Using colon cancer PDX models, it has been recently demonstrated that this can also be simulated in this model system. While initial treatment resulted in tumor regression, a regrowth was observed shortly after treatment suspension. Further treatment cycles were able to re-induce tumor regression by a combination treatment, whereas the single treatments failed to demonstrate activity in recurrent tumors (Schmieder et al. 2014).

These methods can also be used to address the questions regarding resistance mechanisms. Development of second-line resistance to anticancer therapies can be induced due to sustained treatment over several generations of a xenografted tumor. The developed resistant tumors can be used to analyze mechanisms of resistance. Models for antiestrogen-resistant breast cancer have been developed, and by comparing gene expression of the parental and the resistant tumors, Her-2 upregulation has been identified as resistance mechanism (Sommer et al. 2003).

Human tumors accumulate genetic and molecular abnormalities, leading to broad heterogeneity. Large panels of molecular-defined and characterized PDX models reflecting tumor heterogeneity have increased impact for predicting the response to new therapeutic agents in the clinic. The reproducibility, renewability, and availability of tumor material are undisputed advantages.

8 Translational Preclinical Studies with PDX Can Identify Predictive Response Marker

Interesting data have been generated in a study using a large set of patient-derived NSCLC xenograft models (Fichtner et al. 2008). In this panel of NSCLC models, heterogeneous response to Sagopilone treatment was determined in an integrative preclinical phase II study (Hammer et al. 2010). Genome-wide gene expression analysis and mutation analysis of selected genes were used to identify potential markers of response and refractoriness and to explore the mechanism of Sagopilone's antitumor activity in vivo. Overexpression of marker genes (e.g., CA9, CA12, EPHA4, ITGA6) together with TP53 gene expression and mutation has been identified as potential predictive marker for response to Sagopilone (Hammer et al. 2010).

A large panel of colorectal cancer PDX models was developed and tested for drug sensitivity in parallel with a streamlined genetic characterization utilizing panel sequencing and gene expression. The study was used to evaluate to what extend PDX model-based technologies can support translational cancer research processes and even replace clinical experiments (Pechanska et al. 2013; Henderson et al. 2014). In this study it has been confirmed that kRas mutations are a strong predictor for resistance to cetuximab (with 86% specificity), and in addition mutations in bRaf and PI3K have been identified as additional predictive biomarker for drug response (Pechanska et al. 2013).

PDX of pancreatic cancer has been also used as a model for translational medicine (Behrens et al. 2014). For pancreatic cancer, similarity between the activity of gemcitabine in PDX models and respective clinical trial data is notable (Garrido-Laguna et al. 2011). Further, PDX can be utilized as a potential screening