Supplementary Information for

# Index markers of chronic fatigue syndrome with dysfunction of TCA and urea cycles

Emi Yamano, Masahiro Sugimoto, Akiyoshi Hirayama, Satoshi Kume, Masanori Yamato, Guanghua Jin, Seiki Tajima, Nobuhito Goda, Kazuhiro Iwai, Sanae Fukuda, Koji Yamaguti, Hirohiko Kuratsune, Tomoyoshi Soga, Yasuyoshi Watanabe, Yosky Kataoka*

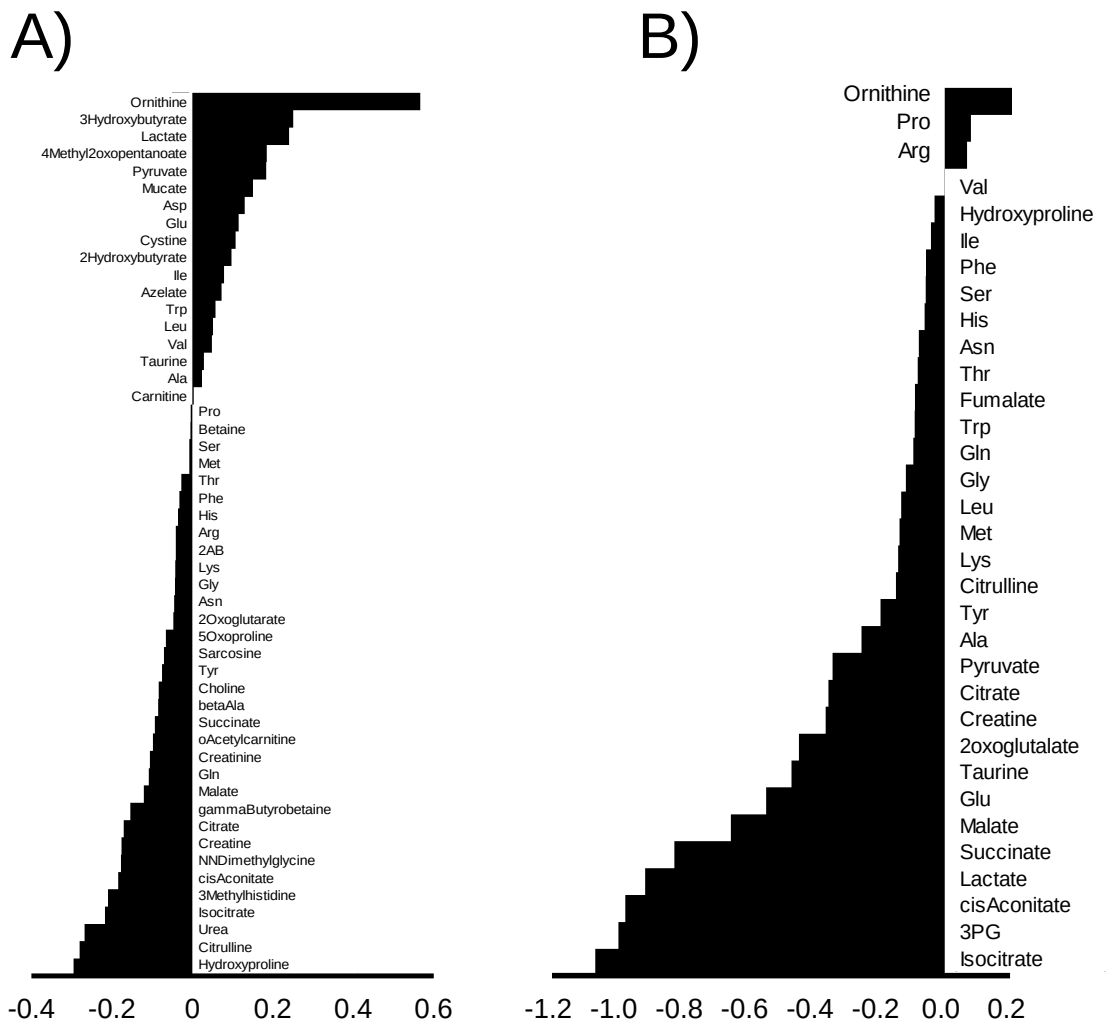


**Figure S1.** $Log_2$ fold changes of the mean concentration between CFS patients and healthy controls for training data **A)** and validation data **B)**.

**Table S1** Comparisons of glucose and representative metabolite concentrations between CFS patients and healthy controls in the training cohort.

| Name | Healthy controls | | CFS patients | | *P* value | Corrected *P* value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Glucose | 85.57 | 7.65 | 87.00 | 5.93 | 0.52 | 0.59 |
| Pyruvate | 130.43 | 30.52 | 148.16 | 47.27 | 0.087 | 0.16 |
| Lactate | 1375.06 | 394.35 | 1624.85 | 839.54 | 0.49 | 0.59 |
| Citrate | 183.63 | 40.98 | 163.10 | 36.03 | 0.010 | **0.049** |
| *cis*-Aconitate | 9.74 | 3.15 | 8.57 | 2.64 | 0.080 | 0.16 |
| 2-Oxoglutarate | 23.13 | 5.38 | 22.39 | 5.17 | 0.63 | 0.63 |
| Succinate | 13.24 | 4.05 | 12.41 | 3.59 | 0.30 | 0.46 |
| Malate | 12.00 | 3.01 | 11.04 | 3.16 | 0.047 | 0.12 |
| Arg | 94.31 | 23.98 | 91.64 | 30.66 | 0.39 | 0.54 |
| Urea | 2426.33 | 622.12 | 2015.10 | 686.34 | 0.0010 | **0.012** |
| Ornithine | 52.15 | 16.36 | 77.25 | 42.24 | 0.023 | 0.083 |
| Citrulline | 38.50 | 11.91 | 31.70 | 8.31 | 0.0030 | **0.026** |
| Glu | 37.59 | 13.71 | 40.71 | 17.38 | 0.55 | 0.59 |
| Gln | 917.43 | 218.58 | 851.15 | 178.37 | 0.16 | 0.27 |

The unit of glucose is mg/dl; the others are μM.

Mann–Whitney *U*-test was performed.

Significant corrected *P* values with a false discovery rate ($P < 0.05$) are in bold type.

SD, standard deviation.

**Table S2**. Ranking using SVM-FS

| Rank | Metabolite |
|---|---|
| 1 | Ornithine |
| 2 | Citrulline |
| 3 | Lactate |
| 4 | Isocitrate |
| 5 | Pyruvate |
| 6 | Succinate |
| 7 | Hydroxyproline |
| 8 | Taurine |
| 9 | Tyr |
| 10 | Val |
| 11 | Gln |
| 12 | Citrate |
| 13 | Trp |
| 14 | Ala |
| 15 | Glu |
| 16 | Leu |
| 17 | Phe |
| 18 | Creatine |
| 19 | Ile |
| 20 | Arg |
| 21 | Thr |
| 22 | *cis*-Aconitate |
| 23 | Pro |
| 24 | 2-Oxoglutarate |
| 25 | Gly |
| 26 | Malate |
| 27 | His |
| 28 | Lys |
| 29 | Ser |
| 30 | Asn |
| 31 | Met |

SVM-FS; Support vector machine–feature selection.