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ANIMAL MODELS OF CANCER BIOLOGY

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Supplement Aims and Scope

This supplement is intended to focus on animal models of cancer biology. Growing human tumors in nude mice, engineering and studying syngeneic animal tumors, perspectives on animal models, and large animal endogenous tumor models are included within the supplement's scope.

Cancer Growth and Metastasis aims to provide researchers working in this complex, quickly developing field with online, open access to scholarly articles on the growth and metastasis of cancer. In a field where the literature is ever-expanding, researchers increasingly need access to up-to-date, high quality scholarly articles on areas of specific contemporary interest. This supplement aims to address this by presenting high-quality articles that allow readers to distinguish the signal from the noise. The editor in chief hopes that through this effort, practitioners and researchers will be aided in finding answers to some of the most complex and pressing issues of our time.

Articles should focus on animal models of cancer biology and may include the following topics:

- Growing human tumors in nude mice: methodology, advantages, cautions
- Engineering and studying syngeneic animal tumors
- Perspectives on animal models
- Large animal endogenous tumor models.

At the discretion of the guest editors other articles on other relevant topics within the scope of the supplement may be included.

Animal models are valuable tools for studying the biology and genetics of human cancers as well as for preclinical investigation of anti-cancer therapeutics and cancer prevention. Various animal models have been generated by genetic engineering, graft transplantation, and viral/physical/chemical induction. Accumulating data from studies using those models have enabled us to gain insight into the genetic mechanisms underlying malignant transformation and cancer progression. Studies from animal models of cancer have been utilized for preclinical investigation of therapeutic efficacy and toxicity of chemicals and biologicals. Tremendous advances have been made in the generation of animal models of cancer, which have become increasingly sophisticated by application of new technologies and integration of clinical information from patients. The goals are to faithfully recapitulate the human malignant diseases in the animal models and apply them as preclinical tools, with the hope of successfully translating the basic knowledge into treatment and prevention of cancer in humans.

The mouse has been the traditional animal model for basic and preclinical studies of cancer, and other organisms including zebrafish play important and complimentary roles as models of cancer research. Genetically engineered mouse and zebrafish models of cancer have been generated by a variety of interventions such as chemical or physical mutagenesis, viral infection, insertion of transgenes, homologous recombination, and the recently developed gene edition. Studies from the genetically engineered models and xenograft models have led to discovery of the molecular basis of tumor initiation, growth, and metastasis, as well as being utilized for anti-cancer

drug discovery and testing. There are numerous publications of research studies regarding generation of animal models of cancer and their pre-clinical applications. A few recently published review articles are cited here for reference.[1–5]

For this supplementary issue, we invited investigators with expertise in various specific areas to contribute articles that focus on cancer biology and genetics using animal models. Several articles focus on mouse models of different types of cancer including pancreatic cancer, melanoma, ovarian cancer, esophageal cancer, and skin cancer. Using a mouse orthotopic model, Padavano et al applied homologous recombination to disrupt the oncogenic *K-RAS* in a human pancreatic adenocarcinoma cell line and examined cancer growth and invasion.[6] These data demonstrate that pancreatic cancer cells with disrupted mutant *K-RAS* exhibited reduced tumor growth and metastasis, and RhoA and RalA GTPase downstream of mutant *K-RAS* are involved in controlling cancer cells migration and invasion. For *in vivo* studies of melanoma, Kuzu et al described a variety of animal models such as genetically engineered mice, patient-derived tumor xenografts, and a topically inducible BRAF mouse model.[7] In addition, the authors compared the advantages and limitations of these various models, and discussed how development of those models may help improve prediction of investigational drugs for therapeutic efficacy in patients with melanoma. Bobbs et al provided an overview on the utility of patient-derived xenograft and genetically engineered mouse models for recapitulating different aspects of ovarian cancer and therapeutic testing.[8] Similarly, Tetreault described tumor xenograft in mice and genetically engineered mice for studying esophageal squamous cell carcinoma and adenocarcinoma.[9]

Several articles in this supplementary issue illustrate the utility of animal models for studying other aspects of cancer and therapy. In a mouse model of colorectal cancer, LeGendre-McGhee et al conducted a time-serial assessment of drug combination interventions using optical coherence tomography (OCT).[10] They demonstrated the feasibility and validity of OCT as a minimally invasive modality for monitoring tumor development and therapeutic efficacy in mouse models of colorectal cancer. Nowotarski et al described mouse models of non-melanoma skin cancer induced by chemicals or ultraviolet B radiation.[11] Based on studies in mice with genetic alteration of epidermal polyamines, they discussed the important roles of dysregulated polyamines in tumor promotion and the survival pathways in epithelia. Animal models of cancer-induced bone pain and the mechanistic insights gained from these models are being reviewed by Slosky et al.[12] They discussed the utility of such models to understand the neuromuscular profile of cancer pain for the goal of developing effective therapeutics for cancer-induced bone pain. Finally, the capability of the genetic mouse models of cancers to recapitulate human tumors by manipulations of single gene versus multiple genes commonly involved in malignancies is reviewed by Lehman and Stairs.[13]

Animal models of cancer biology are becoming more sophisticated by application of new technology, and they play ever increasingly important roles in mechanistic studies and pre-clinical research. Modeling animals is essential for investigation of not only tumor growth and metastasis, but also tumor-associated inflammation and microenvironment, cancer stem cells, tumor heterogeneity, and therapeutic resistance. The recently developed CRISPR-Cas9 system for editing the genomes of model animals as well as cell lines for animal xenograft models is expected to facilitate recapitulation of human malignancies. Animal models, particularly zebrafish, that enable high-throughput screening for drug discovery, drug validation, and developmental toxicity will play a unique role in pre-clinical oncology. Furthermore, application of patient-derived tumor xenograft in animal models is expected to help personalize treatment using chemo- and targeted therapeutics. The recently introduced Nonobese Diabetic Severe Combined ImmunoDeficient Gamma (NSG™) mice will provide the platforms for patient-derived xenograft to develop immunotherapeutics for patients with malignant diseases.

Translating animal models of cancer in combination with molecular tumor profiling and developing clinically useful targeted therapeutics are expected to produce a positive impact towards the goal of precision treatment that is personalized for patients with malignant diseases. This supplementary issue, *Animal Models of Cancer Biology*, is intended to provide new insights and updated information on the use of animal models for studying different aspects of malignant diseases. We hope it will stimulate discussion and collaboration among scientists, clinicians, and health care providers for the goal of understanding the mechanisms of malignant neoplasia and translating the knowledge into advancement of care for patients with cancer. On behalf of the editorial office of *Cancer Growth and Metastasis*, we wish to express our sincere gratitude to the reviewers for their time and efforts on the manuscripts in this supplementary issue. Their critical comments are greatly appreciated, and their constructive suggestions have helped assure and improve the quality of the manuscripts.

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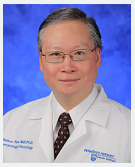

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