**Supplemental Table 2: Amino acids and their metabolites, and potential markers of fish protein intake in urine.**

**(Mean values and standard deviations)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Zucker fa/fa rats |  | Long-Evans rats |  |  |  |  |
|  |  | Control Group |  | Baked Salmon group |  | Control Group |  | Baked Salmon group |  | P Control Diet x strain | P dietZucker | P dietLong-Evans |
| µmol per mmol creatinine |  | Mean | SD |  | Mean | SD |  | Mean | SD |  | Mean | SD |  |  |  |  |
| Alanine  |  | 49.6 | 14.3 |  | 44.0 | 10.0 |  | 30.2 | 5.4 |  | 26.6 | 10.2 |  | 0.013 | 0.47 | 0.46 |
| Asparagine |  | 12.2 | 2.5 |  | 7.8 | 1.5 |  | 8.4 | 3.1 |  | 6.6 | 2.1 |  | 0.055 | 0.0055 | 0.26 |
| Betaine |  | 66.5 | 14.1 |  | 66.4 | 22.4 |  | 40.6 | 18.0 |  | 38.5 | 6.0 |  | 0.028 | 1.00 | 0.79 |
| Creatine |  | 21.4 | 3.4 |  | 1553.2 | 377.4 |  | 3.2 | 0.4 |  | 336.5 | 128.0 |  | 3.7x10-7 | 8.6x10-6 | 8.1x10-5 |
| Cysteine (total) |  | 40.4 | 11.0 |  | 31.9 | 14.6 |  | 19.7 | 9.3 |  | 10.0 | 2.2 |  | 0.0081 | 0.31 | 0.033 |
| Asymmetric dimethyl-arginine |  | 0.10 | 0.04 |  | 0.39 | 0.45 |  | 0.02 | 0.01 |  | 0.05 | 0.03 |  | 0.0019 | 0.18 | 0.094 |
| Symmetric dimethyl-arginine |  | 3.6 | 0.3 |  | 4.0 | 0.7 |  | 1.9 | 0.5 |  | 2.6 | 0.4 |  | 0.00015 | 0.18 | 0.043 |
| Dimethylglycine |  | 55.1 | 14.7 |  | 53.5 | 10.0 |  | 22.9 | 11.3 |  | 20.8 | 8.3 |  | 0.0026 | 0.83 | 0.73 |
| Glutamic acid |  | 25.0 | 18.8 |  | 16.1 | 5.2 |  | 15.1 | 5.1 |  | 17.1 | 16.3 |  | 0.25 | 0.30 | 0.78 |
| Glycine |  | 55.8 | 12.4 |  | 49.3 | 7.4 |  | 46.0 | 5.6 |  | 43.1 | 8.6 |  | 0.12 | 0.31 | 0.51 |
| Histidine |  | 17.5 | 2.2 |  | 13.8 | 3.3 |  | 7.0 | 2.1 |  | 7.1 | 2.0 |  | 2.0x10-5 | 0.059 | 0.96 |
| 1-MeHis |  | 5.5 | 2.9 |  | 170.1 | 111.7 |  | 3.5 | 3.2 |  | 81.5 | 76.9 |  | 0.30 | 0.0098 | 0.032 |
| 3-MeHis |  | 7.9 | 1.3 |  | 30.4 | 8.7 |  | 3.0 | 1.4 |  | 18.0 | 4.4 |  | 0.00024 | 0.00031 | 1.3x10-5 |
| Homocysteine (total) |  | 1.83 | 0.21 |  | 1.68 | 0.72 |  | 1.08 | 0.21 |  | 0.68 | 0.11 |  | 0.0028 | 0.67 | 0.0021 |
| Isoleucine |  | 9.5 | 3.1 |  | 7.2 | 2.0 |  | 9.3 | 5.1 |  | 4.3 | 3.2 |  | 0.95 | 0.17 | 0.068 |
| Kynurenine |  | 0.12 | 0.05 |  | 0.08 | 0.02 |  | 0.41 | 0.30 |  | 0.18 | 0.15 |  | 0.060 | 0.079 | 0.11 |
| Leucine |  | 17.3 | 5.4 |  | 12.1 | 4.1 |  | 11.9 | 5.0 |  | 8.0 | 6.1 |  | 0.12 | 0.10 | 0.25 |
| Lysine |  | 40.8 | 9.7 |  | 39.0 | 11.3 |  | 29.1 | 8.1 |  | 28.6 | 10.5 |  | 0.057 | 0.78 | 0.93 |
| Methionine  |  | 18.4 | 8.3 |  | 13.1 | 7.2 |  | 23.4 | 17.2 |  | 6.8 | 2.7 |  | 0.57 | 0.28 | 0.042 |
| Methionine sulfoxide |  | 2.4 | 1.0 |  | 1.8 | 1.2 |  | 3.4 | 1.8 |  | 1.7 | 0.8 |  | 0.28 | 0.39 | 0.049 |
| Ornithine  |  | 5.7 | 2.0 |  | 5.0 | 1.9 |  | 2.0 | 0.5 |  | 2.0 | 0.9 |  | 0.0015 | 0.57 | 0.87 |
| Phenylalanine |  | 11.4 | 3.1 |  | 9.1 | 2.8 |  | 5.1 | 1.6 |  | 4.0 | 2.3 |  | 0.0018 | 0.23 | 0.38 |
| Proline |  | 28.2 | 6.3 |  | 23.6 | 7.3 |  | 17.7 | 3.5 |  | 11.9 | 2.5 |  | 0.0066 | 0.29 | 0.0083 |
| Sarcosine |  | 3.0 | 0.8 |  | 3.1 | 1.0 |  | 2.3 | 1.8 |  | 1.9 | 0.9 |  | 0.40 | 0.96 | 0.62 |
| Serine |  | 28.4 | 8.2 |  | 20.4 | 4.2 |  | 16.6 | 3.5 |  | 15.8 | 5.7 |  | 0.011 | 0.066 | 0.78 |
| Threonine |  | 52.1 | 9.5 |  | 48.5 | 5.1 |  | 34.2 | 7.5 |  | 28.7 | 7.5 |  | 0.0069 | 0.45 | 0.24 |
| TMAO |  | 59.2 | 13.2 |  | 141.5 | 32.7 |  | 25.8 | 10.6 |  | 105.7 | 13.4 |  | 0.0012 | 0.00081 | 4.5x10-7 |
| Trimethyllysine |  | 4.6 | 1.1 |  | 10.2 | 4.8 |  | 0.2 | 0.1 |  | 2.3 | 1.2 |  | 4.6x10-6 | 0.033 | 0.0013 |
| Tryptophan |  | 2.9 | 0.7 |  | 2.1 | 0.6 |  | 2.5 | 1.4 |  | 1.2 | 0.7 |  | 0.55 | 0.079 | 0.081 |
| Tyrosine |  | 11.9 | 2.4 |  | 9.3 | 3.0 |  | 6.1 | 1.7 |  | 4.8 | 2.3 |  | 0.0013 | 0.16 | 0.30 |
| Valine |  | 22.5 | 4.9 |  | 18.6 | 4.8 |  | 12.2 | 4.7 |  | 8.8 | 6.6 |  | 0.0059 | 0.21 | 0.33 |
| KTR |  | 45.0 | 26.4 |  | 37.3 | 5.1 |  | 269.8 | 302.9 |  | 138.5 | 47.7 |  | 0.14 | 0.50 | 0.32 |

Urine values are shown for *n* 5 in Control Group and *n* 6 rats in Baked Salmon Group in the Zucker fa/fa rat experiment, and for *n* 6 in Control Group and *n* 6 rats in Baked Salmon Group in the Long-Evans rat experiment. p <0.05 were considered significant. Groups are compared within each experiment using Independent Samples T Test assuming equal variances. Control Groups in each rat experiment are compared using Independent Samples T Test assuming equal variances.

1-MeHis; 1-methylhistidine, 3-MeHis; 3-methylhistidine, TMAO; Trimethylamine N-oxide, KTR; kynurenine:Trp ratio multiplied with 1000.

**Supplemental Table 3: Amino acids and metabolites thereof and potential markers of fish intake in plasma**

**(Mean values and standard deviations)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Zucker fa/fa rats |  | Long-Evans rats |  |  |  |  |
|  |  | Control Group |  | Baked Salmon group |  | Control Group |  | Baked Salmon group |  | P Control Diet x strain | P dietZucker | P dietLong-Evans |
| µmol/L |  | Mean | SD |  | Mean | SD |  | Mean | SD |  | Mean | SD |  |  |  |  |
| Alanine  |  | 395 | 104 |  | 416 | 54 |  | 466 | 43 |  | 442 | 38 |  | 0.16 | 0.67 | 0.34 |
| Arginine |  | 5.8 | 2.1 |  | 33.8 | 23.1 |  | 142.3 | 14.5 |  | 164.2 | 18.3 |  | 6.6x10-9 | 0.025 | 0.045 |
| Asparagine |  | 56.1 | 7.8 |  | 52.6 | 2.0 |  | 70.5 | 5.9 |  | 68.5 | 6.7 |  | 0.0071 | 0.31 | 0.60 |
| Aspartic acid |  | 24.0 | 8.5 |  | 17.1 | 1.9 |  | 11.7 | 2.0 |  | 11.6 | 3.0 |  | 0.0071 | 0.084 | 0.92 |
| Betaine |  | 71.1 | 8.8 |  | 80.7 | 8.2 |  | 90.4 | 15.7 |  | 84.1 | 12.5 |  | 0.037 | 0.092 | 0.46 |
| Creatine |  | 94 | 21 |  | 224 | 16 |  | 173 | 34 |  | 288 | 31 |  | 0.0015 | 9.6x10-7 | 1.0x10-4 |
| Cystathionine |  | 0.47 | 0.11 |  | 0.48 | 0.07 |  | 0.93 | 0.14 |  | 0.70 | 0.15 |  | 0.00020 | 0.92 | 0.019 |
| Cysteine (total) |  | 174 | 12 |  | 204 | 27 |  | 211 | 19 |  | 228 | 28 |  | 0.0041 | 0.045 | 0.26 |
| Asymmetric dimethyl-arginine |  | 0.64 | 0.03 |  | 0.77 | 0.07 |  | 0.76 | 0.11 |  | 0.68 | 0.08 |  | 0.044 | 0.0043 | 0.21 |
| Symmetric dimethyl-arginine |  | 0.36 | 0.04 |  | 0.35 | 0.02 |  | 0.39 | 0.06 |  | 0.37 | 0.05 |  | 0.33 | 0.64 | 0.50 |
| Dimethylglycine |  | 8.4 | 2.7 |  | 10.1 | 2.0 |  | 8.6 | 1.8 |  | 8.4 | 2.3 |  | 0.88 | 0.27 | 0.84 |
| Glutamine |  | 515 | 61 |  | 478 | 37 |  | 735 | 47 |  | 688 | 53 |  | 7.9x10-5 | 0.24 | 0.13 |
| Glutamic acid |  | 128 | 45 |  | 106 | 15 |  | 84 | 19 |  | 93 | 23 |  | 0.056 | 0.29 | 0.47 |
| α-keto-glutaric acid |  | 45.5 | 12.1 |  | 40.8 | 10.1 |  | 21.7 | 6.6 |  | 17.5 | 1.9 |  | 0.0025 | 0.50 | 0.17 |
| Glutathione (total) |  | 22.0 | 9.4 |  | 16.3 | 4.9 |  | 5.3 | 1.2 |  | 5.1 | 1.3 |  | 0.0018 | 0.22 | 0.79 |
| GSSG  |  | 9.3 | 4.0 |  | 8.3 | 2.5 |  | 2.0 | 0.8 |  | 1.6 | 0.6 |  | 0.0017 | 0.62 | 0.35 |
| GSH  |  | 12.6 | 6.3 |  | 7.9 | 2.5 |  | 3.3 | 1.2 |  | 3.5 | 1.0 |  | 0.0057 | 0.12 | 0.77 |
| GSSG/GSH |  | 0.86 | 0.39 |  | 1.07 | 0.19 |  | 0.69 | 0.34 |  | 0.47 | 0.25 |  | 0.46 | 0.26 | 0.23 |
| Glycine |  | 124 | 24 |  | 135 | 12 |  | 288 | 41 |  | 309 | 61 |  | 2.5x10-5 | 0.34 | 0.51 |
| Histidine |  | 60.4 | 4.2 |  | 54.2 | 4.1 |  | 54.2 | 4.4 |  | 54.1 | 3.8 |  | 0.040 | 0.035 | 0.98 |
| 1-MeHis |  | 5.9 | 0.6 |  | 41.0 | 10.9 |  | 13.6 | 1.3 |  | 33.6 | 3.8 |  | 6.6x10-7 | 5.6x10-5 | 2.5x10-7 |
| 3-MeHis |  | 2.79 | 0.09 |  | 4.06 | 0.11 |  | 5.08 | 0.84 |  | 5.09 | 0.96 |  | 0.00020 | 6.3x10-9 | 0.99 |
| Homocysteine (total) |  | 2.42 | 0.41 |  | 2.21 | 0.34 |  | 7.14 | 2.20 |  | 5.77 | 1.23 |  | 0.0011 | 0.36 | 0.21 |
| 3-Hydroxy-isobutyrate |  | 24.4 | 6.9 |  | 21.0 | 2.8 |  | 19.0 | 1.5 |  | 17.5 | 1.9 |  | 0.093 | 0.30 | 0.16 |
| Isoleucine |  | 84.3 | 12.1 |  | 83.1 | 13.7 |  | 101.3 | 8.3 |  | 94.8 | 6.5 |  | 0.022 | 0.89 | 0.16 |
| Leucine |  | 135 | 25 |  | 134 | 23 |  | 151 | 8 |  | 148 | 12 |  | 0.17 | 0.95 | 0.59 |
| Lysine |  | 301 | 20 |  | 319 | 45 |  | 361 | 32 |  | 360 | 34 |  | 0.0062 | 0.42 | 0.99 |
| Methionine  |  | 46.8 | 6.6 |  | 44.9 | 1.7 |  | 59.0 | 3.7 |  | 54.4 | 5.8 |  | 0.0037 | 0.53 | 0.13 |
| Methionine sulfoxide |  | 1.41 | 0.71 |  | 1.06 | 0.20 |  | 1.38 | 0.23 |  | 1.31 | 0.13 |  | 0.91 | 0.27 | 0.54 |
| Ornithine  |  | 148 | 21 |  | 129 | 21 |  | 64 | 11 |  | 52 | 7 |  | 1.3x10-5 | 0.18 | 0.048 |
| Phenylalanine |  | 70.2 | 11.4 |  | 71.2 | 3.0 |  | 66.0 | 1.6 |  | 68.8 | 5.4 |  | 0.39 | 0.84 | 0.26 |
| Proline |  | 121 | 30 |  | 116 | 23 |  | 138 | 15 |  | 129 | 12 |  | 0.26 | 0.75 | 0.28 |
| Serine |  | 188 | 22 |  | 197 | 17 |  | 242 | 20 |  | 252 | 14 |  | 0.0022 | 0.45 | 0.36 |
| Threonine |  | 206 | 30 |  | 242 | 64 |  | 269 | 50 |  | 264 | 29 |  | 0.035 | 0.27 | 0.81 |
| TMAO |  | 1.59 | 0.54 |  | 2.23 | 0.68 |  | 0.88 | 0.17 |  | 0.97 | 0.34 |  | 0.013 | 0.12 | 0.59 |
| Trimethyllysine |  | 1.13 | 0.07 |  | 1.26 | 0.11 |  | 1.38 | 0.21 |  | 1.28 | 0.13 |  | 0.032 | 0.054 | 0.32 |
| Tryptophan |  | 104 | 12 |  | 106 | 11 |  | 107 | 7 |  | 125 | 19 |  | 0.59 | 0.83 | 0.053 |
| Tyrosine |  | 79.7 | 17.7 |  | 63.6 | 10.4 |  | 76.4 | 5.1 |  | 77.7 | 12.5 |  | 0.67 | 0.093 | 0.83 |
| Valine |  | 198 | 33 |  | 192 | 34 |  | 202 | 13 |  | 200 | 19 |  | 0.78 | 0.76 | 0.82 |
| KTR |  | 18.3 | 3.5 |  | 18 | 3 |  | 18.9 | 2.7 |  | 15 | 2 |  | 0.75 | 0.99 | 0.0067 |

Plasma and serum values are shown for *n* 5 in Control Group and *n* 6 rats in Baked Salmon Group in the Zucker fa/fa rat experiment, and for *n* 6 in Control Group and *n* 6 rats in Baked Salmon Group in the Long-Evans rat experiment. p <0.05 were considered significant. Groups are compared within each experiment using Independent Samples T Test assuming equal variances. Control Groups in each rat experiment are compared using Independent Samples T Test assuming equal variances.

1-MeHis; 1-methylhistidine, 3-MeHis; 3-methylhistidine, TMAO; Trimethylamine N-oxide, GSSG; oxidised glutathione, GSH; reduced glutathione), KTR; kynurenine:Trp ratio multiplied with 1000.

**Supplemental Table 4: Circulating concentrations of fat-soluble vitamins, B vitamins and tryptophan pathway metabolites**

**(Mean values and standard deviations)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Zucker fa/fa rats |  | Long-Evans rats |  |  |  |  |
|  |  | Control Group |  | Baked Salmon group |  | Control Group | Baked Salmon group |  | P Control Diet x strain | P dietZucker | P dietLong-Evans |
|  |  | Mean | SD |  | Mean | SD |  | Mean | SD |  | Mean | SD |  |  |  |  |
| *Fat soluble vitamins* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| all-trans retinol (umol/L) |  | 1.87 | 0.28 |  | 1.78 | 0.11 |  | 1.59 | 0.19 |  | 1.62 | 0.14 |  | 0.076 | 0.47 | 0.82 |
| 25-OH Vitamin D (total) (ng/mL) |  | 27.4 | 6.7 |  | 28.3 | 5.3 |  | 13.9 | 2.6 |  | 12.2 | 2.1 |  | 0.0013 | 0.81 | 0.24 |
| alpha-tocopherol (umol/L) |  | 91.6 | 9.6 |  | 73.4 | 13.2 |  | 37.8 | 5.1 |  | 41.3 | 9.6 |  | 7.7x10-7 | 0.031 | 0.45 |
| gamma-tocopherol (umol/L) |  | 3.8 | 0.6 |  | 3.8 | 0.9 |  | 0.6 | 0.1 |  | 0.8 | 0.2 |  | 2.6x10-7 | 1.0 | 0.026 |
| *B vitamins* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Thiamine (nmol/L) |  | 166 | 33 |  | 169 | 19 |  | 179 | 7 |  | 169 | 15 |  | 0.40 | 0.89 | 0.19 |
| Thiamine monophosphate (nmol/L) |  | 646 | 80 |  | 596 | 78 |  | 404 | 68 |  | 391 | 55 |  | 0.00041 | 0.32 | 0.72 |
| Riboflavin (nmol/L) |  | 88.1 | 24.3 |  | 61.3 | 10.8 |  | 58.3 | 6.2 |  | 47.9 | 5.6 |  | 0.017 | 0.037 | 0.013 |
| Flavin mononucleotide (nmol/L) |  | 61.0 | 3.6 |  | 49.9 | 5.7 |  | 54.5 | 8.8 |  | 46.1 | 8.0 |  | 0.16 | 0.0048 | 0.11 |
| Nicotinic acid (nmol/L) |  | <LOD |  | <LOD |  | <LOD |  | <LOD |  |  |  |  |
| Nicotinamide (nmol/L) |  | 4494 | 1139 |  | 4678 | 849 |  | 2593 | 612 |  | 2683 | 530 |  | 0.0063 | 0.77 | 0.79 |
| N1-methyl-nicotinamide (nmol/L) |  | 469 | 275 |  | 521 | 277 |  | 515 | 144 |  | 652 | 271 |  | 0.73 | 0.77 | 0.30 |
| Pyridoxal 5'-phosphate (nmol/L) |  | 1200 | 118 |  | 1227 | 135 |  | 963 | 111 |  | 971 | 132 |  | 0.0074 | 0.74 | 0.91 |
| Pyridoxal (nmol/L) |  | 451 | 87 |  | 422 | 45 |  | 844 | 132 |  | 759 | 72 |  | 0.00030 | 0.49 | 0.20 |
| 4-Pyridoxic acid (nmol/L) |  | 69.5 | 9.2 |  | 58.4 | 11.1 |  | 25.4 | 4.7 |  | 19.2 | 3.6 |  | 2.8x10-6 | 0.11 | 0.028 |
| Pyridoxine (nmol/L) |  | <LOD |  | <LOD |  | <LOD |  | <LOD |  |  |  |  |
| *Tryptophan pathway metabolites* |  |  |  |  |  |  |  |  |  |  |
| Kynurenic acid (nmol/L) |  | 81.8 | 12.5 |  | 86.5 | 13.7 |  | 72.7 | 10.6 |  | 54.7 | 6.0 |  | 0.23 | 0.57 | 0.0047 |
| Kynurenine (µmol/L) |  | 1.89 | 0.33 |  | 1.92 | 0.31 |  | 2.02 | 0.29 |  | 1.80 | 0.26 |  | 0.49 | 0.88 | 0.20 |
| Anthranilic acid (nmol/L) |  | 94.1 | 23.5 |  | 72.3 | 13.6 |  | 52.8 | 11.1 |  | 38.7 | 7.4 |  | 0.0039 | 0.086 | 0.027 |
| 3-Hydroxy-kynurenine (nmol/L) |  | 4.4 | 0.9 |  | 7.6 | 4.2 |  | 30.1 | 3.0 |  | 28.0 | 5.9 |  | 1.8x10-8 | 0.14 | 0.46 |
| Xanthurenic acid (nmol/L) |  | 13.9 | 2.6 |  | 16.8 | 3.7 |  | 35.6 | 3.6 |  | 29.4 | 3.0 |  | 1.4x10-6 | 0.17 | 0.0087 |
| 3-Hydroxy-anthranilic acid (nmol/L) |  | 4.41 | 1.17 |  | 5.07 | 0.89 |  | 6.80 | 1.44 |  | 9.24 | 4.28 |  | 0.015 | 0.31 | 0.22 |
| Picolinic acid (nmol/L) |  | 107 | 16 |  | 112 | 25 |  | 138 | 16 |  | 119 | 12 |  | 0.011 | 0.70 | 0.037 |
| Quinolinic acid (nmol/L) |  | 295 | 60 |  | 617 | 268 |  | 905 | 324 |  | 1107 | 585 |  | 0.0026 | 0.028 | 0.47 |
| *Others* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Choline (umol/L) |  | 16.5 | 1.6 |  | 16.0 | 1.8 |  | 12.8 | 0.8 |  | 11.2 | 1.4 |  | 0.00078 | 0.65 | 0.033 |
| Methylmalonic acid (umol/L) |  | 0.36 | 0.07 |  | 0.34 | 0.03 |  | 0.26 | 0.08 |  | 0.26 | 0.06 |  | 0.065 | 0.49 | 0.94 |

LOD, level of detection (LODs were 1 nmol/L for pyridoxine and 20 nmol/L for nicotinic acid)

Plasma and serum values are shown for *n* 5 in Control Group and *n* 6 rats in Baked Salmon Group in the Zucker fa/fa rat experiment, and for *n* 6 in Control Group and *n* 6 rats in Baked Salmon Group in the Long-Evans rat experiment. p <0.05 were considered significant. Groups are compared within each experiment using Independent Samples T Test assuming equal variances. Control Groups in each rat experiment are compared using Independent Samples T Test assuming equal variances.