Reviewer's report

Title: Epidermal growth factor mediates detachment from and invasion through collagen I and Matrigel in Capan-1 pancreatic cancer cells

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Reviewer: Surinder Batra

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General
Reviewer's report: The manuscript entitled "Epidermal growth factor mediates detachment from and invasion through collagen I and Matrigel in Capan-1 pancreatic cancer cells" by Shirk and Kuver, is well-written and easy to follow. The authors hypothesized that EGF receptor and integrin signaling pathways interacted in mediating cellular adhesion and invasion in pancreatic cancer, and that invasiveness correlated with cell detachment from the extracellular matrix. Using the pancreatic tumor cell line, Capan-1, as a model system, the authors examined the role of EGF in mediating adhesion to and invasion through collagen I and Matrigel. They found that adhesion to collagen I and Matrigel could be inhibited by EGF treatment. Moreover, this loss of adhesion could be reversed by inhibitors of PI3K and erbB2 receptor signaling, but not by an inhibitor of protein synthesis. Although the process of EGF-induced de-adhesion in Capan-1 cells per se is not novel (ref. 26), the data presented brings new insights into the underlying mechanisms. This reviewer feels the paper is suitable for publication contingent upon completion of the changes requested below:

1) The statement "The inhibition of adhesion to collagen I elicited by EGF acted specifically via activation of erbB1..." in Results is not supported by the data in this section and should be moved over to the next section.
2) The concentrations of inhibitors used should be provided as they may have an impact on the interpretation of the data. This is particularly relevant to those for which no conspicuous effect was observed, since no control has been used to test the efficacy of the reagent(s).
3) Paragraph #1 in the Discussion: The statement "The lack of EGF secretion by these cells suggests that the drive to invasiveness in these cells is provided by cell-cell interactions" is not supported by the data presented in the paper as no targeted inhibition of EGF (e.g., silencing by siRNA) has been used to prove that the invasiveness seen in the unstimulated control is indeed attributable to EGF (Fig. 3). i.e., EGF may just enhance the invasive potential of the cells.
4) A major point made on the activation of FAK in the Discussion section is not supported by any result in this manuscript.
5) No attempt is made in the Discussion to explain the differences in the results observed by the authors and other investigators (Ref. 26) although the same experimental system was used.