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Press release

## **Shigellosis: how the bacterium neutralizes our immune defenses**

**Institut Pasteur researchers working together with Inserm have recently discovered how *Shigella*, the bacterium responsible for an acute inflammatory disease of the intestine, is able to destroy our initial immune defenses so that it can survive and invade the mucosa. An understanding of such mechanisms opens up useful therapeutic possibilities both for the treatment of shigellosis and for all intestinal infectious diseases.**

The *Shigella* bacterium is responsible for bacillary dysentery in humans; this is one of the most severe diarrheal diseases, causing between 600,000 and one million deaths across the world each year. To defend the organism against infectious attacks, epithelial cells in the intestine secrete antimicrobial peptides, which constitute a first line of immune defense against all the pathogens in the digestive tract. Most intestinal inflammatory diseases, including the widespread Crohn's disease, are partially caused by a lack of synthesis of these bactericidal molecules of innate immunity; this emphasizes their vital role in the organism's defense.

The team from the Molecular Microbial Pathogenesis Unit (Institut Pasteur/Inserm Unit 786), led by Philippe Sansonetti, recently used *in vivo* and *in vitro* approaches to reveal the strategies developed by *Shigella* to counter-attack the protective action of these antimicrobial molecules. The researchers have proven that the bacterium is able to inhibit the transcription of genes coding for antibacterial peptides, in particular those which are the most bactericidal against this pathogen, and therefore to suppress their expression. *Shigella* also prevents the participation of dendritic cells, which have a key role in the immune response, in blocking the epithelial attraction signals of these cells. "*We know the Shigella molecules that control these mechanisms,*" explains Philippe Sansonetti. "*This is therefore the first experimental demonstration of the capacity of a bacterium to directly manipulate the expression of these innate antimicrobial components. This illustrates the extent to which a pathogen has been able to adapt its survival strategy in accordance with our own defense systems.*"

Having deciphered the strategy used by *Shigella*, the scientists are currently developing research to try to find molecules which are able to stimulate – preventively or curatively – the

synthesis of antimicrobial peptides. *“This program offers encouraging therapeutic possibilities,”* adds Philippe Sansonetti, *“as this medication could provide hope for a treatment not only for shigellosis but also in general for all infectious or inflammatory intestinal diseases.”*

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**Source:**

*“Virulent Shigella subverts the host innate immune response through manipulation of antimicrobial peptide genes expression”*, **Journal of Experimental Medicine**, published on line on April 21 2008.

<http://www.jem.org/cgi/content/abstract/jem.20071698v1?papetoc>

Brice Sperandio (1,2), Béatrice Regnault (3), Jianhua Guo (4), Zhi Zhang (4), Samuel L. Stanley Jr. (4), Philippe J. Sansonetti (1,2) & Thierry Pédrón (1,2).

(1) Molecular Microbial Pathogenesis Unit, Institut Pasteur, Paris, France

(2) Inserm Unit 786, Institut Pasteur, Paris, France

(3) DNA Micro-arrays Platform, Institut Pasteur, Paris, France

(4) Department of Medicine, Washington University School of Medicine, St Louis, MO, USA

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**Contact:**

- Institut Pasteur Press Department:

Marion Doucet – +33 (0)1 45 68 89 28 – [marion.doucet@pasteur.fr](mailto:marion.doucet@pasteur.fr)

Nadine Peyrolo – +33 (0)1 45 68 81 47 – [nadine.peyrolo@pasteur.fr](mailto:nadine.peyrolo@pasteur.fr)

- Inserm Press Department:

Anne Mignot – +33 (0)1 44 23 60 73 – [presse@inserm.fr](mailto:presse@inserm.fr)