|  |  |
| --- | --- |
| Relative increase in CLN3Q352X | Relative decrease in CLN3Q352X |
| Pyruvic acid | Glycerol |
| 3-Hydroxymethylglutaric acid | Pantothenic acid |
| Malic acid | Glycerol-3-phosphate |
| Myo-inositol | Creatinine |
|  | Proline |
|  | Pentose\_1 |
|  | Serine |
|  | γ-aminobutyric acid |
|  | Pentose\_2 |
|  | 3-Hydroxybutyric acid |
|  | Butanoic acid |
|  | Fructose |
|  | N-Acetyl-L-aspartic acid |
|  | Glycine |
|  | Threonine |
|  | Methionine |
|  | Leucine |
|  | Phenylalanine |
|  | Isoleucine |
|  | Glutamic acid |
|  | Valine |
|  | Erythronic acid |
|  | Cysteine |
|  | Alanine |
|  | Mannose |
|  | Aspartic acid |

**Table 1.** Metabolic changes detected by hierarchical clustering and ANOVA.

**Table 2.** List of significant (p<0.05) metabolic changes detected by Mann-Whitney test between genotypes. Arrows show the trend of the change in the CLN3Q352X cerebral organoids, compared to the Control ones.

|  |  |
| --- | --- |
| Metabolite | P value |
| Pyruvic acid ↑ | 0.0079 |
| meso-Erythritol ↓ | 0.0079 |
| Glycerol\_3TMS ↓ | 0.0079 |
| Pantothenic acid ↓ | 0.0079 |
| Glycerol-3-phosphate ↓ | 0.0079 |
| Lysine ↓ | 0.0079 |
| Creatinine ↓ | 0.0079 |
| Proline ↓ | 0.0079 |
| Tryptophan ↓ | 0.0079 |
| Pentose\_1 ↓ | 0.0079 |
| Serine ↓ | 0.0079 |
| γ-amino butyric acid ↓ | 0.0079 |
| Tyrosine ↓ | 0.0079 |
| Carbonic acid ↓ | 0.0079 |
| Pentose\_2 ↓ | 0.0159 |
| 3-Hydroxybutyric acid ↓ | 0.0159 |
| Succinic acid ↑ | 0.0159 |
| Spermidine ↓ | 0.0317 |

|  |  |
| --- | --- |
| Metabolite | P value |
| Tryptophan ↓ | 0.0079\* |
| Lysine ↓ | 0.0079\* |
| γ-amino butyric acid ↓ | 0.0079\* |
| Creatinine ↓ | 0.0079\* |
| Ethanolamine ↓ | 0.0556 |
| Ethanolamine phosphate ↓ | 0.0556 |
| Lactic acid ↓ | 0.0952 |
| Valine ↓ | 0.0952 |
| Glutamine ↓ | 0.0952 |
| Isoleucine ↓ | 0.1508 |
| Leucine ↓ | 0.1508 |
| Dopamine ↑ | 0.1508 |
| Glutamic acid ↓ | 0.3095 |
| Aspartic acid ↓ | 0.6667 |
| *Myo*-inositol ↑ | 0.6667 |
| Taurine ↓ | 0.8016 |

**Table 3.** List of changes in metabolites related to cerebral tissue. Arrows show the trend of the change in the CLN3Q352X cerebral organoids, compared to the Control ones. Asterisk mark significant changes.