

Poster presentation

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## Immunomediated growth and regression of pancreatic tumors *in vivo*

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We are using a novel spontaneous pancreatic adenocarcinoma tumor model to investigate immunotherapeutic approaches against pancreatic cancer.

Crossbreeding of p53 knockout mice with TGF- $\alpha$  transgenic mice which overexpress TGF- $\alpha$  in the pancreas and thus develop fibrosis and ductal pancreatic cancer at the age of one year dramatically accelerates tumor development and represents the first model of pancreatic adenocarcinoma with genetic alterations as well as characteristics similar to the human disease.

We have established a total of 28 murine adenopancreatic cell lines (mPACs) derived from 6 different TGF- $\alpha$  p53-/- mice. *In vivo* growth kinetics were analysed in normal syngenic mice and showed that some cell lines progress after *in vivo* injection to form lethal tumors while others grow during the first 10 days and then regress. Next, these tumors were injected into scid beige and in nude mice. In these mice progressors and regressors grow progressively indicating that the regression in normal euthymic mice is an immunemediated response.

Cytotoxic T cell responses against MHC I positive mPACs are induced after immunization with irradiated mPACs and can be found in mice with spontaneous pancreatic carcinomas. Injection of mPAC leads to the induction of IFN- $\gamma$  secreting CD8 T cells *in vivo*, which can also be found in tumor bearing mice.

This new model opens the possibility to investigate spontaneous immune responses against pancreatic cancers in a genetically well defined tumor model, which mimics human adenocarcinoma.