



Article

Human Milk Oligosaccharide-Stimulated *Bifidobacterium* Species Contribute to Prevent Later Respiratory Tract Infections

Shaillay Kumar Dogra, Francois-Pierre Martin, Dominique Donnicola, Monique Julita [†], Bernard Berger and Norbert Sprenger ^{*}

Nestlé Institute of Health Sciences, Société des Produits Nestlé S.A., 1000 Lausanne 26, Switzerland; ShaillayKumar.Dogra@rd.nestle.com (S.K.D.); Francois-Pierre.Martin@rd.nestle.com (F.-P.M.); dominique.donnicola@rdls.nestle.com (D.D.); bernard.berger@rdls.nestle.com (B.B.)

^{*} Correspondence: Norbert.sprenger@rdls.nestle.com; Tel.: +41-21-7858-532

[†] Retired.

Table S1. Loadings of 5 independent rounds of sPLSDA modeling to separate controls and cases for bronchitis ($n = 52$) and LRTI.

| Bronchitis case-control | | | | | | | | | | | | |
|--------------------------|--|-----------|----------|----------|-----------|-----------|------|---------|------|---------|------|------|
| Component 1 | | round 1 | | round 2 | | round 3 | | round 4 | | round 5 | | mean |
| Feature | | value | rank | value | rank | value | rank | value | rank | value | rank | rank |
| % Acetate | | -0.453 | 2 | -0.506 | 1 | | | -0.516 | 1 | -0.456 | 2 | 1.5 |
| Product | | -0.314 | 4 | -0.449 | 3 | | | -0.381 | 2 | -0.463 | 1 | 2.8 |
| Lactobacillus | | | | | | 0.392 | 3 | | | | | 3.0 |
| Bifidobacterium | | | | | | | | -0.307 | 4 | | | 4.0 |
| % Valerate | | | | | | | | | | 0.381 | 4 | 4.0 |
| Fucosyl-Glycans | | -0.266 | 6 | -0.388 | 4 | -0.616 | 1 | -0.290 | 5 | -0.155 | 8 | 4.8 |
| Succinate | | 0.456 | 1 | 0.178 | 6 | 0.442 | 2 | 0.240 | 7 | 0.138 | 9 | 5.0 |
| % Butyrate | | 0.320 | 3 | 0.057 | 10 | 0.250 | 5 | 0.227 | 8 | 0.388 | 3 | 5.8 |
| % Propionate | | 0.134 | 12 | 0.489 | 2 | | | 0.281 | 6 | | | 6.7 |
| Enterococcus | | -0.242 | 7 | | | | | | | | | 7.0 |
| % 5-Aminovalerate | | 0.307 | 5 | 0.045 | 11 | 0.232 | 6 | 0.217 | 9 | 0.370 | 5 | 7.2 |
| Tyrosine | | 0.146 | 11 | 0.266 | 5 | | | | | | | 8.0 |
| Isoleucine | | | | 0.114 | 8 | | | | | | | 8.0 |
| Trabulsella | | | | | | | | 0.119 | 10 | 0.268 | 6 | 8.0 |
| AAT | | -0.179 | 9 | -0.158 | 7 | -0.171 | 7 | | | -0.070 | 10 | 8.3 |
| Calprotectin | | 0.004 | 16 | | | 0.138 | 8 | 0.378 | 3 | | | 9.0 |
| Phenylalanine | | | | 0.074 | 9 | | | | | | | 9.0 |
| Escherichia | | 0.238 | 8 | 0.033 | 12 | 0.025 | 9 | | | | | 9.7 |
| Elastase | | -0.156 | 10 | | | | | | | | | 10.0 |
| Enterobacteriaceae_Other | | | | | | -0.020 | 10 | | | | | 10.0 |
| Mode of delivery | | | | | | | | 0.009 | 13 | 0.160 | 7 | 10.0 |
| Lactate | | | | -0.003 | 13 | | | -0.099 | 11 | | | 12.0 |
| Carnobacteriaceae_Other | | | | | | | | 0.088 | 12 | | | 12.0 |
| Neopterin | | -0.075 | 13 | | | | | | | | | 13.0 |
| Ruminococcus | | 0.046 | 14 | | | | | | | | | 14.0 |
| Streptococcus | | -0.041 | 15 | | | | | | | | | 15.0 |
| LRTI case-control | | | | | | | | | | | | |
| Component 1 | | round 1 | | round 2 | | round 3 | | round 4 | | round 5 | | mean |
| Feature | | value | rank | value | rank | value | rank | value | rank | value | rank | rank |
| Product | | -0.463 | 2 | -0.404 | 3 | -0.555 | 1 | -0.477 | 1 | -0.375 | 2 | 1.8 |
| % Acetate | | -0.537 | 1 | -0.468 | 2 | -0.540 | 2 | -0.351 | 3 | -0.372 | 3 | 2.2 |
| Fucosyl-glycans | | -0.399 | 3 | -0.218 | 5 | -0.425 | 3 | -0.444 | 2 | -0.281 | 5 | 3.6 |
| % Propionate | | 0.342 | 4 | 0.351 | 4 | 0.307 | 4 | 0.272 | 5 | 0.430 | 1 | 3.6 |
| AAT | | | | -0.106 | 7 | | | | | | | 7.0 |
| Succinate | | 0.236 | 6 | 0.638 | 1 | 0.051 | 9 | 0.247 | 6 | 0.091 | 14 | 7.2 |
| % Butyrate | | 0.240 | 5 | 0.013 | 10 | 0.215 | 5 | 0.184 | 9 | | | 7.3 |
| Actinomyces | | | | | | 0.089 | 8 | 0.187 | 8 | 0.261 | 6 | 7.3 |
| % 5-Aminovalerate | | 0.220 | 7 | | | 0.198 | 6 | 0.176 | 10 | | | 7.7 |
| Carnobacteriaceae_Other | | 0.037 | 12 | | | | | 0.282 | 4 | | | 8.0 |
| Enterobacteriaceae_Other | | | | | | | | | | 0.217 | 8 | 8.0 |
| Escherichia | | 0.137 | 9 | 0.105 | 8 | | | 0.164 | 12 | 0.231 | 7 | 9.0 |
| Isoleucine | | | | | | | | | | 0.213 | 9 | 9.0 |
| Bifidobacterium | | -0.189 | 8 | | | | | -0.209 | 7 | -0.155 | 13 | 9.3 |
| Trabulsella | | 0.045 | 10 | | | 0.172 | 7 | 0.172 | 11 | 0.202 | 10 | 9.5 |
| Enterococcus | | | | -0.128 | 6 | | | -0.121 | 13 | | | 9.5 |
| % Valerate | | | | 0.043 | 9 | 0.011 | 10 | | | | | 9.5 |
| Tyrosine | | | | | | | | 0.054 | 16 | 0.317 | 4 | 10.0 |
| Phenylalanine | | | | | | | | | | 0.197 | 11 | 11.0 |
| Ruminococcus | | | | | | | | | | 0.175 | 12 | 12.0 |
| Tyrosine | | 0.032 | 13 | | | | | | | | | 13.0 |
| Veillonella | | | | | | | | -0.093 | 14 | | | 14.0 |
| Calprotectin | | 0.038 | 11 | | | | | 0.039 | 18 | | | 14.5 |
| Mode of Delivery | | | | | | | | 0.087 | 15 | | | 15.0 |
| Streptococcaceae_Other | | | | | | | | | | 0.002 | 15 | 15.0 |
| Lactate | | | | | | | | -0.044 | 17 | | | 17.0 |
| AUC-ROC comp 1 | | | | | | | | | | | | |
| p-value | | 0.78 | 0.76 | 0.82 | 0.80 | 0.74 | | | | | | |
| p-value | | 0.0005423 | 0.001198 | 6.62E-05 | 0.0002183 | 0.003409 | | | | | | |
| Component 2 | | | | | | | | | | | | |
| Component 2 | | round 1 | | round 2 | | round 3 | | round 4 | | round 5 | | mean |
| Feature | | value | rank | value | rank | value | rank | value | rank | value | rank | rank |
| Elastase | | -0.949 | 1 | | | -0.966 | 1 | -0.911 | 1 | | | 1 |
| Lipocalin | | | | | | | | | | 0.8797 | 1 | 1 |
| Bifidobacterium | | | | | | | | | | | | 1 |
| Veillonella | | | | -0.861 | 1 | | | -0.409 | 2 | | | 2 |
| Neopterin | | -0.23 | 2 | | | | | | | | | 2 |
| Enterobacteriaceae_Other | | | | | | -0.241 | 2 | | | -0.338 | 2 | 2 |
| AAT | | -0.216 | 3 | -0.435 | 2 | -0.092 | 3 | | | | | 3 |
| total scfa | | | | -0.263 | 3 | | | | | | | 3 |
| Calprotectin | | | | | | | | 0.061 | 3 | | | 3 |
| Lactate | | | | | | | | | | 0.3339 | 3 | 3 |
| AUC-ROC comp 1+2 | | | | | | | | | | | | |
| p-value | | 0.87 | 0.82 | 0.85 | 0.89 | 0.81 | | | | | | |
| p-value | | 6.17E-06 | 7.15E-05 | 1.57E-05 | 1.63E-06 | 0.0001127 | | | | | | |
| Component 2 | | | | | | | | | | | | |
| Component 2 | | round 1 | | round 2 | | round 3 | | round 4 | | round 5 | | mean |
| Feature | | value | rank | value | rank | value | rank | value | rank | value | rank | rank |
| Neopterin | | | | -0.695 | 1 | | | | | | | 1 |
| Veillonella | | | | | | -0.968 | 1 | -0.766 | 1 | -0.722 | 1 | 1 |
| Lactate | | 0.9432 | 1 | | | | | | | 0.6775 | 2 | 2 |
| Streptococcus | | 0.3204 | 2 | | | | | | | | | 2 |
| Lactate | | | | 0.6792 | 2 | | | | | | | 2 |
| Phenylalanine | | | | -0.236 | 3 | -0.226 | 2 | -0.462 | 2 | | | 2 |
| AlphaAT | | -0.088 | 3 | | | | | | | | | 3 |
| % Valerate | | | | | | | | | | 0.1418 | 3 | 3 |
| Calprotectin | | | | | | | | 0.113 | 4 | | | 4 |
| Streptococcaceae_Other | | | | | | | | -0.005 | 5 | | | 5 |
| Bifidobacterium | | | | | | 0.1114 | 3 | | | | | 3 |
| Enterococcus | | | | | | | | -0.432 | 3 | | | 3 |
| AUC-ROC comp 1+2 | | | | | | | | | | | | |
| p-value | | 0.84 | 0.87 | 0.76 | 0.81 | 0.76 | | | | | | |
| p-value | | 2.02E-06 | 3.21E-07 | 3.38E-04 | 1.26E-05 | 0.0002508 | | | | | | |

direction of cases direction of controls

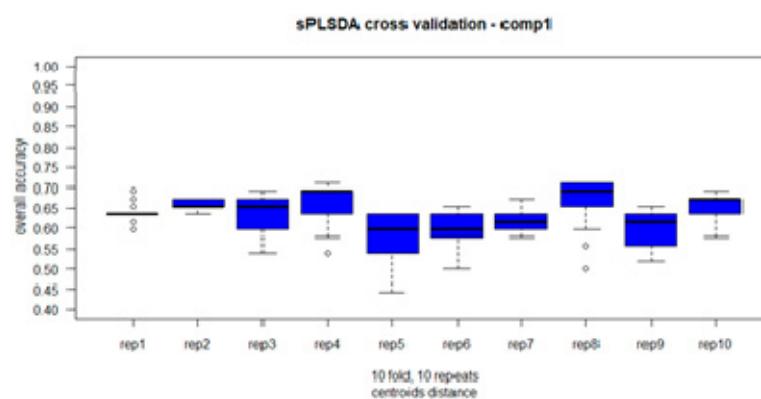
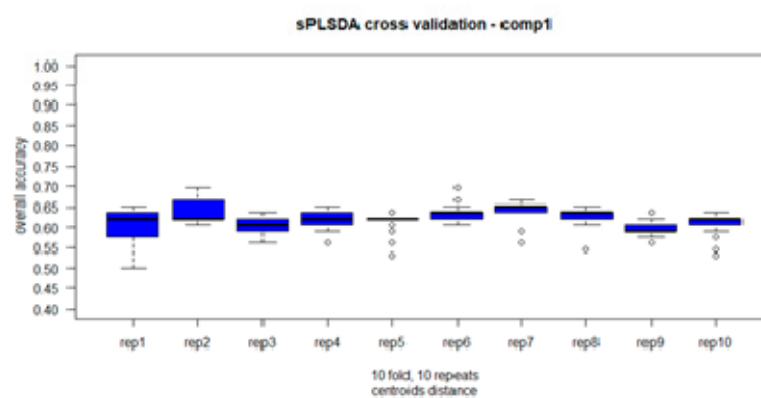
Bronchitis cases vs controls**LRTI cases vs controls**

Figure S1. Representative sPLS-DA model accuracy to separate cases from controls.