Double Humanized PD-1&CTLA-4 Mouse

**Strain Name:** C57BL/6-Pdcd1<sup>em1(hPDCD1)</sup> Ctl4<sup>em1(hCTLA4)</sup>/Smoc  
**Strain Background:** C57BL/6  
**Cat. No.:** IT-HU-00079

Double humanized PD-1 and CTLA-4 mice provide a unique and valuable model for evaluating human specific, combinatorial antibody therapies.

**Construction strategy**

On the C57BL/6 background, the full-length coding sequence of human CTLA-4 gene was placed immediately downstream of the start codon of the mouse endogenous Ctl4 gene, followed by a poly(A) element. This guarantees an exclusive expression of human CTLA-4 in the double humanized mice. A similar construction strategy was used for the Pdcd1 gene replacement.

**Validation data**

PD-1 expression in stimulated T cells
Figure 1. The expression of human PD-1 and CTLA-4 in double humanized PD-1&CTLA-4 mice was confirmed by FACS.

**Efficacy studies**

Figure 2. In vivo validation of double humanized PD-1&CTLA-4 mice. Double humanized mice were inoculated with MC38 cells, and randomly assigned to different groups (n=8) when the tumor grew to a volume of 100 mm³. A combinatorial treatment of anti-CTLA-4 and anti-PD-1 demonstrated a noticeable efficacy improvement compared to the same dose of single agent (top) without affecting the animal body weight (bottom).
Re-challenge studies

Figure 3. As shown in the previous figure, animals of group 1-4 received different doses of either single agent or combinatorial treatment. This graph showed the progression of the tumor implanted in the cured, G4 mice, implicating a systematic anti-tumor effect induced by the combinatorial antibody treatment.
Immune Checkpoint Humanized Mouse Models

Being recognized as a top scientific breakthrough in 2013, cancer immunotherapy is predicted to be one of the most promising research areas for improving patient outcomes. Although many immunotherapy breakthroughs may still lie ahead, important clinical advances have been made in the past few years for some of the deadliest cancers, reaffirming the potential of immunotherapy for many types of patients.

However, it is worth noting that drug candidates developed to interfere with human proteins may not comparably interact with their murine counterparts. It is therefore critical to develop humanized mouse models to enable in vivo efficacy evaluation of cancer immunotherapies.

Immune Checkpoint Humanized Mouse Models available at ingenious targeting laboratory

| 4-1BB | PD-1/PD-L1 |
| CD40 | PD-1/TIGIT |
| CD47 | PD-1/TIM3 |
| CD73 (NT5E) | PD-L1 |
| CTLA4 (C57BL/6) | PD-L1/CTLA4 |
| CTLA4 (BALB/c) | PD-L1/LAG3 |
| KDR | PD-L1/OX40 |
| LAG3 | PD-L1/TIGIT |
| OX40 | SIRPA |
| OX40/CTLA4 | SIRPA/CD47 |
| PD-1 (C57BL/6) | TIGIT |
| PD-1 (BALB/c) | TIM3 (C57BL/6) |
| PD-1/4-1BB | TIM3 (BALB/c) |
| PD-1/CD40 | TNFRSF1B |
| PD-1/CTLA4 | And more to come! |
| PD-1/LAG3 | |
| PD-1/OX40 | |

To get to know more about these models, visit our website www.genetargeting.com or contact our scientific experts at inquiry@genetargeting.com
About ingenious targeting laboratory

ingenious targeting laboratory (ingenious) has been a leading global provider of custom genetically modified mouse, rat, and rabbit models for over 20 years. As one of the very first mouse gene targeting companies, our trusted service is built on two decades’ worth of successful animal model creation for investigators, organizations, and companies worldwide. Our models have been published in hundreds of journals including Science, Nature, and Cell, making us one of the most validated and respected production companies in the industry. We are excited to add catalog mouse models to our service repertoire by means of our collaboration with Shanghai Model Organisms Center (SMOC).