Supplementary Material

Table S.1 Detailed Clinical Description of Patients with Genetic Variants Identified

Gene	Age	Risk Factor	Clinical Description
SPAST (MIM: 604277)	10	N/A	Spastic quadriplegia; born 4.12 lbs at 36 weeks gestation by C-section. Has a twin and is twin B. History of delayed milestones beginning around 8-10 months old. Diagnosed with CP[a] at 2 years old. Abnormal MRI at 6 years old showed mild degree of peritrigonal incomplete myelination. Surgical history includes right pelvic and femoral osteotomy and dorsal rhizotomy. Patient was a GMFCS[b] 3 before surgery, but after surgery progressed to GMFCS[b] 4. Patient receives physical therapy.
L1CAM (MIM: 308840)	13	N/A	Diplegic CP[a], GMFCS[b] 3+; born 8 lbs at 39 weeks gestation by C-section. History of hydrocephalus. History of motor and language delays. He is unable to write but can read in Spanish at a 1st grade level. Surgical history includes bilateral calcaneal osteotomies and medial reefing.
ATM (MIM: 607585)	6	Intraventricular stroke	Quadriplegic CP[a] with right hemiparesis; born 6 lbs 8oz. by C-section. History of intraventricular stroke and unspecified cerebrovascular disease/stroke. Spent one week in the hospital after birth due to seizures, currently no seizures. Patient has multiple cafe au lait spots and a history of global developmental delays.
SCN2A (MIM: 182390)	13	N/A	Spastic hemiplegic CP[a]; born 9.2 lbs at 40 weeks gestation. History of seizures onset at 19 months. Abnormal MRI at 3 years old shows borderline thin corpus callosum. Patient is non-verbal. Patient has a history of neuro-muscular scoliosis and congenital microcephaly.

SMARCB1 (MIM: 601607)	10	Prematurity, birth asphyxia	Spastic CP[a]; born 6.2 lbs at 28 weeks gestation by vaginal delivery. History of hypoxia. History of severe scoliosis, global developmental delays, cortical visual impairment, nystagmus, strabismus, developmental delay, duplicated right collecting system with mild right hydronephrosis, sensorineural hearing loss, and short stature.
ZSWIM6 (MIM: 615951)	5	Intraventricular hemorrhage/ stroke	Spastic hemiplegic CP[a]; born 6 lbs at 37.5 weeks gestation by cesarean section delivery. History of Intraventricular hemorrhage/stroke. History of developmental delays, attention deficit disorder and autism.
PPT1 (MIM: 600722)	4	N/A	Quadriplegic CP[a]; born 7 lbs at 36 weeks gestation by vaginal delivery. Patient has microcephaly, global developmental delays, seizures onset at 4 years old, profound hypotonia, and distal spasticity. Patient has a paternally inherited *CDK5RAP2* mutation associated with microcephaly type, primarily a recessive disorder that was clinically confirmed on whole exome sequencing. *CDK5RAP2* deletion/duplication analysis was normal.
SCN2A (MIM: 182390)	5	Intraventricular hemorrhage	Spastic quadriplegia; born 7.3 lbs at 40 weeks gestation by emergency cesarean section delivery. Patient has severe global developmental delays, absent speech, cortical blindness, precocious puberty, hirsutism, contractures, dysmorphic features, and seizures onset at 2.5 years old.
GNAO1 (MIM: 139311)	15	Intraventricular hemorrhage, birth asphyxia	Right sided hemiplegia; born 8.1 lbs at 40 weeks gestation by vaginal delivery. Patient has parkinsonism, developmental delays, right sided hemiparesis, spasticity, difficulty walking, and significant ataxia toe walking. Patient had a normal MRI at 2 years old.
MECP2 (MIM: 300005)	1	Birth asphyxia	Spastic hemiplegia; born 5.98 lbs at 40 weeks gestation by cesarean section delivery. Failure to thrive, global developmental delay, generalized hypotonia, spasticity, history of metatarsus adductus, mild dysmorphism, and hypotonia

PANK2 (MIM: 606157)	19	Birth asphyxia	Spastic quadriplegia; born 7.02 lbs at 40 weeks gestation by vaginal delivery. History of generalized dystonia, severe scoliosis, developmental delays, and hypothyroidism. Patient is neurogenic bladder - intermittent catheter dependent. Surgical history includes permanent gastrostomy. History of hospitalization for aspiration pneumonia. Diagnosis of pantothenate kinase-associated neurodegeneration (PKAN) due to mutation in the *PANK2* gene.
SCN1A (MIM: 182389)	14	Birth asphyxia, intraventricular stroke/hemorrhage	Spastic quadriplegic CP[a]; born 6.5 lbs at 36 weeks gestation by C-section. History of developmental delays, Seizures, FT uncomplicated birth. Septic infection onset at 6 months old and frequent aspiration pneumonias since initial infection. Abnormal MRI at 5 years old showed cerebral atrophy and temporal arterial stenosis.
COL4A1 (MIM: 120130)	11	Birth asphyxia	Spastic quadriplegic CP[a]; born at 6.12 lbs at 39 weeks gestation by vaginal delivery. History of aspiration. inability to breath with oxygen desaturation as of 6 months
DOCK6 (MIM: 614194)	1	Periventricular stroke	Left-sided Hemiplegia; born 5 lbs at 39 weeks gestation by induced vaginal delivery. History of developmental delays, microcephaly, retinal and eye findings. Abnormal MRI at 11 months old showed thin or partially absent corpus callosum. History of chronic mild left hemiparasis and right gaze preference, failure to thrive, and possible aicardi syndrome. Epilepsy onset at 1 years old and abnormal EEG concerning for hemihypsarrhythmi. Periventricular leukomalacia on MRI at 14 months old.
COL12A1 (MIM: 120320)	40	Prematurity	Spastic quadriplegic CP[a]; GMFCS[b] II that progressed to GMFCS[b] III from ages 10 to 24. Born 8.4 lbs at 31 weeks gestation by vaginal delivery. Patient has mild S-shaped thoracolumbar scoliosis and mild thoracic kyphosis, chronic hip pain, and arthralgia of left knee.
GARS1 (MIM: 600287)	30	Birth asphyxia	Quadriplegic CP[a], dystonic CP[a]; born 8 lbs at 39 weeks gestation by vaginal delivery. History of psychiatric issues and chronic bilateral low back pain with sciatica.

ABCD1 (MIM: 300371)	42	Prematurity, birth asphyxia	Spastic hemiplegic CP[a]; born prematurely 8.4 lbs at 30 weeks gestation by vaginal delivery. History of birth asphyxia. Right-hand dominant spastic hemiplegic with mild degenerative changes of the knees. Diagnosed with spastic diplegic CP[a] at 2 years old.
MFN2 (MIM: 608507)	42	Prematurity, birth asphyxia	Spastic hemiplegic CP[a]; born prematurely 8.4 lbs at 30 weeks gestation by vaginal delivery. History of birth asphyxia. Right-hand dominant spastic hemiplegic with mild degenerative changes of the knees. Diagnosed with spastic diplegic CP[a] at 2 years old.
TENM4 *(*MIM: 610084)	27	Prematurity	Left hemiplegic CP[a], GMFCS[b] 1; born prematurely 3 lbs at 33 weeks gestation by vaginal delivery, NICU for 7 weeks.
ZFHX3 (MIM: 104155)	38	N/A	Spastic diplegic CP[a]; born 5lbs, 13 oz. at 31 weeks gestation by vaginal delivery. Delayed in physical development such as walking and standing. Patient has bipolar disorder and hypothyroidism. Patient experiences tremors of his extremities that occur with increasing stress and exhaustion.
CSMD1 (MIM: 608397)	28	Prematurity	Spastic diplegic CP[a]; born prematurely 7.5 lbs at 28 weeks gestation by vaginal delivery. Suffers from occasional back pain when she walks. Surgical history includes a rhizotomy at age 15. Patient currently received physical therapy. Patient is a high functioning individual and works as an after school teacher. Has a history of depression. Family history is significant for mother with schizophrenia and depression and who passed away at 38 years old.

CP[a]; cerebral palsy, GMFCS[b]; gross motor function classification system

Table S.2 Genes Previously Associated with CP in Literature

Gene	Source
ADD3 (MIM: 601568)	Van Eyk, Corbett and MacLennan (15)
AGAP1 (MIM: 608651)	McMichael et al. (10)
AKT3 (MIM: 611223)	Matthews et al. (19)
ALDH18A1 (MIM: 138250)	Spastic Paraplegia Foundation (18)
ALK (MIM: 105590)	Jin et al. (20)
ALS2 (MIM: 205100)	Van Eyk, Corbett and MacLennan (15)
AMPD2 (MIM: 102771)	Takezawa et al. (17)
AP4B1 (MIM: 607245)	Van Eyk, Corbett and MacLennan (15)
AP4E1 (MIM: 607244)	Van Eyk, Corbett and MacLennan (15)
AP4M1 (MIM: 602296)	Van Eyk, Corbett and MacLennan (15)
AP4S1 (MIM: 607243)	Van Eyk, Corbett and MacLennan (15)
ASXL1 (MIM: 612990)	Matthews et al. (19)
ATL1 (MIM: 606439)	Jin et al. (20)
ATP1A3 (MIM: 182350)	Matthews et al. (19)
ATP8A2 (MIM: 605870)	Matthews et al. (19)
CACNA1A (MIM: 601011)	Takezawa et al. (17)
CACNA2D3 (MIM: 606399)	Presented at the ICPGC[a] meeting 2019 (23)
CD99L2 (MIM: 300846)	McMichael et al. (10)
CDC42BPA (MIM: 603412)	Presented at the ICPGC[a] meeting 2019 (23)
CDK5RAP1 (MIM: 608200)	Presented at the ICPGC[a] meeting 2019 (23)
CHRNA1 (MIM: 100690)	Matthews et al. (19)
COL4A1 (MIM: 120130)	Van Eyk et al. (21)
CSTB (MIM: 601145)	Matthews et al. (19)
CTNNB1 (MIM: 116806)	Takezawa et al. (17)
CYP2U1 (MIM: 615030)	Takezawa et al. (17)
CYP7B1 (MIM: 603711)	Spastic Paraplegia Foundation (18)
DARS2 (MIM: 610956)	Presented at the ICPGC[a] meeting 2019 (23)
DDC (MIM: 107930)	Lee et al. (22)
DDHD2 (MIM: 615003)	Spastic Paraplegia Foundation (18)
DGKZ (MIM: 601441)	Matthews et al. (19)
DGUOK (MIM: 601465)	Van Eyk, Corbett and MacLennan (15)
DHX32 (MIM: 607960)	Jin et al. (20)
DMXL1 (MIM: 605671)	Presented at the ICPGC[a] meeting 2019 (23)
EHMT1 (MIM: 607001)	Matthews et al. (19)
ELP2 (MIM: 616054)	Van Eyk, Corbett and MacLennan (15)
EPHA4 (MIM: 602188)	Matthews et al. (19)
ERLIN2 (MIM: 611605)	Van Eyk, Corbett and MacLennan (15)
FA2H (MIM: 611026)	Spastic Paraplegia Foundation (18)
FBXO31 (MIM: 609102)	Jin et al. (20)
GAD1 (MIM: 605363)	Van Eyk, Corbett and MacLennan (15)
GCH1 (MIM: 600225)	Lee et al. (22)
GCDH (MIM: 608801)	Matthews et al. (19)

GLUD1 (MIM: 138130)	Presented at the ICPGC [a]meeting 2019 (23)
GNAO1 (MIM: 139311)	Takezawa et al., Matthews et al. (17,19)
GPAM (MIM: 602395)	Presented at the ICPGC[a] meeting 2019 (23)
GRIN3A (MIM: 606650)	Presented at the ICPGC[a] meeting 2019 (23)
HNRNPL (MIM: 603083)	Presented at the ICPGC[a] meeting 2019 (23)
HSPD1 (MIM: 118190)	Spastic Paraplegia Foundation (18)
ITPA (MIM: 147520)	Matthews et al. (19)
ITPR1 (MIM: 147265)	Van Eyk, Corbett and MacLennan (15)
KANK1 (MIM: 607704)[b]	Van Eyk, Corbett and MacLennan, Matthews et al. (15,19)
KCNC3 (MIM: 176264)	Van Eyk, Corbett and MacLennan (15)
KCNJ6 (MIM: 600877)	Matthews et al. (19)
KCNQ2 (MIM: 602235)	Van Eyk, Corbett and MacLennan (15)
KDM2A (MIM: 605657)	McMichael et al. (10)
KDM5A (MIM: 180202)	Presented at the ICPGC meeting 2019 (23)
KDM5C (MIM: 314690)	McMichael et al. (10)
KIDINS220 (MIM: 615759)	Matthews et al. (19)
KIF1A (MIM: 601255)	Van Eyk et al. (21)
KMT2C (MIM: 606833)	Matthews et al. (19)
L1CAM (MIM: 308840)	McMichael et al. (10)
MAP3K3 (MIM: 602539)	Presented at the ICPGC[a] meeting 2019 (23)
MAP3K4 (MIM: 602425)	Presented at the ICPGC[a] meeting 2019 (23)
MAST1 (MIM: 612256)	McMichael et al. (10)
MECP2 (MIM: 300005)	Matthews et al. (19)
MRTFA (MIM: 606078)	Presented at the ICPGC[a] meeting 2019 (23)
MTCL1 (MIM: 615766)	Presented at the ICPGC[a] meeting 2019 (23)
MTMR1 (MIM: 300171)	Van Eyk et al. (21)
NAA10 (MIM: 300013)	Matthews et al. (19)
NAA35 (MIM: 617989)	McMichael et al. (10)
NBAS (MIM: 608025)	Matthews et al. (19)
PAK3 (MIM: 300142)	Matthews et al., McMichael et al. (10,16)
PALM (MIM: 608134)	Matthews et al. (19)
PANK2 (MIM: 606157)	Van Eyk, Corbett and MacLennan (15)
PDAP1 (MIM: 607075)	Presented at the ICPGC[a] meeting 2019 (23)
PDE10A (MIM: 610652)	Presented at the ICPGC[a] meeting 2019 (23)
PLP1 (MIM: 300401)	Matthews et al. (19)
PLXNA2 (MIM: 601054)	Matthews et al. (19)
PTK7 (MIM: 601890)	Presented at the ICPGC[a] meeting 2019 (23)
RANBP2 (MIM: 601181)	Matthews et al. (19)
REEP1 (MIM: 609139)	Spastic Paraplegia Foundation (18)
RFX2 (MIM: 142765)	McMichael et al. (10)
RHOB (MIM: 165370)	Jin et al. (20)
ROBO1 (MIM: 602430)	Presented at the ICPGC[a] meeting 2019 (23)
SCN2A (MIM: 182390)	Takezawa et al. (17)

SCN3A (MIM: 182391)	Matthews et al. (19)
SCN8A (MIM: 600702)	McMichael et al. (10)
SLC2A1 (MIM: 138140)	Presented at the ICPGC[a] meeting 2019 (23)
SPAST (MIM: 604277)	Van Eyk, Corbett and MacLennan, Matthews et al., Takezawa et al. (15–17)
SPG7 (MIM: 602783)	Spastic Paraplegia Foundation (18)
SPG11 (MIM: 610844)	Spastic Paraplegia Foundation (18)
SPTBN2 (MIM: 604985)	Van Eyk, Corbett and MacLennan (15)
ST3GAL5 (MIM: 604402)	Van Eyk, Corbett and MacLennan (15)
STXBP1 (MIM: 602926)	Van Eyk, Corbett and MacLennan, Takezawa et al. (13,17)
TAS (MIM: 313850)[c]	Presented at the ICPGC[a] meeting 2019 (23)
TBCK (MIM: 616899)	Matthews et al. (19)
TCF4 (MIM: 602272)	Matthews et al. (19)
TENM1 (MIM: 300588)	McMichael et al. (10)
TH (MIM: 191290)	Presented at the ICPGC[a] meeting 2019 (23)
TMEM67 (MIM: 609884)	Matthews et al. (19)
TRAPPC12 (MIM: 614139)	Presented at the ICPGC[a] meeting 2019 (23)
TUBA1A (MIM: 602529)	McMichael et al. (10)
TUBB4A (MIM: 602662)	Matthews et al. (19)
UBE3A (MIM: 601623)	Van Eyk, Corbett and MacLennan (15)
WARS2 (MIM: 604733)	Presented at the ICPGC[a] meeting 2019 (23)
WASHC5 (MIM: 610657)	Spastic Paraplegia Foundation (18)
WDR45 (MIM: 300526)	Matthews et al. (19)
WIPI2 (MIM: 609225)	McMichael et al. (10)
WNT8B (MIM: 601396)	Presented at the ICPGC[a] meeting 2019 (23)
ZFYVE26 (MIM: 612012)	Spastic Paraplegia Foundation (18)
ZNF238 (MIM: 608433)	Van Eyk, Corbett and MacLennan (15)

ICPGC[a]; International Cerebral Palsy Genomics Consortium, Imprinted inheritance in one of the referenced sources[b], Designated with a % in OMIM, signifying the entry describes a confirmed mendelian phenotype or phenotypic locus for which the underlying molecular basis is not known[c]