standard for the evaluation of immunological therapies. In the last years, transgenic mice stimulating the differentiation of cotransplanted human hematopoietic stem cells have been developed. These mice will develop a functional human immune system, allowing the analysis of new immune therapies (Alcantar-Orozco et al. 2013; Cook et al. 2013; Futakuchi and Singh 2013; Reisfeld 2013; Stromnes et al. 2014).

The establishment and maintenance of patient-derived xenografts are time and cost intensive. Depending on the tumor type, engraftment rate of P1-generation ranges from 15% to 80% and usually takes 2–3 months. The following conservation, characterization, and validation process need further 4–6 months setting the time lines between 6 and 9 months.

These time lines are challenging for the use of the PDX for individual drug response prediction studies. Data will not be available for first-line treatments; however, it could be of valuable help for planning second-line therapies after tumors relapsed.

Working with in vivo tumor models set high demands on the qualification of the scientific personal and the laboratories (clean room, biobanking equipment, and molecular biology).

10 Outlook

Depending on the stage of the drug discovery program, different models are required. For primary in vitro screening, cell lines can be utilized easily from the available large panels or generated by genetic engineering. They can be selected based on the target or the question to be answered. For secondary in vitro screening, larger panels of tumor cell lines with known sensitivity or resistance to available standard drugs are used for further profiling.

Classical 2D cell cultures lack the cellular interactions and structural properties of their donor tissues divesting spatial in vivo-like organization and intra-tumor heterogeneity. This frequently results in different gene expression profiles and drug response readouts. To better mimic the tumor's composition, in vitro 3D models for various solid tumor entities have been established and currently studied with increasing intensity.

Often a differential pattern of sensitivity can be observed using in vivo models. This gap between in vitro and in vivo activity constrains that in vivo experiments are still crucial and remain an integral part to evaluate tumor response in the near future.

Although mouse xenograft models derived from established human cancer cell lines have undoubtedly enhanced the understanding of the antitumor activity of novel anticancer agents, these models have several disadvantages. Depending on the number of cell passages, xenografts can behave very differently to the primary tumor (Haddad and Yee 2008), and combined with other deficiencies in preclinical approaches (Sharpless and Depinho 2006), this can reduce the relevance of established xenograft models for predicting the probability of success of anticancer