The linkage of human circadian rhythms and hepatocellular carcinoma (HCC) through network analysis.

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Human circadian rhythms connect internal biological clock and external environmental through earth's day and night alternating. The human circadian clocks, present in each organs, are controlled by a main pace-maker situated in SCN (suprachiasmatic nuclei) of hypothalamus which is synchronized to the daily photoperiod. Clock disturbances are involved in many diseases like diabetes, obesity, depression, bipolar disease, and many types of cancers like breast cancer, colon cancer as well as hepatocellular carcinoma which is the third most life claiming cancer around the world.

In this work the protein- protein interaction networks were analyzed using Cytoscape software.

The human circadian network consists of 2151 nodes and 75821 interactions making it a huge network. It is very centralized with the value of 0.235. The density of the network is 0.033 and heterogeneity of 1.012. The characteristic path length is 2.373 while the average number of neighbors is equal to 70.5. Recently we performed a network analysis on gene expression data obtained in our group from HepG2 cells, a liver cancer cell line that lacks the viral infection, identifying 26 HUB genes [1]. Among these genes, 20 of them resulted present in the human circadian rhythm network. All these 20 genes had high degree values in the circadian network, ranging from 287 to 77 indicating that they control a large number of functional interactions and the information flow through the circadian network. However, by merging the network of genes involved in human circadian rhythms as well HepG2, we found that 83 hub nodes are common. This establishes strong relationships between liver cancer and circadian rhythms.

[1] Singh S, Colonna G, Di Bernardo G, Bergantino F, Cammarota M, Castello G, et al. The gene expression profiling of hepatocellular carcinoma by a network analysis approach shows a dominance of intrinsically disordered proteins (IDPs) between hub nodes. Mol Biosyst. 2015; doi:10.1039/c5mb00434a