Reviewer's report

Title: Elevated IGFIR expression regulating VEGF and VEGF-C predicts lymph node metastasis in human colorectal cancer

Version: 1 Date: 13 October 2009

Reviewer: Paolo Bruzzi

Reviewer's report:

The paper describes the correlation between frequency of expression of insulin-like growth factor-I receptor (IGFIR), or of the vascular endothelial growth factors (VEGFs), with the pathological features in 98 colorectal cancer tissue samples with 26 samples of adjacent normal tissue and in 38 colorectal adenomas. The sample size is small, but the methods are straightforward and clearly described, and apparently free from major bias. The results confirm the study hypothesis, in that a strong correlation is indeed present, particularly with the presence of lymph node metastases. Focus on clear and direct questions and simplicity are the great merits of this paper, that perhaps would have been improved by a more refined statistical analysis. However, since this can be considered as a small, pilot, hypothesis generating study, whose findings warrant confirmation in a larger series of cases, I am satisfied with the simple analyses presented. Yet, some statements are frankly naïf, and I suggest that the paper is reviewed by a statistician.

Minor Points

Page 9 “The frequency of positive IGFIR staining in colorectal adenoma was higher than that in normal tissues, but …. there was no statistical difference between these two groups (P = 0.265)

Replace with….but the difference was not statistically significant (P=0.265)

Last paragraph of page 10 “...with the severity of lymph node metastasis. Patients were divided into three groups according to the number of metastatic lymph nodes: ....”All the analyses in this paragraph are statistically flawed: the association with N positivity (N0 vs N+) was already shown in the preceding analysis, which is repeated here without adding anything. This analysis should have been limited to N+ patients. -Table 3 Useless –information in table 2 is sufficient

Table 1 and table2 : Add percentages (by row) to facilitate the interpretation, and delete the columns ‘low’

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**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:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests