and the intracellular domains where kept murine to enable salt bridges interaction, interaction with the CD3 zeta and the signaling into mouse cells.

**Results** T cells from CD3 epsilon epitope humanized mice are found in comparable frequency in spleen, blood and bone marrow from WT mice. B cells, monocytes, dendritic cells and NK frequencies are also similar to the frequencies of these cell types in WT mice, suggesting that the humanization of the epitope of CD3 epsilon did not alter the immune cells distribution in these mice. Activation of T cells with antibodies targeting human CD3 (clone SP34) induced CD4 and CD8 T cell proliferation, as well as production of IL-2 and IFN-gamma. The CD3 functionality was demonstrated in vitro by the ability of B cells to produce IgM upon activation of T cells, suggesting a proper cooperation between T and B cells. Additionally, a first class of T-cell engagers targeting both human CD3 and a tumoral antigen, induced tumor cell lysis of MC38-Ag in a concentration-dependent manner. A second class of T cell engagers, also targeting CD3 and a tumoral antigen, showed an anti-tumor effect in vivo, and this effect was also shown to be dose-dependent.

**Conclusions** These data suggest that the CD3 epsilon N-terminal epitope humanized mouse model enables the assessment of efficacy and mechanism of action of T-cell engagers. This model is currently being intercrossed with immunostimulatory humanized mouse models to provide new opportunities for assessment of bi-specific antibodies targeting the CD3 and immunostimulatory molecules. This model is the first generation of a broader program aiming at developing a Pan CD3 humanized model, where the gamma, delta and epsilon chains of the CD3 complex will be humanized. The Pan CD3 humanized mice are currently being investigated for immune responses and would provide a broader tool for assessment of T-cell engagers.

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