Novel long non-coding RNAs of relevance for ulcerative colitis pathogenesis

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Introduction

LncRNAs have become a growing field of research. They are involved in diverse biological processes including expression regulation, and chromatin modification. Many lncRNAs have been characterized as involved in the occurrence and development of various human diseases, including cancer [1]. A growing body of evidence implies a role for lncRNAs in UC by modulating the intestinal barrier, regulating the expression of inflammatory cytokines, and polarization of macrophages [2, 3].

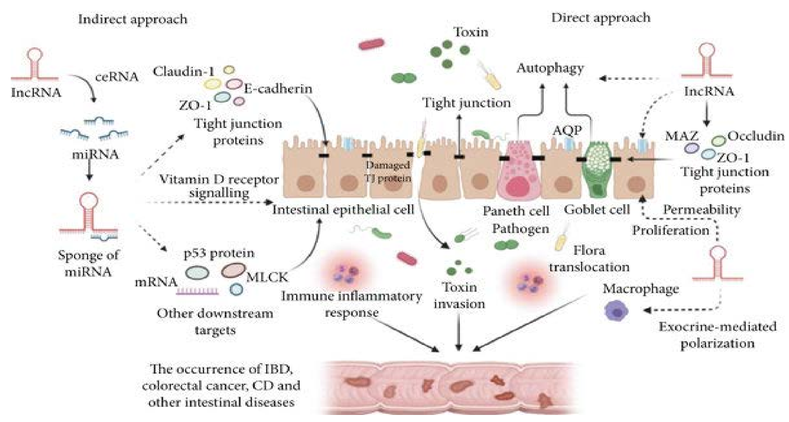

Figure 1. Involvement of lncRNA in intestinal mucosal barrier integrity by both direct and indirect approaches.

Problems

Accurate quantification of lncRNA transcripts is challenging due to the low expression of lncRNAs, and their exons overlap protein-coding exons on the same strand.

Aims

The study aimed to define the role of uncharacterized long non-coding RNAs (lncRNAs) in treatment-naïve ulcerative colitis (UC).

Method

TO overcome difficulties in lncRNA transcript quantification, multiple and “stringent” strategies were applied. New insights in the regulation of functional genes and pathways of relevance for UC through expression of lncRNAs are expected

Conclusion

This study identified a set of 15 yet uncharacterized lncRNAs which may be of importance for UC pathogenesis. These lncRNAs may serve as potential diagnostic biomarkers and might be of use for the development of UC treatment strategies in the future. The proposed method can also be helpful to quantify low-expressed lncRNA transcripts in other datasets.

Solution

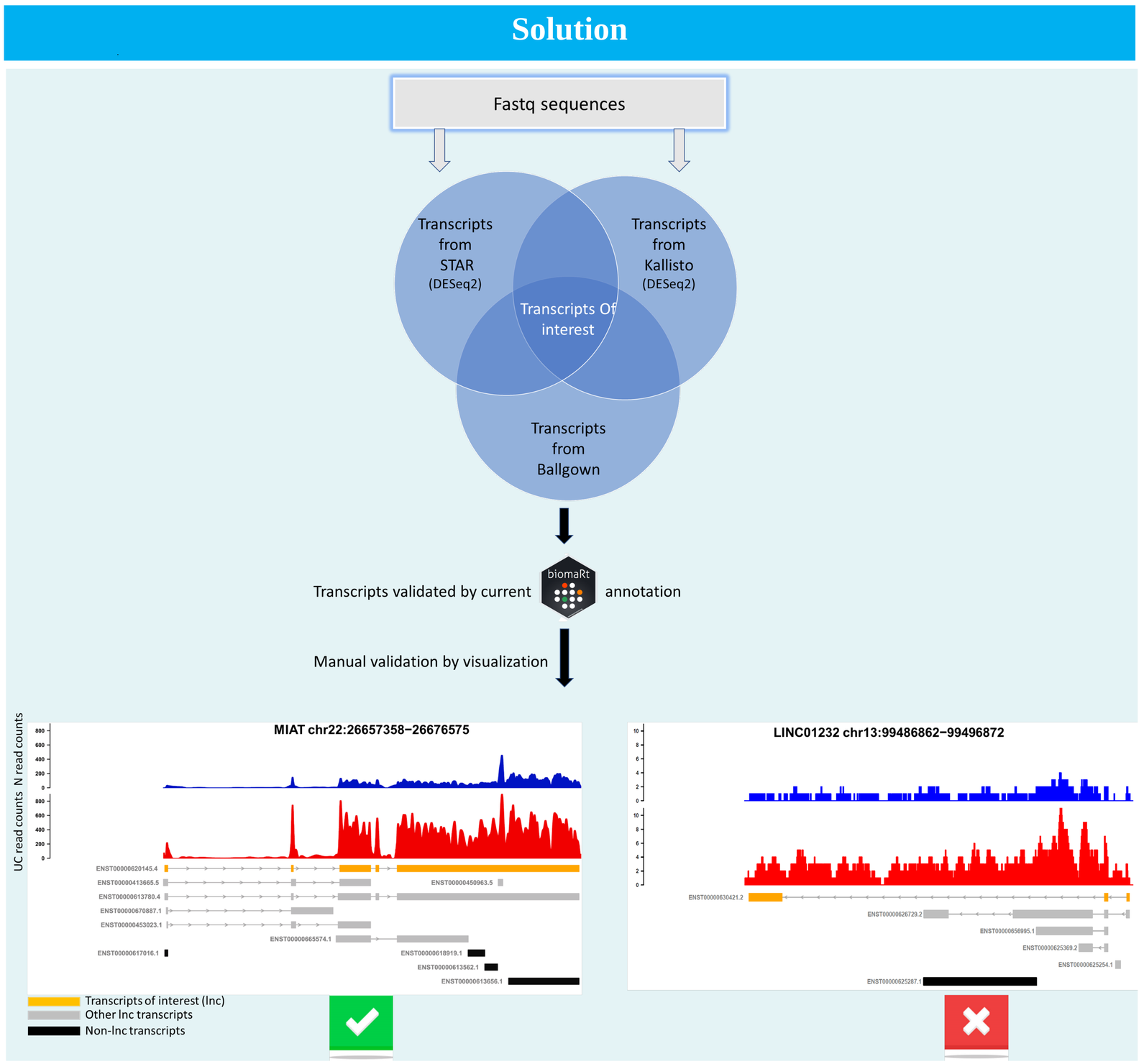

Figure 2. Common differentially expressed transcripts were selected from three methods; DESeq2 on STAR generated count matrix and transcripts obtained from Kallisto aligner and Ballgown. LncRNA’s transcripts were validated in the current biomaRt annotation. The lower part of the figure shows the manual validation by visualization. Average read counts for normal (blue) and UC (red). Read counts are shown on the y-axis. lncRNA transcripts in orange are valid candidates. Transcripts in grey are lncRNA transcripts that were not considered candidates. And transcripts in black are not annotated as lncRNA.

Biological application

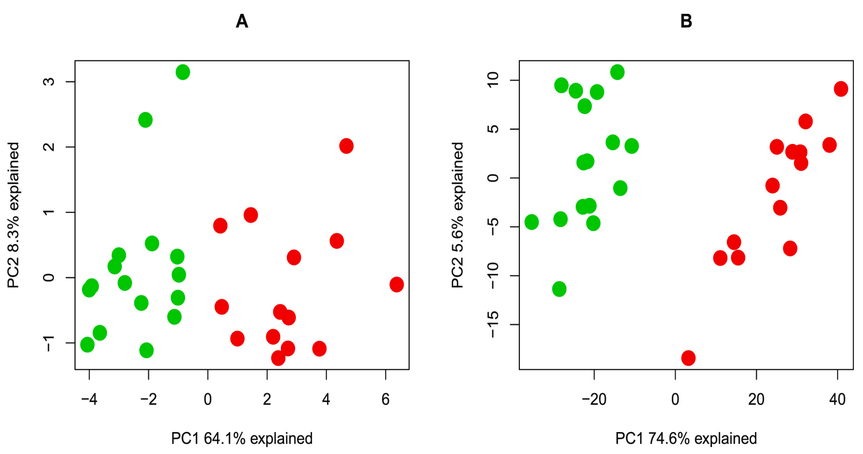

Figure 3. Principal component analysis (PCA). (A) PCA depicting 15 uncharacterized lncRNA transcripts presenting the difference between UC (n = 14; red)) and normal controls (n = 16; green). The first two components explain 64.1% and 8.3% of the variability in the lncRNA expression data. (B) PCA of differentially expressed coding transcripts (n = 686) which correlate to the uncharacterized lncRNAs (n = 15) presenting the difference between UC (n = 14; red) and normal controls (n = 16; green). The first two components explain 74,6% and 5.6% of the variability in the expression data.

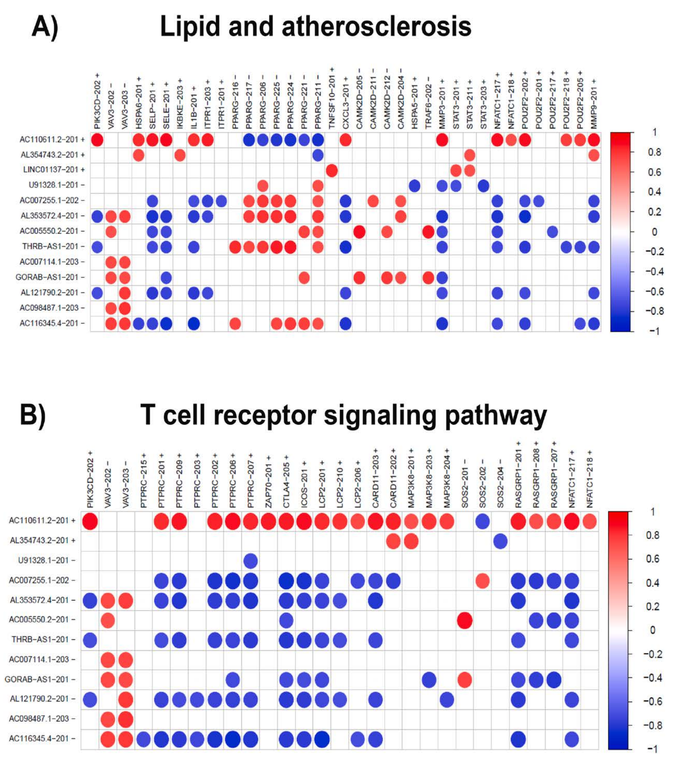

Figure 4. Co-expression plot of KEGG enriched pathways between lncRNA transcripts and their correlated protein coding transcripts. Co-expression plots of lipid and atherosclerosis pathway (A) and T cell receptor signaling (B) are indicated. LncRNA transcripts are listed on the x-axis, correlated protein coding transcripts on the y-axis. Transcript names are followed by a ‘+’ up regulated or a ‘-’ down regulated. Red dots indicate lncRNA transcript and protein coding transcript expression are positively correlated. Blue dots indicate where the lncRNA transcript and protein coding transcript expression are negatively correlated. Only correlations with an absolute value greater than 0.85 are shown.

References

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