Syngeneic tumor models have long been used in cancer research. The recent clinical success of anti-CTLA-4 and anti-PD1 antibodies contributed to increasing the interest around syngeneic models to evaluate cancer immunotherapy. Surprisingly, although they were initially thought to be immuno-suppressive, classic anticancer therapies, such as chemotherapy or radiotherapy, can promote antitumor immunity, thus synergizing with cancer immunotherapies. Suitable models in which to evaluate combination therapies are in great demand. To meet this demand, Crown Bioscience has established a large collection of syngeneic models that covers most tumor types. Our syngeneics have been extensively profiled in vivo using anti-PD1, anti-PD-L1, and anti-CTLA-4 antibodies, providing necessary information for selecting the appropriate models and doses for combination therapy. Most recently, we have generated detailed gene expression and mutation profiles for our models, as well as performed RNAseq to identify transcripts from alternative gene splicing, post-transcriptional modifications, and gene fusion. Moreover, our FACS analysis to isolate subpopulation of T cells, such as effector and regulatory T cells, provides insights about each checkpoint inhibitor’s effect on immune cells. Combining the in vivo immunotherapy profiles of our syngeneic models with comprehensive profiling data will enable models selection based on specific targets and the development of combination therapies that may in the near future benefit patients.

**Methods**

Animals and syngeneic models

Immunocompetent mice (e.g. C57BL/6, BALB/c or C3H) were used to generate syngeneic models. A suspension of tumor cells in 0.1ml PBS was inoculated into the right lower flank of each mouse.

Procedures

Treatment with the immunotherapeutic antibodies were started when mean tumor size reached 80-120 mm³. 6-10 tumor bearing mice were included in each group.

Endpoints

Tumor volume was calculated using the formula: V(mm³) = (D x d)²/2, where D and d are the long and short diameters of the tumor, respectively. The tumor size is then used to calculate the TGI (tumor growth inhibition) values. Tumor samples were collected for FACS, IHC, IF and RNAseq analysis.

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