Supplemental Table 1. Young IL 10$^{tm}$ mice metabolite measurements (full table, p-values unadjusted)

| Metabolite | | Control n=5 | IL 10$^{tm}$ n=6 | | P value |
|---|---|---|---|---|---|
| **Cit** | | 94.45 | 73.5167 | ↓ | 0.0036684 |
| **Orn** | | 73.55 | 56.8167 | ↓ | 0.0100904 |
| **PC ae C38:2** | | 4.95467 | 3.52205 | ↓ | 0.0103952 |
| **PC ae C38:3** | | 1.97635 | 1.52756 | ↓ | 0.0129673 |
| **lysoPC a C14:0** | | 8.68146 | 6.66934 | ↓ | 0.0206697 |
| **SM (OH) C14:1** | | 1.72292 | 1.26118 | ↓ | 0.021117 |
| **PC ae C36:3** | | 2.00604 | 1.7431 | ↓ | 0.0218773 |
| **lysoPC a C16:1** | | 5.7321 | 4.32297 | ↓ | 0.025716 |
| **PC ae C36:2** | | 9.64386 | 8.07114 | ↓ | 0.0276785 |
| **SM (OH) C22:2** | | 1.85736 | 1.47848 | ↓ | 0.032493 |
| **PC aa C36:3** | | 95.9061 | 81.4081 | ↓ | 0.0334162 |

Supplemental Table 2. Middle aged IL 10$^{tm}$ metabolite measurements (full table, p-values unadjusted)

| Metabolite | | Control n=12 | IL 10$^{tm}$ n=19 | | P value |
|---|---|---|---|---|---|
| **Kynurenine / Trp** | * | 0.0099273 | 0.0158913 | ↑ | 4.44E-05 |
| **PC ae C42:1** | * | 0.688724 | 0.927056 | ↑ | 0.0001366 |
| **PC aa C40:6** | | 36.2821 | 53.1196 | ↑ | 0.0004424 |
| **PC aa C40:4** | | 1.71318 | 2.33144 | ↑ | 0.0008275 |
| **PC aa C40:1** | | 0.288054 | 0.346857 | ↑ | 0.0012507 |
| **lysoPC a C26:1** | | 0.315676 | 0.434985 | ↑ | 0.0012549 |
| **PC ae C42:4** | | 0.283372 | 0.385398 | ↑ | 0.0013905 |
| **PC ae C40:5** | | 0.957944 | 1.27838 | ↑ | 0.0016083 |
| **PC ae C36:5** | | 1.60583 | 2.41199 | ↑ | 0.001617 |
| **PC aa C42:5** | | 0.226678 | 0.293754 | ↑ | 0.0019018 |
| **PC aa C32:3** | | 0.177071 | 0.230479 | ↑ | 0.0023928 |
| **SM (OH) C14:1** | | 1.80553 | 1.33645 | ↓ | 0.0027591 |
| **PC aa C34:3** | | 10.4825 | 14.5773 | ↑ | 0.0028308 |
| **PC ae C36:4** | | 2.50391 | 3.42155 | ↑ | 0.0028347 |
| **PC aa C38:4** | | 116.879 | 156.955 | ↑ | 0.0032746 |
| **Kynurenine** | | 1.21658 | 1.63516 | ↑ | 0.0035013 |
| **lysoPC a C28:1** | | 0.636165 | 0.81616 | ↑ | 0.0035348 |

| | | | | |
|---|---|---|---|---|
| **PC aa C38:6** | 76.1241 | 106.147 | ↑ | 0.0039363 |
| **PC aa C36:5** | 6.59467 | 9.30779 | ↑ | 0.0042725 |
| **PC ae C34:3** | 0.827801 | 1.14532 | ↑ | 0.0042915 |
| **PC ae C38:5** | 2.79781 | 3.75849 | ↑ | 0.0043954 |
| **PC ae C32:1** | 0.521774 | 0.664599 | ↑ | 0.0062371 |
| **PC ae C42:0** | 1.01761 | 1.17576 | ↑ | 0.0063958 |
| **PC ae C42:5** | 0.687499 | 0.817973 | ↑ | 0.0068315 |
| **PC aa C34:4** | 0.50192 | 0.662721 | ↑ | 0.0080307 |
| **PC ae C30:2** | 0.100309 | 0.119044 | ↑ | 0.0085778 |
| **PC ae C38:0** | 2.06255 | 2.77453 | ↑ | 0.0098392 |
| **Serotonin** | 9.05709 | 3.34308 | ↓ | 0.0125052 |
| **PC ae C30:1** | 0.208129 | 0.278508 | ↑ | 0.0126652 |
| **c4-OH-Pro** | 4.46417 | 5.58789 | ↑ | 0.0129227 |
| **PC aa C38:0** | 1.22125 | 1.56823 | ↑ | 0.0159307 |
| **PC aa C42:6** | 0.468822 | 0.552634 | ↑ | 0.0162391 |
| **PC aa C40:5** | 4.05247 | 5.21375 | ↑ | 0.0170496 |
| **PC ae C40:4** | 1.64796 | 2.09069 | ↑ | 0.0180223 |
| **PC ae C38:6** | 1.43781 | 1.84396 | ↑ | 0.0198495 |
| **PC ae C34:1** | 2.34154 | 2.89283 | ↑ | 0.019872 |
| **Gly** | 196.983 | 243.263 | ↑ | 0.0202694 |
| **PC aa C38:5** | 35.0897 | 44.7049 | ↑ | 0.0204442 |
| **PC ae C32:2** | 0.218689 | 0.26545 | ↑ | 0.0214631 |
| **PC aa C42:4** | 0.606987 | 0.665631 | ↑ | 0.022113 |
| **PC aa C36:4** | 127.586 | 162.928 | ↑ | 0.0225723 |
| **PC aa C36:6** | 0.349633 | 0.451909 | ↑ | 0.0270209 |
| **PC aa C42:1** | 0.206177 | 0.246872 | ↑ | 0.0301884 |
| **PC ae C38:4** | 3.91691 | 4.87044 | ↑ | 0.033847 |
| **PC aa C36:2** | 249.656 | 297.116 | ↑ | 0.0373519 |
| **SM C20:2** | 0.285843 | 0.348296 | ↑ | 0.0425698 |
| **lysoPC a C18:0** | 167.607 | 199.504 | ↑ | 0.0443904 |
| **PC aa C32:1** | 3.15613 | 4.09743 | ↑ | 0.0476246 |
| **PC aa C40:3** | 0.381395 | 0.45225 | ↑ | 0.047744 |
| **PC ae C36:0** | 0.39648 | 0.476158 | ↑ | 0.0478637 |
| **PC aa C38:3** | 24.9592 | 31.1117 | ↑ | 0.0492607 |

Supplemental Table 3. Old age IL 10$^{tm}$ mice metabolite measurements (full table, p-values unadjusted)

| ID | | Control n=20 | IL 10$^{tm}$ n=16 | | p-value |
|---|---|---|---|---|---|
| **Kynurenine / Trp** | * | 0.0122069 | 0.0244054 | ↑ | 7.07E-07 |
| **alpha-AAA** | * | 6.325 | 2.98062 | ↓ | 2.98E-06 |
| **Trp** | * | 108.88 | 69.95 | ↓ | 5.46E-05 |
| **SM C18:0** | * | 4.54467 | 1.92527 | ↓ | 0.0001196 |
| **lysoPC a C20:4** | * | 81.891 | 44.5328 | ↓ | 0.0001547 |
| **lysoPC a C16:1** | * | 4.88079 | 2.87555 | ↓ | 0.0002673 |
| **lysoPC a C18:1** | | 52.288 | 34.843 | ↓ | 0.0007301 |
| **PC ae C34:2** | | 1.89739 | 2.73332 | ↑ | 0.0012113 |
| **lysoPC a C16:0** | | 233.357 | 163.846 | ↓ | 0.0014066 |
| **PC aa C36:0** | | 2.41212 | 1.65315 | ↓ | 0.0017975 |
| **SM C18:1** | | 1.19859 | 0.760069 | ↓ | 0.0025144 |
| **lysoPC a C24:0** | | 0.949746 | 0.710284 | ↓ | 0.0032113 |
| **Fisher ratio** | | 1.95602 | 2.34761 | ↑ | 0.0034275 |
| **PC aa C40:3** | | 0.272867 | 0.351153 | ↑ | 0.0037729 |
| **PC ae C42:1** | | 0.563257 | 0.879288 | ↑ | 0.0038765 |
| **SM (OH) C14:1** | | 1.35906 | 0.945649 | ↓ | 0.0043295 |
| **lysoPC a C18:2** | | 164.512 | 125.249 | ↓ | 0.0044795 |
| **PC ae C42:3** | | 0.895231 | 0.624062 | ↓ | 0.005439 |
| **PC ae C38:3** | | 0.905353 | 1.24644 | ↑ | 0.0056297 |
| **Kynurenine** | | 1.2398 | 1.62625 | ↑ | 0.0075272 |
| **C16:2-OH** | | 0.0707002 | 0.079037 | ↑ | 0.0076157 |
| **PC aa C34:1** | | 49.5688 | 36.2751 | ↓ | 0.010824 |
| **PC ae C42:0** | | 0.866178 | 1.03258 | ↑ | 0.0110601 |
| **PC ae C36:2** | | 4.78344 | 6.3887 | ↑ | 0.0114751 |
| **PC ae C36:3** | | 1.0802 | 1.35751 | ↑ | 0.0117932 |
| **SM (OH) C16:1** | | 0.397161 | 0.29129 | ↓ | 0.0125727 |
| **SM (OH) C24:1** | | 0.473738 | 0.381408 | ↓ | 0.0170087 |
| **Thr** | | 262.065 | 173.288 | ↓ | 0.0186021 |
| **PC aa C40:6** | | 57.7794 | 40.2682 | ↓ | 0.0195769 |
| **PC aa C38:6** | | 92.2034 | 64.7815 | ↓ | 0.0216498 |
| **PC aa C40:2** | | 0.204337 | 0.254761 | ↑ | 0.0225663 |
| **PC ae C38:2** | | 2.27925 | 3.18833 | ↑ | 0.0241852 |
| **lysoPC a C18:0** | | 191.04 | 144.447 | ↓ | 0.0246072 |
| **Phe** | | 74.175 | 90.5813 | ↑ | 0.0265114 |
| **Serotonin** | | 4.71245 | 1.76533 | ↓ | 0.0271002 |

| | | | | |
|---|---|---|---|---|
| **PC ae C38:0** | 1.90518 | 1.46673 | ↓ | 0.0316329 |
| **PC aa C36:3** | 44.266 | 55.8637 | ↑ | 0.0326819 |
| **PC aa C32:0** | 9.2091 | 7.48208 | ↓ | 0.0410201 |
| **C16:1-OH** | 0.156217 | 0.168695 | ↑ | 0.0429336 |
| **PC aa C42:5** | 0.205434 | 0.242672 | ↑ | 0.0449734 |
| **PC ae C30:2** | 0.0993353 | 0.0837001 | ↓ | 0.0455536 |
| **PC aa C24:0** | 0.33076 | 0.257438 | ↓ | 0.0475861 |
| **PC ae C44:5** | 0.289386 | 0.250126 | ↓ | 0.0477549 |
| **Tyr / Phe** | 0.823069 | 0.728002 | ↓ | 0.0479037 |

**Supplemental Table 4.** Demographics of young versus old including age, sex, BMI, systolic BP, Diastolic BP, IL6, TNFα, TNFα R1 (mean & SD).

| | Young (n=50) | Old (n=116) | p-value |
|---|---|---|---|
| Age , mean(std) | 25.6 (6.2) | 77.6 (5.9) | <0.0001 |
| Gender, male, n(%) | 34 (68.0) | 66 (56.9) | 0.18 |
| BMI | 26.1 (6.6) | 28.0 (5.9) | 0.074 |
| Systolic BP | 113.9 (14.6) | 132.8 (20.1) | <0.0001 |
| Diastolic BP | 73.3 (10.9) | 73.4 (11.3) | 0.96 |
| IL6 | 0.69 (0.63) | 2.04 (4.45) | 0.046 |
| TNFa | 2.01 (1.16) | 3.07 (1.28) | <0.0001 |
| TNFa receptor1 | 793.65 (298.20) | 1454.01 (659.77) | <0.0001 |

**Supplemental Table 5**. Average CV's for metabolites in 14 non-frail individuals CV= stdev (of all 4 visits)/ average (of all 4 visits)

Individual variability in blood metabolites can provide information which can help identify candidate metabolites for biomarkers of aging or disease. In order to understand the variability of the metabolites we measured, we performed metabolomics analysis on serum samples collected from fourteen pre-frail individuals four times over a six-month timespan at two-month intervals. This longitudinal collection allowed for the quantification of the variance of each metabolite over the six-month interval. We calculated the average (intra-assay) CV for each metabolite using the CV over the six-month period for each metabolite for each individual patient, and then averaging the CV's from all fourteen subjects. Most of the metabolites had relatively low CV with only 16 metabolites having CV's > 0.3

| Metabolite | Average CV | Standard Deviation |
|---|---|---|
| PC aa C34:2 | 0.078 | 0.04 |
| PC aa C36:2 | 0.112 | 0.051 |
| Fisher ratio | 0.114 | 0.044 |
| Non essential AA | 0.129 | 0.061 |
| PC aa C36:4 | 0.134 | 0.074 |
| Tyr / Phe | 0.134 | 0.081 |
| PC aa C34:1 | 0.137 | 0.064 |
| PC aa C38:4 | 0.138 | 0.075 |
| PC ae C42:5 | 0.14 | 0.098 |
| Total AA | 0.143 | 0.063 |
| PC ae C44:3 | 0.148 | 0.082 |
| PC aa C38:6 | 0.15 | 0.096 |
| PC ae C42:1 | 0.151 | 0.083 |
| PC ae C44:6 | 0.151 | 0.105 |
| Glucogenic AA | 0.153 | 0.118 |
| PC ae C40:4 | 0.154 | 0.123 |
| PC ae C34:1 | 0.155 | 0.09 |
| PC aa C40:6 | 0.156 | 0.091 |
| PC aa C42:5 | 0.156 | 0.075 |
| PC ae C40:2 | 0.156 | 0.114 |
| PC ae C44:5 | 0.157 | 0.09 |
| PC aa C42:0 | 0.158 | 0.09 |
| PC aa C36:3 | 0.158 | 0.091 |
| PC ae C40:6 | 0.159 | 0.11 |

| | | |
|---|---|---|
| Phe | 0.162 | 0.093 |
| SM C16:1 | 0.162 | 0.11 |
| PC ae C42:4 | 0.163 | 0.127 |
| PC aa C40:5 | 0.163 | 0.08 |
| PC ae C42:2 | 0.164 | 0.089 |
| SM C24:1 | 0.165 | 0.105 |
| PC ae C38:4 | 0.165 | 0.12 |
| SM C16:0 | 0.167 | 0.093 |
| PC aa C28:1 | 0.167 | 0.1 |
| PC aa C38:5 | 0.168 | 0.097 |
| PC aa C42:6 | 0.168 | 0.091 |
| Orn / Arg | 0.168 | 0.079 |
| Gly | 0.168 | 0.116 |
| Val | 0.171 | 0.074 |
| PC ae C40:3 | 0.171 | 0.13 |
| PC ae C36:4 | 0.171 | 0.104 |
| PC aa C32:0 | 0.171 | 0.082 |
| PC aa C42:1 | 0.172 | 0.107 |
| PC ae C36:1 | 0.172 | 0.133 |
| PC aa C38:3 | 0.173 | 0.088 |
| PC aa C42:2 | 0.173 | 0.093 |
| PC aa C40:3 | 0.174 | 0.08 |
| PC ae C40:1 | 0.174 | 0.11 |
| PC ae C40:5 | 0.175 | 0.114 |
| SM C26:1 | 0.175 | 0.1 |
| Gln | 0.175 | 0.121 |
| SM (OH) C16:1 | 0.175 | 0.105 |
| SM (OH) C14:1 | 0.177 | 0.107 |
| PC aa C38:0 | 0.178 | 0.107 |
| Ala | 0.179 | 0.126 |
| PC ae C38:6 | 0.18 | 0.127 |
| PC ae C38:5 | 0.181 | 0.114 |
| PC ae C42:3 | 0.181 | 0.121 |
| PC ae C38:0 | 0.183 | 0.12 |
| PC aa C40:4 | 0.183 | 0.093 |
| PC ae C34:2 | 0.184 | 0.125 |
| PC ae C34:0 | 0.186 | 0.11 |
| PC aa C42:4 | 0.187 | 0.064 |
| PC ae C32:2 | 0.188 | 0.129 |
| AAA | 0.188 | 0.11 |
| SM C24:0 | 0.188 | 0.101 |
| PC ae C36:5 | 0.189 | 0.108 |
| Total DMA / Arg | 0.189 | 0.11 |

| | | |
|---|---|---|
| SM C18:0 | 0.189 | 0.086 |
| SM C18:1 | 0.189 | 0.1 |
| C2 / C0 | 0.189 | 0.133 |
| C18:2 | 0.19 | 0.091 |
| C0 | 0.19 | 0.112 |
| PC ae C36:3 | 0.191 | 0.126 |
| PC aa C32:3 | 0.192 | 0.113 |
| SM (OH) C22:2 | 0.194 | 0.112 |
| SM (OH) C24:1 | 0.194 | 0.106 |
| PC aa C36:0 | 0.196 | 0.105 |
| PC ae C38:3 | 0.196 | 0.126 |
| lysoPC a C18:0 | 0.197 | 0.101 |
| PC ae C32:1 | 0.198 | 0.109 |
| lysoPC a C16:1 | 0.199 | 0.126 |
| SM (OH) C22:1 | 0.199 | 0.109 |
| PC ae C36:0 | 0.199 | 0.113 |
| PC aa C34:3 | 0.199 | 0.089 |
| C4 | 0.2 | 0.09 |
| PC ae C36:2 | 0.2 | 0.174 |
| Kynurenine / Trp | 0.201 | 0.081 |
| PC aa C36:1 | 0.202 | 0.107 |
| lysoPC a C16:0 | 0.202 | 0.096 |
| PC aa C40:2 | 0.205 | 0.112 |
| Met-SO / Met | 0.208 | 0.082 |
| SM C26:0 | 0.208 | 0.113 |
| lysoPC a C20:4 | 0.21 | 0.087 |
| lysoPC a C17:0 | 0.21 | 0.148 |
| Lys | 0.211 | 0.122 |
| PC aa C30:0 | 0.212 | 0.083 |
| PC aa C36:6 | 0.213 | 0.111 |
| ADMA / Arg | 0.213 | 0.082 |
| PC ae C38:2 | 0.214 | 0.115 |
| Pro | 0.214 | 0.071 |
| Essential AA | 0.216 | 0.115 |
| Arg | 0.218 | 0.117 |
| PC ae C34:3 | 0.219 | 0.143 |
| Cit / Arg | 0.22 | 0.105 |
| lysoPC a C18:1 | 0.221 | 0.117 |
| SM C20:2 | 0.221 | 0.108 |
| PC ae C30:2 | 0.223 | 0.101 |
| PC aa C34:4 | 0.223 | 0.105 |
| Trp | 0.224 | 0.158 |

| | | |
|---|---|---|
| total DMA | 0.226 | 0.142 |
| Thr | 0.226 | 0.09 |
| PC ae C44:4 | 0.226 | 0.155 |
| Ser | 0.227 | 0.089 |
| C18:1 | 0.227 | 0.126 |
| Tyr | 0.231 | 0.12 |
| H1 | 0.231 | 0.139 |
| Cit | 0.234 | 0.092 |
| PC aa C36:5 | 0.235 | 0.116 |
| Orn | 0.236 | 0.137 |
| C2 | 0.238 | 0.131 |
| PC aa C32:1 | 0.239 | 0.096 |
| Cit / Orn | 0.241 | 0.099 |
| lysoPC a C20:3 | 0.241 | 0.081 |
| PC aa C32:2 | 0.242 | 0.086 |
| Kynurenine | 0.247 | 0.152 |
| SDMA / Arg | 0.249 | 0.178 |
| BCAA | 0.253 | 0.127 |
| C3 | 0.254 | 0.124 |
| Glu | 0.262 | 0.081 |
| Asn | 0.262 | 0.126 |
| ADMA | 0.267 | 0.176 |
| PC aa C38:1 | 0.272 | 0.164 |
| SDMA | 0.28 | 0.233 |
| Taurine | 0.28 | 0.17 |
| Serotonin / Trp | 0.297 | 0.183 |
| C5 | 0.301 | 0.215 |
| Putrescine / Orn | 0.302 | 0.194 |
| lysoPC a C18:2 | 0.303 | 0.134 |
| Serotonin | 0.309 | 0.108 |
| Met | 0.31 | 0.176 |
| PC ae C38:1 | 0.321 | 0.159 |
| SM C22:3 | 0.326 | 0.308 |
| Ile | 0.33 | 0.168 |
| Leu | 0.331 | 0.169 |
| Met-SO | 0.349 | 0.211 |
| Asp | 0.385 | 0.15 |

**Supplemental Table 6.** Demographics of all older patients stratified by risk status into non-frail and frail groups

| | Non-frail (n=83) | Frail (n=33) | p-value |
|---|---|---|---|
| Age , mean(std) | 76.7 (5.7) | 79.8 (5.9) | 0.01 |
| Gender, male, n(%) | 39 (47.0) | 27 (81.2) | 0.0008 |
| BMI | 26.65 (3.45) | 31.4 (8.5) | <0.0001 |
| Systolic BP | 133.03 (17.17) | 132.4 (25.0) | 0.066 |
| Diastolic BP | 74.19 (11.27) | 71.5 (11.5) | 0.53 |
| IL6 | 1.96 (3.69) | 2.22 (1.76) | 0.22 |
| TNFa | 3.07 (1.35) | 2.73 (0.93) | 0.058 |
| TNFa receptor1 | 1288.01 (580.40) | 1862.70 (677.35) | 0.0002 |
| Walking time for 4m (sec) | 3.75 (0.93) | 7.77 (3.58) | <0.0001 |
| Grip strength | 26.65 (9.93) | 19.04 (6.57) | <0.0001 |

**Supplemental Table 7.** Downstream kynurenine pathway metabolites & ratios ranked correlations with IL-6, TNFα, TNFαR1, and IFNγ levels, and frailty status, walking speed, and grip strength

| IL-6 | | | | TNFα | | | | TNFαR1 | | | | IFNγ | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Metabolite | Estimate | P-value | $R^2$ | Metabolite | Estimate | P-value | $R^2$ | Metabolite | Estimate | P-value | $R^2$ | Metabolite | Estimate | P-value | $R^2$ |
| KYN/PA | 0.276 | 0.00995 | 0.109 | TRP/5HT | 3.324 | 0.00229 | 0.10390 | KYN/PA | 0.360 | 0.000776 | 0.1574 | KA/KYN | -0.286 | 0.0101 | 0.108 |
| | | | | KYN/5HT | 2.633 | 0.00281 | 0.07430 | KYN/QA | 0.338 | 0.00110 | 0.1546 | KYN/AA | 0.289 | 0.0210 | 0.119 |
| | | | | AA/5HT | 0.923 | 0.0192 | 0.0759 | KA/XA | 0.350 | 0.00112 | 0.158 | | | | |
| | | | | 3HK/5HT | 0.532 | 0.0315 | 0.0433 | TRP/3HK | -0.330 | 0.00113 | 0.1303 | | | | |
| | | | | XA/KA | -0.253 | 0.0323 | 0.0719 | XA/TRP | 0.298 | 0.00370 | 0.1185 | | | | |
| | | | | 5HT/KA | -0.232 | 0.0364 | 0.0769 | KA/QA | 0.295 | 0.00442 | 0.1155 | | | | |
| | | | | TRP/KA | -0.220 | 0.0374 | 0.0607 | KA | 0.295 | 0.00580 | 0.1119 | | | | |
| | | | | KYN/QA | 0.236 | 0.0387 | 0.0649 | KA/PA | 0.281 | 0.00730 | 0.1089 | | | | |
| | | | | | | | | TRP/AA | -0.306 | 0.0147 | 0.126 | | | | |
| | | | | | | | | TRP/KA | -0.236 | 0.0252 | 0.0904 | | | | |
| | | | | | | | | 3HK/PA | 0.230 | 0.0293 | 0.0621 | | | | |
| | | | | | | | | XA/KYN | -0.218 | 0.0383 | 0.0603 | | | | |

| Frailty Status | | | Grip Strength | | | | Walking Speed | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Metabolite | OR | P-value | Metabolite | Estimate | P-value | $R^2$ | Metabolite | Estimate | P-value | $R^2$ |
| 3HK/TRP | 2.683 | 0.00251 | TRP/QA | 0.197 | 0.0211 | 0.1406 | TRP/XA | 0.308 | 0.00148 | 0.14020 |
| TRP/AA | 0.281 | 0.0179 | TRP/3HK | 0.187 | 0.0350 | 0.1473 | 3HK/TRP | -0.308 | 0.00158 | 0.14580 |
| KA/PA | 2.043 | 0.0314 | TRP/XA | 0.189 | 0.0405 | 0.1189 | 3HK/PA | -0.243 | 0.0154 | 0.1096 |
| PA/3HK | 0.377 | 0.0321 | | | | | TRP/KA | 0.231 | 0.0179 | 0.0930 |
| KYN/3HK | 0.418 | 0.0343 | | | | | 5HT/TRP | -0.199 | 0.0355 | 0.0424 |
| 3HK/XA | 1.797 | 0.0371 | | | | | 3HK | -0.205 | 0.0401 | 0.0720 |
| XA/AA | 0.342 | 0.0374 | | | | | PA/KA | 0.201 | 0.0420 | 0.0938 |
| KA/KYN | 1.845 | 0.0386 | | | | | | | | |
| 3HK | 1.786 | 0.0393 | | | | | | | | |
| KA/XA | 1.928 | 0.0415 | | | | | | | | |

**Supplemental Table 8**. Metabolite abbreviation list

| **Acylcarnitines** | | | |
|---|---|---|---|
| C0 | Carnitine | C10:1 | Decenoylcarnitine |
| C2 | Acetylcarnitine | C10:2 | Decadienylcarnitine |
| C3 | Propionylcarnitine | C12 | Dodecanoylcarnitine |
| C3:1 | Propenoylcarnitine | C12:1 | Dodecenoylcarnitine |
| C3-OH | Hydroxypropionylcarnitine | C12-DC | Dodecanedioylcarnitine |
| C4 | Butyrylcarnitine | C14 | Tetradecanoylcarnitine |
| C4:1 | Butenylcarnitine | C14:1 | Tetradecenoylcarnitine |
| C4-OH(C3-DC) | Hydroxybutyrylcarnitine | C14:1-OH | Hydroxytetradecenoylcarnitine |
| C5 | Valerylcarnitine | C14:2 | Tetradecadienylcarnitine |
| C5:1 | Tiglylcarnitine | C14:2-OH | Hydroxytetradecadienylcarnitine |
| C5:1-DC | Glutaconylcarnitine | C16 | Hexadecanoylcarnitine |
| C5-DC(C6-OH) | Glutarylcarnitine (Hydroxyhexanoylcarnitine) | C16:1 | Hexadecenoylcarnitine |

| | | | |
|---|---|---|---|
| C5-M-DC | Methylglutarylcarnitine | C16:1-OH | Hydroxyhexadecenoylcarnitine |
| C5-OH (C3-DC-M) | Hydroxyvalerylcarnitine (Methylmalonylcarnitine) | C16:2 | Hexadecadienylcarnitine |
| C6 (C4:1-DC) | Hexanoylcarnitine (Fumarylcarnitine) | C16:2-OH | Hydroxyhexadecadienylcarnitine |
| C6:1 | Hexenoylcarnitine | C16-OH | Hydroxyhexadecanoylcarnitine |
| C7-DC | Pimelylcarnitine | C18 | Octadecanoylcarnitine |
| C8 | Octanoylcarnitine | C18:1 | Octadecenoylcarnitine |
| C9 | Nonaylcarnitine | C18:1-OH | Hydroxyoctadecenoylcarnitine |
| C10 | Decanoylcarnitine | C18:2 | Octadecadienylcarnitine |
| | | | |
| **Amino Acids & Biogenic Amines** | | | |
| Ala | Alanine | Ac-Orn | Acetylornithine |
| Arg | Arginine | ADMA | Asymmetricdimethylarginine |
| Asn | Asparagine | SDMA | Symmetricdimethylarginine |
| Asp | Aspartate | total DMA | Total dimethylarginine |
| Cit | Citrulline | alpha-AAA | alpha-Aminoadipic acid |
| Gln | Glutamine | Carnosine | Carnosine |
| Glu | Glutamate | Creatinine | Creatinine |
| Gly | Glycine | Histamine | Histamine |
| His | Histidine | Kynurenine | Kynurenine |
| Ile | Isoleucine | Met-SO | Methioninesulfoxide |
| Leu | Leucine | Nitro-Tyr | Nitrotyrosine |
| Lys | Lysine | OH-Pro | Hydroxyproline |
| Met | Methionine | PEA | Phenylethylamine |
| Orn | Ornithine | Putrescine | Putrescine |
| Phe | Phenylalanine | Sarcosine | Sarcosine |
| Pro | Proline | Serotonin | Serotonin |
| Ser | Serine | Spermidine | Spermidine |
| Thr | Threonine | Spermine | Spermine |
| Trp | Tryptophan | Taurine | Taurine |
| Tyr | Tyrosine | | |
| Val | Valine | | |
| **Monosaccharides** | | | |
| H1 | Sum of Hexoses (including Glucose) | | |

SM sphingomyelin

PC Phosphatidylcholine

Aa acyl-acyl

Ae acyl-alkyl

**Supplemental Tables 9 & 10.** The standards (**Supplemental Table 9**) and internal standards (**Supplemental Table 10**) were characterized using the MRM ion transitions and their voltages: declustering potentials (DP), collision energies (CE), and collision cell exit potentials (CXP) are listed below. Quinolinic Acid was characterized using spectra for picolinic acid and is reported as only the area under the curve ratio with the internal standard.

**Supplemental Table 9.**

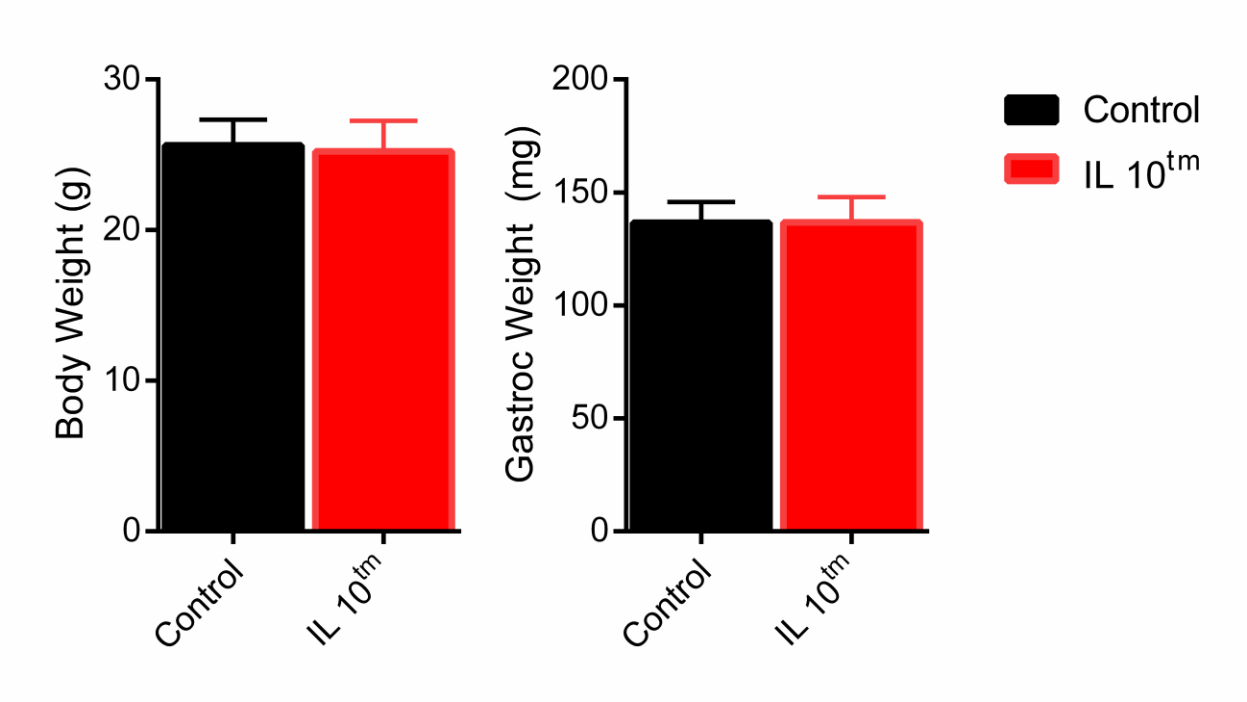
| Analyte | Q1/Q3 | DP | CE | CXP |
|---|---|---|---|---|
| 3-Hydroxy Kynurenine | 226.0/209.1 | 20 | 11 | 10 |
| Kynurenine | 209.0/94.0 | 20 | 19 | 15 |
| Xanthurenic Acid | 206.2/160.0 | 56 | 27 | 10 |
| Kynurenic Acid | 189.9/144.0 | 55 | 25 | 8 |
| Picolinic Acid | 124.0/78.0 | 10 | 25 | 10 |
| Tryptophan | 205.1/118.0 | 39 | 35 | 11 |
| Anthranilic Acid | 138.2/120.0 | 36 | 15 | 8 |
| Serotonin | 177.0/160.1 | 26 | 13 | 8 |

*Quinolinic Acid was characterized using spectra for picolinic acid and is reported as only the area under the curve ratio with the internal standard.

**Supplemental Table 10.**

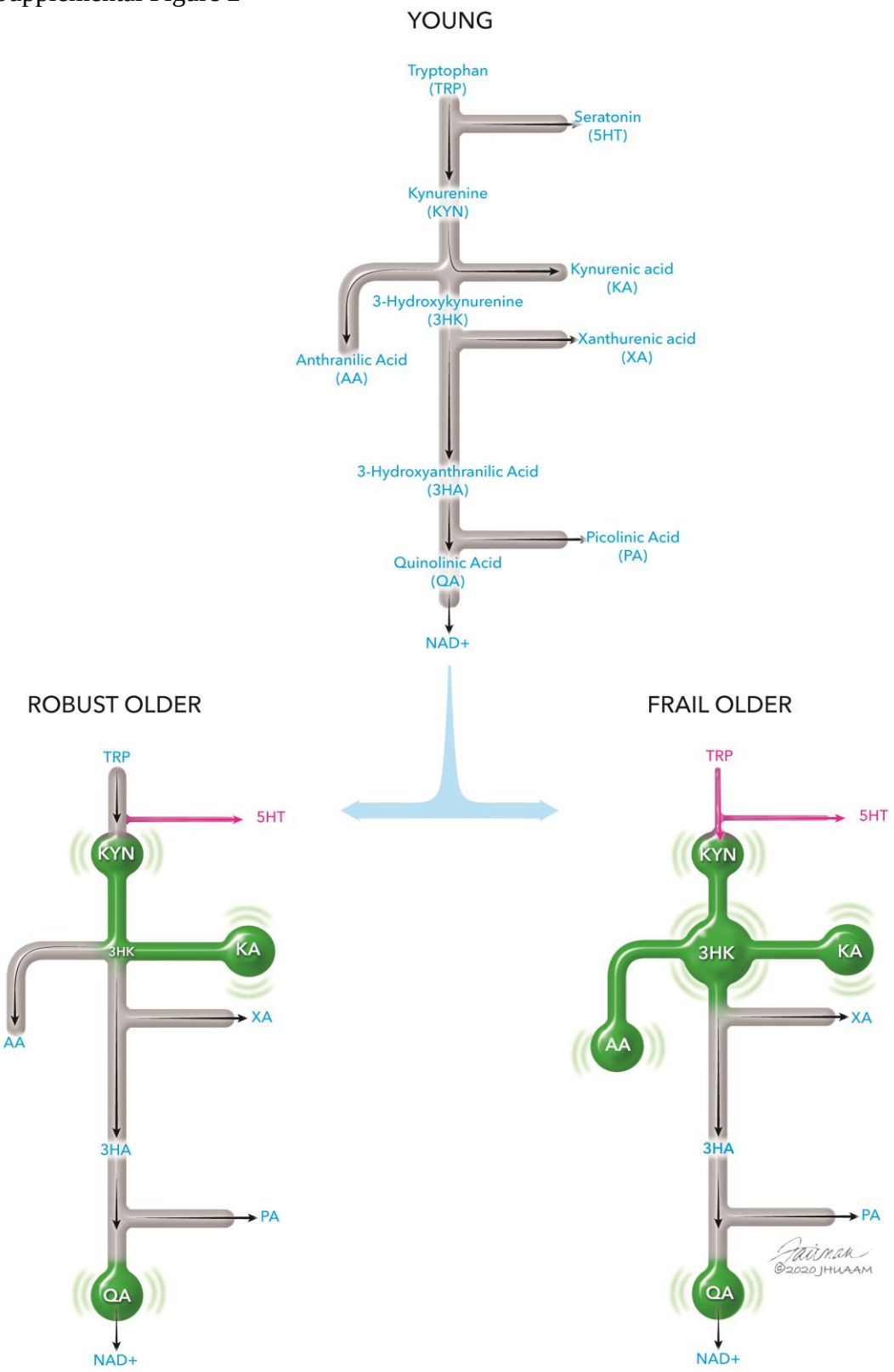
| Internal Standard | Q1/Q3 | DP | CE | CXP |
|---|---|---|---|---|
| $D_4$-KYN | 231.0/98.0 | 20 | 19 | 15 |
| $D_4$-XA | 210.0/164.0 | 56 | 27 | 10 |
| $D_5$-KA | 195.0/149.2 | 55 | 27 | 8 |
| $D_4$-PA | 128.1/82.1 | 10 | 25 | 10 |
| $D_5$-TRP | 210.1/122.0 | 30 | 35 | 10 |
| $D_3$-5HT | 181.1/164.1 | 26 | 13 | 10 |

**Supplemental Figure 1**



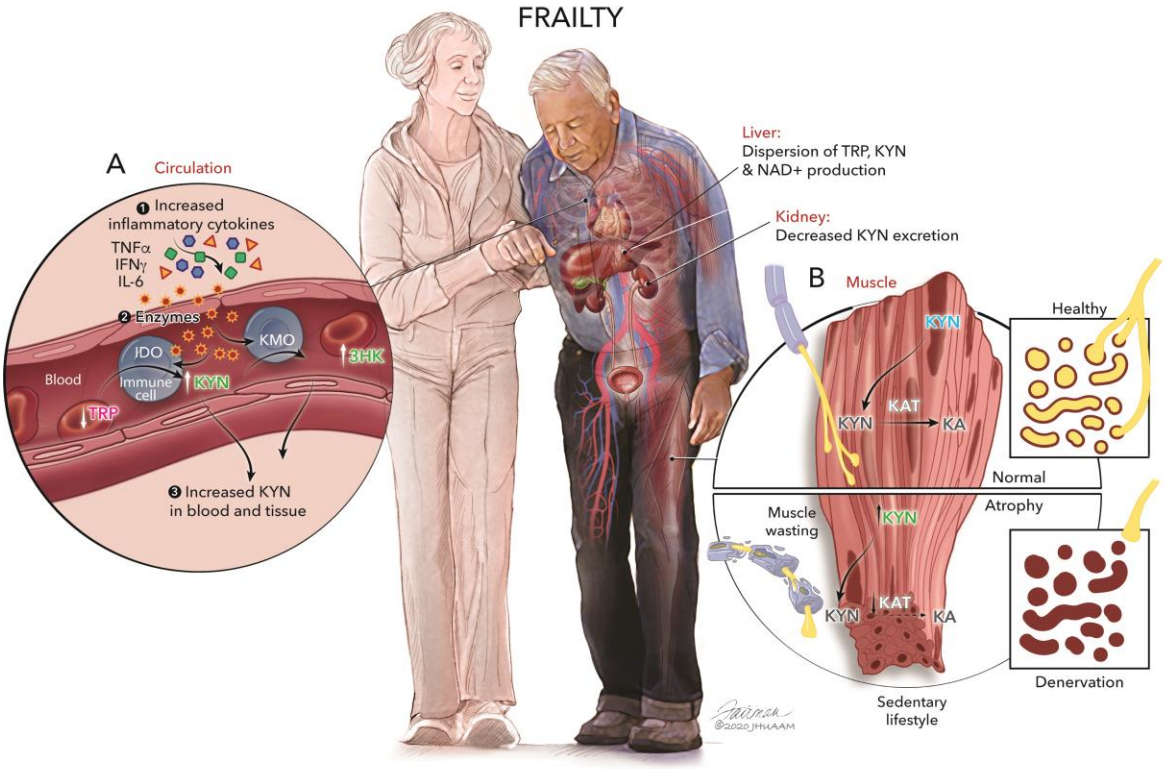

Supplemental Figure 1. Body weight and gastrocnemius weight from 3 month old IL $10^{tm}$ and control mice (n=10 per group)

Supplemental Figure 2




Supplemental Figure 2. Summary of kynurenine pathway changes with age & frailty

Supplemental Figure 3




Supplemental Figure 3. Schematic summarizing the physiological connections between inflammation, kynurenines and neuromuscular integrity. (A) Increased levels of inflammation trigger IDO and KMO in immune cells to produce more kynurenines. (B) These kynurenines can damage neuromuscular junctions leading to decreased neuromuscular integrity.