



SDI Review Form 1.6

PART 1:

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	2013_IJBcRR_3847
Title of the Manuscript:	The Soluble Ectodomain but not Intracellular Domain of Jagged1 Regulates the Expression and Proteolytic Shedding of E-Cadherin

General guideline for Peer Review process is available in this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)

- This form has total 7 parts. Kindly note that you should use all the parts of this review form.



SDI Review Form 1.6

PART 2: Review Comments

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
<u>Compulsory</u> REVISION comments	Major points. It seems to me that some of the conclusions (the title in the first instance) are not fully supported by the experimental results shown, and I would like the authors to comment on the following points. Line 286: <i>“levels of the protein remained unaltered in lysates from JICD transfected cells”</i> Line 289: <i>“The levels of soluble E-cadherin in the conditioned medium from JICD-transfected cells were unaltered”</i>. The same statements are repeated in the Discussion section (lines 340-342) and in the Conclusion (lines 350-352). From Figure 3A, I would say that the level of E-	



SDI Review Form 1.6

cadherin, as detected by immunoblotting, is in the lysate slightly higher in cells over-expressing JICD than in the control (although the standard deviation is high) and, in the medium, that it is nearly two times higher in cells over-expressing JICD than in the control (Figure 3C). Overall, it seems that over-expression of JICD is associated with an increased level of E-cadherin, over-expression of sJAG1 is associated with a decreased level of E-cadherin, with over-expression of full length WT-JAG1 somewhat in the middle (but closer to sJAG1). This trend seems to be confirmed by mRNA levels for E-cadherin, with JICD > WT-JAG1 > sJAG1. Is it possible that over-expression of the intra- and extra-cellular parts of Jagged1 have opposite effects?

In the Discussion, the authors comment on the correlation between Jagged-1 over-expression, E-cadherin levels, and Notch signaling. Actually, no



SDI Review Form 1.6

	experimental evidence of Notch signaling activation is reported, nor Notch activation is measured in any way. Therefore, I would limit the discussion to what is actually measured, i.e. levels of E-cadherin. As Notch receptors as well as Notch ligands and E-cadherin all undergo ADAM-mediated shedding, is it possible that what is observed is actually a competition of different substrates for the same ADAM enzyme?	
--	--	--



SDI Review Form 1.6

Minor REVISION comments	The precision given for expression levels (%) (two decimals) is highly optimistic. I think it would be more sensible to round the values to the closest integer number. Line 169: “... <i>the exact ADAM cleavage site within Jagged1 has not been determined</i>”. Actually, it has been recently reported (Biochem. Biophys. Res. Commun. 2013, 432: 666-671) that Jagged-1 (in fact, a recombinant protein corresponding to the juxtamembrane region) is cleaved at E1054 by ADAM17 catalytic domain. This should be mentioned in the text, or as a footnote added in proof. In Figure 2, I would swap the position of panels D and E, so that in the upper part we would have the results of the anti-C-terminal Jagged antibody, in the lower part those for the anti-N-terminal Jagged, with the left part for the lysate, and the right part for the medium.	
--------------------------------	--	--



SDI Review Form 1.6

	In panel E, what is the “+’ve Control”?	
	In Reference 12, the publication year is missing.	
<u>Optional/General</u> comments		

Note: Anonymous Reviewer