**Background and Aim**

- Preclinical evaluation of novel immune cell therapies, checkpoint inhibitors, and immune cell engagers

**Summary and Outlook**

- We successfully established a fully humanized mouse model for immune oncology by co-transplantation of PDX and human HSC or immune cells (PBMCs, NK or T cells).
- We observed engraftment of PDX on most humanized mice, however, in some cases, it was delayed and seems to be dependent on HLA matching.
- We see different therapeutic effects of checkpoint inhibitors like Nivolumab, Pembrolizumab, or Ipilimumab with strong to minor responders or resistant tumors.
- Comparing tumor growth and checkpoint inhibitor activity in the pancreatic cancer PDX Panc12975 on four different humanized mouse models, humanization with HSC provided best results in comparison to single immune cells.
- We demonstrated in our preclinical studies the eligibility of the humanized models for research in tumor immunology, evaluation of new therapies and combinations, as well as the identification and validation of biomarkers for immune therapy.
- Combination therapies with radiation using mouse strains improving engraftment of HSC (NOD-EXL mice) and immune cells (NOD-IL-15 mice) are under investigation.

**Evaluation of Immuno Therapies in Human HSC - PDX Models**

- Delayed engraftment of glioma PDX on humanized mice with HSC, minor efficacy of checkpoint inhibitor Ipilimumab.
- Efficacy of checkpoint inhibitor Ipilimumab could be shown in Nivolumab-resistant Lymphoma model.

**Evaluation of Immuno Therapies with PDX Model Panc12975 on Four Different Humanized Mouse Models**

- Comparable engraftment of Panc12975 on HSC-humanized and non-humanized mice, efficacy of checkpoint inhibitors Nivolumab and Pembrolizumab could be shown in Panc12975 PDX model.
- Treatment with checkpoint inhibitor Nivolumab or Pembrolizumab in PBMC-humanized mice showed no effect on tumor growth in Panc12975 PDX model.
- Treatment with checkpoint inhibitor Nivolumab or Pembrolizumab on NK-cell humanized mice showed no effect on tumor growth in Panc12975 PDX model.