Reviewer's report

Title: Expression and Prognostic Significance of THBS1, Cyr61 and CTGF in Esophageal Squamous Cell Carcinoma

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Reviewer: Giovanni Zaninotto

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The Authors measured the expression of three proteins, THBS1, CTGF and Cyr61, in esophageal squamous cancer cell by immunohistochemistry and Western blotting. The samples studied were obtained from representative areas of paraffin blocks obtained from specimens from 80 patients who underwent esophagectomy. Protein overexpression was defined as intense staining in >25% of tumor cells.

Western-blot analysis revealed high CTGF and Cyr61 protein levels in the ESSC tissues. THBS1 was overexpressed in the vast majority of ESSC, while Cyr61 and CTGF were overexpressed in about 50% of patients.

These findings were correlated with the patients' clinico-pathological data (TNM) and survival, and the Authors said that two of these proteins (CTFG and Cyr61) were independent prognostic factors of survival.

Comments

Major points:

1. Being a clinician involved in the daily treatment of patients with esophageal cancer, I am keen to read about new biological markers that could shed light on the oncogenesis and help us establish the prognosis of our patients, but when time-proven and universally-accepted prognostic factors such as the TNM are challenged, I tend to be skeptical. It is hard to see why a worse survival is associated with THBS1, given that THBS1 overexpression is inversely correlated with regional lymph node invasion (virtually all N0 patients, i.e. 94%, but only 72% of N1 patients overexpressed this protein). To justify this claim, the Authors should show separate survival curves for each TNM stage and level of protein overexpression.

2. More information should be given on the number of nodes harvested from each patient.

3. The present TNM classification divides Stage II patients into IIA (no nodes involved) and IIB (metastasis to regional nodes): the Authors would be well advised to use the currently-adopted classification.

4. It is also hard to follow the reasoning that patients overexpressing CTGF and Cyr61 show such a poor survival, given that the two markers are almost equally overexpressed in patients in stages I/II and stage III (see point 1).
Minor points:
1. The Ms has several misspellings and grammatical errors.
2. In table 1 there are 46 N0 patients and 45 patients in Stages I/II: is that correct?

Level of interest: An article of limited interest

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interest's below.