

Supplementary information about the two human patients with *SHANK3* duplication

Individual 1.

At the time of evaluation, she was an 11 year-old girl attention deficit hyperactivity disorder (ADHD), combined type. This was treated with Adderall XR 25 mg by mouth daily, with minimal improvement on her behavior, as reported by her adoptive mother. The girl had a history of developmental delay and learning problems, requiring an individualized educational plan. Multiple behavioral problems were reported, including poor impulse control, short attention span, kleptomania, destructive behavior, and easy distractibility by auditory stimuli.

She had a history of two generalized tonic-clonic seizures, both at the age of 2 years, without any associated fevers, toxic exposures, traumas of hypoxia.

Physical examination was significant for minor dysmorphic features, including upslanting palpebral fissures, epicanthus inversus, and a pinched nose with anteverted nares.

The patient had brain imaging by magnetic resonance tomography at 2 years of age, which revealed a structurally normal brain.

Chromosome microarray analysis revealed a heterozygous interstitial duplication of chromosome 22q13.33, with a minimal size of 64 kb (chr22:49,461,602-49,525,130) and a maximal size of 240 kb (chr22:49,451,468-49,691,432), with 39 oligonucleotides within the duplicated interval. Coordinates are based on hg18.

Individual 2.

He was a 35 year-old male with a longstanding history of bipolar disorder and epilepsy. He had generalized tonic-clonic seizures since childhood, with several episodes of status epilepticus. At the time of evaluation, he was treated with levetiracetam, providing excellent seizure control, and he had been seizure free for more than two years.

He reported having had significant learning problems in school, and had received special education during middle school. He managed to graduate from high school when he was 20 years old. During adolescence, he was diagnosed with bipolar disorder, based on mood swings, and anger management problems. He has been hospitalized three times in an inpatient psychiatric facility. He reported several suicide attempts. At the age of 35 years, he is receiving social security disability benefits, being unable to hold a job. He never had any brain imaging.

Chromosome microarray analysis revealed a heterozygous interstitial duplication of chromosome 22q13.33, with a minimal size of 115 kb (chr22:51,063,071-

51,178,264) and a maximal size of 302 kb (chr22:51,002,394-51,304,566) with 46 oligonucleotides within the duplicated interval. Coordinates are based on hg19.