



Integrating epigenetic datasets in cancer using a network based approach highlights tumor specific pathways

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Abstract

Background

Cancer is a complex disease which involves many different types of alterations in both coding and non-coding parts of the genome. In order to understand the effects of these alterations, and uncover the pathways behind them, we used a network approach to integrate epigenetic data from various cancer projects and corresponding datasets from Roadmap.

Observations

Using relationships from chromatin interaction data, we have combined protein-protein interaction networks with regulatory networks composed of promoters and enhancers. Various sources of alterations, such as epigenetic modifications are mapped onto the nodes of the network, creating a weighted graph. Using network clustering tools such as BioNet, we have found several significantly altered subnetworks enriched in differentially methylated and histone modified promoters and enhancers. These network modules are consistent with known tissue-specific or cancer-related pathways, and show enrichment for differentially expressed genes. Interestingly, we find many examples of genes which appear to be solely regulated through epigenetic modification of enhancers. We show that extending the gene network to the regulatory context uncovers more specific pathways.

Conclusion

This study has shown strong evidence of pathway (dis)regulation through epigenetic alterations in cancer. With the rapidly increasing amount of available epigenetic data in the public domain, we believe such approach will be very useful in understanding the regulatory landscape of the diseases and provide support for integration of genomic datasets.