### Supplementary Table 2 Clinical features of patients with recurrent DDX3X variants

| Variant position | Variant type | AA position (CSM) | Years/sex | Seizure type | Other findings | Neurologic findings | Non-neurologic findings | Brain findings | MRI | Ref. |
|------------------|--------------|-------------------|-----------|--------------|----------------|--------------------|------------------------|----------------|-----|------|
| c.236G>A/p.R79K  | De novo      |                   | 29/M      | NS ID        | Progressive spastic paraparesis, behavior problems, decreased lower extremity strength | Macrocephaly, dysarthria | Learning disorder, mixed expressive-receptive language disorder | CCH, VE      | (13) |
| c.236G>A/p.R79K  | De novo      |                   | 25/M      | NS ID        | Progressive spastic paraparesis, tremor, behavior problems, decreased lower extremity strength | Learning disorder, mixed expressive-receptive language disorder | CCH, VE      | (13) |
| c.828_831delAG   | De novo      | D1 (Ia)           | 15/F      | NS Moderate  | Normal          | Dysmorphic features | NP                     | (21)          |
| c.828_831delAG   | De novo      | D1 (Ia)           | 12/F      | NS Mild      | Normal          | Dysmorphic features | NP                     | (21)          |
| c.1126C>T/p.R376C| De novo      | D1                | 4/F       | NS Severe    | Hypotonia, movement disorder | Hyperlaxity, visual problems | CCH                  | (10)          |
| c.1126C>T/p.R376C| De novo      | D1                | 8/F       | NS Severe    | Movement disorder, behavior problems | Hyperlaxity, skin abnormalities, precocious puberty | Normal                  | (10)          |
| c.1126C>T/p.R376C| De novo      | D1                | 3/M       | NS Mild      | Hypotonia, behavior problems | Normal                  | CCH, VE      | (10)          |
| c.1535_1536delA  | De novo      | D2(Va)            | 18/F      | NS Moderate  | Normal          | Hyperlaxity, precocious puberty | Normal                  | (10)          |
| c.1535_1536delA  | De novo      | D2(Va)            | 10/F      | NS Mild      | Hypotonia       | Normal                  | VE                     | (10)          |
| c.1535_1536delA  | De novo      | D2(Va)            | 10/F      | NS ID        | Hypotonia, ADHD | Microcephaly, dysmorphic features | CCH, VE      | (22)          |
| c.1600C>T/p.R534C| De novo      | D2(VI)            | 47/F      | NS Severe    | Hypotonia       | Microcephaly, short stature, CCH, dysmorphic features, polymicrogyria unilateral renal agenesis, difficulty feeding as a child | Normal                  | (18)          |
| c.1600C>T/p.R534C| De novo      | D2(VI)            | 1/F       | GTCS DD      | Dystonia and choreoathetoid movements | IUGR, poor feeding, low Abnormal weight, frequent apnea signal in the episodes, central blindness thalamus | Normal                  | (18)          |
| c.1703C>T/p.P568L| De novo      | CTE               | 11/F      | NA Severe    | Hypotonia, movement disorder | Microcephaly, visual problems, scoliosis, low weight | CCH, VE      | (10)          |
| c.1703C>T/p.P568L| De novo      | CTE               | 10/F      | IS Severe    | Hypotonia       | Microcephaly, short stature, CCH, VE, delayed hypermobility, visual delayed problems, hearing loss, myelination dysmorphic features, scoliosis, respiratory distress, VSD | CCH, VE, VE, delayed | (18)          |
| c.1703C>T/p.P568L| De novo      | CTE               | 7/F       | NS ID/DD     | Hypotonia with decreased muscle mass | Microcephaly, short stature, VE, delayed cortical visual impairment, myelination dysmorphic features | CCH, VE      | (18)          |

AA: Amino Acid; ADHD: Attention Deficit Hyperactivity Disorder; AS: Absence Seizures; ASD: Atrial Septal Defect; CCH: Corpus Callosum Hypoplasia; CM: Cortical Malformation; CSM: Conserved Sequence Motifs; CTE: C-terminal extensions of DDX3X; D1/D2: The functional core of DDX3X, composed
of two RecA-like domains; DD: Developmental Delay; F: Female; GTCS: Generalized Tonic-Clonic Seizures; ID: Intellectual Disability; IS: Infantile Spasms; IUGR: Intrauterine Growth Retardation; M: Male; MRI: Magnetic Resonance Imaging; NA: Not Available; NP: Not Performed; NS: No Seizures; PDA: Patent Ductus Arteriosus; Ref.: Reference; VE: Ventricular Enlargement; VSD: Ventricular Septal Defect. Variants c.1244T>A/p.I415N and c.1052G>A/p.R351Q were not listed as comprehensive clinical presentations were unavailable.