Improved “humanized” mouse models should help to overcome current limitations given by xenogeneic barrier between humans and mice. Establishment of a functional human immune system and a corresponding human microenvironment in laboratory animals will strongly support further research.

Drug discovery, systems biology, and translational research are moving closer together to address all the new hallmarks of cancer, increase the success rate of drug development, and increase the predictive value of preclinical models.

Keywords

Mouse models · Patient-derived xenograft (PDX) · Preclinical oncology · Translational research

1 Introduction

Tumor biology research and preclinical drug discovery both depend heavily on specific in vivo disease models. Historically, basic research and drug characterization were based on a handful of preclinical tumor models from each indication. Given our current knowledge about tumor heterogeneity, we can now understand why results from studies with 2–3 lung cancer models could have been only lowly predictive for the clinical outcome and a risky development work was a burden to clinicians and patients.

Almost in parallel with the new millennium, processes have changed substantially. This has been driven by increasing costs for the clinical development in contrast to often disappointing improvements for the patients. Growing insight into the fundamental genetic basics of the disease through analysis of gene expression and mutations and the development of fascinating new technologies in genetic engineering and bioinformatics – key word systems biology – have provided the technical basis for this paradigm shift.

As consequence, primary pharmacology processes in preclinical cancer research have changed, and the elementary task is the establishment of the right model and access to appropriate tools for each step of the drug discovery process (as shown in Fig. 1). This also requires former single disciplines to work more and more together, forming a more and more integrated process of preclinical drug discovery.

2 Demands on Target Identification and Validation Models

Innovative technologies in target identification and validation have also changed the request on the disease models. Have been a small number of extensively characterized tumor cell cultures and mouse models the standard for many decades, the target-driven approaches now require models reflecting better the clinical situation. Genotype-dependent stratification of patient cohorts to predict efficacy