Murein lytic enzyme TgaA of Bifidobacterium bifidum MIMBb75 modulates dendritic cell maturation through its cysteine- and histidine-dependent amidohydrolase/peptidase (CHAP) amidase domain

Bifidobacteria are Gram-positive inhabitants of the human gastrointestinal tract that have evolved close interaction with their host and especially with the host's immune system. The molecular mechanisms underlying such interactions, however, are largely unidentified. In this study, we investigated the immunomodulatory potential of Bifidobacterium bifidum MIMBb75, a bacterium of human intestinal origin commercially used as a probiotic. Particularly, we focused our attention on TgaA, a protein expressed on the outer surface of MIMBb75's cells and homologous to other known bacterial immunomodulatory proteins. TgaA is a peptidoglycan lytic enzyme containing two active domains: lytic murein transglycosylase (LT) and cysteine- and histidine-dependent amidohydrolase/peptidase (CHAP). We ran immunological experiments stimulating dendritic cells (DCs) with the B. bifidum MIMBb75 and TgaA, with the result that both the bacterium and the protein activated DCs and triggered interleukin-2 (IL-2) production. In addition, we observed that the heterologous expression of TgaA in Bifidobacterium longum transferred to the bacterium the ability to induce IL-2. Subsequently, immunological experiments performed using two purified recombinant proteins corresponding to the single domains LT and CHAP demonstrated that the CHAP domain is the immune-reactive region of TgaA. Finally, we also showed that TgaA-dependent activation of DCs requires the protein CD14, marginally involves TRIF, and is independent of Toll-like receptor 4 (TLR4) and MyD88. In conclusion, our study suggests that the bacterial CHAP domain is a novel microbe-associated molecular pattern actively participating in the cross talk mechanisms between bifidobacteria and the host's immune system. © 2014, American Society for Microbiology.