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Comparative study of the immunomodulatory activities of lactobacilli strains in porcine intestinal epithelial cells: effect on the innate antiviral immune response

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Lactobacillus rhamnosus CRL1505 and L. plantarum CRL1506 are immunomodulatory probiotic strains (immunobiotics) with the ability to improve the intestinal antiviral response and the protection against viral infections as demonstrated in animal models and clinical trials. In order to advance in the understanding of the mechanisms involved in the antiviral capacities of both immunobiotic strains, we have previously performed comparative transcriptomic studies in porcine intestinal epithelial (PIE cells). These cells were stimulated with L. rhamnosus CRL1505 or L. plantarum CRL1506 and then challenged with the TLR3 agonist poly(I:C). The immunotranscriptomic response of PIE cells was evaluated 12 h after poly(I:C) challenge. Our results showed that both immunobiotic strains significantly improved the expression of IFN-α and IFN-β as well as the antiviral factors RNASE4, RNASEL, OAS1, OASL, MX1, and MX2 when compared to controls. In addition, both lactobacilli strains increased the expression of cytokines (IL-1β, IL-6), chemokines (CCL4, CCL20, CCL28, AMCF-II, CXCL10), and enzymes involved in prostaglandin biosynthesis (PTGES, PTGER4). For the majority of these genes, their expression in CRL1505-tretaed PIE cells was significantly higher than in cells treated with the CRL1506 strain. Furthermore, only L. rhamnosus CRL1505 differentially regulated the expression of CXCL2, CXCL5, and CXCL11. Then, our transcriptomic analysis successfully allowed us to identify a group of genes that can be used as prospective biomarkers for the screening of new antiviral immunobiotics in PIE cells (Albarracin et al, 2017, Front Immunol 8:57).

The aim of this work was to evaluate whether the immunotranscriptomic changes induced by L. rhamnosus CRL1505 and L. plantarum CRL1506 in PIE cells are unique and not sheared by non-immunomodulatory strains of the same species. For this purpose, we evaluated the effect of different L. rhamnosus and L. plantarum strains on the antiviral response of PIE cells. The immunomodulatory L. rhamnosus IBL027, and L. plantarum MPL16 and the non-immunomodulatory L. rhamnosus CRL489, L. rhamnosus CRL576, and L. plantarum CRL681 strains were used. The CRL1505 and CRL1506 strains were used as positive controls. PIE cells were seeded at 104 cells per well in 12-well type I collagen-coated plates and stimulated with lactobacilli (108 cells/ml) for 48 h. Then cells were challenged with poly(I:C) (60 μg/ml) for 12 h. Two-step real-time qPCR was performed to characterize the expression of biomarker genes in PIE cells. The following genes were evaluated: IFN-α, IFN-β, A20, TLR3, RIG-I, RNASEL, MX2, OAS1, CCL4, CXCL5, IL-15, EPCAM, SELE, SELL, PTGS2, PTGER4, PLA2G4A, and PTGES.

L. plantarum MPL16, a strain that is able to modulate bacterial-mediated inflammation in PIE cells, induced an immunotranscriptomic profile that was similar to the observed for L. rhamnosus CRL1505 with increases of IFN-β, A20, RNASEL, MX2, OAS1, as well as CXCL5, EPCAM, SELE, PTGS2, and PLA2G4A. The expression of those genes in CRL1505- and MPL16-treated PIE cells was significantly higher than in the other groups. Of interest, L. rhamnosus IBL027, a strain that is able to improve the immune response to mucosal antigens, induced an immunotranscriptomic profile in PIE cells that was similar to the observed for L. plantarum CRL1506. The non-immunomodulatory L. rhamnosus CRL489, L. rhamnosus CRL576, and L. plantarum CRL681 strains induced modest increases in IFN-α, IFN-β, SELE, and SELL, while the other studied genes were not different from control PIE cells challenged with poly(I:C).

The results of this work confirm that the effect of L. rhamnosus and L. plantarum strains on the innate antiviral immune response of PIE cells is a strain-specific property. Moreover, our study indicates that the set of biomarkers genes (IFN-α, IFN-β, A20, TLR3, RIG-I, RNASEL, MX2, OAS1, CCL4, CXCL5, IL-15, EPCAM, SELE, SELL, PTGS2, PTGER4, PLA2G4A, and PTGES) would allow an efficient screening of new antiviral immunobiotics in PIE cells. This study is of importance since it verified that these biomarker genes are able to bluntly allow the selection of immunobiotic strains with the ability to beneficially modulate the innate antiviral immune response.

REFERENCES

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