**Supplementary Materials:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Biochemical** | **Patient 3** | **Patient 4** | **Patient 5** |
| 1-methylhistidine | 0.976 | -0.068 | -0.722 |
| 1-methylimidazoleacetate | -0.665 | -0.042 | 2.110 |
| 1-palmitoylglycerol (16:0) | 3.584 | 3.146 | 2.518 |
| 3-methylhistidine | 1.362 | 0.499 | 0.398 |
| 4-imidazoleacetate | -1.101 | -2.255 | 1.176 |
| anserine | -0.445 | -0.450 | NA |
| beta-alanine | 0.121 | 0.860 | -0.308 |
| carnosine | NA | -0.805 | 1.866 |
| cis-urocanate | 3.667 | 2.766 | 6.509 |
| citramalate | 1.552 | 0.303 | NA |
| glutamate | -0.773 | -0.235 | 1.393 |
| glutamine | -0.383 | 0.219 | 0.874 |
| histidine | -1.258 | -1.256 | -0.009 |
| hydantoin-5-propionic acid | -1.126 | -0.961 | NA |
| imidazole lactate | 0.010 | -0.319 | 0.661 |
| imidazole propionate | 3.507 | 3.284 | 2.662 |
| N-acetyl-1-methylhistidine\* | 0.599 | -1.216 | NA |
| N-acetyl-3-methylhistidine\* | NA | NA | NA |
| N-acetyl-aspartyl-glutamate (NAAG) | -0.032 | -0.944 | 0.189 |
| N-acetylcarnosine | 0.122 | 1.037 | -1.243 |
| N-acetylglutamate | -0.880 | -0.728 | 0.915 |
| N-acetylglutamine | NA | NA | -0.121 |
| N-acetylhistidine | -0.744 | -1.135 | 4.115 |
| pyroglutamine | -0.405 | -1.944 | 1.244 |
| trans-urocanate | 4.925 | 5.013 | 8.591 |

**Table 3**: Untargeted metabolomics identifies multiple intermediates in histidine metabolism in plasma for possible urocanic acidemia. Shown above are Z-Scores for patients found in our database with a pattern of abnormalities suggestive of an underlying deficiency in urocanase enzymatic activity.

|  |  |
| --- | --- |
| **Biochemical** | **Patient 6** |
| 1-methylhistamine | 1.440 |
| 1-methylhistidine | 0.173 |
| 1-methylimidazoleacetate | 1.872 |
| 3-methylhistidine | -0.901 |
| 4-hydroxyglutamate | -0.883 |
| 4-imidazoleacetate | 2.802 |
| anserine | -0.335 |
| beta-alanine | -0.540 |
| carboxyethyl-GABA | 1.771 |
| carnosine | NA |
| cis-urocanate | 2.854 |
| citramalate | NA |
| formiminoglutamate | NA |
| gamma-aminobutyrate (GABA) | 2.599 |
| gamma-carboxyglutamate | -2.162 |
| glutamate | 1.061 |
| glutamine | 1.385 |
| histamine | 2.011 |
| histidine | 4.433 |
| homocarnosine | 1.695 |
| hydantoin-5-propionic acid | -1.230 |
| imidazole lactate | -0.316 |
| imidazole propionate | 2.037 |
| N-acetyl-1-methylhistidine\* | NA |
| N-acetyl-3-methylhistidine\* | NA |
| N-acetyl-aspartyl-glutamate (NAAG) | -0.135 |
| N-acetylcarnosine | -1.172 |
| N-acetylglutamate | -1.532 |
| N-acetylglutamine | -1.398 |
| N-acetylhistamine | NA |
| N-acetylhistidine | 1.022 |
| N-methyl-GABA | 0.490 |
| N-methylglutamate | NA |
| pyroglutamine\* | -0.210 |
| trans-urocanate | 7.493 |

**Table 4**: Untargeted metabolomics identifies multiple intermediates in histidine metabolism in urine for possible urocanic acidemia. Shown above are Z-Scores for a single patient found in our database with a pattern of abnormalities suggestive of an underlying deficiency in urocanase enzymatic activity.