Intestinal epithelial NAIP/NLRC4 restricts systemic dissemination of the adapted pathogen Salmonella Typhimurium due to site-specific bacterial PAMP expression

ID 4527123
Author(s) Hausmann, Annika; Böck, Desirée; Geiser, Petra; Berthold, Dorothée L.; Fattinger, Stefan A.; Furter, Markus; Bouman, Judith A.; Barthel-Scherrer, Manja; Lang, Crispin M.; Bakkeren, Erik; Kolinko, Isabel; Diard, Médéric; Bumann, Dirk; Slack, Emma; Regoes, Roland R.; Pilhofer, Martin; Sellin, Mikael E.; Hardt, Wolf-Dietrich
Author(s) at UniBasel Bumann, Dirk ; Diard, Médéric ;
Year 2020
Title Intestinal epithelial NAIP/NLRC4 restricts systemic dissemination of the adapted pathogen Salmonella Typhimurium due to site-specific bacterial PAMP expression
Journal Mucosal Immunology
Volume 13
Number 3
Pages / **Article-Number** 530-544
Inflammasomes can prevent systemic dissemination of enteropathogenic bacteria. As adapted pathogens including Salmonella Typhimurium (S. Tm) have evolved evasion strategies, it has remained unclear when and where inflammasomes restrict their dissemination. Bacterial population dynamics establish that the NAIP/NLRC4 inflammasome specifically restricts S. Tm migration from the gut to draining lymph nodes. This is solely attributable to NAIP/NLRC4 within intestinal epithelial cells (IECs), while S. Tm evades restriction by phagocyte NAIP/NLRC4. NLRP3 and Caspase-11 also fail to restrict S. Tm mucosa traversal, migration to lymph nodes, and systemic pathogen growth. The ability of IECs (not phagocytes) to mount a NAIP/NLRC4 defense in vivo is explained by particularly high NAIP/NLRC4 expression in IECs and the necessity for epithelium-invading S. Tm to express the NAIP1-6 ligands-flagella and type-III-secretion-system-1. Imaging reveals both ligands to be promptly downregulated following IEC-traversal. These results highlight the importance of intestinal epithelial NAIP/NLRC4 in blocking bacterial dissemination in vivo, and explain why this constitutes a uniquely evasion-proof defense against the adapted enteropathogen S. Tm.
Publisher Nature
ISSN/ISBN 1933-0219 ; 1935-3456
edoc-URL https://edoc.unibas.ch/76478/
Full Text on edoc Available;
Digital Object Identifier DOI 10.1038/s41385-019-0247-0
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/31953493
Document type (ISI) Journal Article