Reviewer's report

Title: APRIL is a novel clinical chemo-resistance biomarker in colorectal adenocarcinoma identified by gene expression profiling.

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Reviewer: Andreas Teufel

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The manuscript presented by Russell et al describes a novel biomarker, APRIL, overexpressed in 5fu/radiation treated colorectal carcinomas and was found to be predictive of outcome of adjuvant 5FU chemotherapy in patients with colorectal cancers.

The manuscript offers a number of unclear points that need to be addressed before publication.

1) As the authors state the microarray experiments may only be seen as screening experiments since the ten samples were from 4 different experimental groups and even within the group were from different tumor stages.
   a. It remains absolutely unclear though, as to why exactly APRIL was of highest interest among regulated genes? The authors describe a group of 17 cell death genes that are differentially regulated. What about the remaining 16?
   b. The authors cite several publications to “support further investigation of a putative functional role for APRIL in clinical 5 FU resistance”. Although these publications demonstrate an already established role of APRIL in cancer development, they don’t seem to deal with 5FU resistancy? Do the other 16 cell death genes not have any publications stating a role in cancer development?

2) The evaluation for a prognostic value for an adjuvant chemotherapeutic treatment in CRC was only investigated in stage III patients. It would be much more interesting to get a result in stage II patients as this may help to identify patients that would benefit from such a treatment in earlier stages not commonly treated with adjuvant chemotherapy.

3) The performance in comparison to established biomarkers is not discussed at all? Does APRIL perform better the previously identified markers?

4) Since the marker is differentially expressed in stromal cells. Is the expression of APRIL in stromal cells associated with differential overall survival?

Level of interest: An article of limited interest

Quality of written English: Acceptable

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