Reviewer's report

Title: Small lytic peptides escape the inhibitory effect of heparan sulfate on the surface of cancer cells

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Reviewer: Masaaki Iigo

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The authors investigated the anticancer activity of chemically modified 9-mer peptides and the influence of heparan sulfate (HS) on the surface of cancer cells on their cytotoxicity.

Bovine lactoferricin and human lactoferricin have cytotoxicity in some tumor cell lines, as reported previously. One reason may be that they have cationic peptides. Cationic peptides may bind to negatively charged peptides, like HS. However, there is not a clear relationship between the binding to HS and cytotoxicity. In this study, similar results are shown in Tables 3 and 4. Cytotoxicity is not depend on HS content.

It is interesting that 9-mer cationic peptides bind to HS. Does lactoferrin also bind to HS on the cells? And does lactoferrin show cytotoxicity against these cell lines? Are there differences between lactoferrin and lactoferricin? Is there merit to be a shorter peptide (unrelated to lactoferricin), compared to lactoferricin in this study? The authors should clearly explain the effects of lactoferricin and shorter peptides bound to HS on cytotoxicity.