Reviewer's report

Title: Targeting Notch signaling for the treatment of pediatric soft tissue sarcomas

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Reviewer: Isabella Screpanti

Reviewer's report:

The review proposed by Rota and colleagues is well constructed and the specific topic of the role of Notch signalling in soft tissue sarcomas is original, presented in an attractive style and appealing for a wide audience.

As mentioned in the manuscript by the authors this topic is very controversial but in the review article this aspect is very well discussed and a wide prospective on the potential factors which may explain the discordance of the role of Notch signaling in STS tumors is clearly emerging.

However, some issues need to be addressed in order to strengthen and clarify the review:

- page 10 lane 2, in the paper by Graziani et al, cited by the authors there is no evidence that Notch/RBP-Jk axis directly repress PTEN expression additionally the current view is that Notch signaling represses PTEN expression through a HES-1-dependent mechanism (see the commentary of Bailis and Pear, Blood 2012). The text should be modified to clarify this issue.

- page 11 lane 24, the role of Numb in sustaining Notch3 degradation is controversial (see Beres et al. Mech Dev 128:247, 2011), the authors should mention that.

- In this review the main subject approached is the role of Notch signaling in STSs tumors whereas the targeting of Notch signaling for the treatment of pediatric soft tissue sarcomas is only discussed as a possible perspective, therefore the title should be modified in order to keep the title in focus with the review topic.

Minor points

- to avoid misunderstanding, when the acronym CSL (derived from CBF-1/RBP-Jk/Su(H)/Lag2, as stated on page 6) is used, it would be better writing CSL/RBP-Jk

- a number of sentences should be shortened and better focused to make easier the reading

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.