Reviewer's report

Title: GIT1 gene deletion delays chondrocyte differentiation and healing of tibial plateau fracture through suppressing proliferation and apoptosis of chondrocyte

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Reviewer: Sowmya Viswanathan

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Understanding the role of GIT1 in healing of tibial fractures, particularly the role in chondrocyte differentiation, proliferation and apoptosis is important in fracture healing and in other joint conditions including osteoarthritis.

The hypothesis that GIT1 deletion results in delayed recovery is only partially supported by the data provided by the authors. The introduction states that "we hypothesize that GIT1 gene expression deletion may decrease the formation of new blood vessels and osteoclasts, which becomes our study focus."

There is no data showing decreased osteoclast formation or blood vessel formation. In particular, they did not label control or experimental group with markers to show differentiation of chondrocytes to specific lineages. There is no labeling in Fig 1 to show decreased osteoclast or blood vessel invasion or decreased osteoblast formation between control and experimental groups.

The behavioral observations between the two groups is descriptive - there is no quantitative or semi-quantitative documentation. For example, rotarod experiments could have been used to quantify differences in locomotion/pain of the two groups. Were the experimental and control groups matched by age and weight? There is no table or information on the mice. It's also unclear whether the experimental and control groups were housed in same or different cages - there seems to be contradictory information with respect to this in the materials and methods section.

I'm not an expert in this area, but could some sort of semi-quantitative scoring or morphometric measurements have been used to quantify the area of the bone callus in the GIT1 group vs. the control group?
The authors use the word delay indicating that at some time point the GIT1 group does differentiate towards bone - but presumably this is after the 14 and 21 day data shown? If the word delay is being used, then some kinetic data indicating resumption of differentiation towards osteoblast lineages, and invasion by osteoclasts and blood vessels, and apoptosis of chondrocytes should be demonstrated. Otherwise, it's hard to see if it's the absence of this vs. a temporal delay.

In the discussion section, I'm unclear why there is an increase in bone mass of GIT1 KO mice if they result in decreased bone callus? Perhaps there's some point here that I missed, but the explanation was not very clear here.

For stats, can they show that the use of the tests is valid and the data is normally distributed with low residuals?

Overall, I thought the study method and experimental results could be further developed to support the original hypothesis.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

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