Topology preservation of disease-specific gene-regulatory subnetworks

Maryam Nazarieh[1,2], Hema Sekhar Reddy Rajula[1] and Volkhard Helms[1]

[1]*Graduate School of Computer Science, and* [2] *Center for Bioinformatics, Saarland University, Saarbruecken, Germany*

Detecting differential expression (DE) of genes between normal and disease tissues is a common approach to get mechanistic insight into disease processes. Unfortunately, various bioinformatics methods for identifying such DE genes yield quite different results. Here, we used four bioinformatics tools to process RNA-Seq data taken from TCGA for matched tumor and normal samples of liver cancer and breast cancer patients. The overlap between the sets of significant DE genes was only 26 % in liver cancer and 28 % in breast cancer. Then, we constructed regulatory sub-networks involving transcription factors, microRNAs, and target genes that we predicted with our TFmiR web server [1] from the four sets of DE genes. We also identified both hotspot degree genes and a minimum set of dominator nodes using our integer linear programming approach described earlier [2]. Interestingly, we found that the topology of the regulatory networks constructed using TFmiR for the different sets of DE genes was highly similar with respect to hub degree nodes and dominator nodes. This suggests that key genes identified in regulatory networks derived from DE genes may give more insight into disease processes than simply inspecting the lists of DE genes.

[1] M. Hamed, C. Spaniol, M. Nazarieh, V. Hems, Nucleic Acid Res 43, gkv418 (2015).
[2] M. Nazarieh, A. Wiese, T. Will, M. Hamed, V. Helms, BMC Systems Biology 10, 88 (2016).