Reviewer's report

Title: The distribution of the therapeutic monoclonal antibodies cetuximab and trastuzumab within solid tumors

Version: 2 Date: 1 September 2009

Reviewer: Arno Schad

Reviewer's report:

In the manuscript of Lee and Tannock the distribution of therapeutic antibodies cetuximab and trastuzumab within different xenograft tumours has been investigated using combined fluorescence and bright field microscopy. Their data suggest a time and dose dependent distribution pattern of cetuximab and trastuzumab in vascularised xenograft tumours.

- Major Compulsory Revisions

1. While the data on cetuximab distribution in EGFR expressing A431 xenograft tumours is based on convincing EGFR staining by cetuximab, the part on trastuzumab and HER2 expression is problematic due to poor quality of the HER2 staining by trastuzumab. Since trastuzumab has been successfully used for immunohistochemistry even in human paraffin embedded tumour tissue (Glazyrin et al. 2007 J Histochem Cytochem 55:25–33), it should be possible to achieve an appropriate staining quality to assess the specificity and sensitivity of the HER2 stainings in the xenograft tumours. (Maybe paraffin sections in conjunction with antigen retrieval would lead to more specific staining signals with better overall morphology.)

2. Two important but easy to perform control experiments are missing: Using standardized diagnostic antibodies for immunohistochemistry it would be easy to assess the endogeneous expression levels of EGFR and HER2 in the different xenograft tumours in comparison to the expression levels detected by the therapeutic antibodies. Additionally, staining of the xenograft tumours from treated animals could differentiate between expression and distribution gradients.

- Minor Essential Revisions

The substrate for HRP should be mentioned in the Methods part.

- Discretionary Revisions

Some comments on possible (if any) signs of initial tumour regression due to treatment would be interesting.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests