The Oncopig Cancer Model: An Innovative Large Animal Translational Oncology Platform

Despite an improved understanding of cancer molecular biology, immune landscapes, and advancements in cytotoxic, biologic, and immunologic anti-cancer therapeutics, cancer remains a leading cause of death worldwide. More than 8.2 million deaths were attributed to cancer in 2012, and it is anticipated that cancer incidence will continue to rise, with 19.3 million cases expected by 2025. The development and investigation of new diagnostic modalities and innovative therapeutic tools is critical for reducing the global cancer burden. Toward this end, transitional animal models serve a crucial role in bridging the gap between fundamental diagnostic and therapeutic discoveries and human clinical trials. Such animal models offer insights into all aspects of the basic science-clinical translational cancer research continuum (screening, detection, oncogenesis, tumor biology, immunogenicity, therapeutics, and outcomes). To date, however, cancer research progress has been markedly hampered by lack of a genotypically, anatomically, and physiologically relevant large animal model. Without progressive cancer models, discoveries are hindered and cures are improbable. Herein, we describe a transgenic porcine model-the Oncopig Cancer Model (OCM)-as a next-generation large animal platform for the study of hematologic and solid tumor oncology. With mutations in key tumor suppressor and oncopenes, $TP_53^{R167H}$ and $KRAS^{G12D}$, the OCM recapitulates transcriptional hallmarks of human disease while also exhibiting clinically relevant histologic and genotypic tumor phenotypes. Moreover, as obesity rates increase across the global population, cancer patients commonly present clinically with multiple comorbid conditions. Due to the effects of these comorbidities on patient management, therapeutic strategies, and clinical outcomes, an ideal animal model should develop cancer on the background of representative comorbid conditions (tumor macro- and microenvironments). As observed in clinical practice, liver cirrhosis frequently precedes development of primary liver cancer or hepatocellular carcinoma. The OCM has the capacity to develop tumors in combination with such relevant comorbidities. Furthermore, studies on the tumor microenvironment demonstrate similarities between OCM and human cancer genomic landscapes. This review highlights the potential of this and other large animal platforms as transitional models to bridge the gap between basic research and clinical practice.