Reviewer’s report

Title: Association of NGAL mRNA Expression with Tumor Progression and MMP-9 in Human Rectal Cancer

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Reviewer: Andreas Friedl

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In the manuscript entitled “Association of NGAL mRNA Expression with Tumor Progression and MMP-9 in Human Rectal Cancer”, Zhang and co-workers describe at the RNA level the overexpression of the lipocalin NGAL in rectal carcinomas compared to normal control mucosa. The authors further demonstrate an association of NGAL overexpression with stage (tumor invasion, lymph node and distant metastasis) and with vessel invasion but not tumor grade. In addition, they show that NGAL correlates with MMP9 at the mRNA level.

This is a descriptive and correlative study. The paper would be stronger if clinical outcome information was available, permitting an evaluation of NGAL as independent marker. However, some novel information is presented. The experimental methods appear overall appropriate and are adequately described. The pertinent literature is sufficiently quoted. On the other hand, a number of weaknesses detract from the overall positive impression:

Major Compulsory Revisions

1. Some of the conclusions are overreaching. For example, the authors state in the abstract and the main manuscript that “NGAL plays an important role in the progression of human rectal cancer”, which is not supported by their correlative data.

2. While the manuscript is overall comprehensible, many passages lack clarity and are tedious to read. Major editing is necessary, possibly by a native English speaker.

3. As the molecule’s name implies, NGAL is expressed at high levels by neutrophils. The authors should confirm by either NGAL immunohistochemistry or even standard H&E histology that neutrophils are not present in large numbers in the NGAL positive carcinomas.

Minor Essential Revisions

1. Table 2 is not sufficiently explained. For example, “sample means” presumably indicate mean CT values for the carcinomas, but this is not stated. The statement below the table “Randomizations 1,000 of 1,000 done” is unclear.

2. The authors assert that NGAL is a proven biomarker for the early diagnosis of malignancy. No such studies exist to the knowledge of this reviewer.
3. The proposed utility of NGAL as marker is not clear. Do the authors suggest an eventual use of NGAL as diagnostic or prognostic marker?

Discretionary Revisions
The discussion section could be shortened by omitting the discourse on the merits of qRT-PCR

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

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

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