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Paper Poster Session
Host-pathogen interactions

Toll-like receptor-4 is essential for Arcobacter butzleri induced colonic and systemic immune responses in gnotobiotic IL-10-/- mice

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Background: The gram-negative bacterium *Arcobacter butzleri* has been shown to be responsible for sporadic cases of human gastroenteritis with abdominal pain and acute or prolonged watery diarrhea. Information about the underlying immunopathological mechanisms of infection *in vivo*, however, is limited. We have recently shown that following *A. butzleri* infection, gnotobiotic IL-10$^{-/-}$ mice exhibited intestinal and systemic pro-inflammatory immune responses. For the first time we investigated the role of Toll-like-Receptor (TLR) -4, the main innate receptor for lipopolysaccharide and lipooligosaccharide of gram-negative bacteria, in murine *Arcobacter* infection in the present study.

Material/methods: The intestinal microbiota of TLR-4 IL-10 double deficient (TLR-4$^{-/-}$ IL-10$^{-/-}$) and IL-10$^{-/-}$ control mice was depleted by broad-spectrum antibiotic treatment. The resulting gnotobiotic (i.e. secondary abiotic) mice were then perorally infected with two different *A. butzleri* strains isolated from a diseased patient (CCUG 30485) or fresh chicken meat (C1), respectively.

Results: Until day 16 after infection gnotobiotic TLR-4$^{-/-}$ IL-10$^{-/-}$ and IL-10$^{-/-}$ control mice were stably colonized with either *A. butzleri* strain at high concentrations. During the course of infection, bacterial fecal loads, however, were slightly lower in the TLR-4$^{-/-}$ IL-10$^{-/-}$ as compared to IL-10$^{-/-}$ control mice. *A. butzleri* infected IL-10$^{-/-}$ mice lacking TLR-4 displayed less pronounced colonic apoptosis that was accompanied by lower numbers of innate and adaptive immune cells including macrophages and monocytes, T lymphocytes, regulatory T cells and B lymphocytes within the colonic mucosa and lamina propria as compared to IL-10$^{-/-}$ control mice. Furthermore, large intestinal pro-inflammatory mediators including nitric oxide, TNF, IL-6 and MCP-1 and, remarkably, of systemic pro-inflammatory cytokines such as IFN-γ and IL-12p70 were lower in *A. butzleri* infected TLR-4$^{-/-}$ IL-10$^{-/-}$ versus IL-10$^{-/-}$ mice.

Conclusions: TLR-4 is involved in mediating *Arcobacter* infection *in vivo*. Further studies are needed to investigate the molecular mechanisms underlying arcobacteriosis in more detail.