Biological Sciences Division

First use of global proteomics to identify bacterial protein abundance changes

Scientists at Pacific Northwest National Laboratory (PNNL) have reported the first systematic investigation using global proteomics to identify changes in the abundance of bacterial proteins associated with macrophage colonization. These results demonstrate the utility of a systematic investigation of changes in the bacterial proteome to identify key proteins of likely importance in detecting bacterial pathogens and developing effective vaccines. The results appear in the September 28 issue of the *Journal of Biological Chemistry*.

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Salmonella enterica serovar Typhimurium (STM) is a facultative intracellular pathogen that can cause gastroenterit is in humans and a lethal infection in mice that lack a functional natural resistance-associated macrophage protein 1 (Nramp1). Because the symptoms resemble human typhoid fever caused by STM, mice infected by STM provide a model system to investigate the development and immunology of typhoid fever in humans.

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To evade host resistance mechanisms, STM must alter its proteome following macrophage infection. To identify new colonization and virulence factors that mediate STM production and development, PNNL researchers have isolated STM cells from RAW 264.7 (a mouse leukemic monocyte cell line) macrophages at various time points following infection and used the PNNL-developed accurate mass and time (AMT) tag proteomic approach to detect the changes in STM protein abundances.

Critical to the identification of key proteins linked to the successful colonization of macrophages, the scientists used the AMT tag proteomic approach to systematically investigate the STM proteins isolated from the macrophages with or without functional Nramp1 at different time-points of infection.

The research team includes Liang Shi, Josh Adkins, Jim Coleman, Athena Schepmoes, Alice Dohlnakova, Heather Mottaz, Angela Norbeck, Samuel Purvine, Nathan Manes, Heather Smallwood, Haixing Wang, Karin Rodland, Dick Smith, and Thomas Squier, all PNNL; John Forbes and Philippe Gros, McGill University, Montreal; Sergio Uzzau, University of Sassari, Italy; and Fred Heffron, Oregon Health Sciences University.

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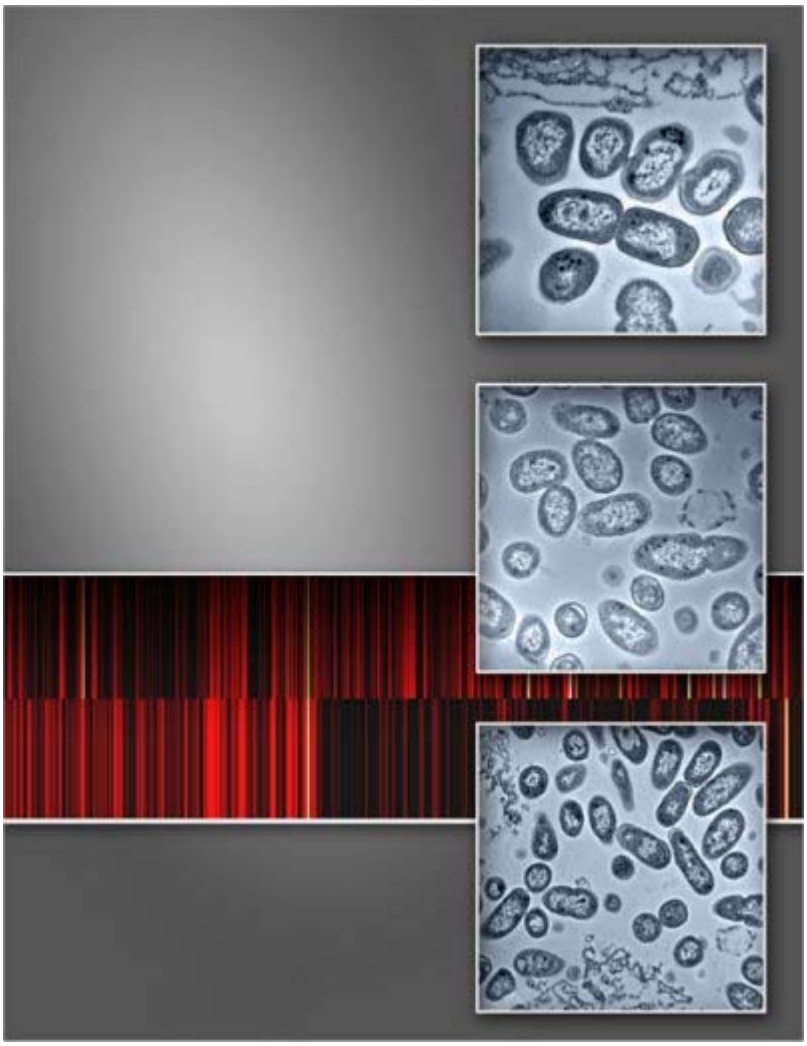

This shows the cells of *Salmonella* isolated from macrophages and the results of proteomic analysis of the isolated *Salmonella* cells. Investigati on of the changes in *Salmonella* protein abundances during the infection resulted in identification of a novel protein that is required for *Salmonella* to replicate inside macrophages. Full Image

Reference

Shi L, JN Adkins, JR Coleman, AA Schepmoes, A Dohnalkova, HM Mottaz, AD Norbeck, SO Purvine, NP Manes, HS Smallwood, H Wang, J Forbes, P Gros, S Uzzau, KD Rodland, F Heffron, RD Smith, and TC Squier. 2006. "Proteomic analysis of *Salmonella enterica* serovar Typhimurium isolated from RAW 264.7 macrophages: identification of a novel protein that contributes to the replication of serovar Typhimurium inside macrophages." *Journal of Biological Chemistry* 281(39):29131-29140.