

## 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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### Regulatory network of inflammation downstream of proteinase-activated receptors.

Ricardo Saban, Michael R D'Andrea, Patricia Andrade-Gordon, Claudia K Derian, Igor Dozmorov, Michael A Ihnat, Robert E Hurst, Cindy Simpson and Marcia R Saban. BMC Physiology 2007, 7:3.

<http://www.biomedcentral.com/1472-6793/7/3>

A recent study published in BMC Physiology by members of the Saban lab at the University of Oklahoma Health Sciences Center (OUHSC) elucidates the role of a unique set of G-protein coupled receptors called protease-activated receptors (PARs) in bladder tissue response to inflammation. Using a combination of large-scale gene expression analysis and Ingenuity Pathways Analysis the research team was able to build a working model for the role of PAR1 and downstream networks in bladder inflammatory response, and generate testable hypotheses regarding PAR1 regulation and bladder inflammation.

The OUHSC team set out to determine the composition of the transcriptome downstream of PAR activation, and the molecular pathways and biological processes impacted by members of that transcriptome. In this study they focused on PAR1, which is well represented in bladder tissue. In order to understand the role of PAR1 in mediating bladder tissue response to inflammation and identify PAR1-dependent transcripts, bladder inflammation was induced with substance P or LPS in wild type or PAR1-/- mice. PAR1-dependent transcripts were defined by cDNA array analysis as those that were up-regulated in response to inflammation in WT mice and failed to be up-regulated in PAR1-/- mice. IPA core analysis then identified the pathways, biological interactions, and functional annotations that were most significant to the PAR1-dependent transcripts (which corresponded to 75 genes). IPA rapidly identified a role for many genes in the PAR1 transcriptome in relevant physiological and cellular processes including cell motility, immune response, inflammation, and renal and urological diseases.

By combining cDNA array results with “in silico genomics network analysis” in IPA, the researchers were able to generate hypotheses and build a working model of PAR1 and the PAR1 transcriptome in inflammation response in the bladder, and design targeted siRNA follow up experiments to test those hypotheses.