

## Ingenuity<sup>®</sup> Science Spotlight:

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



### **mSin3A corepressor regulates diverse transcriptional networks governing normal and neoplastic growth and survival.**

Jan-Hermen Dannenberg, Gregory David, Sheng Zhong, Jaco van der Torre<sup>1</sup>, Wing H. Wong<sup>2</sup> and Ronald A. DePinho. *Genes & Development* 19:1581-1595, 2005.

<http://www.ncbi.nlm.nih.gov/pubmed/15998811?dopt=Abstract>

Sin3 is a component of an evolutionarily conserved multi-protein corepressor complex that mediates gene silencing in eukaryotes. The mammalian Sin3 corepressor complex (mSin3) associates with histone deacetylases (HDACs) and achieves transcriptional silencing through the chromatin-modifying activities of these enzymes. A wide range of sequence-specific DNA-binding transcription factors can recruit the mSin3/HDAC complex to the regulatory region of a target gene. The mSin3/HDAC complex activity is essential to cellular differentiation and development, proliferation, and apoptosis. Aberrant interactions between transcription factors and the mSin3/HDAC complex are associated with the pathogenesis of cancer as well as other diseases.

mSin3 includes two splice forms called mSin3A and mSin3B. Investigators applied IPA to the mSin3A transcriptome to better define the roles of this corepressor component. Network analysis confirmed several known transcription factor nodes through which mSin3A modulates gene expression, including the Myc-Mad, E2F, and p53 transcriptional networks. Furthermore, the network analysis identified new mSin3A interactions, revealing unexpected connections between mSin3A and networks regulated by FOS, PPAR, STAT, and FALZ. PPAR is especially noteworthy because the mSin3A transcriptome includes many genes involved in mitochondrial respiration and metabolism, and the PPAR pathway, which is implicated in mitochondrial respiration and metabolism, appears to be regulated by histone deacetylation.