

485 TIGIT/PVRIG HUMANIZED MICE-AN IDEA MODEL FOR STUDYING ANTI-PVRIG ANTIBODIES

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Background The poliovirus receptor (PVR)-associated immunoglobulin structural domain (PVRIG) is expressed as a single transmembrane protein mainly in CD8⁺ T cells and CD16⁺ and CD16⁺NK cells. In the tumour microenvironment, PVRIG binding to the receptor PVR inhibits T cell activation and attenuates the killing effect of NK cells, thereby contributing to the immune escape of tumour cells.

Methods We used gene editing technology to replace the murine extracellular region of Pvrig gene with the corresponding human PVRIG gene fragment in BALB/c-hTIGIT background mice. Humanized PVRIG was expressed mainly in NK cells of BALB/c-hTIGIT/hPVRIG mice, with an expression profile similar to that of wild-type mice.

Results Our data showed that anti-TIGIT antibodies and anti-PVRIG antibodies could significantly inhibit tumor growth in BALB/c-hTIGIT/hPVRIG CT26 tumor bearing mice. Furthermore, within the tumor-infiltrating lymphocytes, there was an increase in cytotoxic CD8⁺ T cells, which accurately mimics the mechanism of action of anti-TIGIT antibodies and anti-PVRIG antibodies.

Conclusions In conclusion, BALB/c-hTIGIT/hPVRIG mice are ideal models for studying the efficacy and pharmacodynamics of anti-PVRIG antibodies as a single agent or in combination with anti-TIGIT therapies.

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