BALB/c-hVTCN1 – AN IDEAL MOUSE MODEL FOR EVALUATING THE EFFICACY AND SAFETY OF HUMAN VTCN1 INHIBITORS

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Background VTCN1, also known as B7-H4, is a protein that is expressed on the surface of certain cells, including tumor cells and immune cells. It belongs to the B7 family of immune checkpoint molecules, which play a crucial role in regulating the immune response. Immune checkpoint molecules can either promote or suppress immune responses, and their dysregulation can contribute to immune evasion by cancer cells.

Methods To evaluate the efficacy and safety of human VTCN1 inhibitors in an immunocompetent mouse model, we developed a humanized VTCN1 mouse model on BALB/c background (BALB/c-hVTCN1), using the CRISPER-CAS9 technology to replace the mouse VTCN1 (mVTCN1) extracellular IgV domain (not including the LQLLNS sequence) of BALB/c mice with the corresponding human VTCN1 (hVTCN1) fragments. In BALB/c-hVTCN1 mouse model, human VTCN1 could be detected in several tissues including heart, lung, breast, liver, kidney, etc. Also, there was no difference in blood leukocyte subpopulations in BALB/c and BALB/c-hVTCN1 mice.

Results Gempharmatech has evaluated the efficacy of VTCN1 inhibitors in preclinical models involves assessing their impact on tumor growth, tumor weight and immune cell infiltration, which demonstrated VTCN1 inhibitors could significantly inhibit tumor growth in BALB/c-hVTCN1 tumor-bearing mouse model.

Conclusions In summary, the VTCN1 humanized mouse model can be used in the preclinical evaluation of mono or combined immune checkpoint blockade with anti-human VTCN1 therapy.

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