

The strain-specific anti-inflammatory capacities of probiotics are driven by NOD2-mediated recognition of specific muropeptides derived from the peptidoglycan.

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i) Introduction and objectives. In genetically susceptible individuals, an inappropriate mucosal immune response against the intestinal flora appears to be the principal mechanism leading to the pathogenesis of inflammatory bowel disease (IBD). Therefore, manipulation of the luminal contents with probiotic strains represents an attractive therapeutic option but beneficial effects were shown to be strain-specific and the precise underlying mechanisms remain often unclear. Therefore we investigated the role of peptidoglycan (PGN) in the protective effect of lactobacilli.

ii) Materials and Methods. TNBS-induced colitis model performed in WT and Nod2-deficient mice was used to unravel the protective role of PGN and derived muropeptide. Bone marrow derived dendritic cells (BMDCs) were differentiated from WT and NF κ B-Luc mice.

iii) Results and Discussion. We showed that direct administration of PGN purified from a protective *Lactobacillus* strain could exert potent anti-inflammatory effects in a Nod2 dependant way. In addition, such PGN induced IL-10-producing regulatory DCs *in vitro*, able to rescue mice from colitis after adoptive transfer and inhibited the TLR2 and TLR4-induced activation of NF- κ B. More interestingly, the observed anti-inflammatory properties were strain-specific, since they were not obtained with PGN derived from a non anti-inflammatory strain. We hypothesized that specific PGN structures might be the driving force behind the selective anti-inflammatory properties of probiotic strains and identified the presence of a specific Nod2 ligand in the protective PGN, which was confirmed to be protective *in vivo*. The work presented points out that PGN and derived muropeptides are active compounds in probiotic functionality and might represent new immune intervention tools for IBD.