Conditional Mouse Models of Cancer

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Abstract The development of inducible and conditional technologies allowed us to generate transgenic mouse models that faithfully recapitulate human tumorigenesis. It is possible to control, in time and space, the development of tumors in almost every mouse tissue. The result is that now we have available mouse models for all major human cancers. Novel noninvasive approaches to tumor imaging will enable us to follow tumor development and metastasis in vivo, as well as the effects of candidate therapeutic drugs. Such new generation tumor models, which accurately emulate the disease state in situ, should provide a useful platform with which to experimentally test drugs targeted to specific gene products, or combinations of genes that control rate-limiting steps of tumor development. In this review, we focus on the different mouse models for colon cancer.

Keywords Colon cancer · Conditional mouse models

Abbreviations

Rb Retinoblastoma
min Multiple intestinal neoplasia
Apc Adenomatous polyposis coli
HNPPCC Hereditary nonpolyposis colorectal cancer
CRC Colorectal cancer
FAP Familial adenomatous polyposis
NSAIDs Nonsteroidal anti-inflammatory drugs
MRI Magnetic resonance imaging
CT Computed tomography
The Ideal Model for Human Cancer

Mouse models of human cancer have played an important role in formulating modern concepts of multistage carcinogenesis, and are providing us with a new set of tools for testing novel therapeutic approaches to cancer treatment. However, as the scientific and medical community’s understanding of human cancer becomes more pronounced, limitations and potential weaknesses of existing models are revealed. There is the expectation that mouse models will mimic human cancer, i.e., tumors developing in transgenic mice should look and behave like the human disease. Mouse tumors should have the same or similar histological features of the corresponding human tumors; they should progress through the same stages and cause the same physiological effects on the host; the same genes and/or pathways should be affected in tumor initiation and progression; the response of a given tumor to a particular therapy in the mouse should accurately reflect the response in human patients; and the results from preclinical testing of experimental therapies in mouse models should predict the efficacy of such therapies in clinical trials in humans.

Certain mouse models recapitulate human disease extremely well. For example, overexpression of c-Myc in the mouse leads to similar pathologies (B cell lymphomas) as it does in man (Adams et al. 1985; Macleod and Jacks 1999). However, identical genetic lesions do sometimes produce very different pathologies in the two species. A good example is the retinoblastoma gene product (Rb). Rb transduces antiproliferative signals and is an important tumor suppressor. In humans, loss of Rb leads to the development of retinoblastoma at an early age, followed by osteosarcomas and small cell lung cancer (Jacks et al. 1992). In mice, however, loss of Rb very rarely causes retinoblastoma (Jacks et al. 1992; Macleod and Jacks 1999); Rb-null mice ex-