Reviewer Report

Title: Efficient and accurate detection of splice junctions from RNA-Seq with Portcullis

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Reviewer Comments to Author:

The authors introduced their methods for the accurate detection of splicing junction from RNA-seq data. The proposed method was based on the classification of splicing junctions into multiple categories of different confidentialities. The categories were based on the novelty of the splicing junction (i.e. whether the junction is annotated in the gene transcript annotation file) and novelty of the splice site (i.e. whether the splice site is annotated).

The classification of splicing junctions is very useful to the field of RNA-seq analysis. It is expected that junctions with novel sites are less reliable than junctions with known sites. However, it would be too arbitrary to simply filter these junctions, especially in human subjects, since many novel events are associated with disease development.

Major comments:

1. The classification-based filtering system could be too stringent for some studies, although the classification itself is useful in many cases without doing the filtering. The authors could emphasize in the abstract and introduction that the system was based on the classification of novel junctions and novel splice sites, and in addition to the filtering function, the classification system would be useful.

2. The simulation procedure could favor the proposed filtering system since all RNA-seq reads were simulated from annotation, which is different from real RNA-seq data in which many reads are generated from unannotated junctions or splice sites. The authors could elaborate more on this limitation in the discussion.

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