

➤ Orthotopic tumor models

Implantation of tumor cells into the organ of origin (“orthotopically”) allows organotypical interaction between tumor cells and surrounding stroma. It has been shown that this interaction affects growth, differentiation, and drug sensitivity of tumor cells. Moreover, tumor cells can spread to metastatic sites in other organs, with specificities comparable to the human situation. However, it must be emphasized that in most orthotopically implanted *in vivo* models using typical immortalized cell lines metastasis occurs but is very heterogeneous and not detectable in all animals after implantation. Reaction Biology started working on more reliable *in vivo* models to address intentions aiming mainly at metastasis. Nevertheless, analysis of the primary tumors of orthotopically implanted cancer cells gives us a very prospective read out when testing a new compound.

➤ Panc1_Luc cells

A human pancreatic duct carcinoma cell line established from a patient with adenocarcinoma.

In order to detect the orthotopically implanted cells, a luciferase expressing cell pool was generated via transduction of a luciferase-neomycin construct and subsequent neomycin selection.

➤ Study outline

Panc1_Luc cells are injected into the pancreas. Tumor cell growth is monitored via *in vivo* bioluminescence imaging (BLI). The animals are randomized into treatment groups according to the luminescence signal. During the study, tumor growth is monitored via BLI once per week, animal behavior is monitored daily and animal weights are measured three times per week.

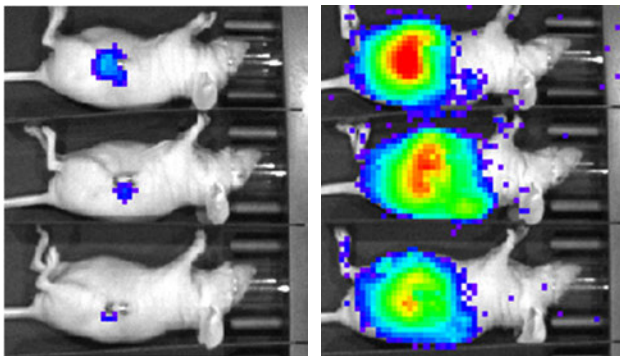


Figure 1: *In vivo* BLI of mice with Panc1_Luc cells injected under the kidney capsule were measured 13 days (left) or 73 days (right) after implantation.

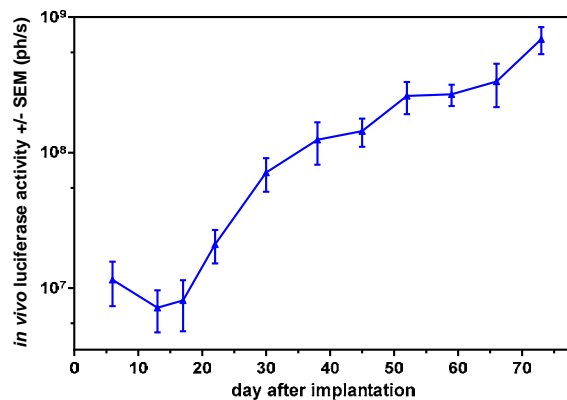


Figure 2: *In vivo* BLI of Panc1_Luc cells growing as liver metastasis tumors *in vivo*, luciferase activity, mean values +/- SEM

➤ Quality assurance

- Routine authentication of tumor cell lines by STR profiling
- Mycoplasma testing of tumor cells by PCR prior to implantation
- Routine health monitoring of sentinel animals (according to FELASA guide lines)
- Adherence to the 5R rules (reduce, refine, replace, responsible, remember)

Note: Graphs depicted are derived from study examples. Each study is a biological system of its own and subject to intrinsic variation.