

Host-microbial relationships in the intestine: sensing commensal and pathogenic bacteria

Marc Lecuit^{1,2,3}, Justin Sonnenburg², Pascale Cossart¹ and Jeffrey I. Gordon²

¹ Unité des Interactions Bactéries Cellules, INSERM U604, Institut Pasteur, Paris-F

² Center for Genome Sciences and Department of Molecular Biology and Pharmacology, Washington University, St Louis, MO USA

³ Department of Infectious Diseases and Tropical Medicine, Necker-Enfants malades Hospital, Paris-5 René Descartes University, Paris-F

Functional genomics studies of the response to mono-association of germ-free mice with *Bacteroides thetaiotaomicron* have revealed that this symbiont modulates expression of genes involved in a broad range of important intestinal functions, including nutrient absorption, angiogenesis, xenobiotic metabolism, and fortification of the innate immune system. To explore the microbial determinants of beneficial versus pathogenic host-bacterial relationships, similar types of functional genomic studies were performed in germ-free mice colonized with *Listeria monocytogenes*, or its closely related non-pathogenic relative, *L. innocua*. The results of functional genomics analyses revealed that the host response to *L. innocua* is very similar to that documented with *B. thetaiotaomicron*. In contrast, *L. monocytogenes* evokes a complex program of host gene expression that includes NF-kappaB-dependent and IFN-responsive pathways. Strikingly, a *L. monocytogenes* mutant for listeriolysin produces a host response that phenocopies that of *L. innocua*. These findings reveal that the presence or absence of a single gene product that allows the microbe to access the cytoplasmic compartment of host cells can profoundly influence the host-bacterial relationship.

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