Reviewer's report

Title: The Ets dominant repressor En/Erm enhances intestinal epithelial tumorigenesis in ApcMin mice

Version: 2 Date: 11 February 2009

Reviewer: Anna Velcich

Reviewer's report:

In this manuscript the authors present solid evidence that the introduction of an artificially engineered repressor of the Ets family of transcription factors in the intestinal epithelial component of the ApcMin mouse significantly increases the tumor phenotype. Interestingly, this is obtained in mice in which the expression of the repressive transgene can be documented at the mRNA, but not at the protein level by IHC and does not affect small intestine architecture. However, there is only incremental addition towards understanding the role of the Ets transcription factors in intestinal tumorigenesis due to the universal nature of the repressor transgene that does not permit the identification of the Ets factor(s) responsible for the modifications of the ApcMin phenotype. The authors should at least determine whether Ets2, the aploinsufficiency of which was shown to impart a phenotype similar to the one described here, and/or Pea3 which regulates TgfβRII expression in the normal epithelium, are targets of the En/Erm repressor by analyzing the expression of their known target genes.

An interesting collateral result from this study is that on the mixed Black6/FVB background ApcMin mice develop increased number of tumors that display stroma invasion. Under this aspect, it would be important to determine whether there is increased nuclear β-catenin expression at the invasion front.

Additional points

Have the authors determined whether expression of En/Erm repressor that cannot be detected by IHC, can be seen by western blot using intestinal epithelial cell enriched cell extracts?

Although the villin promoter is mostly active in the small intestine, it also functions in the colon. Since ApcMin mice develop also colonic tumors, albeit at reduced number, is there also a modulation of the colonic tumor phenotype in TgEn/Erm ApcMin mice?

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

Quality of written English: Acceptable

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