786-O: Kidney cancer tumor model xenograft – orthotopic

IN VIVO PHARMACOLOGY

➢ 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.

➢ 786-O_Luc cells

A human renal cell 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

786-O_Luc cells are injected under the kidney capsule. 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.

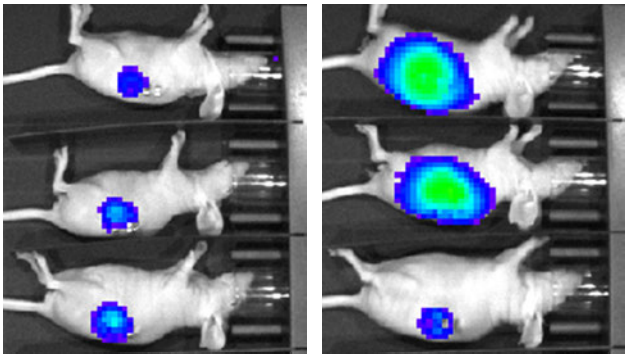

Figure 1: *In vivo BLI of mice with 786-O_Luc cells injected under the kidney capsule were measured 9 days (left) or 66 days (right) after implantation.*

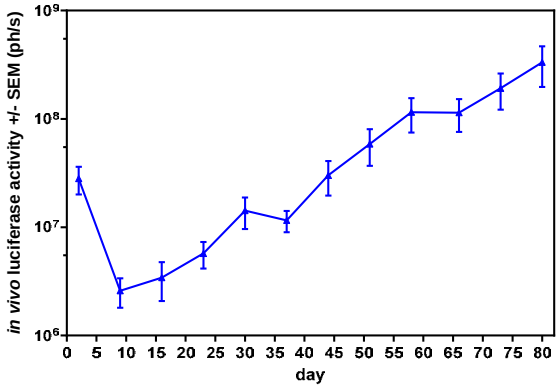

Figure 2: *In vivo BLI of 786-O_Luc cells orthotopically implanted into the kidney, luciferase activity, mean values +/- SEM.*

➢ Quality Assurance

- Routine authentication of tumor cell lines by STR profiling
- Mycoplasma testing of implanted tumor cells by PCR just prior to implantation
- Routine health monitoring of sentinel animals (according to FELASA guide lines)
- Animal work according 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.