What can competing endogenous RNA-networks tell us about viral response in Atlantic Salmon?

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We know now that only a small fraction of the genome codes for proteins. The remaining fraction contains non-coding transcripts that control the expression of other genes, influencing specific pathways and, ultimately, production traits and health status. Here we explored these gene interactions according to the competing endogenous RNA (ceRNA) hypothesis, using whole transcriptome sequencing data from gill tissue of Atlantic salmon (*Salmo salar*) infected with Pilchard orthomyxovirus (POMV) but showing no clinical signs of disease.

Introduction

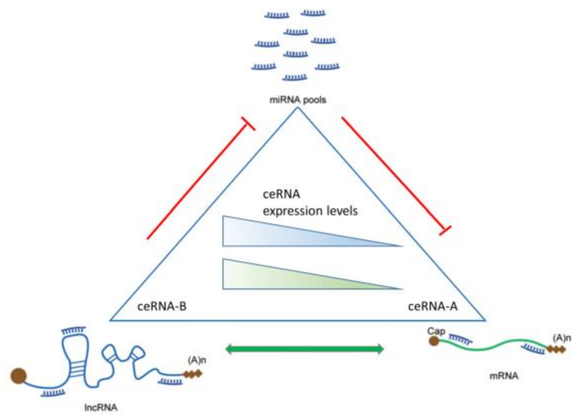

Figure 1: Competing endogenous RNAs regulate other RNA transcripts by competing for shared microRNAs (miRNAs). In our model, the increased expression of a long non-coding RNA (lncRNA) would result in the sequestering of a target miRNA which, in turn, would result in the increased expression of a messenger RNA (mRNA) previously targeted my that miRNA. The opposite would occur with the deceased expression of the lncRNA (Figure adapted from: Fiannaca et al. (2020) BMC Bioinformatics 21, 199).

Material and Methods

The mRNA, miRNA and lncRNA expression data was generated from gill samples of Atlantic salmon collected early during the POMV viral challenge trial (days 8 to 12) to uncover potential biomarkers of early infection, and late during the challenge trial (day 19) to elucidate potential markers of resistance to POMV. Control samples were also collected. A bioinformatic pipeline was developed to generate ceRNA networks for early and late infection, using miRanda[1] and RNAhybrid[2] for miRNA target prediction, and PCIT[3] for co-expression analysis.

Figure 2: Mass Atlantic salmon death due to Pilchard orthomyxovirus outbreak.

Results

Based on ceRNA hypothesis, we identified a cluster of transcripts around miRNA ssa-miR-125b-3-3p which are differentially expressed in early infection and involved in anti-viral response, suggesting they are important players in early infection. The ceRNA network also pointed to a selenoprotein (selja) downregulated in fish sampled late during the challenge, and its associated regulatory non-coding RNAs, which may be associated with viral clearance and the return to homeostasis.

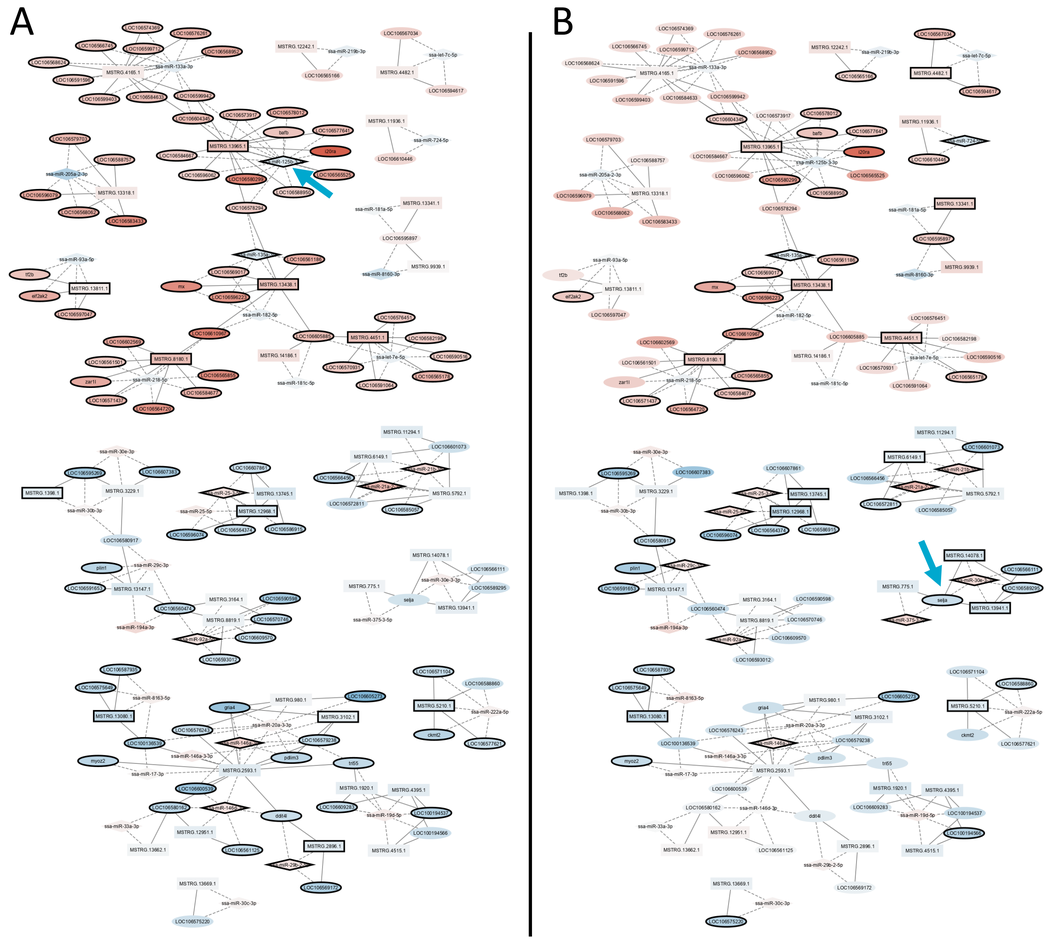

Figure 3: Competing endogenous RNA network for early (A) and late (B) subclinical fish. Black borders indicate differentially expressed transcripts in comparison to the control group. Nodes in red and blue shades represent upregulated and downregulated transcripts in comparison to the control, respectively, and the intensity of the shades correspond to the log2 fold change. The shape of the node indicates mRNA (ovals), lncRNA (rectangles) and miRNA (diamonds). Links or edges represent positive (solid lines) and negative (dotted lines) co-expression values.

Conclusion

This study provides the basis for further investigations using molecular tools to overexpress or inhibit miRNAs to confirm the functional impact of the interactions presented here on gene expression and their potential application at commercial level.

FOR FURTHER INFORMATION

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