Reviewer's report

Title: Heparan sulfate mediates trastuzumab effect in breast cancer cells

Version: 1 Date: 30 July 2013

Reviewer: Elda Tagliabue

Reviewer's report:

While the revised version of the manuscript was actually improved, in my opinion, the paper is still disjointed. It is, in fact, difficult to understand why transfection of HPSE-1 was considered a valid tool for understanding the role of HS in trastuzumab activity if HPSE-1 upmodulation also changes the expression levels of HER2. In my opinion, experiments showing correlation of trastuzumab activity and HS expression, as well as physical interaction between trastuzumab and HS and inhibition of trastuzumab activity by both anti-HS antibody and eparin, can represent by themselves convincing proofs of the role of HS in trastuzumab efficacy. On the contrary, it is still difficult to fully appreciate the part of the manuscript concerning trastuzumab capability to change GAG production.

Major Compulsory Revision

1. it should be better to firstly present data demonstrating that HER2 interacts with HS and that the block of HS decreases susceptibility of tumor cells to trastuzumab, and in sequence, those showing the capability of trastuzumab to affect expression of GAG as well as of HPSE-1 expression to modify HER2 levels.

Minor essential Revision.

2. English editing

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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