platform for clinical trials as it could be shown in a prospective study that the combination of *nab*-paclitaxel and gemcitabine is effective in pancreatic PDX. This outcome is correlated with the clinical efficacy of the combination. Indeed, in a randomized phase III study, this regime has shown to provide a survival benefit for patients with advanced pancreatic cancer, and it is likely to become a standard of care in this setting (Von Hoff et al. 2013).

In another PDX study with gemcitabine, the expression of gemcitabine-activating enzyme deoxycytidine kinase was identified as a predictor of drug efficacy. A subsequent analysis of this marker in clinical samples confirmed these results (Rubio-Viqueira et al. 2006; Sebastiani et al. 2006).

9 Current Limitations

One disadvantage of PDX is the loss of the human tumor microenvironment during engraftment of patient material. This may affect tumor progression and is discussed as one reason for the low take rate of breast and prostate xenografts (Hidalgo et al. 2014). A review of Fang and DeClerk (2013) showed clearly the impact and benefit of the tumor microenvironment as target for anticancer treatment. Several integrin inhibitors (EMD 121974, CNTO 95, MEDI-522) that impair the communication between tumor cells and extracellular matrix are under clinical investigation (Dechantsreiter et al. 1999; O'Day et al. 2011; Hersey et al. 2010). The therapeutic potential of the tumor surrounding tissue is discussed for several entities, like pancreatic (Rossi et al. 2014), breast (Nwabo Kamdje et al. 2014), and prostate cancer (Chiarugi et al. 2014). However, after xenotransplantation, the human stromal components are replaced by a murine texture within 3–9 weeks (Hylander et al. 2013). With respect to therapeutic approaches targeting the human tumor microenvironment, the classical PDX models are therefore less feasible. The stroma replacement can be decelerated by the engraftment of large, non-disrupted tissue fragments and by the use of NOD/SCID mice with knockdown of IL2Ry (Bankert et al. 2001, 2011). In addition, the cotransplantation of human fibroblasts has been evaluated to generate PDX models with a more "humanized" microenvironment (Hoffmann unpublished results).

As mentioned earlier, a human microenvironment is strongly needed for another pillar of tumor therapy – the activation of immune reactions. Xenotransplanted human tumor cells are growing well in immunodeficient mice, very similar to the patient where they have escaped the body's immune control. Whereas in the patient a functional immune system is present and can be redirected against the tumor cells, the currently used immunodeficient mouse strains are mainly lacking functional immune cells (i.e., tumor-associated macrophages, dendritic cells, cytotoxic T-cells) and secretion of inflammatory cytokines (Fang and DeClerk 2013; Duechler et al. 2014; daChuna et al. 2014; Paulsson et al. 2014). Consequently, the preclinical evaluation of immunotherapeutic strategies in PDX has certain limitations. Therefore, the less predictive syngeneic mouse models or the cotransplantation of human peripheral blood mononuclear cells has been the