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Introduction

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Cancers are complex diseases with diverse molecular etiologies, intimate interactions between tumor and stromal cells, and rapid mutability to adapt to different environments. Therefore, predictive preclinical models require accurate engineering for the induction of cancer *in situ*. The genetically engineered mouse (GEM) is the leading mammalian model for basic genetic research of human cancers.

After decades of investigations, the scientific community came to realize that studying biologically and genetically relevant mouse models is of critical importance. Recently, a murine lung cancer model was used to identify genetic modifiers of therapeutic response in a "co-clinical trial" that mirrors an ongoing human clinical trial in patients with KRAS mutant lung cancers [1]. A pancreatic cancer model helped to uncover a potential major impediment to the treatment of this disease, namely their impermeability to drug perfusion [2]. Basic findings obtained from mouse models are *en route* to be tested in drug efficacy studies in humans, e.g., trials of gemcitabine with IPI-926 and GDC-0449 in combination with gemcitabine and erlotinib or Abraxane.

Despite some success, there are still many challenges ahead to maximize the value of the mouse as a cancer model. In this issue of *Cancer and Metastasis Reviews*, we provide an up-to-date discussion on animal models for several prominent human cancers. Dr. Swartling et al. will describe numerous murine brain tumor models in the context of normal brain development and the potential for these animals to impact research of glioma and medulloblastoma, the most commonly occurring malignant brain tumors in adults and in children, respectively. Drs. Dine and Deng will review features of over 20 distinct breast cancer-associated gene 1 (BRCA1) mutant mice, including null, hypomorphic, isoform, conditional, and point mutations, and their applications to cancer prevention and therapeutic treatment. Drs. Johnson and Fleet will provide an overview of the mechanisms driving human colorectal cancer, discuss the approaches for modeling colon cancer in animals, and describe diet- and chemical-induced cancer models as well as GEM models. Drs. Cook and Pardee will highlight various carcinogen-induced, viral and transposon-induced, and GEM models of acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia and describe their contributions to the improved understanding and treatment of these cancers while acknowledging limitations. Although many mouse models of lung adenocarcinoma exist, only a few mouse models of lung squamous cell carcinoma have been developed. Dr. You et al. will review the applications of mouse lung squamous cell carcinoma models with different stages of squamous lesions and squamous cell carcinomas to cancer development and chemoprevention studies. Drs. Qiu and Su will summarize the currently available animal models for pancreatic cancer and the advances in pancreatic cancer animal modeling, compare and contrast the advantages and disadvantages of three major categories of models: carcinogen-induced, xenograft and allograft, and GEM models, and highlight the combinations of these models with various newly developed strategies and cell lineage labeling systems. Drs. Irshad and Abate-Shen will describe GEM models for prostate cancer with some historical perspectives and focus on their strengths and limitations in relation to human

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prostate cancer. Finally, skin cancer is the most prevalent of all cancers with over two million cases of non-melanoma skin cancer each year and 75,000 melanoma cases in 2012. Dr. Gober et al. will discuss some of the important animal models that have been useful to identify critical pathways involved in basal cell carcinoma, squamous cell carcinoma, and melanoma.

With an increasing diversity of GEM models available, it is important to keep in mind that a given GEM model only partly recapitulates human disease. Many GEM models are generated using inbred mouse strains. Inbred models represent, at best, single individual, and therefore it may be difficult to successfully translate information garnered into human populations [3]. Nevertheless, appropriate mouse studies will provide valuable hypotheses to be tested in the clinic.

Reference

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