Appendix S1

Study #	Year	Indication	Location	CNV	Size (kb)/%	Inheritance	Gene/Disease	Category	Outcome	Phenotype well known	Data available regarding likelihood of an affected fetus
1	2018	Prior pregnancies Trisomy 21 and Trisomy 16	15q12q13.1	Loss	90	unknown	Partial loss of *OCA2*, associated with oculocutaneous albinism type 2 (AR)	Likely carrier	Full term, healthy	Yes	Yes
2	2018	Mom with retinitis pigmentosa; NT 3.3	17p11.2	Gain	21	unknown	Partial gain of *FLCN*, associated with Birt-Hogg-Dube syndrome with losses; 1 case report of a full copy gain	CNV with OMIM Morbid Genes	Preterm, induction for chorioamnionitis	Yes	No
3	2018	Uncle spina bifida; NT 3.6	12q12	Gain	1450	paternal	Gain of *IRAK4, ADAMTS20, TWF1, NELL2*. Diseases only associated with loss	CNV with OMIM Morbid Genes	Full term, healthy	Yes	Yes
4	2018	Prior pregnancy skeletal dysplasia; AMA	7p21.2	Loss x 2	50	maternal and paternal	Loss in intron of *ISPD,* associated with Walker-Warburg syndrome. Loss only described in exon deletions.	CNV with OMIM Morbid Genes	Full term, healthy	Yes	Yes
5	2017	Complex cardiac defect; Parents are 1st cousins	[ROH]	ROH	17.50%	[ROH]	58 genes identified associated with cardiac defects	Large ROH	NND, 7 wks. Mildly dysmorphic. WES neg.	No	Yes
6	2017	AMA; CVS mosaic Trisomy 18	Xp22.31	Loss	1694	unknown	Female with loss of 8 genes, including *STS*, associated with X-linked ichthyosis. Females may have minor skin manifestations or corneal opacities; UPD18 confirmed (not an imprinted gene)	Likely carrier	Full term, unknown health status	Yes	Yes
7	2017	Niece with hand with 1 finger; known consanguinity	[ROH]	ROH	5.30%	[ROH]	110 genes, but none likely to be related to the family history	Large ROH	Preterm delivery; sacral dimple, mild conductive hearing loss	No	Yes
8	2017	AMA; Family h/o epilepsy	16p13.3	Loss	50	maternal	Loss of promoter and a non-protein coding exon of transcript variants of *RBFOX1*, associated with epilepsy and autism spectrum disorder with losses of protein-coding exons	CNV with OMIM Morbid Genes	Full term, healthy	Yes	Yes
9	2017	AMA; 2 sons with autism	16p13.11	Gain	1555	unknown	Gain in *NDE1* and *MYH11*, associated with 16p13.11 Microduplication Syndrome with incomplete penetrance and variable expressivity. Same CNV as an affected brother (other not tested)	Incomplete penetrance	Termination	Yes	Yes
10	2017	AMA; Family history of developmental delay	8p22	Gain x 2	1288	maternal	Gain x 2 in *DLC1* associated with cancer if deleted	CNV with OMIM Morbid Genes	Full term, healthy	Yes	Yes

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11	2018	Abnormal analytes	2q13	Gain	1703	paternal	7 genes associated with autism spectrum disorder, developmental disorder, but with incomplete penetrance.	Incomplete penetrance	Full term, healthy	Yes	Yes
12	2014	AMA; club foot, enlarged NT, oligohydramnios; paternal uncle with club foot	2p21	Gain	378	de novo	Gain in *DYNC2LI1*, *ABCG5, ABCG8* and *LRPPRC*. No reports of abnormal phenotype with copy gains.	CNV with OMIM Morbid Genes	Delivered at 36 weeks, unknown outcome	Yes	Yes
13	2014	AMA	3p26.2p26.1	Loss	265	unknown	Deletion of single exon of *SUMG1* gene, associated with multiple sulfatase deficiency (AR)	Likely carrier	Both parents sequenced, did not have mutation of this gene. Full term birth, healthy.	Yes	Yes
14	2014	AMA	16p12.2	Gain	604	paternal	Gain in *UQRC2*; losses associated with mitochondrial complex III deficiency nuclear type 5	CNV with OMIM Morbid Genes	Full term birth, healthy	Yes	Yes
15	2015	AMA, prior fetus with Trisomy 21, RPL	16p13.11	Loss	407	paternal	Loss in *ABCC6* and *MYH11*, associated with vascular and connective tissue disorders in loss of function mutations. Overlaps with 16p13.11 microdeletion syndrome, but does not involve the strongest causative candidate gene.	CNV with OMIM Morbid Genes	Full term birth; healthy	Yes	No
16	2015	Abnormal analytes; unilateral cleft lip/palate	2p25.3	Gain	838	paternal	Gain in *TPO*; loss of function mutations associated with thyroid dyshormonogenesis 2A.	CNV with OMIM Morbid Genes	Full term birth; cleft lip/palate; SGA; developmental delay; ALL; seizures. Panel of 500 cancer genes showed no pathogenic germline alterations.	Yes	Yes
17	2015	AMA; abnormal analytes	2q11.1q11.2	Gain	1446	unknown	Gain of *TMEM127, CNNM4, SNRNP200, SEMA4C* and 34 other genes. Only loss of function variants associated with disease	CNV with OMIM Morbid Genes	Full term birth; SGA, speech delay	Yes	Yes
18	2015	AMA	8p23.2	Gain	1110	maternal	Gain of *CSMD1*, associated with developmental delay and autistic features in single nucleotide variants	CNV with OMIM Morbid Genes	Full term birth; healthy	Yes	Yes

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			16p13.3	Loss	17	maternal	Loss of *HBA1* and *HBA2*, associated with alpha thalassemia. Mother known alpha thalassemia trait, father with normal MCV and hemoglobin electrophoresis.	Likely carrier		Yes	Yes
19	2015	Renal pelviectasis, echogenic bowel	16p13.3	Loss	17	unknown	*HBA1* and *HBA2*, likely alpha thalassemia trait	Likely carrier	Full term birth; unknown postnatal findings	Yes	Yes
20	2015	NIPT high risk for Angelman syndrome	15q11.2	Loss	26	maternal	Loss within intron 1 of *SNRPN*, associated with Angelman syndrome, but downstream of imprinting center. Rare deletions in healthy controls	CNV with OMIM Morbid Genes	Full term birth; unknown postnatal findings	Yes	Yes
21	2015	Bilateral club feet	22q11.21	Loss	730	unknown	LCR B to D deletion in 22q11.21; does not include *TBX1*, thought to be responsible for DiGeorge syndrome. Does contain *CRKL*, sometimes involved in cardiac anomalies.	Incomplete penetrance	Elective termination	Yes	Yes
22	2015	AMA	7q36.2	Loss	175	maternal	Loss of *DPP6*, associated with autosomal dominant mental retardation and microcephaly with loss of function mutations	CNV with OMIM Morbid Genes	No microcephaly on prenatal ultrasound. Full term, unknown status	Yes	Yes
23	2015	NT 3.5mm	Xp22.31	Gain	1659	paternal	Female with gain in in *STS,* associated with X-linked ichthyosis in males if deleted	CNV with OMIM Morbid Genes	Full term, no postnatal abnormal findings	Yes	Yes
24	2016	Fetus with tetralogy of Fallot; prior child with DiGeorge syndrome	Xq25	Loss x 2	1567	maternal	Male with loss of *ACTRT1*, not associated with a disease	Large size	Termination given uncertainty with VUS	No	Yes
25	2016	Prior pregnancy XXX	4p15.1	Gain	3985	paternal	Duplication involving *PCDH7*; deletions associated with an increased risk of epilepsy	CNV with OMIM Morbid Genes	Full term birth, large for gestational age, otherwise no abnormal findings	No	Yes
26	2016	Fetus with suspected posterior urethral valves; NT 3.2mm	12q24.31q24 .32	Loss	1237	unknown	Large loss without OMIM Morbid genes	Large size	Developed poor cardiac output with severe biventricular dysfunction, and severe intracranial hemorrhage/ infarction	No	Yes

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27	2016	Twin A- bilateral club feet; Twin B- cystic hygroma, pelviectasis. Growth discordance (Twin B larger)	6q24.2	Loss	37	maternal	Both twins with deletion of *PEX3*, associated with Zellweger syndrome (AR). Biochemical analysis for Zellweger from amniocytes was negative.	Likely carrier	Preterm birth; twin A with normal postnatal findings, twin B with Sotos syndrome diagnosed by WES	Yes	Yes
28	2016	Abnormal analytes	13q12.12	Gain	1393	paternal	Gain of 7 genes, associated with disease with loss of function variants	CNV with OMIM Morbid Genes	Full term birth; unknown postnatal findings	No	Yes
29	2016	Abnormal analytes, echogenic bowel	1q41	Loss	51	unknown	Loss in *USH2A*, associated with Usher syndrome type IIA (AR)	Likely carrier	Full term birth, healthy	Yes	Yes
30	2016	Abnormal analytes, tetralogy of Fallot and single umbilical artery	3p26.3	Loss	1849	unknown	Loss consistent with 3p26 microdeletion syndrome, which has incomplete penetrance, and only 1 case reported with conotruncal anomalies.	Incomplete penetrance	Full term birth; confirmed tetralogy of Fallot, vascular ring with right aortic arch, congenital accessory tragus; decreased attention, conductive hearing loss, probable submucosal cleft palate	Yes	Yes
31	2016	Abnormal analytes; myelomeningocele	22q11.23	Gain	1314	unknown	LCR F-H distal duplication (not overlapping with 22q11.2 microdeletion syndrome), associated with developmental delay, ADHD, abnormal facial features, seizure, and renal anomalies, but of incomplete penetrance. No findings of neural tube defects.	Incomplete penetrance	Termination	Yes	Yes
32	2016	AMA; prior male fetus with deletion in Xp22.31	Xp22.31	Loss	1683	maternal	Female with loss of *STS* gene, associated with X-linked ichthyosis. Female carriers can have minor skin manifestations or corneal opacities.	Likely carrier	Full term birth, healthy	Yes	Yes
33	2016	AMA	4q34.3	Gain	1761	paternal	Gain without OMIM Morbid genes.	Large size	Full term birth, healthy	No	Yes

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34	2016	AMA; abnormal analytes	22q13.2q13.33	Loss	7808	unknown	Twin A with loss of 59 OMIM genes, including *SHANK3*, associated with Phelan-McDermid syndrome. Loss appears in ~10-20% of cells, consistent with low level mosaicism.	Mosaicism	Karyotype confirmed mosaic ring chromosome 22. Termination (resulting in reduction from DCDA twins to singleton)	Yes	Yes
35	2016	AMA; abnormal analytes	16p13.3	Loss	21	unknown	Loss of *HBA1* and *HBA2* genes, associated with likely alpha thalassemia trait. Father known alpha thalassemia trait, mother with normal MCV.	Likely carrier	Full term birth, no abnormal findings	Yes	Yes
36	2017	NT 3.1mm	8q23.1	Loss	113	unknown	Female with loss of 2 exons of *ZFPM2*, associated with autosomal dominant 46,XY sex reversal, CDH, and cardiac anomalies, associated with incomplete penetrance	Incomplete penetrance	Unknown	Yes	Yes
37	2017	Stage 3 TTTS	2q36.3	Loss	57	unknown	Loss of *SLC19A3*, associated with thiamine metabolism dysfunction syndrome 2 (AR)	Likely carrier	Preterm labor (PPROM, cord prolapse day after amnioreduction); unknown postnatal findings	Yes	Yes
38	2017	Abnormal analytes	1p36.22	Loss	1368	de novo	Loss of 6 OMIM genes, in a region found in some cases of 1p36 deletion syndrome, though typically larger deletions are implicated. Suggested critical region not included in this loss	CNV with OMIM Morbid Genes	Termination	Yes	Yes
39	2017	NIPT XXX; another child with autism (no genetic evaluation)	15q11.2	Loss	476	unknown	BP1 to BP2 deletion, with 4 OMIM Morbid genes (not including those associated with Prader Willi or Angelman syndromes) associated with developmental delay, intellectual disability and behavioral disturbances (including autism), but incomplete penetrance (about 10%). No evidence of Trisomy X.	Incomplete penetrance	Unknown	Yes	Yes
40	2017	AMA; 2 second degree relatives with intellectual or behavioral issues	15q11.2	Loss	1276	maternal	BP1 to between BP2 and BP3 deletion, not specifically associated with a well-described deletion syndrome. Includes 6 OMIM Morbid genes (not including those associated with Prader Willi or Angelman syndromes), including *MAGEL2 (*variably can have a Prader-Willi or autism phenotype).	CNV with OMIM Morbid Genes	Full term birth, no abnormal findings	Yes	Yes

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41	2017	Abnormal analytes	16p13.3	Loss	17	unknown	Loss of *HBA1* and *HBA2* genes on the same allele. Likely alpha thalassemia trait. Maternal aunt with alpha thalassemia trait, mother with low MCV, father with normal alpha thalassemia mutation analysis.	Likely carrier	Full term birth, no abnormal findings	Yes	Yes
42	2017	Pericardial effusion, dilated 4th ventricle, possible VSD; parents 1st cousins	[ROH]	ROH	4.80%	[ROH]	Large ROH, including 150 genes with autosomal recessive inheritance related to ultrasound findings. 60Mb ROH on chromosome 11 could represent UPD, which can be associated with Beckwith-Wiedemann syndrome or Silver-Russell syndrome	Large ROH	Termination	No	Yes
43	2018	Hydrops, polyhydramnios, "suspected cardiac defect"	1q13.5q14.1	Gain	1012	unknown	9 OMIM Morbid genes, but no diseases associated with copy gains.	CNV with OMIM Morbid Genes	Unknown	No	Yes
44	2018	Hypoplastic left heart, echogenic bowel, single umbilical artery, absent cavum septum pellucidum	16p13.3	Loss x 2	0.258	unknown	Small, homozygous loss of exon 3 of *HBA2* (no probes for exons 1 or 2). Most likely consistent with alpha thalassemia trait, with homozygous deletion in "trans". Unlikely to be related to ultrasound findings	Likely carrier	Unknown	Yes	Yes
45	2018	AMA; abnormal analytes; prior pregnancy with CDH (terminated; normal karyotype)	16p13.3	Loss	17	unknown	Loss of *HBA1* and *HBA2* genes, associated with likely alpha thalassemia trait. Mom with normal MCV.	Likely carrier	Unknown	Yes	Yes
46	2018	NT 3.1mm	16p13.3	Loss	17	unknown	Loss of *HBA1* and *HBA2* genes, associated with likely alpha thalassemia trait. Mom with normal MCV.	Likely carrier	Full term, healthy	Yes	Yes
47	2017	AMA; abnormal analytes	13q21.32	Gain	1007	maternal	Partial duplication of *PCDH9*, minimally associated with autism spectrum disorder in full duplications or deletions	CNV with OMIM Morbid Genes	Preterm birth due to preeclampsia; no abnormal postnatal findings	Yes	Yes
48	2017	AMA	6p12.2	Loss	217	unknown	Loss of 3 OMIM genes, including *EFHC1*, associated with an autosomal dominant form of juvenile-onset myoclonic epilepsy and juvenile-onset absence epilepsy in loss of function mutations	CNV with OMIM Morbid Genes	Unknown	Yes	Yes
49	2014	Bilateral cleft lip/palate, "suspicion of cardiac anomaly"	6q16.3q21	ROH	10442	[ROH]	Large ROH on chromosome 6, suggestive of UPD. UPD6 has imprinted genes associated with transient neonatal diabetes and IUGR	Large ROH	Termination; autopsy confirmed bilateral cleft lip, no cardiac anomaly	Yes	Yes

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50	2015	AMA; family history of myotonic dystrophy	13q31.3	Loss	149	unknown	Intronic deletion of *GPC6*, associated with omodysplasia-1 with loss of function variants	CNV with OMIM Morbid Genes	Full term birth; no anomalies	Yes	Yes
51	2015	AMA	15q14q23	ROH	29677	[ROH]	Large ROH suggestive of maternal UPD on chromosome 15, which had imprinted genes associated with Prader Willi syndrome	Large ROH	Methylation studies confirmed Prader Willi syndrome. Pregnancy terminated.	Yes	Yes
52	2015	AMA, mother with intermediate allele for Fragile X	13q12.11	Loss	306	unknown	Loss of *GJB6,* associated with nonsyndromic hearing loss (AR)	Likely carrier	Sequencing of *GJB6* was normal, confirming carrier status.	Yes	Yes
53	2016	AMA; nephew with Cutis Marmorata Congenita	16p13	Loss	17	paternal	Loss of *HBA1* and *HBA2* genes, associated with alpha thalassemia	Likely carrier	Sequencing panel for alpha globin mutations was normal, confirming alpha thalassemia trait.	Yes	Yes
54	2017	Fetal congenital diaphragmatic hernia	6q24.2	Loss	37	unknown	Loss of *PEX3,* associated with an autosomal recessive form of Zellweger syndrome	Likely carrier	Sequencing of *PEX3* was normal, confirming carrier status	Yes	Yes
55	2018	AMA, abnormal analytes	1q23.1	Loss	436	unknown	Loss of *SPTA1*, associated with hereditary elliptocytosis (AR)	Likely carrier	Sequencing of *SPTA1* and *PCD15* genes confirmed carrier status.	Yes	Yes
			10q21.1	Loss	434	unknown	Loss of *PCD15*, associated with autosomal recessive deafness and Usher syndrome type 1.	Likely carrier		Yes	Yes

Abbreviations: ADHD = attention deficit hyperactivity disorder, ALL = acute lymphoid leukemia, AMA = advanced maternal age, AR = autosomal recessive, CDH = congenital diaphragmatic hernia, CNV = copy number variant, CVS = chorionic villous sample, DCDA = dichorionic diamniotic, IUGR = in utero growth restriction, MCV = mean corpuscular volume, NIPT = noninvasive prenatal testing, NND = neonatal demise, NT = nuchal translucency, PPROM = preterm premature rupture of membranes, ROH = regions of homozygosity, RPL = recurrent pregnancy loss, SGA = small for gestational age, TTTS = twin twin transfusion syndrome, UPD = uniparental disomy, VSD = ventricular septal defect, VUS = variant of uncertain significance, WES = whole exome sequencing