NIH3T3-ErbB2-Rrep mouse model

IN VIVO TESTING SERVICES

➢ ErbB2

ErbB2/HER2 is a member of the EGFR family consisting of three further receptor, namely ErbB1/EGFR, ErbB3/HER3 and ErbB4/HER4. Lacking a known ligand, ErbB2 is assumed to be activated by receptor-heterodimerization with any of the three other receptors, ultimately resulting in phosphorylation of the intracellular kinase domain und subsequent downstream signalling. The overexpression of ErbB2 is pathologically associated with tumor growth, especially in the context of breast cancer, making it a bona fide target for the development of novel anti-cancer drugs.

➢ NIH3T3-ErbB2-Rrep

NIH3T3/Toff/ErbB2 cells were generated by stable transfection of NIH3T3 cells with three vectors (pUHD-15-1, pTBC1-Hygro, and pTBC-HER2/SEAP). Clones were selected with hygromycin (Schiffer I. B. et al., Cancer Res 2003;63:7221-7231).

The cells express the human ErbB2 cDNA under the control of a Tet-inducible promoter. ErbB2 is expressed in the absence of doxycycline and expression is inhibited in the presence of doxycycline. Thus this cell line provides an excellent tool for the test of substances directed against ErbB2.

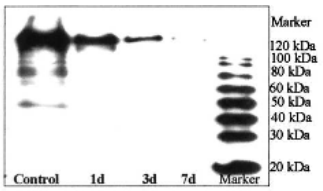

Figure 1:
Characterization of the cell line.
The cells were kept in the presence of the regulator doxycycline for up to 7 days. ErbB2 expression was checked using a HER-2 antibody. (from Schiffer I. B. et al., Cancer Res 2003;63:7221-7231)

➢ Tumor growth *in vivo*

NIH3T3-ErbB2-Rrep cells harvested from tissue culture flasks were implanted into the subcutaneous space of the left flank of the mice. At an average size of 400 mm3, the mice were randomized into two groups, and one group received the anti-ErbB2 antibody Herceptin. As shown in Figure 2, treatment by Herceptin resulted in tumor regression.

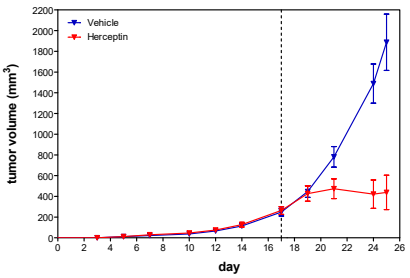

Figure 2:
Growth curve of subcutaneously implanted NIH3T3-ErbB2-Rrep cells in vivo.
The blue line indicates the growth of the untreated, the red of the Herceptine treated tumors

➢ Immunofluorescence

As shown in figure 3, the addition of doxycycline to the mice in the drinking water ablates exogenous ErbB2 expression in the tumors.

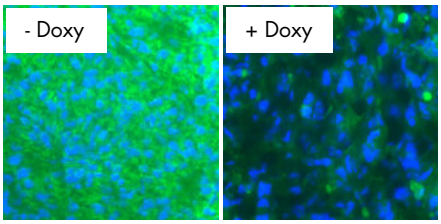

Figure 3: *Immunofluorescence staining of NIH3T3-ErbB2-Rrep tumors. On the left, a tumor of an untreated mouse is shown. The tumor on the right panel was extracted from a mouse treated with doxycycline. ErbB2 positive cells are green, the nuclei are counterstained with DAPI (blue).*