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Lactobacillus acidophilus W37 Supports Intestinal Health and Immune Function Function

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Lactobacillus strains are interesting probiotic strains which might have immune modulatory and other beneficial health effects, but each strain can be different in its activity. Here we tested three *Lactobacillus* strains, *L. acidophilus*W37, *L. brevis* W63 and *L. casei* W56, for their modulatory effects towards small intestinal epithelial cells *in vitro* and whether the most potent strain *L. acidophilus* W37 could have immune supportive effects in neonatal piglets.

Caco-2 cells differentiated to small intestinal epithelial cells were exposed to *L. acidophilus* W37, *L. brevis* W63 and *L. casei* W56 (10^7 CFU/mL) for 6 hours. During exposure, trans-epithelial electrical resistance (TEER) was measured to determine the integrity of the confluent epithelialmonolayer. To determine the effect of the *Lactobacillus* strains on gene expression and related canonical pathways, RNA of Caco-2 cells was harvested after 6 hours incubation hybridized to Affymetrix Human Gene 1.1 ST arrays and Ingenuity Pathway Analysis (IPA) analysis was performed. Additionally, the potential beneficial effect of *L. acidophilus*W37 on intestinal integrity was studied using Caco-2 cells challenged with *Salmonella* Typhimurium (STM) DT12. In neonatal piglets, *L. acidophilus*W37 combined with long chain inulin type fructanFrutafit®TEX! was tested to enhance efficacy of vaccination against *Salmonella* Typhimurium. Treatments were given daily via oral drenches as of day 2 after birth until sacrifice. Piglets were weaned on day 24 and vaccinated with a single dose of Salmoporc STM®. To analyze the effect on protection againstSTM, animals were challenged with this pathogen before sacrifice. Blood was sampled prior and post vaccination to quantify antibody titers and characterisation of immune cells.

In the Caco-2 cell model, *L. acidophilus* W37 enhanced TEER by 15% ($p<0.01$) after 6 hours, while the strains *L. brevis* W63 and*L. casei* W56 had almost no effect on TEER.Transcriptomic data also showed that *L. acidophilus*W37 induced much more pronounced effects then the other 2 *Lactobacillus* strains. Most genes modulated by *L. acidophilus* W37 were related to intestinal barrier function, inflammation and bacterial stimulation of the epithelial layer.Many genes involved in the regulation of tight junctions were upregulated (*e.g.* CLDN 3, -4, Rab13)which fits the change in TEER. *L. acidophilus* W37 seems to impact epithelial-immune interactions via NFkB signaling and the upregulation of markers of follicle-associated epithelium (FAE) indicates that*L. Acidophilus* W37 might support epithelial cell differentiation towards tissue with enhanced intestinalimmune sampling capacity. Challenging Caco-2 cells with STM showed a drop in TEER of 24% ($p<0.01$) compared to medium control. This drop was only 3.9% ($p<0.05$) in cells pretreated for 17 hours with *L. acidophilus*W37 compared to medium control, illustrating the beneficial effect of this strain during STM infection.In piglets, the combination of *L. acidophilus* W37 and Frutafit® TEX! enhanced antibody titters against STM. This positive effect of *L. acidophilus* W37 on vaccination efficacy is indicative for its immunomodulatory potential.

These results demonstrate that *L. acidophilus* W37can have beneficial effects on intestinal barrier function and aninteresting immune supportive activity. *L. acidophilus* W37 is therefore potentially useful to support intestinal health to e.g. STM burden in society and immune health for those groups that have a low immune fitness.

Biography:

Dr. Nicole de Wit is a Senior Research Scientist at Wageningen Food & Biobased Research with major expertise in gut physiology. At the department of Human Nutrition of Wageningen University, she previously explored the role of nutrition, and especially high fat diets, on intestinal physiology at the molecular level in various mouse models. In her current job at Wageningen Food & Biobased Research, she is involved in multiple projects that study the role of fibres and pre- and probiotics in gastrointestinal health using *in vitro* models as well as animal models (piglets) and human intervention trials. For instance, she studied the immunomodulatory effect of probiotic strains by exploring their potential to support vaccination efficacy. She is also involved in public private partnership (PPP) projects in which the role of nutrition is studied to improve quality of life of irritable bowel syndrome (IBS) patients and how personalized dietary advice on fibre intake can empower consumers to make the right choices for improved health or reduced health risk.