

Ingenuity[®] Science Spotlight:

Articles featured in the Ingenuity Science Spotlight represent some of the best and most diverse examples of how IPA[®] has contributed to research across multiple platforms, research areas, and research goals.



"Although genes within the circadian regulatory framework are known to coordinate transcription in a variety of biological pathways, the extent to which cancer-relevant transcripts may be influenced by alterations in circadian gene expression remains unclear. Using Ingenuity's extensive, manually curated database of functional interactions, we were able to identify canonical gene networks which were influenced by the core circadian gene CRY2, thereby advancing our understanding of the circadian system's role in tumorigenesis."

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Clock-Cancer Connection in Non-Hodgkin's Lymphoma: A Genetic Association Study and Pathway Analysis of the Circadian Gene Cryptochrome 2.

Hoffman AE, Zheng T, Stevens RG, Ba Y, Zhang Y, Leaderer D, Yi C, Holford TR, Zhu Y. Cancer Res. 2009 Mar 24. [Epub ahead of print].

http://www.ncbi.nlm.nih.gov/pubmed/19318546?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Researchers from the Department of Epidemiology and Public Health, Yale University School of Medicine, and the Dept of Community Medicine and Health Care, University of Connecticut Health Center studied Cryptochrome 2(CRY2), a core circadian gene and transcriptional repressor, to examine its role in non-Hodgkins lymphoma(NHL) tumorigenesis. Genetic analysis was performed to identify the association between genetic variants in CRY2 and risk of NHL. Three SNPs were identified and findings were confirmed by CRY2 diplotype studies. To further determine the functional effects of CRY2, the gene was silenced in vitro and the gene expression differences in CRY2 knockdown and normal cells were studied using whole genome microarray. IPA was used to analyze the differentially expressed molecules to determine whether CRY2 influences any biological pathways that may be relevant for lymphomagenesis. The subsequent identification of several genes important for cancer that are affected by CRY2, and their known relevance to hematological malignancies, provides a novel panel of promising biomarkers for NHL risk and prognosis for further investigation.

IPA network analysis showed that the genes significantly altered by CRY2 knockdown were associated with immune response and hematological system development, and were predicted to have significant effects on disease processes including cancer. A key network included molecules important for DNA repair, cell migration and metastasis, apoptosis, cell proliferation, and angiogenesis. The network was made of twenty-seven significantly up-regulated molecules and only two downregulated molecules, which is consistent with the role of CRY2 as a transcriptional repressor. By using IPA network analysis and IPA functional analysis in conjunction with genetic association studies, researchers were able to suggest that CRY2 may play an important role in HNL development.