Reviewer’s report

Title: Activation of MEK1 or MEK2 isoform is sufficient to fully transform intestinal epithelial cells and induce the formation of metastatic tumors

Version: 2 Date: 29 September 2008

Reviewer: georges baffet

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The manuscript by Voisin et al. describes studies showing that activation of either MEK1 or MEK 2 isoform is sufficient to fully transform intestinal epithelial cells and to promote tumor formation and progression in vivo. Activation of MEK1 or MEK2 up-regulates the expression of matrix metalloproteinase and protects cells from undergoing anoikis. Overall, this is a strong manuscript and well executed. This study represents an area of interest for the understanding and treatments of invasive human colon carcinoma cells.

Comments:

1/ Did the authors look at the morphology of exponentially proliferating cells and E cadherin expression in 10% FBS stimulated cells where the MEK activity is higher after MEK1 (and MEK2 ?) transfection.

2/ Figure 4: The authors could discuss the discrepancy between results of urokinase receptor mRNA expressions after MEK1DD and MEK2DD transfections and the role of the MAPK dependent-urokinase receptor expression in cell invasion.

3/ Authors should precise that they get the same efficiency of transduction in the four cell lines analyzed in this study allowing experiments without cellular selection.

Silencing MEK 1 and MEK 2 are very efficient and well executed. MEK 2 inhibition always suppressed cell proliferation to a higher extends than MEK 1 inhibition. It is surprising that MEK1 or MEK 2 inhibitions lead to same inhibition of ERK1/2 phosphorylation in HCT116 whereas inactivation of MEK2 totally abolished the proliferation. What’s the cell phenotype after MEK1 and MEK2 inhibitions together(lethal or not)? Kinases could have distinct functions according to cell origins.

Level of interest: An article of importance in its field

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