IECV 2024 Conference

The 2nd International Electronic Conference on Vaccines

27–29 November 2024 | Online

MDPI

Development of Nanobodies Targeting TIGIT for Cancer Immunotherapy

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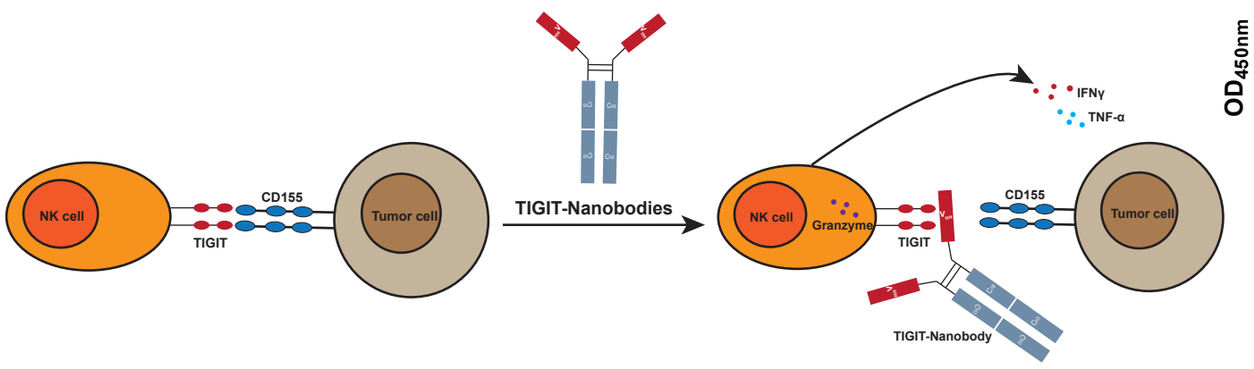
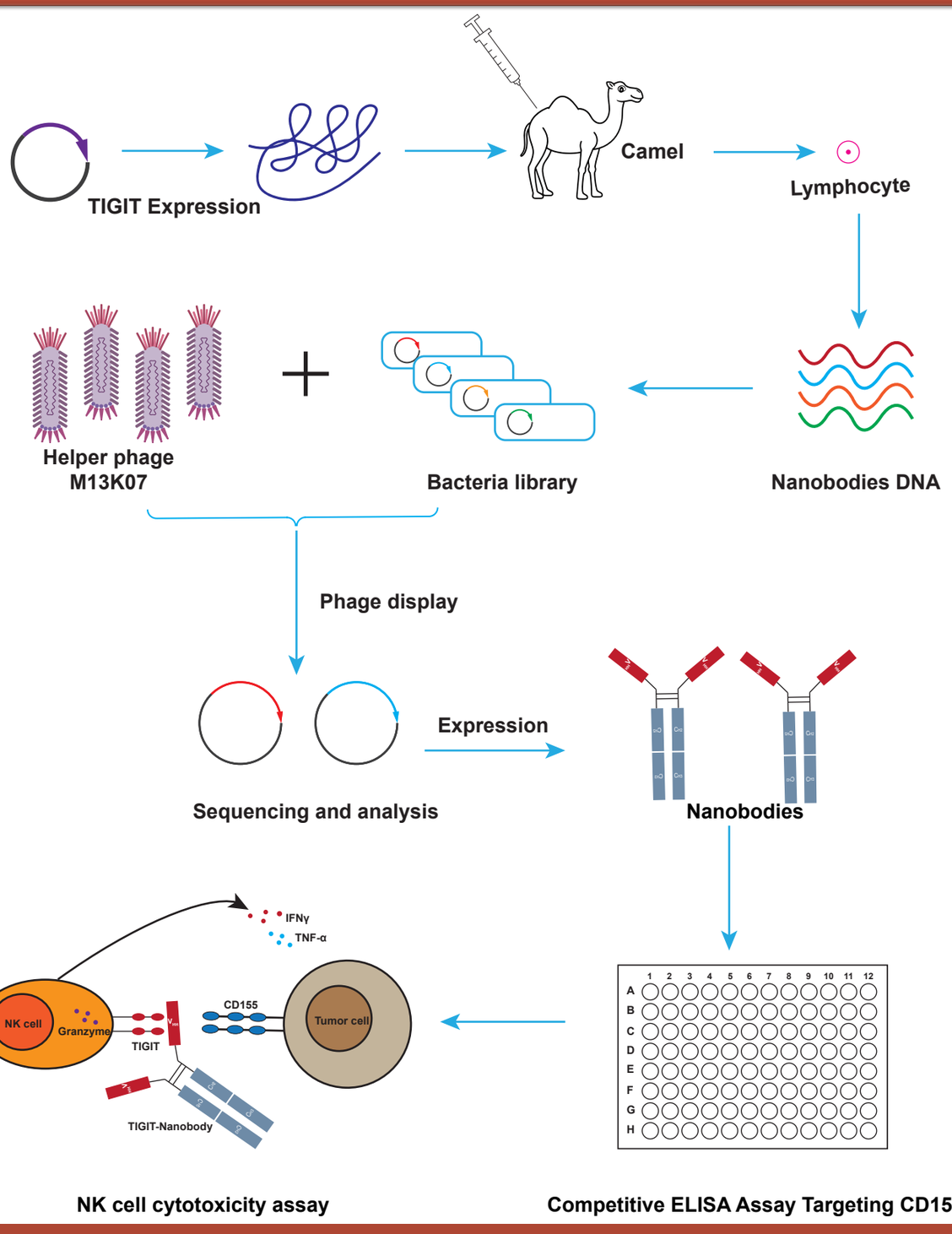
INTRODUCTION & AIM

1. Apart from traditional cancer treatments, immunotherapy has also garnered significant attention in recent decades.
2. Cancer immunotherapy targeting immune checkpoint molecules, such as programmed cell death-1 (PD-1) and its ligand programmed death-ligand-1 (PD-L1), has transformed the paradigm of cancer treatment. However, given that less than 50% of tumor patients respond to monoclonal antibody (mAb) therapies targeting PD-1/PD-L1, there is still significant room for improvement. Targeting other immune checkpoints, such as TIGIT (also known as T cell immunoreceptor with Ig and ITIM domains), represents a promising strategy.
3. To this end, we will screen high-affinity, highly specific TIGIT nanobodies and validate their functionality through in vitro assays and animal experiments to explore new possibilities in tumor treatment.

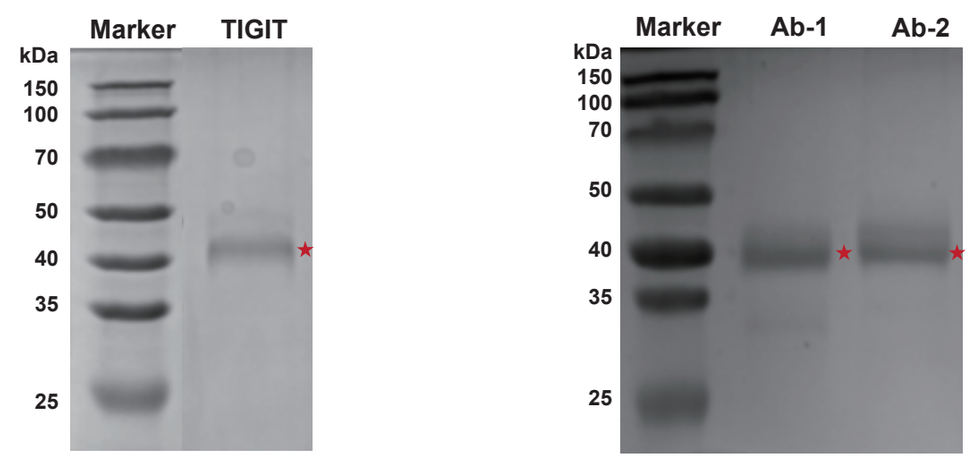


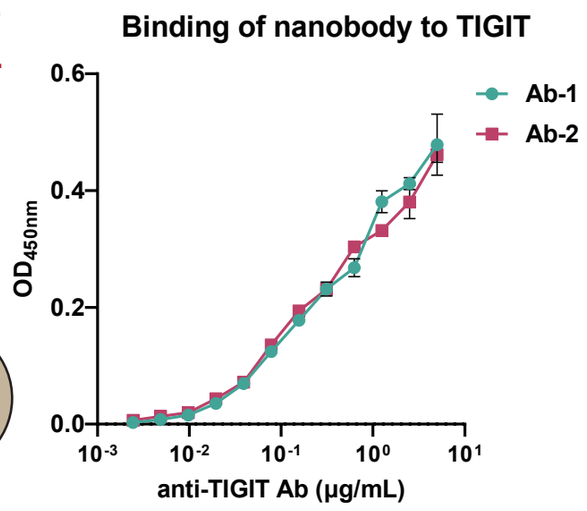
METHOD

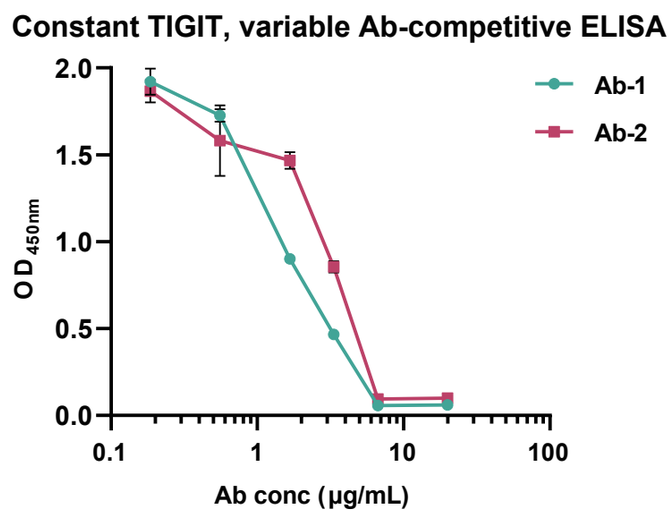


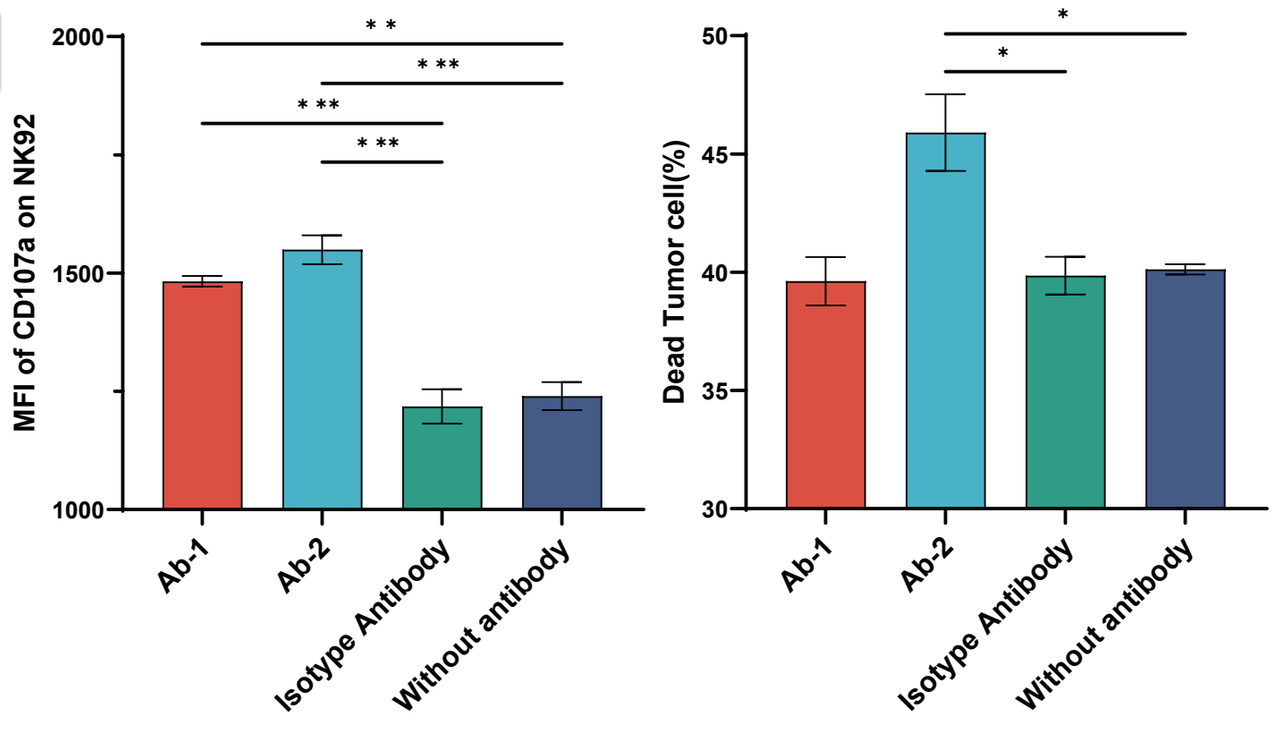
RESULTS

SDS-PAGE analysis of TIGIT and TIGIT nanobodies









CONCLUSION&FUTURE

1. In binding and competition assays, the selected TIGIT nanobodies can effectively bind to TIGIT and compete with CD155 for TIGIT binding.
2. The viabilities of K562 cells were significantly reduced when the nanobodies were added, indicating that nanobodies effectively block TIGIT on NK cells from binding to CD155 on tumor cells.
3. These findings suggest that the screened nanobodies have promising potential for further evaluation in tumor-bearing mouse models.
4. These nanobodies might offer significant benefits in clinical settings by improving patient selection and therapeutic outcomes in cancer immunotherapy.