

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.



Identification of Novel Candidate Oncogenes and Tumor Suppressors in Malignant Pleural Mesothelioma Using Large-Scale Transcriptional Profiling.

Gavin J. Gordon, Graham N. Rockwell, Roderick V. Jensen, James G. Rheinwald, Jonathan N. Glickman, Joshua P. Aronson, Brian J. Pottorf, Matthew D. Nitz, William G. Richards, David J. Sugarbaker, and Raphael Bueno. *American Journal of Pathology*. 2005; 166:1827-1840.

<http://www.ncbi.nlm.nih.gov/pubmed/15920167?dopt=Abstract>

Malignant pleural mesothelioma (MPM) is a highly lethal and poorly understood cancer. With limited treatment options, patients usually survive less than two years following diagnosis. Although MPM has been classified into three histological subtypes, there is no correlation between survival and response to treatment or histological classification.

In this study, 40 MPM tumor specimens, nine normal lung tissue samples and five cell lines were evaluated using the Affymetrix7 GeneChip7 U133A array. After applying clustering methods, two possible subclasses of MPM (C1 or C2) were grouped, representing distinct expression patterns. A total of 113 genes were differentially expressed in the C1 and C2 subclasses. Histological markers of 54 genes showed different expression levels between MPM histological classes. The study identified 328 upregulated genes and 311 downregulated genes as MPM tumor markers. Quantitative RT PCR, western blotting, and MPM tissue arrays validated expression of subset markers. The results showed that transcription and translation are coupled by NME2 (transcription factor) and CR1 (CREB binding protein).

IPA was used to discover novel pathogenic pathways during MPM progression. Analysis of the 328-upregulated genes in MPM tumor vs. normal tissues identified twelve networks. Seven networks that shared at least one gene were combined and are displayed in Figure 7 of this paper. Five genes were shared by at least two pathways. Two of them, SP1 and SPARC, have not been previously described in MPM studies. SP1, a transcription factor, regulates many cancer-related genes. SPARC is a matrix-associated protein. Pathway analysis showed that SPARC interacts with VTN and may function in angiogenesis in the context of MPM tumorigenesis. The functional pathways and networks generated by Ingenuity Pathways Analysis assisted in understanding MPM pathogenesis and tumorigenesis.