The past few years have witnessed a renaissance in the field of cancer immunotherapy, relating largely to the clinical advances associated with the development of immunomodulatory agents, e.g. monoclonal antibodies targeting the immune inhibitory pathways (CTLA-4 and PD-1/PD-L1). Often, the preclinical efficacy assessments are based on the evaluation of surrogate anti-mouse target antibodies using mouse syngenic tumor models, which are highly efficient in an immune-competent system. However, this strategy is limited due to the fact that the immune systems in human and mouse are different, and a surrogate molecule needs to be tested in these syngenic models. Here we set out to validate mouse models that harbor human immune cells by pre-engrafting the immuno-deficient mice with human PBMC (the Mixeno™ model), and use them for efficacy evaluation of the humanized anti-PD-1 antibody. PD-L1 high-expression human tumor cell lines are selected for these in vivo models. Based on the preliminary result, the Mixeno™ models are hopefully becoming useful tools in immunotherapeutic antibody development, and may greatly increase the clinical translatability of animal studies.

Three Types of In Vivo Models for Immunotherapy

- **Subcutaneous model (14 models)**: Breast cancer, colon cancer, liver cancer, melanoma, pancreatic cancer, prostate cancer, renal cancer. HCC827 cell line was identified as a high PD-L1 expression cell line, and selected to develop in vivo model for in vivo efficacy evaluation, though correlation between PD-L1 expression level and the efficacy by anti-PD-1 antibody therapy is still not clear.
  - BMS-936558 produced 50% tumor growth inhibition in the HCC827 Mixeno™ Model.
  - Mixeno™ Models are hopefully becoming the useful tools for in vivo evaluation of immunotherapeutic agents, but more investigation is required to determine many parameters about the status of the human immune components along with the immunotherapeutic treatment.

### References