

disadvantage regarding cost and time economy due to their larger size and generation time when compared to mice. For some specific approaches (e.g., physiological/anatomic and hormone-related questions, experimental handling, need of organ material, and PK studies), the laboratory rat might be the better option.

6 Humanized Mice

A current challenge is to overcome the limitations of “classical” mouse xenograft models: the lack of a functional immune background as well as the replacement of the human neoplastic microenvironment by mouse stromal components. Tumor-stroma interactions and blockade of the immune response are well-known factors promoting the tumor growth (Goubran et al. 2014; Wang et al. 2014). The development of appropriate models for the preclinical evaluation of approaches targeting these mechanisms is the focus of tumor model developers. Especially cancer immunologists are limited in their research to immune competent mice with syngeneic tumor models. Given differences in the homology between human and murine proteins or pathways are making the development difficult and less predictive.

Recent approaches have been based on the cotransplantation of human cancer cells as well as human immune or stromal cells into an immunodeficient mouse. As an example, hematopoietic stem cells, engineered NK and T-cells, or mononuclear cells from the peripheral blood have been successfully engrafted on tumor-bearing NOD/SCID mice and used for the evaluation of T-cell-activating therapies (Zhou et al. 2014; Brischwein et al. 2006; Schlereth et al. 2005; Dreier et al. 2003; Fu et al. 2014; Wege et al. 2014; Thibaudeau et al. 2014; Rongvaux et al. 2014; Alcantar-Orozco et al. 2013). Several groups are working on the generation of humanized mouse models for oncological purposes. Fu et al. (2014) established a humanized ovarian tumor stroma due to the transplantation of normal ovarian tissues. The development of a human immune system after implantation of hematopoietic stem cells for a breast cancer xenograft model was described by Wege et al. (2014). The injection of CD34⁺ cells into specific genetically modified mice results in the production of functional human monocytes, macrophages, and NK cells (Rongvaux et al. 2014).

In summary, xenotransplantation of patient tumors on “increasingly humanized mice” will strongly support predictive preclinical oncology research and moreover provide a fundamental basis for “personalized medicine.”

7 Scopes of Patient-Derived Xenografts

Classical 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 (Cree et al. 2010). To better mimic the tumor’s composition, in vivo PDX