**Online supplementary data:**

**Table A** Fasting plasma lipids status of volunteers recruited to a double-blind, placebo-controlled, randomized cross-over during supplementation with a candidate prebiotic (xylo-oligosaccharide, XOS, 8g/day), probiotic (*Bifidobacterium animalis* subsp. *lactis*, Bi-07, 109 CFU/day) or synbiotic (XOS + Bi-07) 1

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | |  | | |  | | | | | | | | P-value | | |
|  | Baseline  (n = 43) | | Δ MDX  (n = 40) | | | Δ Bi-07  (n = 42) | | Δ XOS  (n = 42) | | Δ XOS + Bi-07  (n = 42) | |  | | Bi-07 | XOS | XOS \* Bi-07 |
|  |  | | | *mM* | | | | | | | | | |  |  |  |
| Total cholesterol | 5.0 | (1.0) | -0.1 | | (0.4) | -0.1 | (0.5) | 0.0 | (0.5) | 0.1 | (0.5) |  |  | 0.789 | 0.238 | 0.881 |
| Triglycerides † | 1.2 | (0.7) | 0.1 | | (0.4) | 0.0 | (0.3) | 0.1 | (0.2) | -0.2 | (0.7) |  |  | 0.938 | 0.404 | 0.566 |
| HDL cholesterol † | 1.4 | (0.5) | -0.1 | | (0.1) | 0.0 | (0.1) | 0.0 | (0.1) | 0.1\* | (0.1) |  |  | 0.242 | 0.005 | 0.909 |
| LDL cholesterol | 3.3 | (0.8) | 0.0 | | (0.4) | -0.1 | (0.4) | 0.0 | (0.4) | 0.1 | (0.4) |  |  | 0.869 | 0.193 | 0.596 |
| Non-esterified fatty acids | 0.49 | (0.25) | 0.03 | | (0.26) | -0.03 | (0.24) | 0.04 | (0.23) | -0.02 | (0.32) |  |  | 0.476 | 0.757 | 0.416 |
| Total cholesterol : HDL cholesterol † | 3.8 | (1.3) | 0.1 | | (0.4) | -0.1 | (0.3) | 0.0 | (0.3) | -0.3 | (0.3) |  |  | 0.150 | 0.062 | 0.814 |

1 Data are mean (SD). P values given are linear mixed-effects models (2x2 factorial approach) for the presence/absence of the prebiotic (XOS) and probiotic (Bi-07) and their interaction (XOS \* Bi-07). \* p = 0.02 compared to MDX, pairwise posts hoc comparisons carried out using contrasts, adjusted using a single-step algorithm. † n = 11, data from first treatment period only.

**Table B** Peripheral blood immune cell phenotypes of volunteers recruited to a double-blind, placebo-controlled, randomised cross-over during treatment with a candidate prebiotic (xylo-oligosaccharide, XOS, 8g/day), probiotic (*Bifidobacterium animalis* subsp *lactis*, Bi-07, 109 CFU/day) or synbiotic (XOS + Bi-07) 1

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | |  | |  | | | | | | | | | P value | | |
|  | Baseline  (n=43) | | Δ MDX  (n = 38) | | Δ Bi-07  (n = 42) | | Δ XOS  (n = 41) | | Δ XOS + Bi-07  (n = 39-42) | | |  | | Bi-07 | XOS | XOS \* Bi-07 |
|  | *% lymphocytes* | | | | | | | | | | | | |  |  |  |
| CD3+ (T cells) | 66.1 | (10.7) | 2.3 | (10.0) | 2.1 | (11.4) | -1.4 | (18.5) | 0.8 | (11.6) |  | |  | 0.621 | 0.201 | 0.357 |
| CD3+CD4+ (T helper cells) | 40.7 | (7.7) | -1.6 | (17.8) | 2.2 | (9.2) | 0.0 | (6.5) | 0.1 | (12.0) |  | |  | 0.326 | 0.793 | 0.472 |
| CD3+CD8+ (cytotoxic T cells) | 23.5 | (8.6) | -1.5 | (7.4) | 0.8 | (4.9) | 0.1 | (4.2) | -0.3 | (5.7) |  | |  | 0.307 | 0.857 | 0.141 |
| CD3+CD16/56+ (NKT cells) † | 4.3 | (4.3) | -0.2 | (1.2) | -0.6 | (1.4) | -0.7 | (0.8) | -0.2 | (1.6) |  | |  | 0.895 | 0.522 | 0.772 |
| CD16/56+ (NK cells) | 15.6 | (7.2) | -1.5 | (4.1) | -0.6 | (5.9) | -0.2 | (5.1) | -0.4 | (4.6) |  | |  | 0.767 | 0.256 | 0.492 |
| CD19+(B cells) | 12.0 | (3.8) | 0.5 | (2.9) | -0.2 | (3.0) | -0.8 | (6.1) | 0.4 | (2.8) |  | |  | 0.832 | 0.470 | 0.128 |
|  | *mean fluorescence intensity* | | | | | | | | | | | | |  |  |  |
| CD3 on T cells † | 61.7 | (6.2) | 2.9 | (4.7) | -1.3 | (4.7) | 1.1 | (3.5) | 1.3 | (5.3) |  | |  | 0.236 | 0.679 | 0.050 |
| CD3 on T helper cells  CD4 on T helper cells | 62.9  527.4 | (6.8)  (67.3) | -0.7 | (8.9) | 0.5 | (5.8) | 0.8 | (4.8) | 1.0 | (6.4) |  | |  | 0.701  0.779 | 0.505  0.985 | 0.940  0.706 |
| 6.0 | (127.6) | 2.4 | (68.5) | 5.1 | (73.8) | 8.7 | (63.9) |  | |  |
| CD3 on cytotoxic T cells  CD8 on cytotoxic T cells (x 10-3) | 56.1  1.2 | (6.7)  (0.3) | 0.8 | (5.0) | 0.0 | (4.9) | 1.4 | (4.3) | 0.2 | (6.7) |  | |  | 0.168  0.463 | 0.804  0.685 | 0.823  0.732 |
| 7.1 | (331.5) | 11.0 | (246.8) | 18.2 | (207.6) | -18.6 | (342.2) |  | |  |
| CD3 on NKT cells †  CD16/56 on NKT cells † | 72.5  32.2 | (14.9)  (8.9) | 4.3 | (4.5) | 0.8 | (11.6) | -2.5 | (11.2) | 1.5 | (10.6) |  | |  | 0.524  0.344 | 0.547  0.027 | 0.354  0.166 |
| 4.3 | (5.3) | -0.3 | (10.6) | -5.1\* | (10.3) | 0.5 | (6.2) |  | |  |
| CD16/56 on NK cells † | 129.6 | (44.8) | 8.1 | (34.6) | -9.0 | (13.0) | -5.9 | (18.6) | -6.7 | (47.0) |  | |  | 0.393 | 0.725 | 0.133 |
| CD19 on B cells † | 180.5 | (35.2) | 15.8 | (27.1) | -8.7 | (32.0) | -3.8 | (25.9) | -1.8 | (42.4) |  | |  | 0.151 | 0.291 | 0.009 |

1 Data are mean (SD). P values given are linear mixed-effects models (2x2 factorial approach) for the presence/absence of the prebiotic (XOS) and probiotic (Bi-07) and their interaction (XOS \* Bi-07). \* significantly different from MDX, pairwise posts hoc comparisons carried out using contrasts, adjusted using a single-step algorithm. † n = 11, data from first treatment period only.**Table C** Ex vivo cytokine production of LPS stimulated whole blood cultures from volunteers recruited to a double-blind, placebo-controlled, randomised cross-over during treatment with a candidate prebiotic (xylo-oligosaccharide, XOS, 8g/day), probiotic (*Bifidobacterium animalis* subsp *lactis*, Bi-07, 109 CFU/day) or synbiotic (XOS + Bi-07) 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | |  | |  | | | | | | | | P value | | |
|  | Baseline  (n = 41-43) | | Δ MDX  (n = 39-41) | | Δ Bi-07  (n = 42) | | Δ XOS  (n = 42) | | Δ XOS + Bi-07  (n = 39-42) | |  | | Bi-07 | XOS | XOS \* Bi-07 |
|  | *pg/ml* | | | | | | | | | | | |  |  |  |
| IFN-γ † | 315.3 | (462.4) | 113.6 | (501.0) | 42.4 | (152.4) | 53.1 | (176.6) | 129.2 | (390.2) |  |  | 0.178 | 0.388 | 0.743 |
| IL-1β † | 733.1 | (742.5) | 124.7 | (461.2) | 53.2 | (256.7) | -135.5 | (255.5) | -72.4 | (547.7) |  |  | 0.083 | 0.995 | 0.265 |
| IL-2 | 6.9 | (13.0) | 0.4 | (16.4) | 2.0 | (15.2) | -1.1 | (13.3) | 0.7 | (17.6) |  |  | 0.480 | 0.597 | 0.995 |
| IL-4 | 3.7 | (7.9) | 2.3 | (11.5) | -1.9 | (8.1) | 1.0 | (6.4) | -1.9 | (11.5) |  |  | 0.035 | 0.814 | 0.705 |
| IL-5 | 2.3 | (6.9) | 2.0 | (9.0) | 0.0 | (6.1) | -3.0 | (9.5) | 1.2 | (11.9) |  |  | 0.609 | 0.317 | 0.059 |
| IL-6 (x 10-3) † | 3.5 | (3.2) | 0.7 | (2.5) | 1.0 | (2.7) | -0.1 | (0.9) | 1.3 | (1.5) |  |  | 0.009 | 0.650 | 0.399 |
| IL-8 (x 10-3) | 1.5 | (1.1) | 0.0 | (0.6) | -0.1 | (0.8) | -0.1 | (0.6) | 0.1 | (0.7) |  |  | 0.416 | 0.269 | 0.252 |
| IL-10 † | 79.7 | (88.8) | 13.7 | (49.7) | 5.1 | (72.9) | -9.3 | (32.2) | -21.0 | (36.3) |  |  | 0.743 | 0.049 | 0.936 |
| IL-12p70 | ND | | 2.0 | (8.8) | 0.8 | (3.8) | 0.3 | (6.0) | -0.4 | (5.1) |  |  | 0.281 | 0.123 | 0.840 |
| TNF-α | 222.8 | (249.6) | 24.1 | (195.7) | 31.9 | (216.5) | 110.5 | (306.4) | 77.2 | (229.5) |  |  | 0.442 | 0.074 | 0.485 |
| TNF-β | 0.6 | (2.9) | -0.7 | (3.0) | 0.0 | (0.3) | -0.1 | (3.8) | -1.0 | (5.7) |  |  | 0.886 | 0.657 | 0.190 |

1 Data are mean (SD). P values given are linear mixed-effects models (2x2 factorial approach) for the presence/absence of the prebiotic (XOS) and probiotic (Bi-07) and their interaction (XOS \* Bi-07). † n = 11, data from first treatment period only.