PC-3: Orthotopic prostate tumor model

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.

➢ PC-3 LN cells

The androgen-independent PC-3 cell line was initiated from a bone metastasis of a grade IV prostatic 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.

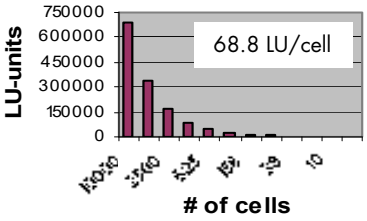


Figure 1: *Luciferase assay. Serial dilutions of a cell lysate were tested for luciferase activity.*

➢ *In vivo* bioluminescence measurement

After surgery, the growth of the cells will be monitored via in vivo bioluminescence imaging (BLI). Using BLI, the animals are randomized into treatment groups according to apparent tumor sizes.

Moreover, once treatment is initiated, effects on the total in vivo bioluminescence signal, and thus primary tumor and potential metastatic loci may be monitored.

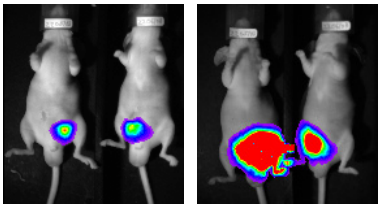
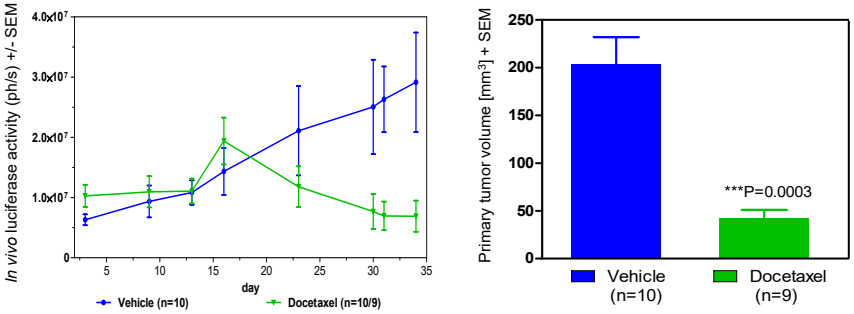


Figure 2: *In vivo BLI. Mice with PC-3 LN cells orthotopically implanted into the prostate were measured one week (left panel) or 6 weeks after surgery.*

➢ Study example

Mice bearing orthotopically implanted PC-3 tumors were treated with Docetaxel (Taxotere®).

Figure 3: *Therapy with Docetaxel. Tumor growth was monitored using BLI (left panel). At necropsy primary tumor volume was determined by caliper measurement (right panel).*



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