

## NPDX ASD Test Results

**Patient ID/MRN:** X12345

**Patient Name:** Doe, John M.

**Date of Birth:** 6/22/2019

**Sex:** M

**Specimen Type:** Blood Plasma

**Test:** NPDX ASD Test v.2

**NeuroPointDX Sample ID:** A00042

**Ordering Physician:** Jane R. Smith, MD

**Specimen Collected Date:** 12/5/2020

**Specimen Received Date:** 12/7/2020

**Report Date:** 12/21/2020

**Report Time:** 16:10:00

### NPDX ASD Test Description

The NPDX ASD Test v.2.0 is comprised of two metabolic panels that measure the levels of metabolites in blood plasma using Mass Spectrometry. One panel measures 32 amines (CPT Code 0063U) and the other panel measures 16 metabolites involved in energy metabolism, mitochondrial metabolites, microbiome derived products and others (CPT Code 0139U). Algorithmic analysis of these metabolite levels is used to identify 23 metabolic subtypes (metabotypes) known to be associated with autism spectrum disorder (ASD) classification using the ADOS-2 behavioural assessment as the reference method. The metabolic subtypes were validated in a clinical study of children 18-48 months old (1,2).

### Result Summary

**POSITIVE** - patient has metabolic signature associated with ASD

The algorithmic analysis indicates patient has form(s) of metabolic dysregulation associated with autism spectrum disorder (ASD). A summary of positive metabotype results is shown below.

- Ethanolamine and Alpha-Ketoglutarate: The sample results indicate a positive metabolic profile associated with ASD. The imbalance detected indicates an increase in concentration of Ethanolamine relative to the concentration of Alpha-Ketoglutarate (6,7,8).
- Ornithine and Carnitine: The sample results indicate a positive metabolic profile associated with ASD. The imbalance detected indicates an increase in concentration of Ornithine relative to the concentration of Carnitine (1,5,6,7,8).
- Ornithine and Lysine: The sample results indicate a positive metabolic profile associated with ASD. The imbalance detected indicates an increase in concentration of Ornithine relative to the concentration of Lysine (1,2,6,7,8).
- Phenylalanine and Citrate: The sample results indicate a positive metabolic profile associated with ASD. The imbalance detected indicates an increase in concentration of Phenylalanine relative to the concentration of Citrate (1,5,6,7,8).
- Taurine and Alpha-Ketoglutarate: The sample results indicate a positive metabolic profile associated with ASD. The imbalance detected indicates an increase in concentration of Taurine relative to the concentration of Alpha-Ketoglutarate (1,5,6,7,8).

### **Additional Findings**

- A total of 27 analytes have tested outside the typical range (see attached table).
- Warning: Patient is not within the validated 18 to 48 month range.

### **Guidance**

Recommend follow up with neurodevelopment/ASD specialist for further evaluation. Some studies indicate dietary modification may be beneficial for patients with amine metabolic (3,4,5,6) or energy related (6,7,8) dysregulations. May want to refer patient to a registered dietitian nutritionist (RDN) for an evaluation of his/her diet and supplement intake.

EXAMPLE

## Metabotype Evaluation

### Alanine and Alpha-Ketoglutarate

- Alanine and Alpha-Ketoglutarate: This metabotype evaluates the level of Alanine relative to Alpha-Ketoglutarate.



### Ethanolamine and 4-Hydroxyproline

- Ethanolamine and 4-Hydroxyproline: This metabotype evaluates the level of Ethanolamine relative to 4-Hydroxyproline.



### Ethanolamine and Alpha-Ketoglutarate

- Ethanolamine and Alpha-Ketoglutarate: This metabotype evaluates the level of Ethanolamine relative to Alpha-Ketoglutarate.



### Ethanolamine and Carnitine

- Ethanolamine and Carnitine: This metabotype evaluates the level of Ethanolamine relative to Carnitine.



### Ethanolamine and Kynurenine

- Ethanolamine and Kynurenine: This metabotype evaluates the level of Ethanolamine relative to Kynurenine.



### Gamma-Aminobutyric Acid and BCAA\* (Leucine, Isoleucine, Valine)

- Gamma-Aminobutyric Acid and BCAA\*: This metabotype evaluates the level of Gamma-Aminobutyric Acid relative to BCAA (Isoleucine, Leucine, Valine).



### Glutamine and BCAA\* (Leucine, Isoleucine, Valine)

- Glutamine and BCAA\*: This metabotype evaluates the level of Glutamine relative to BCAA (Leucine, Isoleucine, Valine).



### Glycine and BCAA\* (Leucine, Isoleucine, Valine)

- Glycine and BCAA\*: This metabotype evaluates the level of Glycine relative to BCAA (Leucine, Isoleucine, Valine).



### Glycine and Citrate

- Glycine and Citrate: This metabotype evaluates the level of Glycine relative to Citrate.



### Lactate and Glutamic Acid

- Lactate and Glutamic Acid: This metabotype evaluates the level of Lactate relative to Glutamic Acid.



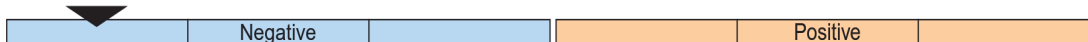
### Lactate and Homoserine

- Lactate and Homoserine: This metabotype evaluates the level of Lactate relative to Homoserine.



### Malate and Proline

- Malate and Proline: This metabotype evaluates the level of Malate relative to Proline.



### Ornithine and BCAA\* (Leucine, Isoleucine, Valine)

- Ornithine and BCAA\*: This metabotype evaluates the level of Ornithine relative to BCAA (Leucine, Isoleucine, Valine).



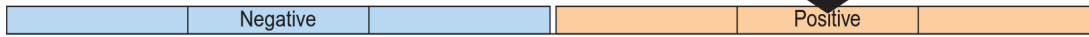
### Ornithine and Carnitine

• Ornithine and Carnitine: This metabotype evaluates the level of Ornithine relative to Carnitine.



### Ornithine and Lysine

• Ornithine and Lysine: This metabotype evaluates the level of Ornithine relative to Lysine.



### Phenylalanine and Citrate

• Phenylalanine and Citrate: This metabotype evaluates the level of Phenylalanine relative to Citrate.



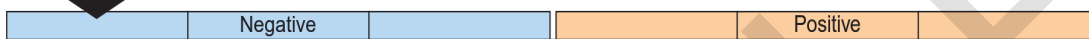
### Pyruvate and Aspartic Acid

• Pyruvate and Aspartic Acid: This metabotype evaluates the level of Pyruvate relative to Aspartic Acid.



### Pyruvate and Homocitrulline

• Pyruvate and Homocitrulline: This metabotype evaluates the level of Pyruvate relative to Homocitrulline.



### Pyruvate and Sarcosine

• Pyruvate and Sarcosine: This metabotype evaluates the level of Pyruvate relative to Sarcosine.



### Taurine and Alpha-Ketoglutarate

• Taurine and Alpha-Ketoglutarate: This metabotype evaluates the level of Taurine relative to Alpha-Ketoglutarate.



### Taurine and Phenylalanine

• Taurine and Phenylalanine: This metabotype evaluates the level of Taurine relative to Phenylalanine.



### Tryptophan and Alpha-Ketoglutarate

• Tryptophan and Alpha-Ketoglutarate: This metabotype evaluates the level of Tryptophan relative to Alpha-Ketoglutarate.



### Xanthine and 4-Hydroxyproline

• Xanthine and 4-Hydroxyproline: This metabotype evaluates the level of Xanthine relative to 4-Hydroxyproline.



\*BCAA: Branched-Chain Amino Acids, including Leucine, Isoleucine and Valine

## Table of Measured Metabolites

#	Analyte	Range (µM)	Result (µM)	Flag
1	4-Hydroxyproline†	0-16	41	High
2	Alanine†	158-314	494	High
3	Arginine†	38-98	169	High
4	Asparagine†	24-64	94	High
5	Aspartic Acid†	3-15	69	High
6	Beta-Alanine‡	1.8-7.8	8.4	High
7	Beta-Aminoisobutyric Acid†	0.5-4.9	2.1	
8	Citrulline†	18-50	38	
9	Ethanolamine†	0-10	14.4	High
10	Gamma-Aminobutyric Acid‡	0.18-0.42	0.33	
11	Glutamic Acid†	11-51	191	High
12	Glutamine†	373-709	837	High
13	Glycine†	113-261	545	High
14	Histidine†	45-106	138	High
15	Homocitrulline‡	0.13-0.48	0.42	
16	Homoserine‡§	0.1-0.13	0.22	High
17	Isoleucine†	31-83	97	High
18	Kynurenine†	1.2-3	2.6	
19	Leucine†	64-164	201	High
20	Lysine†	77-181	199	High
21	Methionine†	11-27	31	High
22	Ornithine†	24-64	98	High
23	Phenylalanine†	35-67	122	High
24	Proline†	93-221	258	High
25	Sarcosine‡	0.6-2.3	1.4	
26	Serine†	77-169	153	
27	Serotonin‡	0.04-0.58	0.79	High
28	Taurine†	24-92	144	High
29	Threonine†	48-140	202	High
30	Tryptophan†	5-57	101	High
31	Tyrosine†	34-82	103	High
32	Valine†	133-273	349	High
33	Alpha-Ketoglutarate‡	5.2-10.2	9.9	
34	Carnitine‡	14.4-39.8	30.9	
35	Citrate‡	82-172	178	High
36	Fumarate‡	0-1	0.9	
37	Hypoxanthine‡	1.4-9	8	
38	Inosine‡§	0.3-4.3	3.7	
39	Lactate‡	556-1862	827	
40	Malate‡	2-5	4	
41	Pyruvate‡	42-135	77	
42	s-Sulfocysteine‡	0-1	0.9	
43	Succinate‡	0-1	3.2	High
44	Urate‡	142-318	276	
45	Xanthine‡	0.7-1.8	1.6	

† Reference values are of typically developing children of 18 to 48 months from Blau et. al (2008), Laboratory Guide to the Methods in Biochemical Genetics. Springer.

‡ Reference values are the 2.5 - 97.5 percentiles obtained from typically developing children 18 to 48 months in the CAMP-01 study (1,2).

§ The lower level of the typical range is below the limit of quantification of this assay.

### **Test Limitations**

Clinical study was performed using fasting, blood-plasma samples from patients 18-48 months of age. Test performance has not been evaluated in patients younger than 18 months or older than 48 months of age. A negative NPDX ASD Test result indicates a metabolic subtype associated with ASD classification has not been identified at this time. A negative result does not guarantee a patient will not be classified as having ASD. Additional information about the NPDX ASD Test may be found at [www.NeuroPointDX.com](http://www.NeuroPointDX.com). These results are interpreted with respect to metabolotypes related to ASD as validated in the CAMP study (1,2). Interpretation of metabolite levels outside the typical range can be obtained by consulting with a physician.

**This test was developed, and its performance characteristics determined, by NeuroPointDX. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA and is certified by CAP as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.**

## **References**

1. Smith, A., et al. Amino acid dysregulation metabolotypes: potential biomarkers for diagnosis and individualized treatment for subtypes of autism spectrum disorder. 2019 *Biological Psychiatry*, 85,(4)345-355.
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4. Novarino et al. 2012 Mutations in BCKD-kinase lead to a potentially treatable form of autism with epilepsy. *Science* 338, 394-397.R[-14]C
5. Garcia-Cazorla et al. 2014 Two novel mutations in the BCKDK (Branched-Chain Keto-Acid Dehydrogenase Kinase) gene are responsible for a neurobehavioral deficit in two pediatric unrelated patients. *Human Mut.* 35 (4), 470-477.5
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