Reviewer's report

Title: Genomic profiling of rectal adenoma and carcinoma by array-based comparative genomic hybridization

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Reviewer: Manny Bacolod

Summary: In this article, the authors subjected 8 rectal adenomas and 8 rectal carcinomas (from 16 different patients) to CGH array analyses. Chromosomal regions of gains and losses were identified. To identify the genes whose expression levels were affected by these aberrations, the authors analyzed publicly available copy number and expression data for 7 CRC cell lines. Finally, the authors examined the expression patterns of these identified genes, in the Oncomine database (for CRC samples).

Although there has been a plethora of publications regarding high resolution copy number analysis of CRCs (using either CGH or SNP array), most of them were focused on colon cancer. So, a study such as this, which focused on rectal tumors (as well as adenoma) is not exactly widely replicated.

A. Major Compulsory Revisions

1. The study would have been much better if the authors analyzed the genome-wide expression of the 16 samples themselves (instead of using the expression data from 7 CRC lines), when trying to figure out which among the resident genes are most relevant in the rectal cancer progression. If tissue samples remained (either fresh froze, or even FFPE), expression analyses can certainly be done. Additional expression data will make up for the low sample size in this study.

2. The authors listed the aberrant (gain, loss) chromosomal regions that are common to the tumors and adenomas. That is fine. In my opinion, I think it is also important to identify the difference between the adenomas and carcinomas (in particular, the gains/losses present in carcinomas, but not in adenomas). Then the authors may ask the next question: which genes had significant expression level change when going from adenoma to carcinoma? The authors may want to pay particular attention to the copy number-dependent, upregulated genes (in carcinoma relative to adenoma), verify their expression at the protein level (or histochemistry), and discuss the possibility of such genes/proteins being therapeutic targets.

3. The authors can strengthen this paper by: sequencing SMAD4 (18q) (and
examine if the gene gets mutated at the adenoma stage), and by checking the expression of MET (7q), if it has significantly increased from adenoma to carcinoma. It wouldn’t hurt to sequence p53, and APC as well.

4. The authors may want to discuss further the difference between rectal and colon tumors (in terms of chromosomal aberrations, etc.), if there are any.

B. Minor Essential Revision

1. The manuscript needs a few minor grammatical corrections. For example, in abstract (methods part): use “interesting” instead of interested.

C. Discretionary Revision

1. Do the authors have information on who among the patients sampled for adenomas eventually developed tumors (and who did not)? If these information are available, the authors may want to examine the difference in chromosomal aberrations between these two groups (subgroup which remained adenoma, subgroup which progressed to cancer).

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

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

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