Reviewer's report

Title: Overexpression of the Duffy Antigen Receptor for Chemokines (DARC) by NSCLC Tumor Cells Results in Increased Tumor Necrosis

Version: 1 Date: 29 April 2004

Reviewer: Stephan Segerer

Reviewer's report:

General
The study by Addison CL is very well performed, and well written.

The authors describe that tumors derived from DARC overexpressing cells:
- are larger in size
- have more necrotic lesions
- have a lower cellularity
- have a reduction in metastatic potential

-----------------------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

- The system, using overexpression of DARC by tumor cells appears to be a very artificial one, and I don't think that important conclusions (as DARC plays a significant role in tumor associated angiogenesis) can be drawn from this system. The function of DARC might be completely different when expression is restricted to endothelial cells. Please describe the evidence for an expression of DARC in tumors and by tumor cells in human disease.

- Speculation about intracellular localization of DARC is included (on page 6, 7, 10) several times in the manuscript, it could be addressed using immunofluorescence and confocal microscopy (does it colocalize with IL-8?)

- What makes DARC overexpressing tumors larger than the normal counterparts? The tumors have a lower cell number and less infiltrating cells. It is not very convincing that larger areas of necrosis makes those tumors bigger. It could be hypothesized that there might be increased proliferation during earlier time points leading to larger tumors, and increased necrosis later on. If the number of cells is decreased and the tumor size increased are there differences in the extracellular matrix? (Extracellular matrix might also be important for the local chemokine milieu)

-----------------------------------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

- Introduction, first sentence: DARC was originally identified as a blood group, and later as a coreceptor for malaria (Erythrocyte receptors for (Plasmodium knowlesi) malaria: Duffy blood group determinants.
- Source and establishment of the IL-8 antibody should be included

- References 7, 13 contain (see comments)

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No