Reviewer's report

Title: DNA methylation alterations of AXIN2 in serrated adenomas and colon carcinomas with microsatellite instability

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Reviewer: Subbaya Subramanian

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Muto et al. describes the analyses of DNA methylation in sessile serrated adenomas (SSA) and colorectal cancers with microsatellite instability (MSI). The authors used an array-based methylation sensitive amplified fragment length polymorphism method to analyze the genome-wide methylations status of SSA and MSI tissue cancer samples.

The authors show that there were no major hypermethylation differences between or within benign and malignant tumors groups regardless of their clinical and genomic parameters. Further, hypomethylation was also found to be less frequent in SSAs compared with MSI or MSS samples. They also conclude that AXIN2 gene had more methylation alterations and hypermethylation of MLH1, when occurs in an adenoma cell with BRAF mutation, drives MSI cancer.

Major essential revisions.

The sample size used in this study seems to be too low to achieve statistical significance. Further, the functional characterization of loss or gain-of-function of AXIN in colon cancer cells will strengthen the conclusion of this study. Additional experimental validations are required substantiate their claim that “hypermethylation of MLH1, when occurs in an adenoma cell with BRAF mutation, drives MSI cancer”

Level of interest: An article of importance in its field

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

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

Declaration of competing interests:

I declare that I have no competing interests