**Supplementary Table 1.** The effect of either MILK or WHEAT diet on cytokines after a LPS challenge. Results are presented as LSMeans and SEM.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Treatment group |  |  |
|  | MILK | WHEAT | SEM | *P*-value |
| *N* | 11 | 9 |  |  |
| IL6 (pg/mL) | 546.1 | 746.7 | 276.46 | 0.499 |
| IL10 (pg/mL) | 70.1 | 53.4 | 35.22 | 0.648 |
| TNFα (pg/mL) | 1146.8 | 1375.3 | 684.34 | 0.748 |
| IL1 β (ng/mL) | 2.3 | 3.8 | 1.53 | 0.350 |

**Supplementary Table 2.** The hematology of MILK and WHEAT groups at day 24/25

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Items |  | Classification |  |  |
|  |  | MILK | WHEAT | SEM | P-values |
| *N* |  | 18 | 18 |  |  |
| Total leukocytes, bill/L |  | 5.77 | 7.58 | 0.685 | **0.009** |
| Total erythrocytes, tril/L |  | 4.11 | 4.23 | 0.214 | 0.563 |
| Haemoglobin (HGB), mmol/L |  | 3.05 | 3.19 | 0.157 | 0.342 |
| Hematocrit (HCT), L/L |  | 0.175 | 0.187 | 0.009 | 0.126 |
| MCH, fmol |  | 0.75 | 0.76 | 0.033 | 0.779 |
| MCHC, mmol/L |  | 17.48 | 16.98 | 0.399 | 0.192 |
| Thrombocytes |  | 1647 | 1287 | 204.0 | 0.069 |
| Mean platelet volume (MPV), fL |  | 17.7 | 17.0 | 1.77 | 0.696 |
| Mean cell volume (MCV), fL |  | 42.8 | 44.5 | 1.23 | 0.157 |
| Mean platelet count, (MPC), g/L |  | 263 | 259 | 4.9 | 0.339 |
| Neutrophils, pct |  | 25.0 | 32.5 | 3.41 | **0.028** |
| Lymphocytes, pct |  | 68.6 | 62.1 | 4.07 | 0.100 |
| Monocytes, pct |  | 2.7 | 2.0 | 0.43 | 0.097 |
| Eosinophils, pct |  | 1.7 | 2.3 | 1.27 | 0.601 |
| Basophils, pct |  | 0.29 | 0.32 | 0.097 | 0.738 |
| Large unstained cells (LUC), pct |  | 1.23 | 0.94 | 0.235 | 0.182 |
| Neutrophils, bill/L |  | 1.52 | 2.56 | 0.379 | **0.007** |
| Lymphocytes, bill/L |  | 3.95 | 4.62 | 0.472 | 0.141 |
| Monocytes, bill/L |  | 0.15 | 0.13 | 0.039 | 0.650 |
| Eosinophil, bill/L |  | 0.05 | 0.18 | 0.100 | 0.193 |
| Basophils, bill/L |  | 0.02 | 0.02 | 0.008 | 0.336 |
| Large unstained cells (LUC), bill/L |  | 0.07 | 0.06 | 0.017 | 0.789 |
| Reticulocytes, pct (estim) |  | 4.55 | 4.82 | 0.537 | 0.601 |
| Absolut reticulocyte, bill/L (estim) |  | 186.3 | 200.4 | 22.86 | 0.512 |

MCH=mean corpuscular hemoglobin, MCHC = Mean corpuscular hemoglobin concentration,

**Supplementary Table 3.** Effects of serum metabolites and electrolytes at weaning.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | Classification |  |  |  |
|  |  | MILK | WHEAT |  | SEM | P-values |
| *n* |  | 18 | 13 |  |  |  |
| Albumin g/L |  | 29.9 | 25.5 |  | 1.75 | **0.013** |
| Total protein, g/L |  | 44.0 | 41.0 |  | 2.08 | 0.127 |
| Basic phosphatase, U/L |  |  |  |  |  |  |
| Alanin amino transferase U/L |  | 16.5 | 13.3 |  | 5.70 | 0.551 |
| Cholesterol, mmol/L |  | 2.7 | 2.0 |  | 0.19 | **<.0001** |
| Creatinine, umol/L  |  | 67.7 | 72.0 |  | 4.51 | 0.311 |
| Iron |  | 2.2 | 1.5 |  | 0.84 | 0.365 |
| Inorganic phosphate, mmol/L |  | 2.2 | 1.7 |  | 0.19 | **0.010** |
| Aspartate amino transferase U/L |  | 36.0 | 14.6 |  | 30.81 | 0.460 |
| Blood urea nitrogen, mmol/L |  | 6.6 | 3.5 |  | 0.64 | **<.0001** |
| Gamma-glutamyl transferase, U/L |  | 20.0 | 22.9 |  | 4.89 | 0.532 |
| Calcium, mmol/L |  | 2.7 | 2.7 |  | 0.09 | 0.869 |
| Magnesium, mmol/L |  | 1.2 | 1.2 |  | 0.06 | 0.462 |
| Sodium, mmol/L  |  | 141.5 | 145.5 |  | 3.84 | 0.277 |
| Potassium, mmol/L  |  | 5.7 | 5.5 |  | 0.62 | 0.669 |
| Glucose, mmol/L |  | 7.0 | 6.4 |  | 0.52 | 0.262 |
| Triglyceride, mmol/L |  | 1.2 | 0.7 |  | 0.15 | **0.001** |

**Supplementary Table 4.** The top ten genes up-regulated and down-regulated by WHEAT treatment compared to MILK treatment. Genes are ranked by fold change and NOISEQ q-value. Genes in bold and italics were also measured by qPCR.

|  |  |  |  |
| --- | --- | --- | --- |
| Gene symbol | Name | Fold Change | *Q* value |
| *PROM2* | Prominin 2 | -8.1 | 0.54 |
| **SAA2** | **Serum amyloid A2** | **-7.9** | **0.65** |
| *PCDH9* | Protocadherin 9 | -4.6 | 0.62 |
| *TACC1* | Transforming acidic coiled-coil-containing protein 1 | -3.1 | 0.59 |
| ***CCL20*** | **C-C motif chemokine 20** | **-2.5** | **0.61** |
| *AQP8* | Aquaporin 8 | -2.4 | 0.62 |
| *FOSL1* | Fos-like antigen 1 | -2.4 | 0.58 |
| *S100A8* | Protein S100-A8 | -2.2 | 0.56 |
| ***SERPINB2*** | **Plasminogen activator inhibitor 2** | **-2.2** | **0.65** |
| *IGSF9* | Immunoglobulin Super Family 9 | -2.1 | 0.58 |
| ***TNIP3*** | **TNFAIP3 interacting protein 3** | **-2.1** | **0.63** |

|  |  |  |  |
| --- | --- | --- | --- |
| Gene symbol | Name | Fold Change | *Q* value |
| *ZP3* | Zona pellucida glycoprotein 3 | 7.1 | 0.59 |
| *HCAR2* | Hydroxycarboxylic acid receptor 2 | 6.1 | 0.56 |
| *CD19\** | B-lymphocyte antigen CD19 | 5.7 | 0.58 |
| *IFGBPL1* | Insulin-like growth factor-binding protein-like 1 | 4.8 | 0.58 |
| *CXCR5\** | C-X-C chemokine receptor type 5 | 4.6 | 0.58 |
| *FCRLA\** | Fc-receptor like protein A | 4.4 | 0.58 |
| *TNFRSF13C\** | B-cell activating factor receptor  | 4 | 0.58 |
| *FCRL1\** | Fc-receptor like protein 1 | 3.4 | 0.58 |
| *CD22\** | B-cell receptor CD22 | 2.7 | 0.58 |
| *LRMP\** | Lymphoid restricted membrane protein | 2.3 | 0.59 |

\*Involved in B-cell function

**Supplementary Table 5.** Effect of milk replacer diet on gut morphology. Results are presented as LSMeans and SEM.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Treatment group |  |  |
|  | MILK  | WHEAT | SEM | *P*-value |
| *n* | 15 | 18 |  |  |
| Villous height, mm | 0.31 | 0.25 | 0.046 | 0.174 |
| Crypt depths, mm | 0.13 | 0.13 | 0.008 | 0.507 |
| Enterocyte height, mm | 0.03 | 0.03 | 0.002 | 0.487 |
| Villous height/Crypt depth ratio | 2.72 | 2.22 | 0.355 | 0.129 |