

# A novel class of Innate Cell Engagers targeting NKp30

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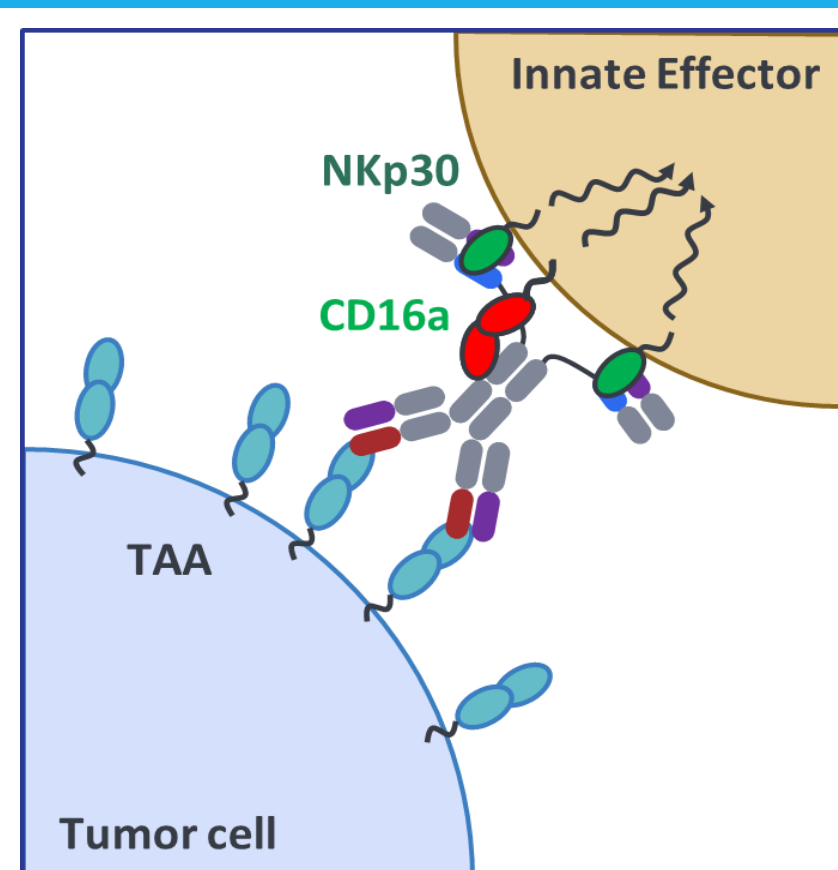
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## Introduction

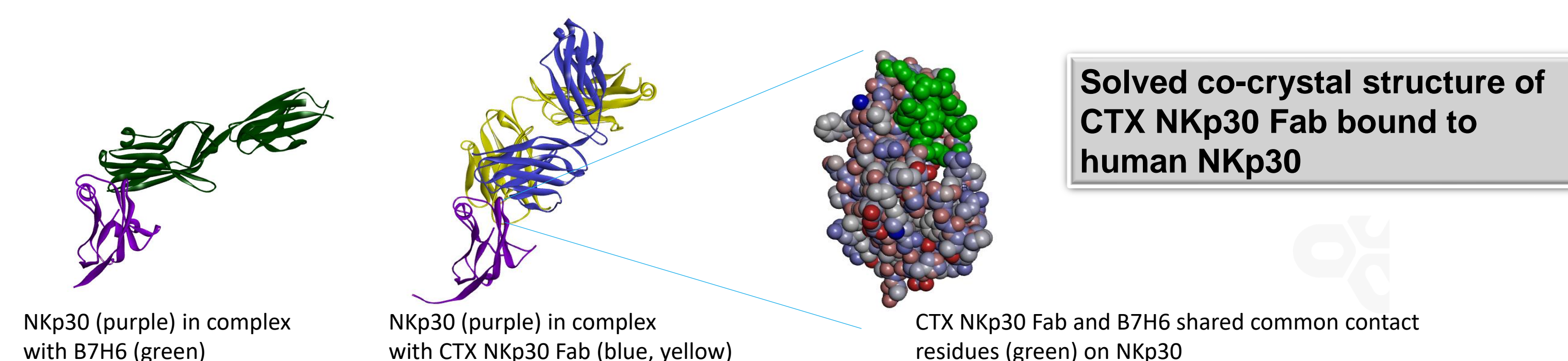
Cancer immunotherapies have demonstrated remarkable clinical benefits and durable responses even for late-stage cancers. Most of the attempts of current therapies in development are focused on harnessing the adaptive immune system by unleashing antitumor T cell responses. However, there is emerging evidence that cancers develop multiple strategies to escape T cell recognition, hence approaches that do not require T cell recognition should be explored. Tumors can be effectively eradicated by natural killer (NK) cells that can elicit potent anti-tumor response in both mouse cancer models and patients. Therefore exploiting therapies that enhance NK response for the treatment of cancer represents a promising and complementary approach to current existing immunotherapies.

## Mechanism of action of Compass multi-specific antibodies

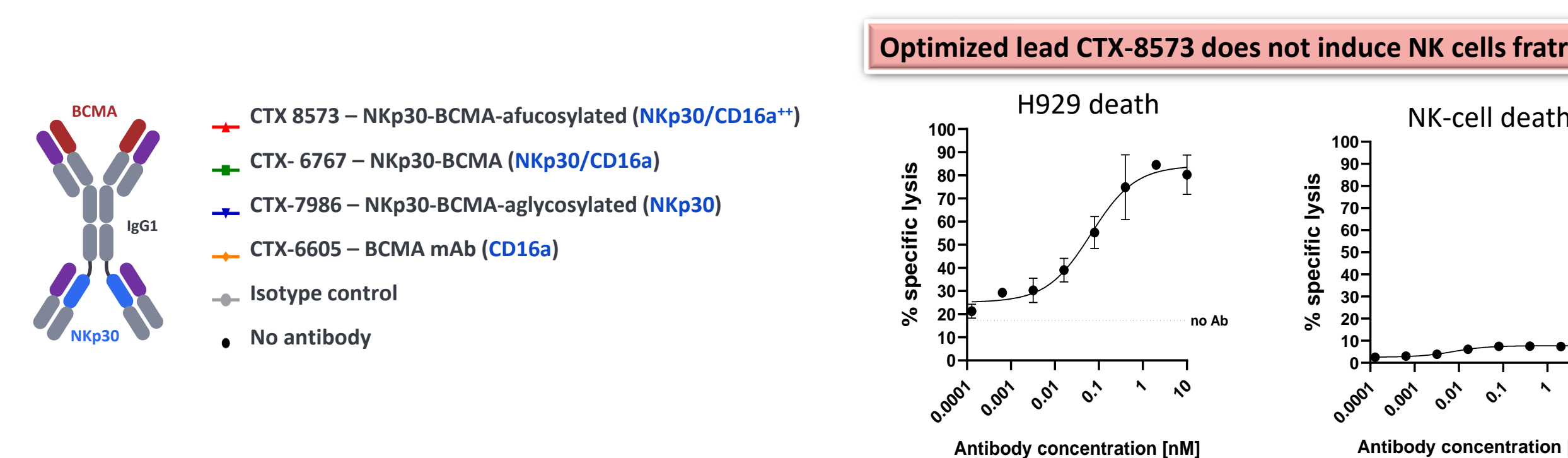
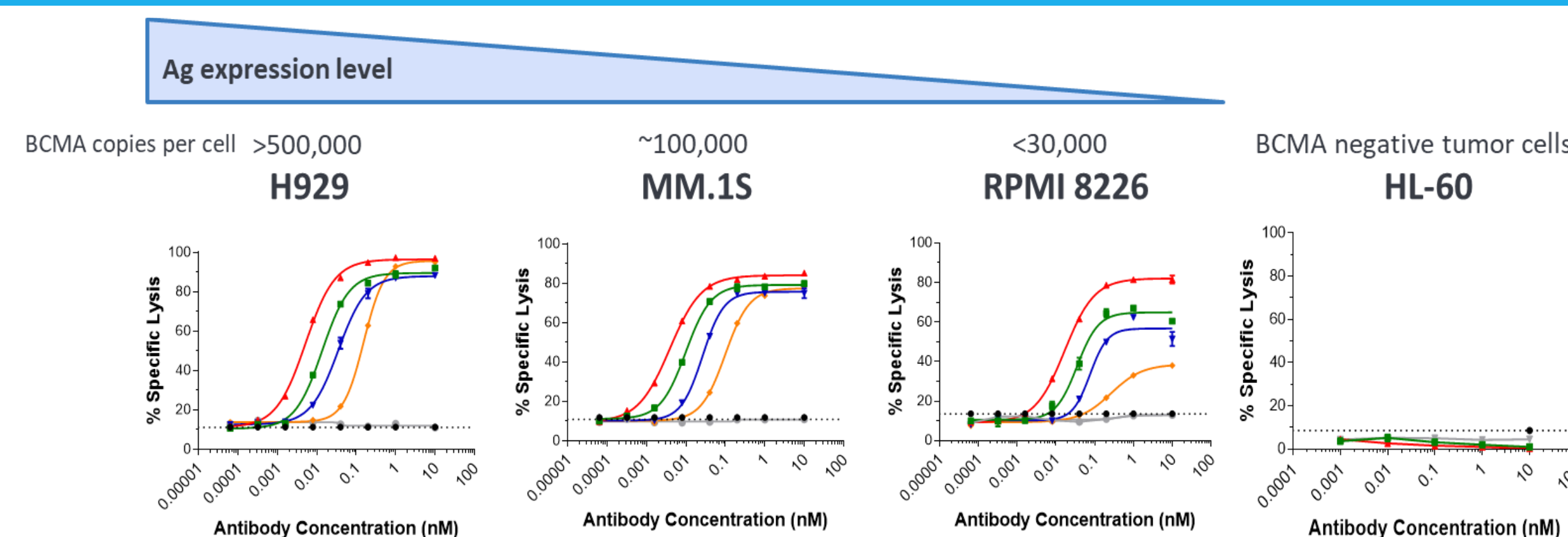


- Target one or more tumor-associated antigens (TAA)
- Engage CD16A through Fc to drive ADCC
- Trigger NK cell activation through NKp30 to synergistically amplify CD16A response or maintain activity in the absence of CD16A expression on NK cells

## Compass NKp30 Fab Binds at similar epitope and orientation as ligand B7-H6

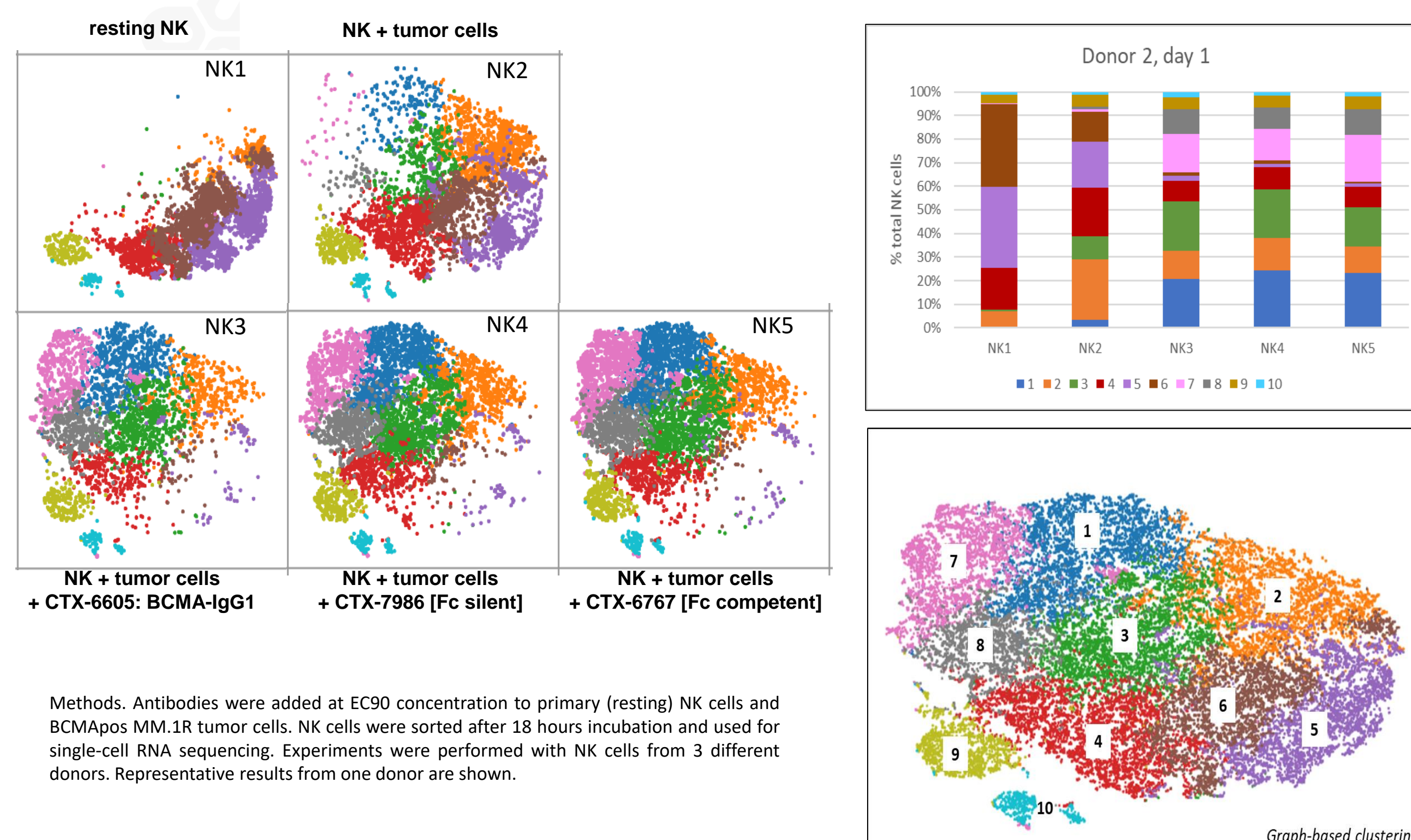


## Compass NKp30xBCMA Lead CTX-8573 induces highly potent and selective lysis of BCMA<sup>pos</sup> tumor cells expressing different levels of antigen

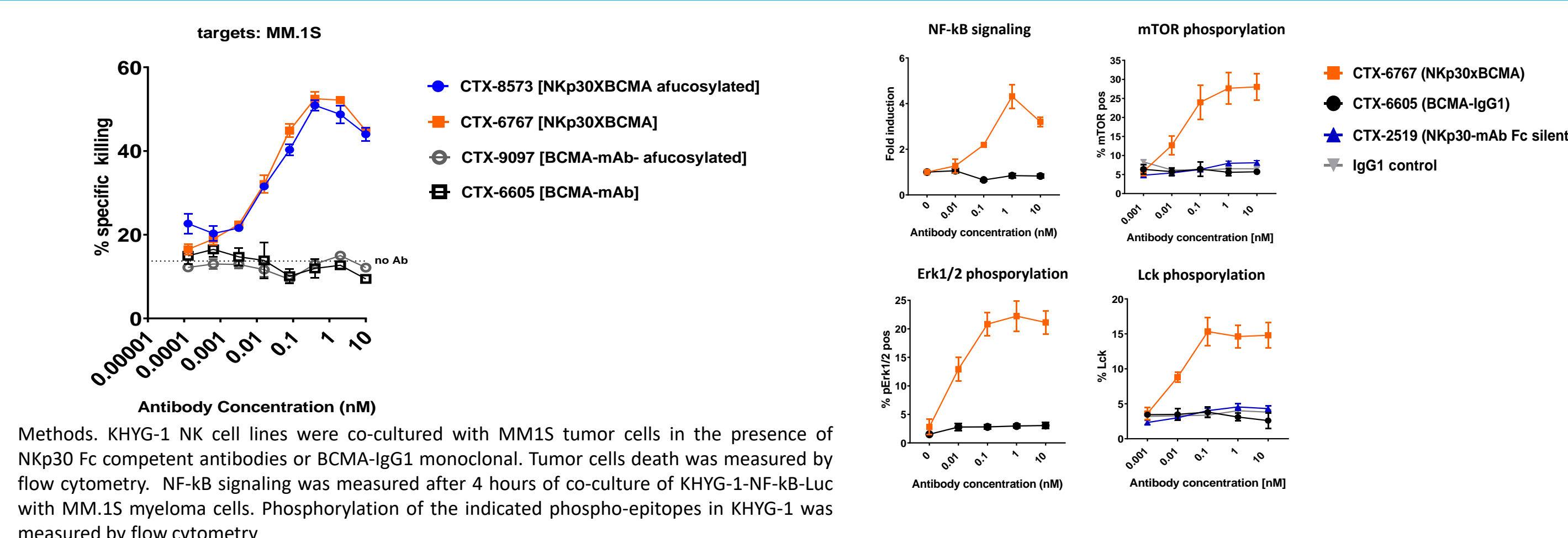


Methods. Primary NK cells were cultured for 4 hours with tumor cells and different concentrations of antibodies. Tumor and NK cells viability was assessed by flow cytometry

## Differential NK cell activation induced by NKp30xBCMA as compared to BCMA-IgG1 monoclonal

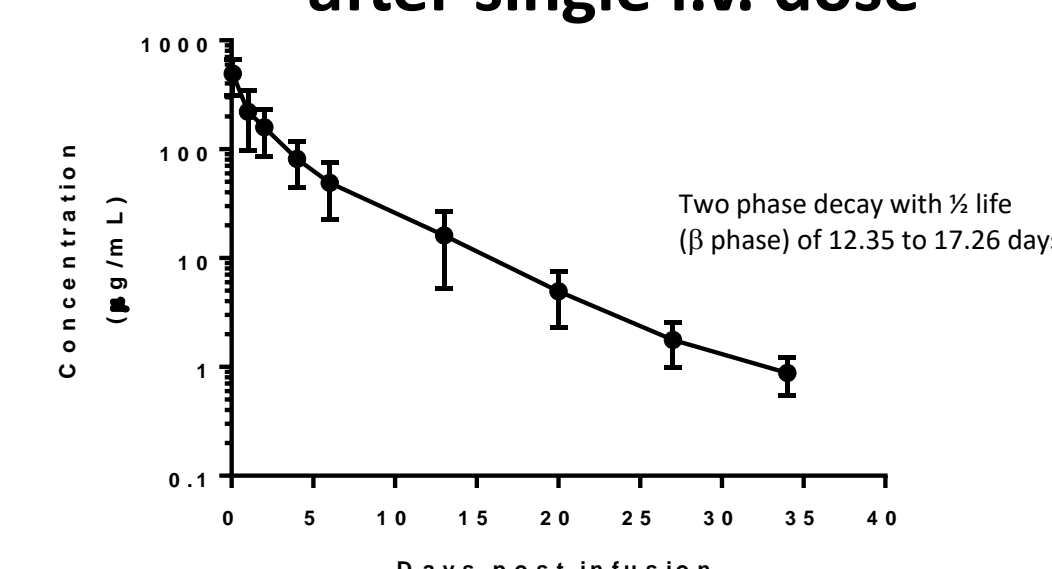


## Activity of NKp30 engagers in the absence of CD16A engagement

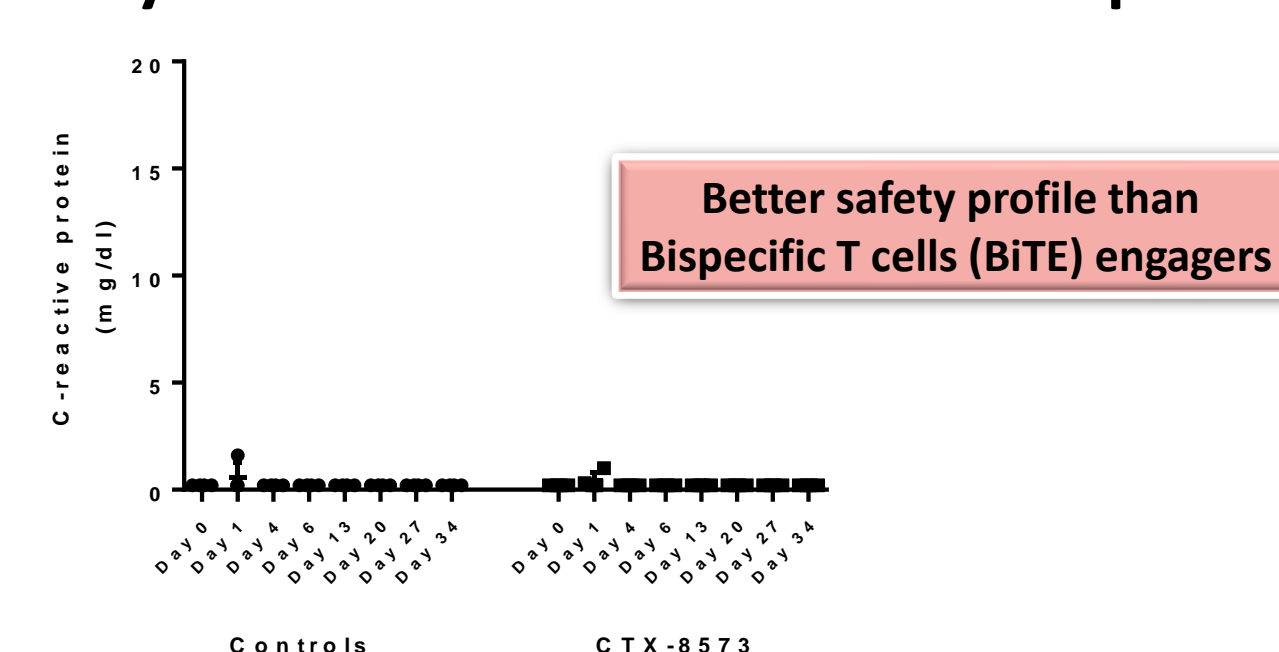


## Pharmacokinetics and safety toxicity profile of NKp30xBCMA in cynomolgus monkeys

### Serum concentrations of NKp30xBCMA after single i.v. dose



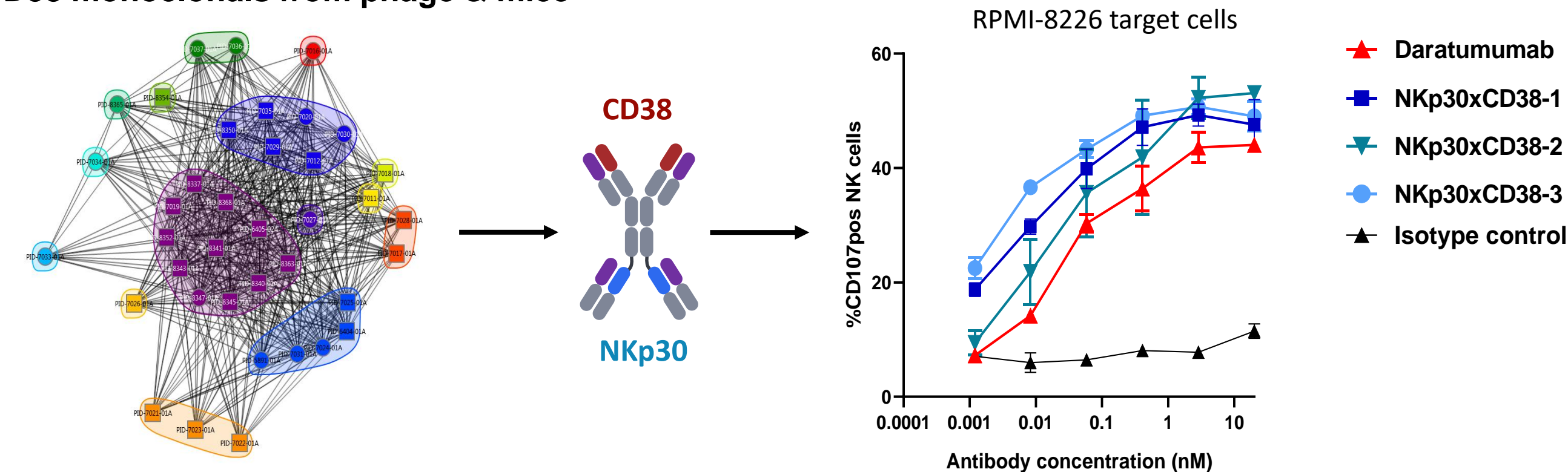
### No systemic induction of C-reactive protein



Methods. Three groups (n=3) of female monkeys received a single i.v. dose of 30 mg/kg of NKp30xBCMA (CTX-8573). Samples were collected at the time indicated. Serum concentrations of NKp30xBCMA were measured by ELISA

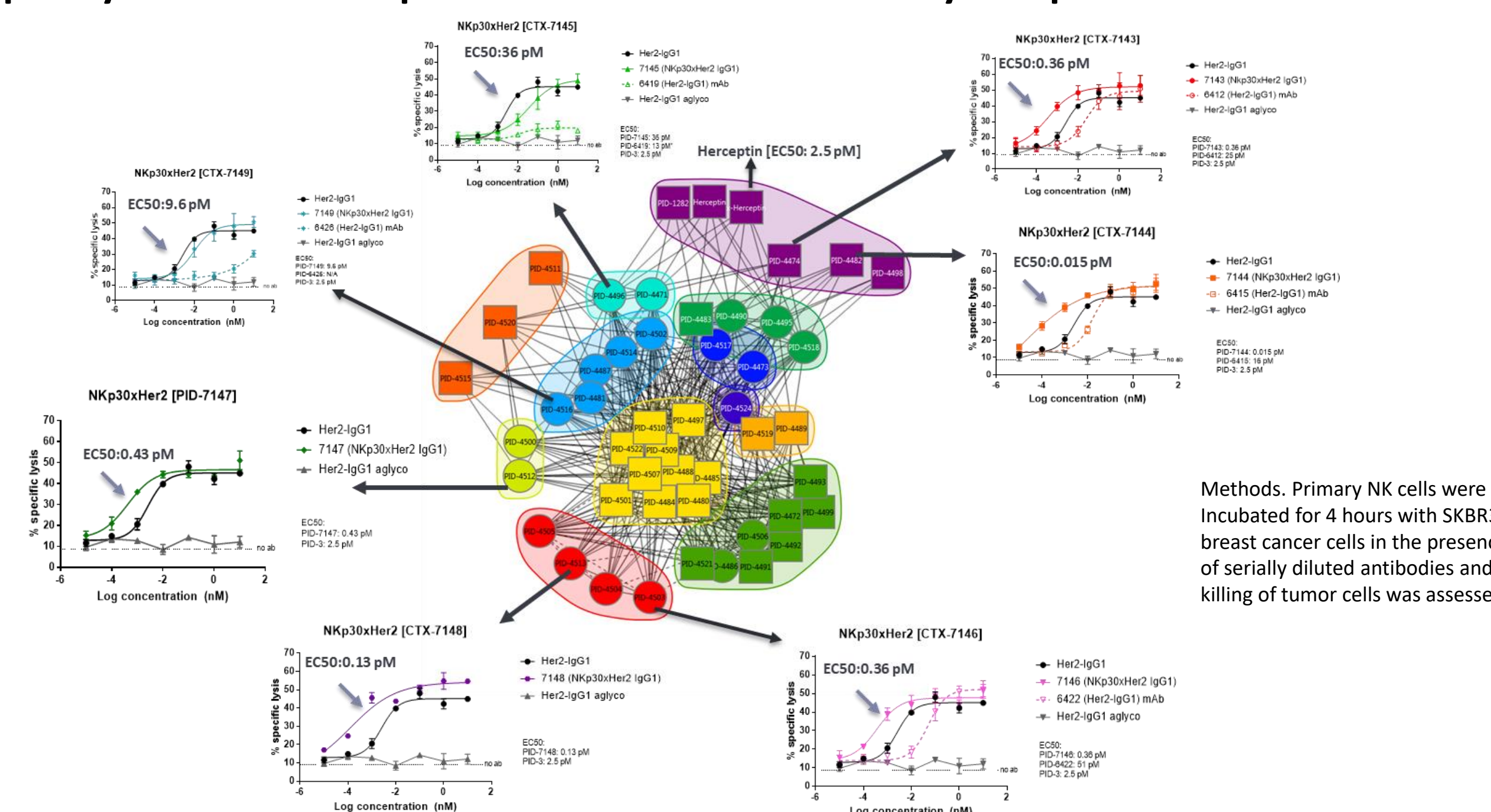
## NKp30xCD38 with enhanced potency compared to Daratumumab

### CD38 monoclonals from phage & mice

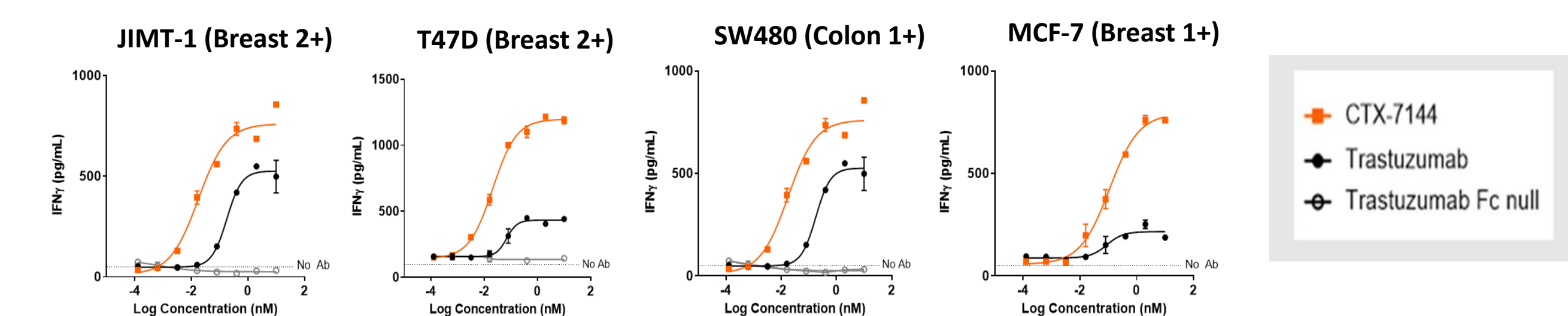


## NKp30XTAA for solid tumors

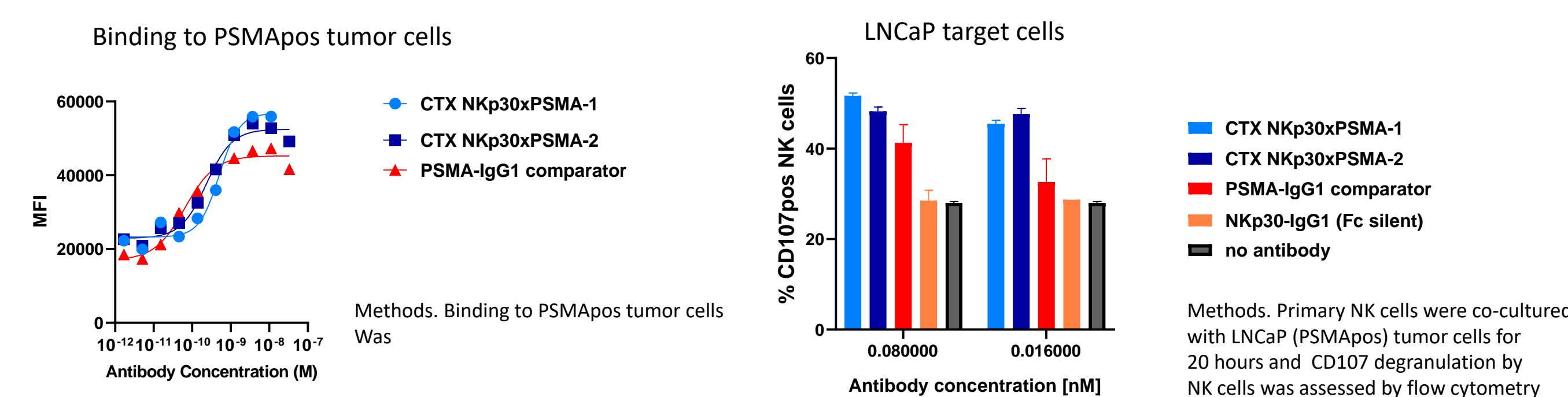
### Epitopically diverse multi-specifics with enhanced activity compared to trastuzumab



### Compass NKp30xHer2 lead has enhanced activity compared with trastuzumab against tumor cells with wide range of Her2 expression



### Compass NKp30xPSMA enhanced NK cells activity towards PSMApos prostate cancer cells



## Summary

➤ Compass has developed a novel class of Innate Cell Engagers that bind to antigens on the surface of tumor cells and engage both NKp30 and CD16A on NK cells.

➤ Compass NKp30 engagers can induce killing of tumor cells expressing different levels of tumor antigen without off-target effects and NK cell depletion.

➤ Compass Innate Cell Engagers display PK similar to monoclonal antibodies and favorable toxicity profile.

➤ Our results provide the rationale for developing multifunctional NKp30 engagers for the treatment of hematological and solid tumors.