

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.



"The possibility of reconstructing cell regulatory networks and expert-curated canonical pathways as delivered by Ingenuity's graphical workspace environment, together with Ingenuity's very detailed proprietary database information and cell- and tissue-specific filters, allowed us to very precisely correlate differential expression profiles with complex tissue responses after consumption of different preparations of a single strain of lactic acid bacteria"

Dr. Peter van Baarlen
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Differential NF-kappaB pathways induction by *Lactobacillus plantarum* in the duodenum of healthy humans correlating with immune tolerance.

van Baarlen P, Troost FJ, van Hemert S, van der Meer C, de Vos WM, de Groot PJ, Hooiveld GJ, Brummer RJ, Kleerebezem M. Proc Natl Acad Sci U S A. 2009 Feb 17;106(7):2371-6.

http://www.ncbi.nlm.nih.gov/pubmed/19190178?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

A multidisciplinary team of researchers from TI Food and Nutrition in The Netherlands published findings from a recent study designed to elucidate the mechanisms by which nonpathogenic food bacteria affect immune response. By generating genome wide expression profiles from healthy adults that had consumed *Lactobacillus plantarum* and analyzing those profiles in IPA, they were able to build a molecular model for the establishment of immune tolerance toward nonpathogenic bacterium. Their approach may help clarify the potential probiotic activities of *L. plantarum*, and may also help elucidate the mechanisms that underlie disproportionate immune responses observed in patients with inflammatory bowel disorders.

Analysis of human intestinal mucosa gene expression profiles in IPA effectively enabled the researchers to walk from molecular profiles of host response to stationary phase, midlog, or dead *L. plantarum* to cellular processes, pathways, and key transcriptional regulators at the core of immune response to the bacterium. Key to their analysis was the ability to use IPA's Contextual Filtering capabilities to reconstruct networks that were specifically anchored on immune response and immune and lymphatic tissue development processes. This enabled them to identify genes that were core regulators of genes altered in response to consumption of bacteria. For example, the key regulators of genes altered by consumption of midlog cultures of bacteria included MYC, PARP1 and cyclin D1 – all potent regulators of cellular proliferation. Midlog gene expression profiles were also associated with upregulation of metabolic and Wnt/Beta Catenin signaling pathways, further supporting their hypothesis that midlog bacteria stimulate proliferation in the small intestine. The key nodes associated with stationary and dead *L. plantarum* included TNF•, NF-kB and JUN. Visualization in IPA of differential regulation of NF-kB subunits enabled them to further hypothesize that RelB dependent NF-kB signaling and AHR signaling

may specifically participate in regulated response to food bacteria, and may provide points to intervene and modulate that response.