

## 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.



### **Bioinformatic identification of FGF, p38-MAPK, and calcium signaling pathways associated with carcinoma *in situ* in the urinary bladder.**

Malene Herbsleb, Ole F Christensen, Thomas Thykjaer, Carsten Wiuf, Michael Borre, Torben F Ørntoft and Lars Dyrskjøt. BMC Cancer, 2008, 8:37 (31 January 2008).

<http://www.biomedcentral.com/content/pdf/1471-2407-8-37.pdf>

Researchers from the Department of Genetics and Biotechnology, University of Aarhus, Denmark have developed a new way to predict the presence or absence of carcinoma *in situ* (CIS) in patients diagnosed with certain types of bladder cancer. Instead of focusing on the best individual markers of bladder cancer, they used IPA to study the involvement of a panel of transcription factors within canonical signaling pathways. IPA identified four signaling pathways where the transcription factors behaved coherently, indicating the whole pathway was affected. Three of these identified pathways were able to classify tissue samples according to CIS status significantly.

The team analyzed all canonical signaling pathways within IPA to find transcription factors that had DNA binding domains. They then used the “My Pathway” features in IPA to find all direct downstream genes in which activation, inhibition, expression, or transcription is affected. Pathways that were significantly affected were FGF signaling, p38 MAPK signaling, cAMP signaling, and Calcium signaling. They found that the ability to predict CIS status based on the transcription factors in the p38 MAPK pathway was the most interesting since it contained the most number of transcription factors and had previously been shown to have a role in bladder cancer. By correlating the respective expression values of the transcription factors in this pathway with the classification of tumor, they were able to formulate a pathway signature for CIS. In particular, they found that genes involved in the p38 MAPK pathway are often upregulated in tumors with concomitant CIS. Moreover, previous studies showed changes in FGF receptor 3 gene levels their results highlight the already-established mechanistic connection between the p38 MAPK pathway and FGFR3 levels.

In this way, the authors were able to identify whole pathways that are associated with a distinct disease course. The advantage of this pathway-based strategy is that small contributions from single genes, which may not be as detectable, can, accumulate within a specific pathway, and thus be more evident.