The manuscript by Ruan & Cui et al., " Expression profiles of circular RNA and interaction networks of competing endogenous RNA in neurogenic bladder following suprasacral spinal cord injury" describes that a set of differentially expressed mRNA and circular RNA might play roles in bladder fibrosis and neurogenic bladder progression after suprasacral spinal cord injury in rats. The authors used the RNA-seq technique to determine the expression profile of mRNAs and circular RNAs and validated the results by qPCR. The authors have employed two assays to test their hypothesis. While the findings are interesting and could be informative, there are challenges in the basic experimental design, the model used, the way the data is presented and analyzed. There are still basic questions that need to be addressed.

Below I provide comments to improve this article.

1. Please provide a schema of the experimental design in Figure 1. The schema would be useful for the reader to understand how the injury was inflicted and the timeline of the bladder tissue collected after suprasacral spinal cord injury.
2. Why was this study conducted using female rats? A gender-balanced study could have been more useful.
3. Fig 1: Need proper labelling of the images. The group and type of staining. What are we looking at? Use the arrows to indicate collagen fibers (blue) and muscle tissue (red). The image should be self-explanatory. Please provide a scale bar for each image. Panels E, F, G, and H have different magnifications than panels A, B, C, and D. Please provide a quantitative analysis of the mission staining signal.
4. The authors should provide H&E and mission staining of a whole neurogenic bladder. Does this condition happen uniformly throughout the bladder or appear in a patchy way at the beginning and then progress? I wonder how that might have an impact on sampling the bladder tissue used for RNAseq (considering 1/3 of the bladder was used).
5. Is there any other molecular marker available for NB? The author should confirm their NB model with more than one marker.
6. Fig 4: What does the Y axis represent? What was the control gene?

7. Fig 5+7: These figures are very difficult to follow. Too many words in each bar graph. Please find a better way to present these bar graphs. Image resolution should be improved.
8. Fig 6: Each panel should have labels. The image should be self-explanatory. An enrichment score is exactly what?
9. Fig 9: These images are practically unreadable. Please increase image resolution or find a better way to present the data.
10. Line 301: Have you checked one or two circRNAs that didn't change in expression as a control?
11. Line 417: What is the average number of circRNAs present in tissue? 3090 is what percent of total known circRNA? It would be great to comment on the coverage of RNAseq here.
12. Line 423: How do you know these are causes of NB? Some of the DECs in the early stages could be responsible for developing NB, but during the advanced stage, the DECs could be the results of cellular response due to NB. Is NB reversible? Is it possible to add back a few downregulated circRNAs or ko few upregulated circRNA to test whether it would reverse the condition?
13. Line 447-what is the relevance? Is this circRNA0722 up/down regulated?
14. Is there a common set of up- or down-regulated circRNA present in all 3 stages? What is the status of specific up- or down-regulated circRNA or mRNA sets found in stage 1 when compared to stage 2 or stage 3? Do they change?
15. Is there any available RNAseq data set from Human NB? The authors should check the correlation of their top 10 hits (circRNAs).