

## 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.



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### **Combined Proteomics and Pathways Analysis of Collecting Duct Reveals a Protein Regulatory Network Activated in Vasopressin Escape.**

Ewout J. Hoorn, Jason D. Hoffert, and Mark A. Knepper . J Am Soc Nephrol. 2005 Oct;16(10):2852-63. Epub 2005 Aug 3.

<http://www.ncbi.nlm.nih.gov/pubmed/16079266?dopt=Abstract>

Certain clinical conditions such as congestive heart failure or inappropriately elevated levels of circulating vasopressin can lead to free-water retention and progressive hyponatremia, a serious and potentially fatal electrolyte disorder. The extent of hyponatremia is limited by vasopressin escape, a physiologic phenomenon that leads to increased water excretion independent of circulating vasopressin levels.

Working with a rat model, scientists at the National Institutes of Health sought to discover proteins from the inner medullary collecting duct that regulate vasopressin escape and the signaling pathways that are involved. Since vasopressin escape is characterized by reduced expression of the water channel aquaporin-2 (AQP2), the researchers focused on the proteins that co-regulate with AQP2, using differential gel electrophoresis (DIGE) to monitor their abundance and MALDI-TOF mass spectrometry to identify them.

The proteins found by DIGE were uploaded into IPA, IPA generated a network of 33 proteins, dubbed the vasopressin escape cluster. It included proteins that were not detected by DIGE, but whose involvement in vasopressin escape was verified by semiquantitative immunoblotting. Thus IPA enabled the discovery of low-abundance proteins, such as transcription factors, not found by DIGE.

The proteins in the vasopressin escape cluster that were identified by IPA, but not DIGE represent hypotheses in that their involvement in vasopressin escape can be tested by semiquantitative immunoblotting to confirm changes in their abundance. The results of this exciting approach implicate several transcription factors (c-myc, c-fos, c-jun, p53), the transcriptional co-factor SRC-1, and regulatory proteins (c-src, RACK1) in vasopressin escape.