Background CD39 catalyze the production of adenosine from ATP by combination with CD73. Adenosine has been recognized as an important modulator in anti-tumour immunity. In the tumor microenvironment, adenosine binds to adenosine receptors could inhibit the cytotoxic activity of T cells and NK cells, thereby suppressing the tumor killing ability of immune system and leading to tumor proliferation and metastasis. Combining inhibitors targeting PD-1/PD-L1 and CD39/CD73 may have synergistic effects in cancer treatment. By blocking PD-1 or PD-L1, the inhibitory signals on immune cells can be relieved, potentially restoring their anti-tumor activity. Additionally, inhibiting CD39/CD73 can reduce adenosine production and alleviate the immunosuppressive effects in the tumor microenvironment. Therefore, the combination therapy can enhance the effectiveness of immune checkpoint blockade by targeting multiple immunosuppressive pathways simultaneously.

Methods Gempharmatech has developed BALB/c-hPD1/hPDL1/hCD39/hCD73 mouse model by crossing BALB/c-hPD1/hPDL1/hCD39 with BALB/c-hPD1/hPDL1/hCD73 mice.

Results Human CD39 and CD73 proteins were mainly expressed on T cells, B cells, NK cells and Treg cells of BALB/c-hPD1/hPDL1/hCD39/hCD73 mice, similar to the expression profiles of CD39 and CD73 proteins in wild-type mice. The immune cell subsets of BALB/c-hPD1/hPDL1/hCD39 mice were identical to those of wild-type mice. Our data showed that anti-CD39 antibody combined with anti-CD73 antibodies could significantly inhibit tumor growth in BALB/c-hPD1/hPDL1/hCD39/hCD73 mice bearing CT26-hPDL1/hCD39/hCD73 tumor cells.

Conclusions In summary, BALB/c-hPD1/hPDL1/hCD39/hCD73 mice are ideal models for studying the efficacy and pharmacodynamics of anti-CD39/CD73 antibodies alone or in combination with anti-PD-1/PD-L1 therapy.