Background and Aim
The preclinical evaluation of novel immune checkpoint modulators is dependent on models with functional human immune cells. In previous experiments, we established humanized mouse models by transplantation of hematopoietic stem (HSC) cells to immunodeficient mice. Transplantation results in the engraftment of a functional human immune system. By co-transplantation of human patient-derived xenografts (PDX), we successfully generated a fully human tumor-immune cell model in mice. These humanized immune-PDX models for melanoma and lung cancer were further characterized by treatment with immunotherapeutic drugs like the CTLA-4 inhibitor ipilimumab and PD-1 inhibitor Nivolumab. In our current studies, we investigated the functionality of the human immune cells and evaluated concepts for combination therapies i.e. with chemotherapy or radiation. We further established new human immune-PDX models from other tumor entities like lymphoma, pancreatic or breast cancer.

Summary and Outlook
In summary, HSC transplantation into immunodeficient mice generates a human immune system. PDX from different entities are characterized by a differential expression of PD-L1 comparable to the clinical situation. Depending on PD-L1 expression, PDX showed a tumor growth delay on humanized mice compared to non-humanized mice. Our humanized models enable preclinical studies on tumor immunology, evaluation of new immune therapies and combinations, as well as the identification and validation of biomarkers for tumor immunotherapy.