N VIVO PHARMACOLOG

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.

SK-OV-3 Luc cells

SK-OV-3 cells originate from the ascites of a woman with adenocarcinoma of the ovary.

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

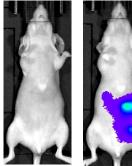
Ascites

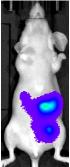
Increased drainage of the lymphatic system as a response to cancer- induced inflammation is what causes the buildup of peritoneal fluid in the abdomen. This fluid is called ascites.

By injecting SK-OV-3 Luc cells into the abdomen of Nude mice, tumor cells that have grown in the resulting ascites can be isolated, cultured and frozen for use in the future.

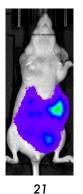
In vivo bioluminescence measurement

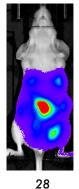
Tumors cells are intraperitoneally injected into the abdomen to initiate ascites production and tumor growth. Thereafter tumor growth is monitored via in vivo bioluminescence imaging (BLI).





14





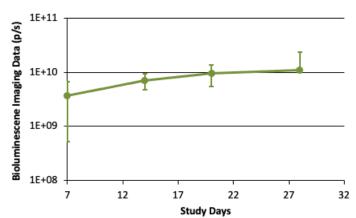


Figure 1: Pictures of in vivo BLI. Mice with orthotopically growing SK-OV-3 Luc ascites measured on day 7, 14, 21 and 28 after injection.

Figure 2: In vivo BLI. In vivo tumor growth of SK-OV-3 Luc was monitored once a week using BLI. Median values +/- SEM.

Study example

If you are interested in receiving information on potential positive controls please reach out to our Business Development team at requests@reactionbiology.com.