Reviewer's report

Title: Systematic genomic identification of colorectal cancer genes delineating clinical stage and metastasis

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Reviewer: Ramon RZ Salazar

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Major: I find the integrative approach provided in this paper of great value and highly intuitive, it can represent a methodological break through in the validation of elastic net regularized regression gene centered methods, but its current clinical application is nule and influenced by the wrong definition of advanced disease where lymph node metastasis is made equivalent to distant metastasis, which is clinically a very inappropriate definition

Minor
On page 17 when the authors try to explain why there are no genes that delineate M status independently, the most important weakness of the whole paper, they claim that this indicates that lymph node metastasis is a sufficient, early indicator for metastatic behaviour. This is a wrong statement and, curiously, the authors correct themselves in the next sentence where they accept the the smaller number of stage IV samples may have affected their sensitivity for identifying genes associated with distant metastasus in other organs

Further down on the las line on page 17 thay claim that dominant inverse association in T status and clinical stage suggest that loss of or lower expression of genes is a more frequent in advanced stage clinical disease, which counterdicts the previous statement describing the frequent direct association in N status and MSI implies that the gain or higher expression genetic aberrations occur more frequently in advanced clinical stage,

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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