

Abstract

Ovarian cancer is the fifth most deadliest cancer among women. Changes in microRNA(miRNA) expression and miRNA/mRNA dysregulation have been associated with ovarian cancer. In this study, we performed a comprehensive analysis of miRNA and mRNA expression in ovarian cancer using an integrative network approach combined with eQTL mapping. Our method is composed of expanding networks from eQTL associations from eQTL mapping, incorporating miRNA target predictions, and then combining the networks into an integrated network. This integrated network includes various types of data, including miRNA eQTL associations, miRNAs and their targets, protein-protein interactions, co-expressions among miRNAs and genes respectively. Applied to ovarian cancer data, we created an integrated network that provided a more inclusive view of miRNA and gene expression in ovarian cancer. In summary, we developed an integrative approach to construct an integrative network that illustrates the complex interplay among miRNA and gene expression from a systems perspective. Such an integrative network can further our understanding of the underlying mechanisms in studying ovarian cancer.

Methods

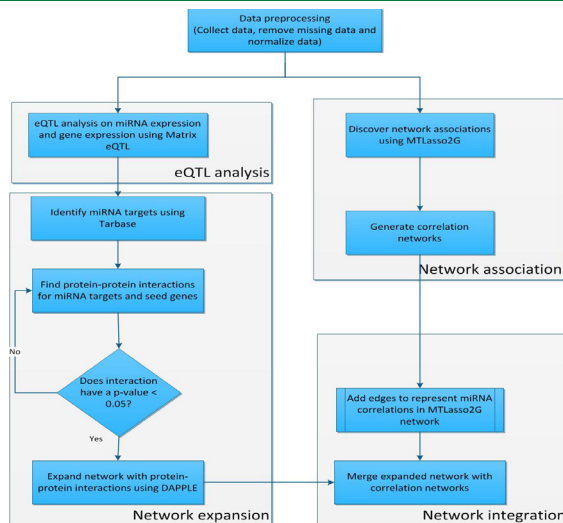


Figure 1: The workflow to create the integrated network.

- Phase 1: eQTL analysis - Perform eQTL analysis between miRNAs and gene expression.
- Phase 2: network association - Discover network association between miRNAs
- Phase 3: network expansion - Expand network with miRNA targets from eQTL analysis.
- Phase 4: network integration - Merge correlation networks and expanded networks.

Results

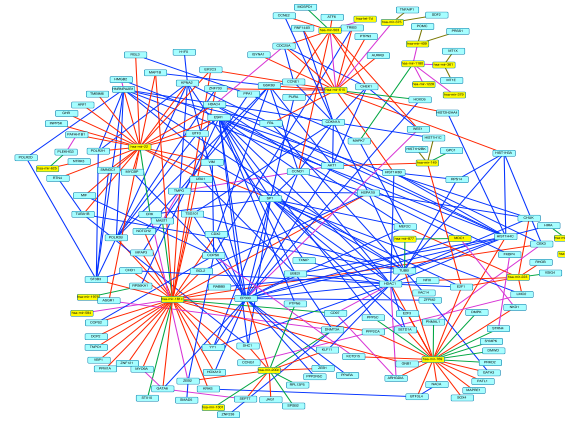


Figure 2: This network incorporated eQTLs, protein-protein interactions from DAPPLE, and miRNA-target interactions from TarBase. miRNAs are shown in yellow nodes, and genes are shown in light blue nodes. eQTLs are shown as green edges, protein-protein interactions are shown as blue edges, miRNA-target interactions are shown as red edges, MTLasso2G correlation interactions are in purple, and MTLasso2G eQTLs are in gold.

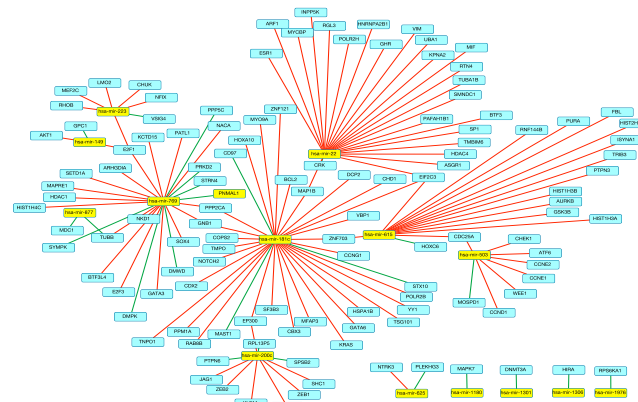


Figure 3: Network containing eQTLs and miRNA target genes obtained from Tarbase. These targets are included in the integrated network.

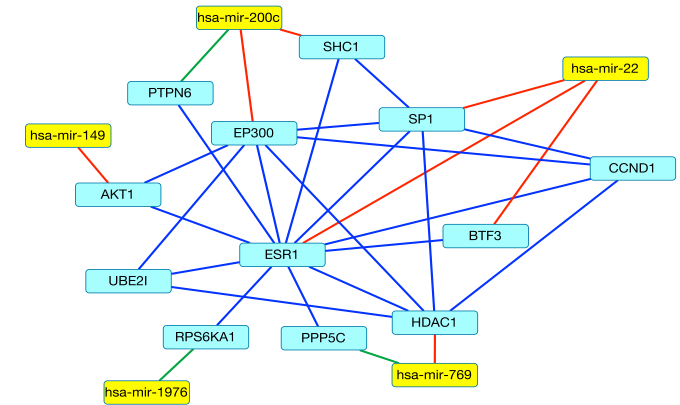


Figure 4: This subnetwork illustrates how the multiple data sources are involved in the integrated network. If the network only contained the eQTLs in green, and the miRNA-target interactions in red, most of the connections would not exist. Adding the protein-protein interactions of the genes, allows us to visualize potential downstream effects.

Conclusion

In this paper we developed a new method of constructing an integrated network by combining an eQTL study and network analysis. We applied our method to TCGA ovarian cancer data and constructed an integrated network of miRNA and gene interactions in ovarian cancer. The generated network contained miRNA to target gene relationships, eQTL associations, protein-protein interactions, the correlations or co-expressions among microRNAs and genes respectively. In the future, we will extend our approach by incorporating multiple sources. Using various data sources, we can exploit the relationships between different molecular components to help understand how ovarian cancer progresses.

References

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