Invasion without a stir

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Bacteria of the genus Salmonella cause most food-borne illnesses. The bacteria attach to cells of the intestinal wall and induce their own ingestion by cells of the intestinal epithelium. Up till now, researchers assumed that Salmonella have to induce the formation of distinctive membrane waves in order to invade these gut cells. Researchers from the Helmholtz Centre for Infection Research in Braunschweig, Germany, now refuted this common doctrine.

"Based on our data, the molecular mechanism of infection employed by Salmonella has to be revised," says Klemens Rottner, head of the HZI research group "Cytoskeleton Dynamics". The group's results have now been published in the current issue of the scientific journal "*Cellular Microbiology*".

Salmonella are highly adaptive bacteria. They can live in the presence and absence of oxygen and thus propagate in the gut. The ingestion by humans occurs mainly via contaminated egg dishes such as mayonnaise or raw milk products as well as meat or sausages. Infections with *Salmonella* lead to severe diarrhea and fever, particularly in patients harbouring a compromised immune system.

Although *Salmonella* are long-known pathogens, the precise mechanisms of infection are incompletely understood. The bacteria inject a protein cocktail using a "molecular syringe" into host cells, leading to dramatic rearrangements of cytoskeletal filaments below the cell membrane. As a result, membrane waves are formed, which enclose the bacteria, and apparently facilitate their invasion. Those characteristic membrane

waves are called "ruffles", the process is known as "ruffling". Until now, researchers regarded the formation of these ruffles as absolutely essential for bacterial entry.

In a collaborative effort, HZI research groups "Cytoskeleton dynamics" and "Signalling and Motility" now succeeded in shedding new light on the infection strategy of *Salmonella*. "We wanted to improve our mechanistic understanding of how *Salmonella* invade their host cells," says Jan Hänisch, who performed most experiments in the course of his PhD-thesis. Cells that were engineered to lack those membrane ruffles normally induced during *Salmonella* infection still engulfed the bacteria. "We showed for the first time that membrane ruffles are not essential for the bacteria to penetrate the host cell membrane." Since ruffling was used so far as signature of successful host cell invasion by this pathogen, the usefulness of such methods has to be reconsidered.

Finally, the researchers discovered a new piece in the puzzle of *Salmonella* entry, called WASH. This novel factor promotes bacterial invasion by contributing to the formation of host cell cytoskeletal filaments important for entry. "Our results have significant impact on the molecular and mechanistic understanding of the infection strategy used by this pathogen," says Rottner, "and on the development of novel strategies to screen for potential inhibitors of the entry process in the future."

More information: Molecular dissection of Salmonellen-induced membrane ruffling versus invasion. Hänisch J, Ehinger J, Ladwein M, Rohde M, Derivery E, Bosse T, Steffen A, Bumann D, Misselwitz B, Hardt WD, Gautreau A, Stradal TE, Rottner K. Cell Microbiol. (2010) 12(1), 84□□doi:10.1111/j.1462-5822.2009.01380.x

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