Of Mice, Dogs, Pigs, and Men: Choosing the Appropriate Model for Immuno-Oncology Research

The immune system plays dual roles in response to cancer. The host immune system protects against tumor formation via immunosurveillance; however, recognition of the tumor by immune cells also induces sculpting mechanisms leading to a Darwinian selection of tumor cell variants with reduced immunogenicity. Cancer immunoediting is the concept used to describe the complex interplay between tumor cells and the immune system. This concept, commonly referred to as the three E’s, is encompassed by 3 distinct phases of elimination, equilibrium, and escape. Despite impressive results in the clinic, cancer immunotherapy still has room for improvement as many patients remain unresponsive to therapy. Moreover, many of the preclinical results obtained in the widely used mouse models of cancer are lost in translation to human patients. To improve the success rate of immuno-oncology research and preclinical testing of immune-based anticancer therapies, using alternative animal models more closely related to humans is a promising approach. Here, we describe 2 of the major alternative model systems: canine (spontaneous) and porcine (experimental) cancer models. Although dogs display a high rate of spontaneous tumor formation, an increased number of genetically modified porcine models exist. We suggest that the optimal immuno-oncology model may depend on the stage of cancer immunoediting in question. In particular, the spontaneous canine tumor models provide a unique platform for evaluating therapies aimed at the escape phase of cancer, while genetically engineered swine allow for elucidation of tumor-immune cell interactions especially during the phases of elimination and equilibrium.