

Reviewer Report

Title: Massive NGS Data Analysis Reveals Hundreds Of Potential Novel Gene Fusions in Human Cell Lines

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Reviewer Comments to Author:

The article presents that bioinformatics analysis and its results for calling candidate fusion genes in RNA-seq data from 935 cancer cell lines. The list of candidate fusion genes is available as a browseable database called LiGeA. On page 1, line 12, the "gene fusion events result from chromosomal rearrangements" should be changed to "oncogenic gene fusion events result from chromosomal rearrangements" because fusion genes occur also in healthy organisms. Fusion of genes is also one of the evolutionary mechanism for creating a new gene in a healthy organism. Not all fusion genes are oncogenic. For example, there are plenty of fusion genes known to exist in healthy people, like for example TTTY15-USP9Y, SLC45A3-ELK4, MSMB-NCOA4. On page 1, lines 37-40, the text "Moreover, each gene fusion predictions differs...chromosomal rearrangements (Mertens et al.; 2015)" should be removed from the article because it is not correct. This is not correct because some fusion gene finder can call very well a certain type of fusion genes whilst all the other fusion caller will miss the and therefore the consensus here is not the best. For example, FusionCatcher is the only fusion finder which is able to call IGH fusions (see: <https://doi.org/10.1182/blood-2016-12-758979>). When searching for a gene using the http://hpc-bioinformatics.cineca.it/fusion/search_for_gene is very slow. This should be fixed. Also it is very important to list and show the fusion genes which are supported only by one fusion finder. For example the fusion DUX4-IGH is known to exist in NALM6 cell line which is one of the 935 cell lines but when looking for it in LiGeA database, it does not show up because the TOPHAT-fusion and EricScript are not able to find fusions which involve DUX4 gene or IGH gene.

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