Reviewer's report

**Title:** Epigenetic inactivation of the NORE1A gene correlates with malignant progression of colorectal tumors

**Version:** 1  **Date:** 23 August 2010

**Reviewer:** Miguel A. Peinado

**Reviewer's report:**

This paper reports the epigenetic inactivation of NORE1A, a member of the RASSF family, in colorectal cancer. Authors have analyzed gene expression and the DNA methylation status of NORE1A promoter CpG island in a series of 80 primary colorectal carcinomas and 10 cell lines. Downregulation of NORE1A is more frequent in advanced stages of the disease. It is concluded that epigenetic inactivation of NORE1A is a frequent event in colorectal cancer and that it might be implicated in the progression of the disease.

Experimental analysis is well performed and presented. The conclusions are consistent with the data, but show no novelty. The design of the study is very modest. Specifically, NORE1A epigenetic activation should be accompanied by the analysis and study of possible associations with other genetic and epigenetic alterations (i.e. K-ras and p53 mutations, microsatellite instability, RASSF1A epigenetic silencing, etc) and additional clinical data (i.e. outcome, location).

Minor issues: The classification of tumors into low and high “expressors” is not justified and has no biological meaning. Taking into account that authors have quantified the expression levels using densitometry, it would be more appropriate to use statistical parameters (mean, SD) to compare the different groups of tumors as it has been done for normal-tumor comparisons.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

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