Syngeneic Models for Developing Cancer Therapeutics Targeting Immune System

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Abstract

Syngeneic tumor models have long been used in cancer research, from mechanistic study to developing cancer therapeutics, especially those that require intact immune system, such as the ADCC effect in many of the antibody therapeutics. Recently, cancer immunotherapy regained its momentum in this field. To meet this demand, Crown has established a large collection of syngeneic models that covers many of the tumor types and mutational profiles. In addition, we've also profiled the models using anti-mouse PD1/PD-L1 antibodies. The syngeneic models display very different responses toward the immunotherapeutics, ranging from shrinking the tumor to stimulating the tumor growth. These results emphasize the need to carefully select models based on the development goals. A single agent development approach would require selecting the models with the best response, while a combination study design would require a model with suboptimal response. Our comprehensive list of syngeneic models and profiling data are essential in developing cancer immunotherapies that may one day benefit the patients.

Method

Animals: C57BL/6 and BALB/c mice purchased from Beijing HFK Bio-Technology Co. Ltd. (HFK, Beijing, China) and Shanghai Laboratory Animal Center (SLAC, Shanghai, China).

Tumor Inoculation: For subcutaneous syngeneic models, each mouse was inoculated at the right flank with tumor cells for tumor development.

Group and Treatment: The treatments for the therapeutic study were started when mean tumor size reached 100 mm$^3$ in subcutaneous model.

Endpoints: Tumor volume was calculated as the formula: $V = (a \times b^2)/2$, where $a$ and $b$ were the long and short diameters of the tumor, respectively.

Statistical Analysis: For comparison between two groups, an independent sample t-test were used. All data were analyzed using SPSS 18.0. $p < 0.05$ was considered to be statistically significant.

Results

Conclusions

The syngeneic models display very different responses toward immunotherapeutics. Careful selection of models based on development goals are necessary, be it single agent or combination therapy.

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