Reviewer's report

Title: The selective COX-2 inhibitor, JTE-522, inhibits growth of pulmonary metastases of colorectal cancer in rats.

Version: 1 Date: 19 November 2004

Reviewer: M. Michael M Wolfe

Reviewer's report:

General
This manuscript by Dr. Kobayashi and colleagues describes the effects of the selective COX-2 inhibitor JTE-522 on the growth and lung metastases of colorectal cancer in a rat tumor model. Several previous studies have documented the inhibitory effect of COX-2 selective inhibition on the growth and metastasis of colorectal cancer (CRC), which decreases the novelty of this current study. As discussed below, some of the methods used in this study need to be more carefully characterized to avoid confusion by potential readers.

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

1. The authors have not provided sufficient information regarding the methods used for evaluating lung metastasis and have not described their method for creating lung sections in dissected lung after rats were sacrificed. The criteria used for section selection should be specified.
2. Along these same lines, the evaluation of immunostaining used by the authors has not been clearly described. The number of positive cells were apparently counted and categorized in order to evaluate the distribution of positive cells. Why then did the authors convert the distribution score to an intensity score?
3. A correlation analysis should be used for evaluation of the association between VEGF score and COX-2 score (Figure 4). The authors did not provide sufficient detail in the legend in this figure, making it difficult to understand.
4. Because colorectal metastasis occurs primarily in the liver, the authors should comment on the clinical significance of their observations in this regard. Pulmonary metastasis in this study certainly occurred as a result of their injection of tumor cells into the tail vein.

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. Table 1 provides a VEGFR score; do they mean VEGF? Please clarify.

Discretionary Revisions (which the author can choose to ignore)

1. It would have been helpful for the authors to perform microvessel staining with a CD31 antibody to evaluate tumor angiogenesis, in addition to their evaluation of VEGF expression. Ideally, VEGF and COX-2 expression in noncancerous tissues surrounding the metastatic lesion should have also been assessed.

What next?: Accept after minor essential revisions
Level of interest: An article of limited interest

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

Statistical review: No