Reviewer's report

Title: The TGFBR1*6A allele is not associated with susceptibility to colorectal cancer in a Spanish population: a case-control study

Version: 1 Date: 16 March 2009

Reviewer: Boris Pasche

Reviewer's report:

TGFBR1*6A is not associated with susceptibility for colorectal cancer in a Spanish population: A case control study

This is an interesting study reporting genotyping of TGFBR1*6A in 400 cases and 400 matched controls in Spain.

- Major Compulsory Revisions

MSI status was assessed in tumor DNA from 120 patients using only one marker, BAT-26. The authors should justify why only one marker was used when standard international guidelines recommend the use of several markers to assess microsatellite instability. Most studies use at least BAT-25 in addition to BAT-26 and this reviewer is not aware of any report in which only BAT-26 was used to assess MSI status.

While the study is powered to detect an OR of 2.0 for *9A/*6A heterozygous individuals and an OR of 3.0 for *6A homozygous individual with 80% power, this should be considered markedly under powered based on the previous studies sided by the authors. Indeed, the OR for heterozygotes has ranged between 1.15 and 1.20 and the OR for homozygotes has not exceeded 2.0. Hence, the study is under powered to detect differences between cases on controls based on the published literature. The authors should acknowledge this weakness.

The authors should cite a recent report by Zeng et al, Cancer Res 2009, 69:678-686, showing that constitutively decreased Tgfbr1 signaling is a potent modified of colorectal cancer development.

The authors should clarify what they mean by "bystander effect" on ASE alterations on page 12, last line.

- Minor Essential Revisions

None

- Discretionary Revisions

None

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I have applied for a patent related to the discovery of TGFBR1 ASE