An exopolysaccharide-deficient mutant of Lactobacillus rhamnosus GG efficiently displays a protective llama antibody fragment against rotavirus on its surface

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Rotavirus is the leading cause of infantile diarrhea in developing countries, where it causes a high number of deaths among infants. Two vaccines are available, being highly effective in developed countries although markedly less efficient in developing countries. As a complementary treatment to the vaccines, a Lactobacillus strain producing an anti-rotavirus antibody fragment in the gastrointestinal tract could potentially be used. In order to develop such an alternative therapy, the effectiveness of Lactobacillus rhamnosus GG to produce and display a VHH antibody fragment (referred to as anti-rotavirus protein 1 [ARP1]) on the surface was investigated. L. rhamnosus GG is one of the best-characterized probiotic bacteria and has intrinsic antirotavirus activity. Among four L. rhamnosus GG strains [GG (CMC), GG (ATCC 53103), GG (NCC 3003), and GG (UT)] originating from different sources, only GG (UT) was able to display ARP1 on the bacterial surface. The genomic analysis of strain GG (UT) showed that the genes welE and welF of the EPS cluster are inactivated, which causes a defect in exopolysaccharide (EPS) production, allowing efficient display of ARP1 on its surface. Finally, GG (UT) seemed to confer a level of protection against

rotavirusinduced diarrhea similar to that of wild-type GG (NCC 3003) in a mouse pup model, indicating that the EPS may not be involved in the intrinsic antirotavirus activity. Most important, GG (EM233), a derivative of GG (UT) producing ARP1, was significantly more protective than the control strain L. casei BL23.