Reviewer's report

Title: Growth and metastases formation of human malignant mesothelioma cell lines orthotopically implanted into the pleural cavity of immunodeficient mice.

Version: 8 Date: 4 October 2005

Reviewer: Amir Onn

Reviewer's report:

General
This is an important paper on an orthotopic model of human mesothelioma in nude mice. The innovation is the orthotopic concept, in which mesothelioma tumor cells may interact with their natural microenvironment, i.e. thoracic endothelial cells, immune system components etc.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The authors present technical paper on a new animal model, which is presumably better representing the human disease. Yet their work lack several important aspects of such a technical paper:
1. Injection into the pleural cavity in mice is not trivial, and I wonder how the authors confirmed that the location of the tip of the injecting needle was actually in the pleural space and not elsewhere. Didn’t they observe parenchymal and/or subcutaneous lesions in cases of needle injected 'too deep' or 'too shallow'? Where exactly in the left chest were the cells injected? How do they explain that the major bulk of tumor in image 2 is in the right chest and not the left? Was this technique associated with induction of pneumothorax? Did mice die of pneumothorax? What about lymph node metastasis?
2. The authors suggest that their model was developed to enable assessment of inflammatory cytokines and growth factors (abstract-background). They would need to demonstrate this advantage and convince the reader that their model is better by presenting relevant data.
3. Section of discussion does not address the limitations of the new technique. One major limitation is lack of pleural effusion in this model, which is a clinical characteristic of mesothelioma. In addition, most patients present with the epithelioid subtype, but the model is of the biphasic subtype. Please correct this section to include these aspects.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. Present a representative H&E slide of mesothelioma tumor invading the lung
2. Provide the immunohistochemistry protocol for CD31
3. Explain if mice were allowed to die of disease or were sacrificed when they became moribund, as required by most authorities

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after discretionary revisions

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

Statistical review: No

Declaration of competing interests:
'I declare that I have no competing interests'