

## **Supplemental Material:**

### **Supplementary Figure 1. Double electron electron resonance signal analysis.** (Left)

Time dependent decay of DEER signal (open circles) with respective fits (in solid line) determined using Tikhonov regularization for the extracellular (A) and intracellular (B) reporter pairs. (Right) The chosen regularization parameter is circled in the respective L-curves from Tikhonov analysis to approximate the best distance distribution as shown in Figure 4.

### **Clinical Information:**

Proband (male) is the eldest of two children and heterozygous for the mutation described herein.

**Patient ID:** AC04-0029-01 (proband)

**Event:** *SLC6A3* *de novo* missense (T356M) mutation

At the time of testing, patient was a 66-69-month-old non-Hispanic male Caucasian diagnosed with autism (on both ADOS and ADIR). Maternal interview on pregnancy provided the following details: Mother experienced anemia during pregnancy (gestational age = 39 weeks). Labor was induced (use of Pitocin) because of failure to progress (Note: no C-section was done). Child was born 8 lbs 6 oz (134 ounces), with no other delivery issues.

Subset and composite scores on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) indicate normal intelligence. Full Scale IQ was Average (94), and the subsets of Verbal-IQ and Performance-IQ was scored as Average (101) and Low

Average (86) respectively, indicating normal intelligence.

ADIR revealed deficits across all four subsets: (1) Reciprocal Social Interaction (score=13; cutoff=10); (2) Abnormalities in Communication (score=13; cutoff=8); (3) Restricted, Repetitive and Stereotyped Patterns of Behavior (score=4; cutoff=3); (4) Development Evident at or before 36 Months (score=1; cutoff=1).

Patient experienced a delay in speech requiring therapy. No history of seizures, gastrointestinal conditions, sleep deficits, and no diet restrictions. Currently taking multivitamins, with no use of other medications (besides amoxicillin, Tylenol, and Benadryl).

No family history for psychiatric illness requiring hospitalization. Known history of Asperger's Disorder (Mother's cousin's son), and depression (Father's paternal uncle).

**Patient ID:** AC04-0029-02 (father)

Father is an adult non-Hispanic Caucasian male. Age at conception of proband is 36. Slightly above normative range of intelligence (IQ=118; Wechsler Adult Intelligence Scale). No presence of broader autism phenotype, and no psychiatric medication use current or past. No co-morbid diagnoses. He holds a postgraduate degree and reports an annual household income of \$81-101k.

**Patient ID:** AC04-0029-03 (mother)

Mother is an adult non-Hispanic Caucasian female. Age at conception of proband is 32.

Above normative range of intelligence (IQ=131; Wechsler Adult Intelligence Scale); no presence of broader autism phenotype, and no psychiatric medication use current or past. No co-morbid diagnoses. She holds a postgraduate degree and reports an annual household income of \$81-101k. No medication use reported for mother before, during, or after pregnancy except for epidural during labor.

**Patient ID:** AC04-0029-04 (sibling)

Sibling is a non-Hispanic Caucasian 3 year old (37 months) of unspecified sex. Normative intelligence (IQ=118; WPPSI). No behavioral problems reported. No medication use endorsed for current or past. No comorbid diagnoses.