Reviewer's report

Title: A comprehensive look at transcription factor gene expression changes in colorectal adenomas.

Version: 2 Date: 29 October 2013

Reviewer: Benjamin Barré

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In this manuscript, the authors analyzed microarray data from colon tumors and normal tissues collected in the same patients, at several centimeters from the tumor site. By using a three-pronged selection procedure, they identified transcription factors deregulated in colon cancer which might be implicated in tumorigenesis. The expression of 261 TF genes is significantly affected in colorectal adenomas such as the relatively unexplored development gene DACH1. However, the implication of these TF is not evaluated/confirmed in colorectal cells. This study requires more evidences of the identified TF implication in the tumorigenesis.

1- The strategy allows to see variations of TF mRNA level but mRNA level does not correlate systematically with the protein level. Moreover the protein level does not reflect the TF activation which in some case require post-translational modification. For example, what is the implication of Smad2, STAT1 or STAT3 in these tumors? The authors have to validated the activation of the TF by using western blot or ChIP.

2- The determination of the genetic alterations of each tumors need to be known. For example in the present study, the authors observed a variation of the TP53 mRNA level but if the p53 is mutated on its DNA binding domain, as it appears frequently in colon cancer, what is the implication of this TF? How many functional TF are in the list of 261?

3- Using the expression levels of the TF genes for a hierarchical clustering analysis, the cancer and normal tissues are separated in the figure 3. It would be appreciated to detail the factors used for this classification and maybe realize a sub-classification of these tumors (and normal tissues).

4- The authors showed definitively that MMR+ cancers present the biggest variation of DACH1 expression level however they need to complemented that critical factors to identified the colon cancers that not presenting DASH1 mRNA variation.

5- To verify if the compaction of the DASH1 gene is methylation independent, the authors could do a southern blot using a probe directed against DASH1 genes. Moreover, it might be interesting to discuss the function of DASH1 with p53 (Cancer Res 2013).
To conclude, this study is not the first analysis the mRNA level in colon cancer (Mol Cancer Res 2007) but it presents an original point of view by staying focused on the TF expression. However the authors have to improve their strategy and approach to support their hypothesis. This article requires major revisions for a publication in BMC.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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