U-87 MG: Orthotopic glioblastoma 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.

➢ U-87 MG Cells (CPQ-290)

U-87 MG cells originate from the brain and represent a human glioblastoma cell line. In order to detect orthotopic growth of implanted cells, a luciferase expressing cell pool was initially generated via transduction with a luciferase-neomycin construct and subsequent neomycin selection.

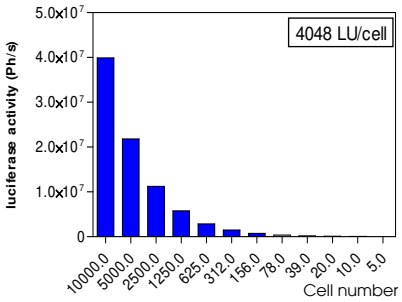

Figure 1: *Luciferase assay. Serial dilutions of a cell lysate were tested for luciferase activity.*

➢ *In vivo* bioluminescence measurement

To initiate orthotopic growth, nude mice are anesthetized and placed in a stereotactic fixation device. Through a burr hole cells will be implanted intracranially into the cerebrum. The growth of the cells will be monitored via in vivo bioluminescence imaging (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 on potential metastatic loci, may be monitored.

Analysis by MRI (Magnetic resonance imaging) is also available, e.g. to monitor edema formation.

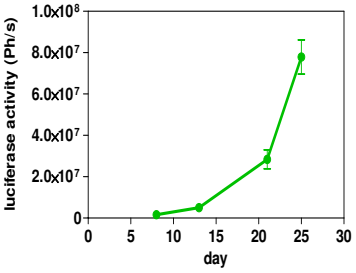

Figure 2: *In vivo BLI In vivo tumor growth of U-87 MG was monitored once a week.*

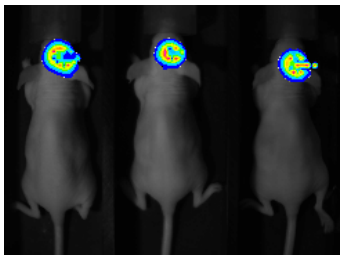

Figure 3: *In vivo BLI In vivo tumor growth of U-87 MG was monitored once a week.*

➢ Study example

Mice bearing orthotopically implanted U-87 MG tumors were treated with two different concentrations of Temodal.

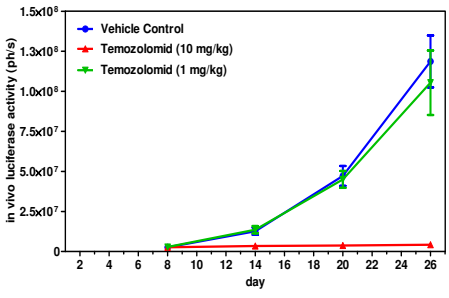

Figure 4: *Treatment with Temodal. In vivo tumor growth was monitored using in vivo bioluminescence.*