Docket #: S23-217

Cross-reactive antibodies targeting NKp46 that enhance cytotoxicity and proliferation in both human and murine NK cells

Stanford scientists have developed cross-reactive antibodies that can bind human and murine NKp46 on NK cells and induce cytotoxicity and proliferation. Species cross-reactivity enables direct testing of the antibody in murine models without modification, providing a better prediction of efficacy in humans.

NKp46 is an emerging NK cell receptor that has recently been receiving attention as a target for increasing NK cell cytotoxicity and proliferation. Currently available antibodies against NKp46 are only capable of binding a single species ortholog (e.g. only human or only murine), which has necessitated significant modifications to the antibody to enable testing in preclinical mouse models. Species cross-reactive antibodies that bind to NKp46 would make it possible to validate an unmodified antibody in preclinical models before progressing into human clinical trials.

The species cross-reactive antibodies displayed nanomolar affinity to human, murine and cyno NKp46. The antibodies enabled NK cell proliferation and expansion. Importantly, bispecific antibodies constructed with these antibodies demonstrated increased cytotoxicity of both human and mouse NK cells towards tumor cells as compared to their monospecific counterparts. Consequently, species cross-reactive antibodies for NKp46 have the potential to optimize preclinical studies and provide a more direct pathway to human clinical trials.

Stage of Development:
Preclinical – *in-vitro* data
Continued research - Validation of the invention to better understand the characteristics and applications

Applications

- Binding of the NKp46 receptor on NK cells
- Incorporation into a bispecific antibody to improve NK cell killing of target cells
- Usage in NK cell expansion kits

Advantages

- Species cross-reactivity for both human and murine NKp46
- Removes the need for modification to enable validation in pre-clinical models before moving to human clinical trials

Patents

- Published Application: WO2025175136

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