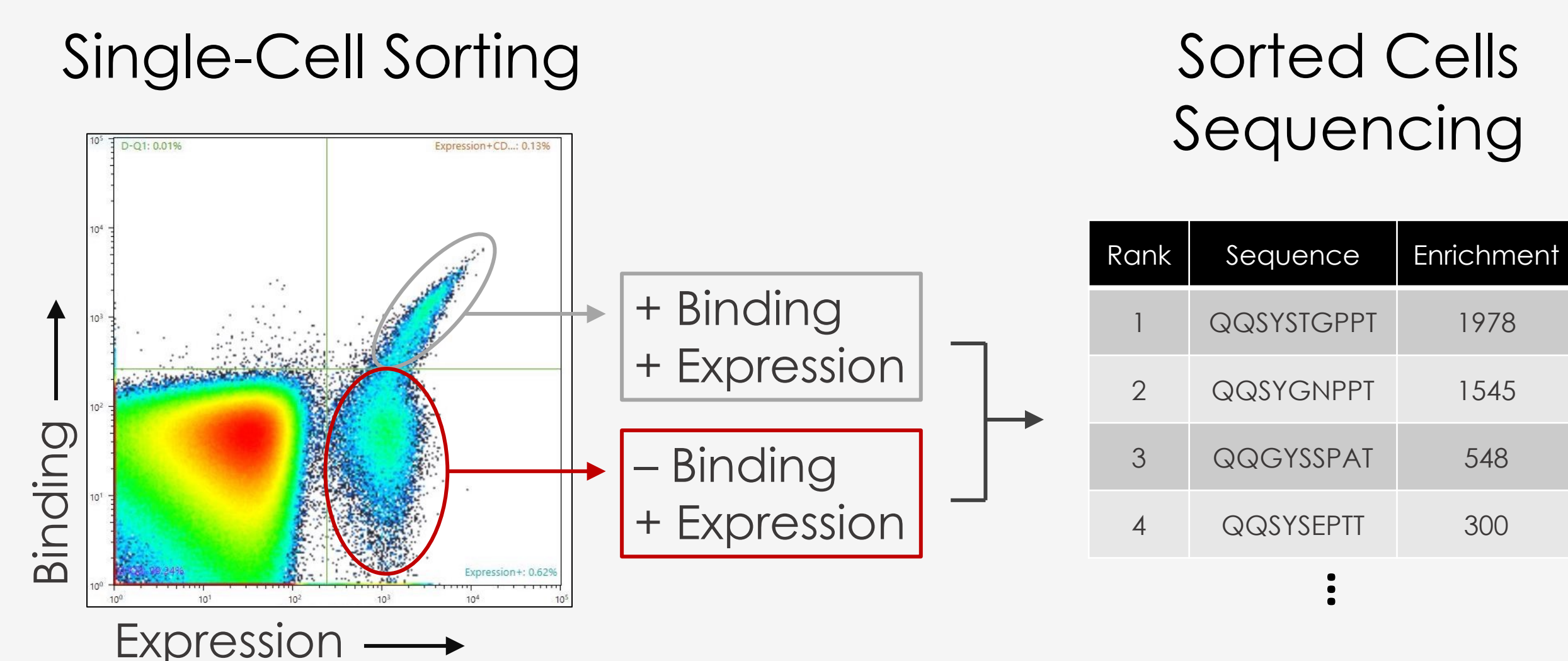
2. Use AI model to predict fully human focused diversity from a template antibody to be optimized



3. Produce a mammalian-display library using AI-predicted focused diversity



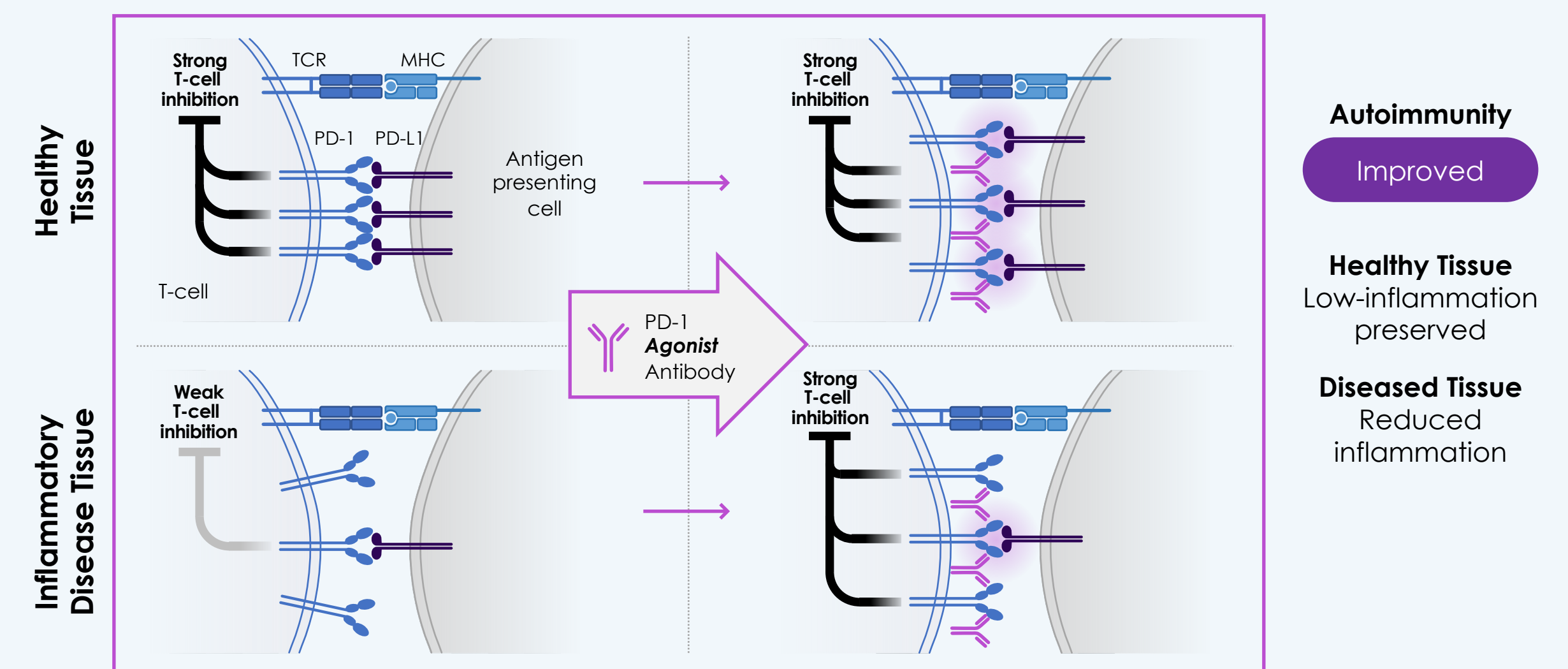
4. Single-cell screen mammalian-display library for expression and binding



Validation

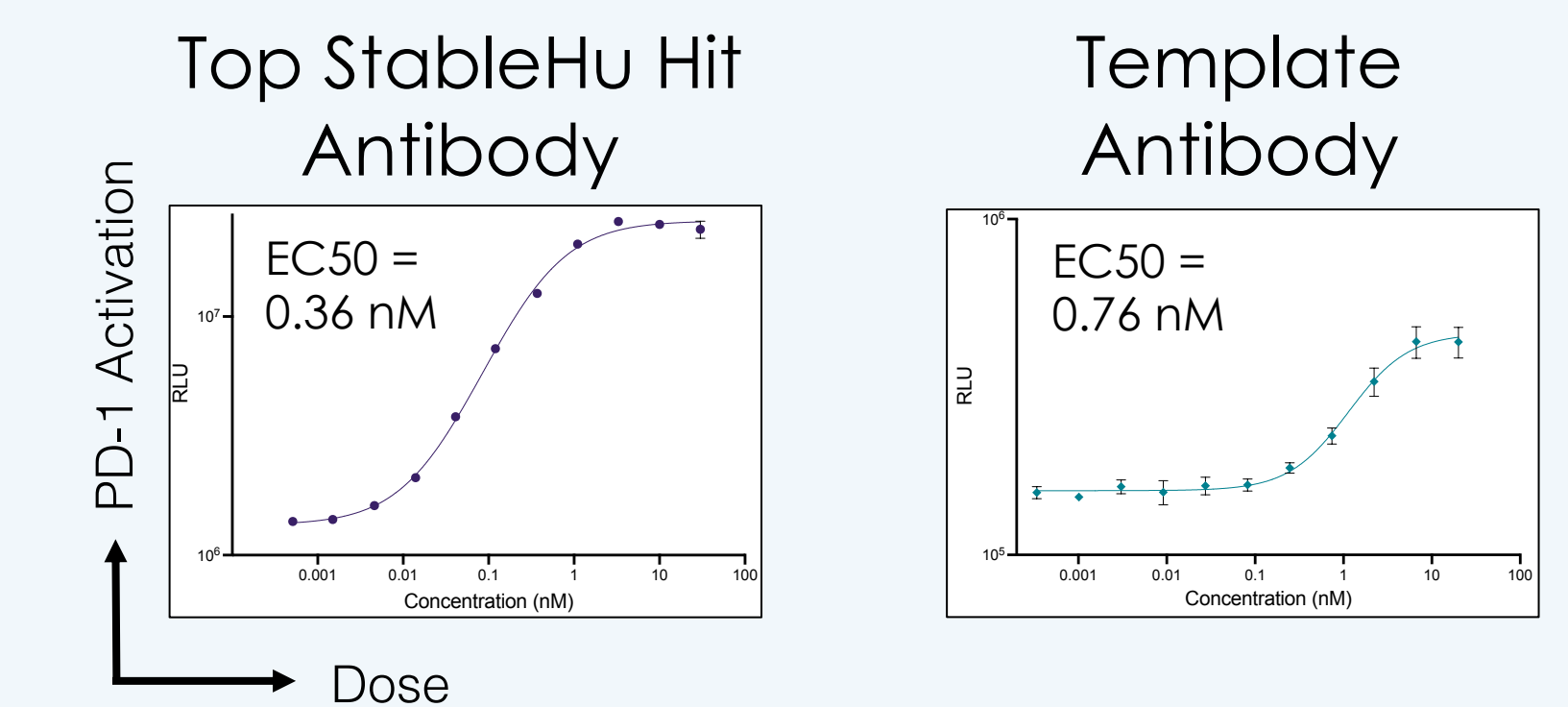
PD-1 Agonist

Agonizing PD-1 without blocking PD-L1 restores activated T-cell suppression



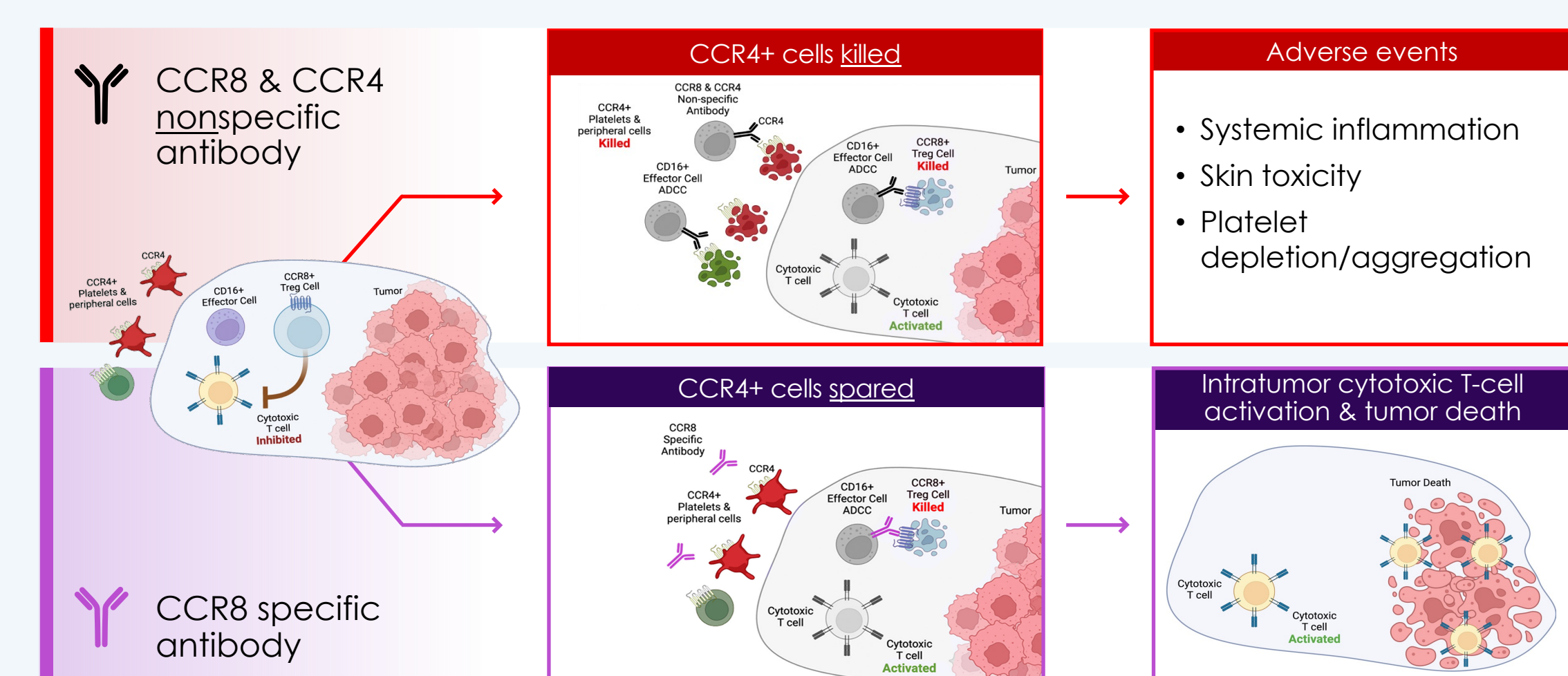
PD-1 Agonist Reporter Assay

Starting from a mouse antibody template, StableHu AI & mammalian-display identified a more potent PD-1 agonist antibody



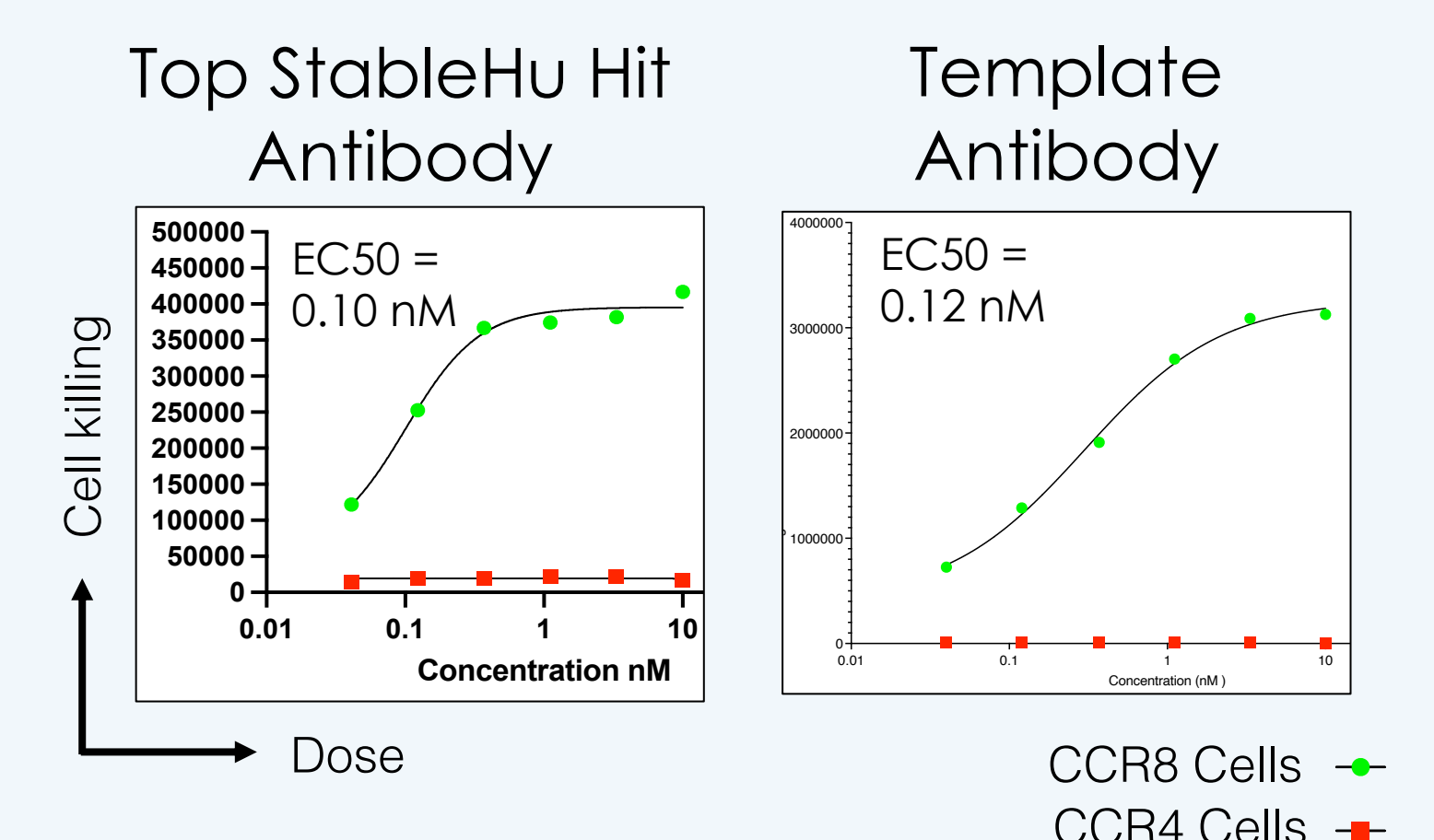
CCR8 GPCR ADCC

Depletion of CCR8+ Treg cells can evoke tumor immunity



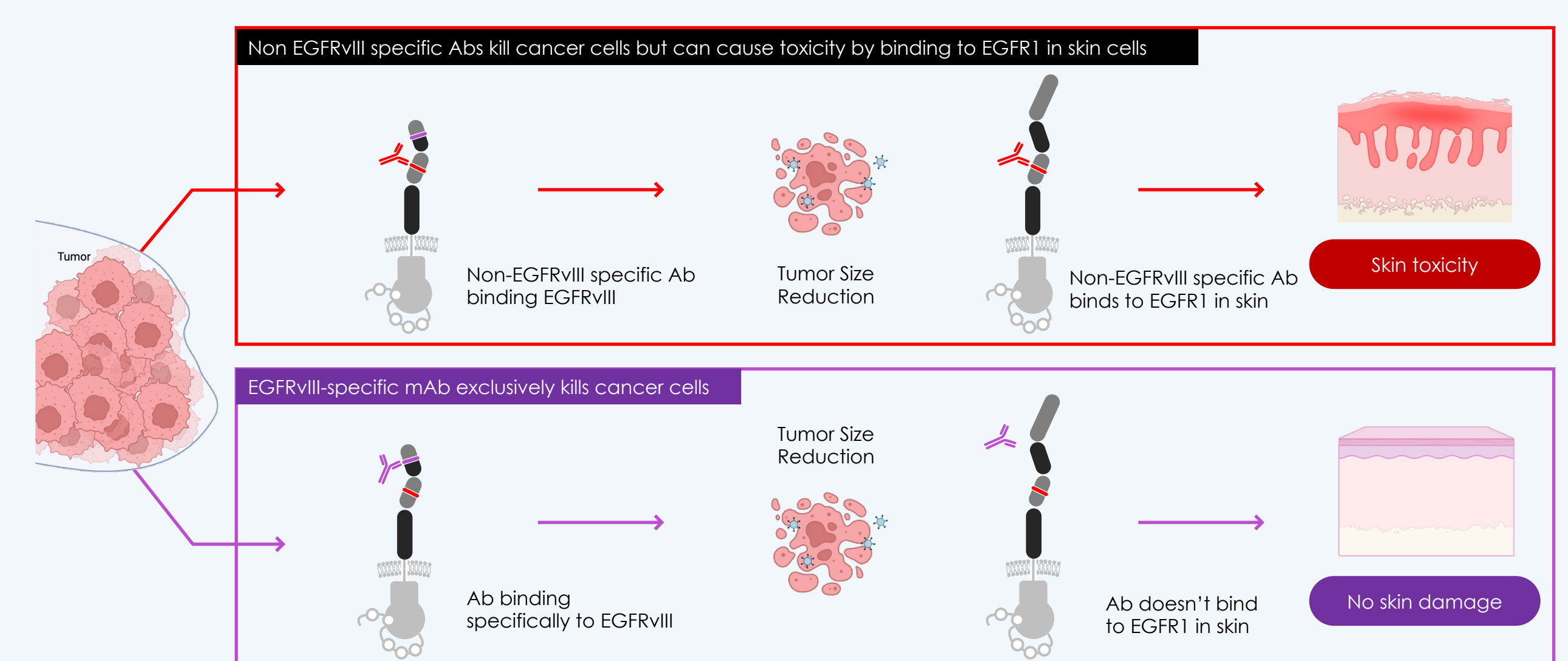
CCR8 ADCC Cell Killing Assay

Starting from a mouse antibody template, StableHu AI & mammalian-display identified a more potent CCR8+ cell killing antibody



EGFRvIII TSA

The EGFRvIII epitope can be targeted to kill tumor cells and preserve EGFR1 healthy cells



EGFRvIII ADCC Cell Killing Assay

Starting from a mouse antibody template, StableHu AI & mammalian-display identified a more potent EGFRvIII+ cell killing antibody

