The present manuscript submitted by the authors on circRNA is considered suitable for publication pending major edits. Despite presenting a fairly complete content regarding the topic it develops, it is recommended to detail a little more information listed below, as well as a review of the English language. However, I consider it is important to emphasize that they bring very interesting information to the field.

- Line 15: The abstract speaks of "covalently closed circRNAs" as if there were another type of closure for circRNA. Does it exist another type of closure for circRNA formation? I believe it sounds slightly redundant.
- Lines 45-49: “Given the prevalence of alternative circRNAs processing, such as exon skipping, intron retention and alternative splicing (Dong et al., 2017; Gao et al., 2016; You et al., 2015; Zhang et al., 2016a), just using back-splicing junction sites (BSJs) to represent different circRNAs restricts our understanding of circRNAs functions and further achievement in evolution among species”. Discuss its importance.
- Line 62-64: “Recent studies unveiled that circRNAs are not only derived from numerous of precursor mRNAs (pre-mRNAs) but also long non-coding RNAs (lncRNAs) (Holdt et al., 2016; Huang et al., 2018; Zhang et al., 2019)”. Is the formation of circRNA from mRNA and lnc-RNA the same? How can this affect the product? Add some information about it in the manuscript.
- Line 72-74: “Therefore, the branch point upstream of a circularized exon is able to attack the downstream splice donor site, resulting in a pre-mRNA intermediate containing a 2’, 5’-phosphodiester linkage”. Is it represented in Figure 1? It would be useful for its understanding its representation on the scheme.
- The abbreviations should be cited the first time they appear in the text, for example, the term ADAR is cited on line 76 and described on line 160.
- Line 83-89: “In this model, canonical splicing appears first followed by further processing of lariat intermediates to generate circRNAs. The details show as follows: first, the 2’ branch point situated within the 3’ downstream attacks the upstream 5’ splice acceptor forming a lariat precursor (Eger et

al., 2018); and then internal back-splicing take place in the same manner to generate a double lariat molecular; finally, the free 3′ hydroxyl group is capable of attacking the upstream splice acceptor site which result in a circRNA containing a 3’ to 5’ phosphodiester linkage”. This sentence is composed of 89 words, it is too long and makes it difficult to understand. It is recommended to make an outline, or to introduce a section in Figure 1, to facilitate its understanding.

- Line 101-103: “Similar to linear isoforms, circRNAs generated from multi-exon genes are alternatively spliced as well, and may further plays important roles in the transcriptome”. I suggest you add a reference here, as well as some examples.
- Line 136-137: “Considering that most of circRNAs are generated after their parent genes have been transcribed completely, the majority of circRNA isoforms may occur post-transcriptionally”. I suggest you add a reference here.
- Line 150-152: “As both repetitive and non-repetitive elements across different flanking introns are capable of forming RNA duplexes, the generation of circRNAs is tissue specific from flies to humans (Zhang et al., 2014)”. What do you mean by this? What relevance does it have to the paragraph?
- Line 161-163: “Differentially expressed RBPs have been reported to mediate pre-mRNA AS in various cell lines (Nilsen et al., 2010), and hence we hypothesize that AS in circRNAs may be regulated by similar mechanism”. Discuss how RBPs act on linear RNAs.
- Line 168: The author's name is not capitalized.
- Line 215-217: “Considering that the expression of circRNAs is often lower than the linear counterparts, even a small amount of undigested linear RNAs may surpass the abundant of cognate circRNAs”. It is a vague statement, I suggest you add a reference here.
- The paragraph that begins on line 218 should follow the previous one, since it refers to this one. Remove the paragraph separation.
- Regarding the figures, in general terms, I suggest the figure captions to be more developed, and so to facilitate the understanding of the schemes.

- Figure 1: In the figure it would be necessary to add, at least in the figure caption, that exons that are not incorporated into a circRNA form a linear RNA. Whenever a cirRNA is formed, a linear RNA is also formed. Also, indicate which type of molecule is the initial 6-exon molecule (pre-mRNA, lnc-RNA...). Can they give the same product?
- Between figure 1 a and b it says "competing of RNA pairing". This is not explained in the main text nor in the figure caption, could you explain what you mean?
- Figure 1d is confusing. Does it degrade if it is not circularized or one part is degraded and another is circularized?
- Figure 1: indicate which specific process is A, B, C, D, at least, in the figure caption.
- Figures 1 and 3 present red arrows, explain their meaning.
- Figure 3: None of the circRNAs depicted contain introns. Does the process that explains the figure attempts to explain this as well? In this case it would be good to introduce an intermediate step of maturation between the AS and the mature circRNA.
- Figure 3c: Another possible option would be Exon 3 and 4. It may be represented as such.
- Add an extra column in the Table 1 and separate the references from the algorithm name. In addition, I recommend reordering the algorithms and mentioning them as they appear in the text, for example, FUCHS (line 246) is explained before CIRCexplorer2 (line 248) in the main text.
- What is the difference between a circRNA formed by alternative-splicing and one formed by alternative back-splicing? I do not think it is clear.