Major Compulsory Revisions:

1. The authors described that cytotoxic activity of a cationic antimicrobial peptide lactoferricin to mammalian cell lines depends on the presence of glycosaminoglycans (GAGs) on the surface of the target cells and also on the level of their sulfation.

Lactoferricin cytotoxic effect on cell lines requires high micromolar concentrations. This raises a question about potential use of CAPs as anti-tumor agents. There is additional factor which can further reduce the activity of CAPs towards cytoplasmic membrane of cancer cells in vivo. This is the inhibition of cationic antimicrobial peptides activity by blood plasma or serum proteins.

Do serum proteins inhibit cytotoxic activity of lactoferrin?

The authors need to address this issue.

2. Anti-tumor and anti-metastatic activity of lactoferricin was documented in literature. The in vivo activity most likely did not involve direct disturbance of cytoplasmic membrane of tumor cells but other mechanisms were involved.


M.Iigo et al., 2008 “Anticarcinogenesis pathways activated by bovine lactoferrin in the murine small intestine”. Biochimie, in press).

These mechanisms may involve more specific interactions with G-protein couple receptors as was described for several other antimicrobial and immunomodulatory peptides such as defensins and LL-37 (see for example, De Yang et al, 2004, Annu Rev Immunol, 22:181).

These references have to be cited and discussed.

Minor Essential Revisions:

P8, third line from bottom, instead “where” should be “were”.

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