# DEList: Identifying Cancer Genes Associated With Circadian Regulator ARNTL2 Using a Novel RNA-Seq Multi-Dataset Strategy

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Circadian disruptions have been implicated in the oncogenesis of multiple cancers. However, the underlying mechanisms linking circadian rhythms and cell cycles remain unclear, posing a significant obstacle to advancing circadian-based cancer diagnosis and treatment in the clinic. This research proposes a systematic data mining pipeline combining differential expression, correlational, and machine learning analyses to investigate the expression of 18 circadian genes in breast, lung, kidney, and thyroid cancer. Through exploration of clinical and demographic subgroups in TCGA, circadian regulator ARNTL2 was identified as upregulated in tumors and correlated with severe cancer grades, demonstrating potential as a cancer biomarker. To further elucidate ARNTL2's role in cancer, a novel multi-dataset strategy was designed to integrate analyses of data from TCGA and GSE72942, a mouse metastasis cell line with ARNTL2 blockade. DElist, a patent-pending list of 80 ARNTL2-regulated, cancer-associated genes was created, with enriched pathways in nuclear division, microtubule binding, and centromeres. RNAscope imaging identified for the first time in situ colocalization of ARNTL2 and HMMR, a DElist gene associated with cell motility and division, in squamous cell lung cancer tissue. These findings have significant clinical applications, as genomic tests based on DElist can support cancer diagnosis and treatment. Furthermore, the proposed multi-dataset strategy can help identify gene signatures for other impactful medical conditions. Finally, the strong circadian-cancer relationship discovered in this research underscores an urgent need for interdisciplinary research in public health, epidemiology, and beyond to develop circadian-based strategies for mitigating disease incidence.

**Awards Won:**
Third Award of $1,000