Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Reddy UM, Page GP, Saade GR, et al. Karyotype versus microarray testing for genetic abnormalities after stillbirth. N Engl J Med 2012;367:2185-93. DOI: 10.1056/NEJMoa1201569

Supplemental Appendix

Reddy et al., *Genetic Abnormalities in Stillbirth: Comparison of Karyotype and Microarray Testing, New England Journal of Medicine, 2012*

Correspondence:
Dr. Uma Reddy
Pregnancy and Perinatology Branch
PPB CDBPM NICHD NIH
6100 Executive Blvd, Rm 4B03-F
Bethesda, MD 20892-7510, USA
E-mail: reddyu@mail.nih.gov

Table of Contents

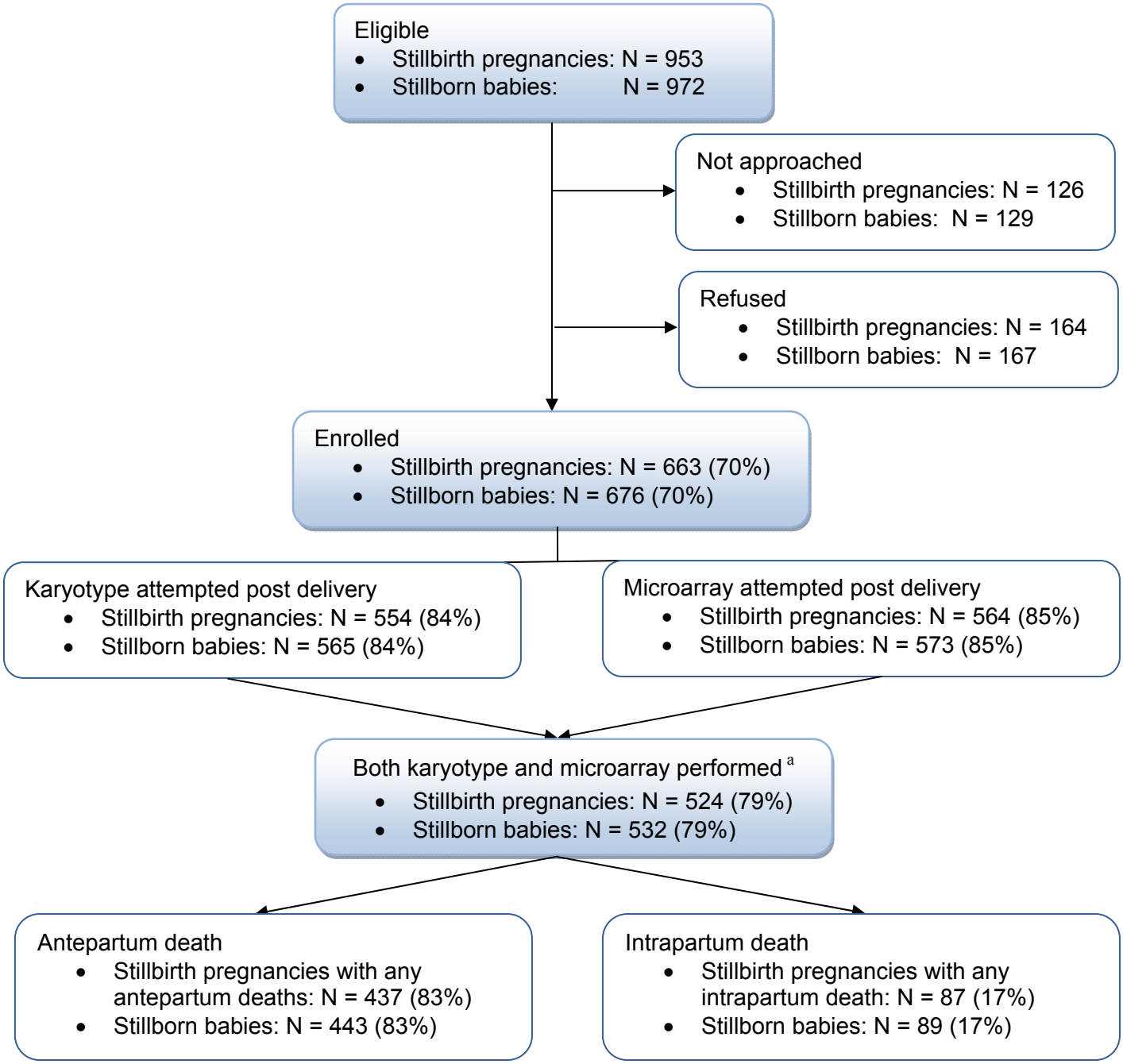
Stillbirth Collaborative Research Network

The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Stillbirth Collaborative Research Network (SCRN) is as follows: *University of Texas Health Science Center at San Antonio* — Donald J. Dudley, Deborah Conway, Josefine Heim-Hall, Karen Aufdemorte, Angela Rodriguez; *University of Utah School of Medicine and Intermountain Health Care* — Robert M. Silver, Michael W. Varner, Kristi Nelson; *Emory University School of Medicine, the Rollins School of Public Health, and Children's Healthcare of Atlanta* — Carol J. Rowland Hogue, Barbara J. Stoll, Janice Daniels Tinsley, Bahig Shehata, Carlos Abramowsky; *Brown University* — Donald Coustan, Halit Pinar, Marshall Carpenter, Susan Kubaska; *University of Texas Medical Branch at Galveston:* George R. Saade, Radek Bukowski, Jennifer Lee Rollins, Hal Hawkins, Elena Sbrana; *RTI International* — Corette B. Parker, Matthew A. Koch, Vanessa R. Thorsten, Holly Franklin, Pinliang Chen; *Pregnancy and Perinatology Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health* — Marian Willinger, Uma M. Reddy; *Columbia University School of Medicine* — Robert L. Goldenberg.

Additional Contributions

We acknowledge the following members of the National Institute of Child Health and Human Development Scientific Advisory and Safety Monitoring Board for their review of the study protocol, materials, and progress: Reverend Phillip Cato, PhD; James W. Collins Jr, MD, MPH; Terry Dwyer, MD, MPH; William P. Fifer, PhD; John Ilekis, PhD; Marc Incerpi, MD; George Macones, MD, MSCE; Richard M. Pauli, MD, PhD; Raymond W. Redline, MD; Elizabeth Thom, PhD (chair), as well as all of the other physicians, study coordinators, research nurses, and patients who participated in the Stillbirth Collaborative Research Network.

Figure S1. Stillbirth cohort description



The SCRN conducted a population-based case-control study of stillbirth with enrollment at the time of delivery. Recruitment was through 59 hospitals in 5 geographic regions defined by state and county lines that included: the State of Rhode Island and Bristol County, MA; DeKalb County, GA; Galveston and Brazoria Counties, TX; Bexar County, TX; and Salt Lake County, UT. The enrollment experience for stillbirths is shown. Stillbirths with post-delivery samples assessed by karyotype and microarray are the focus of this paper for comparison. Both were attempted on 532 stillbirths. Results are provided for all 532 stillbirths and for the subset that were antepartum deaths.

[a] Both karyotype and microarray were performed in 532 stillbirths. This included 492 singleton stillbirths, 19 twin gestations with 1 stillbirth, 4 twin gestations with 2 stillbirths but only one assessed by karyotype and microarray, 8 twin gestations with 2 stillbirths and both assessed, and 1 triplet gestation with 1 stillbirth.

Figure S2. Case 1

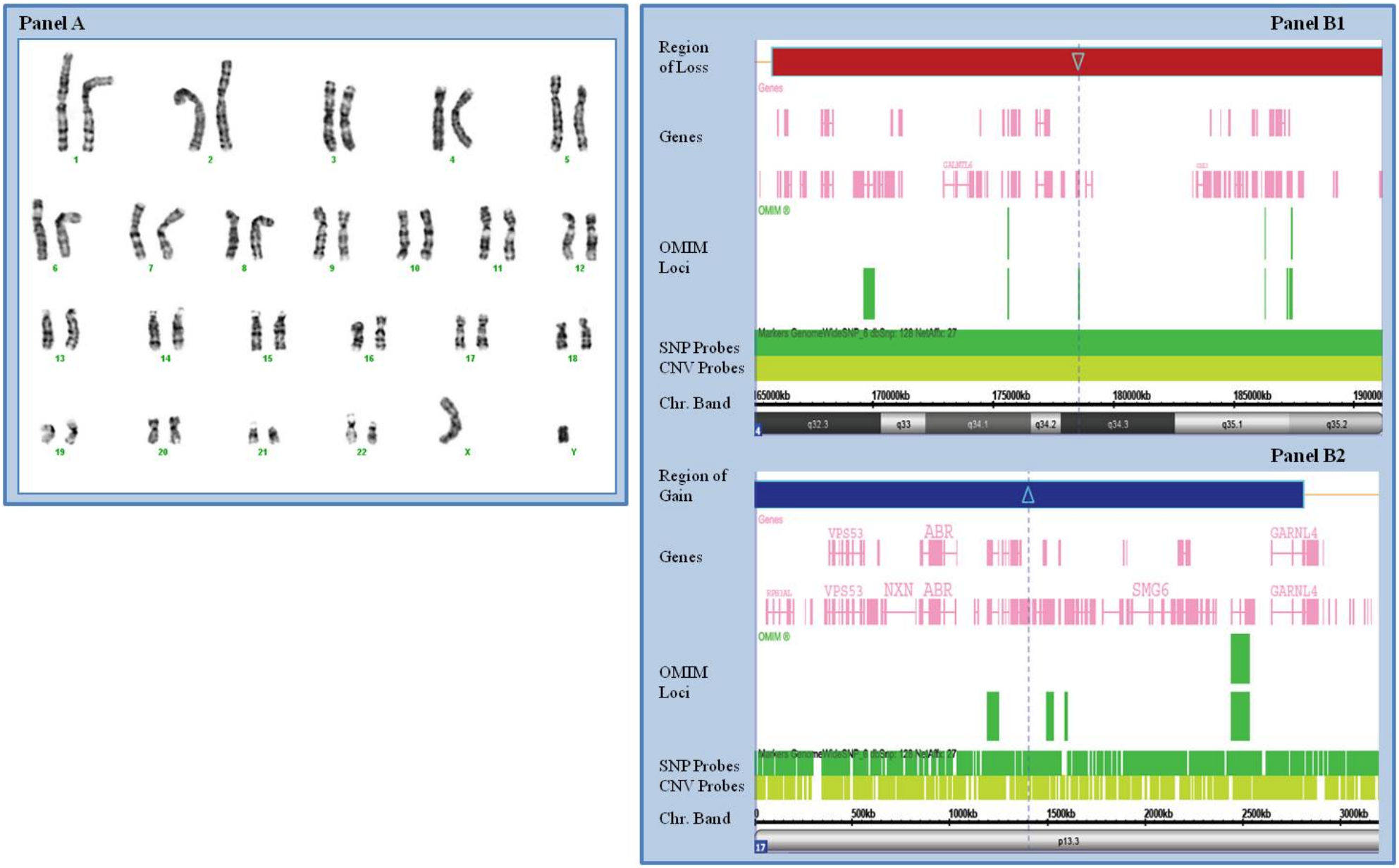
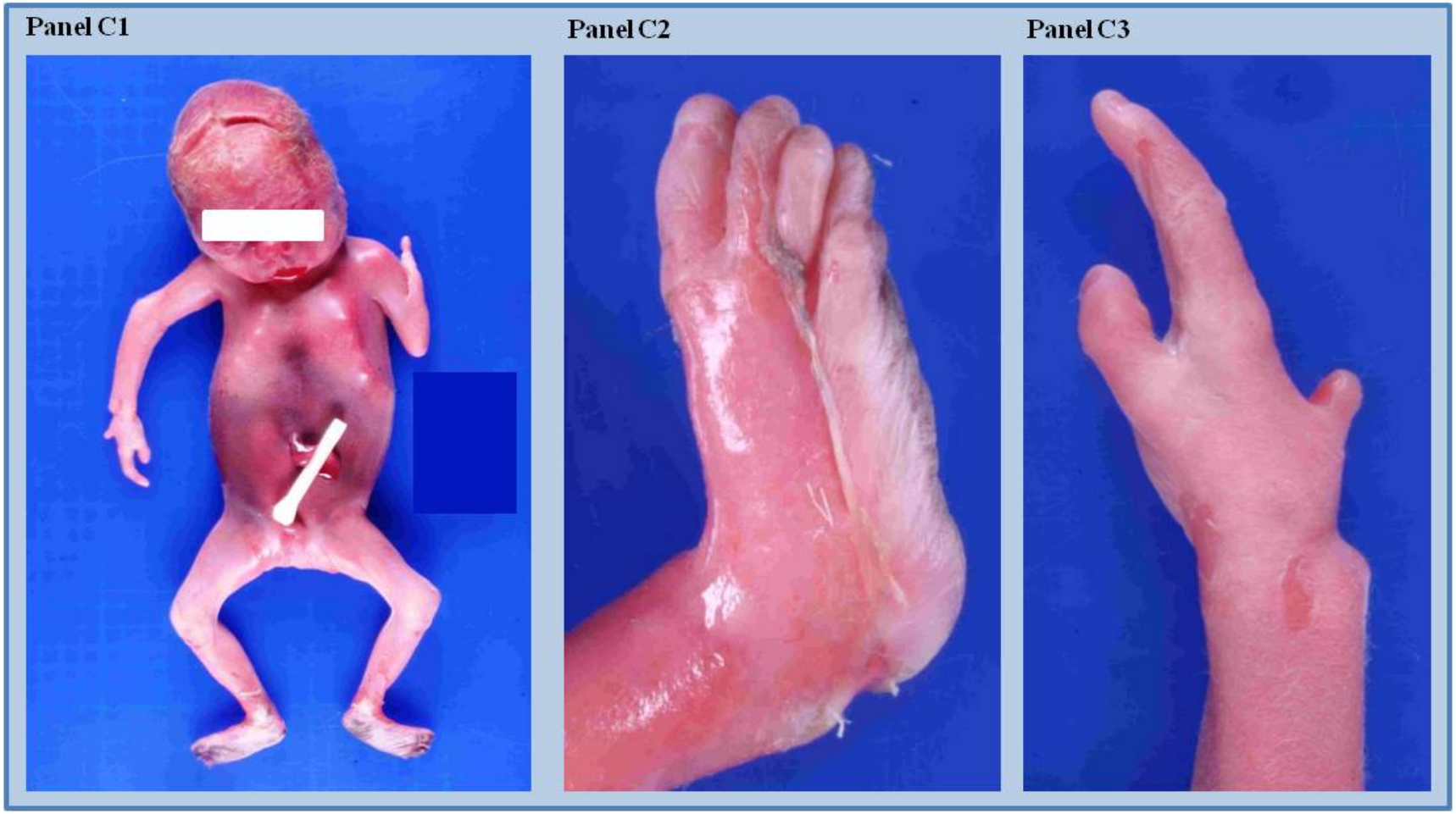


Figure S2. Case 1 (Continued)



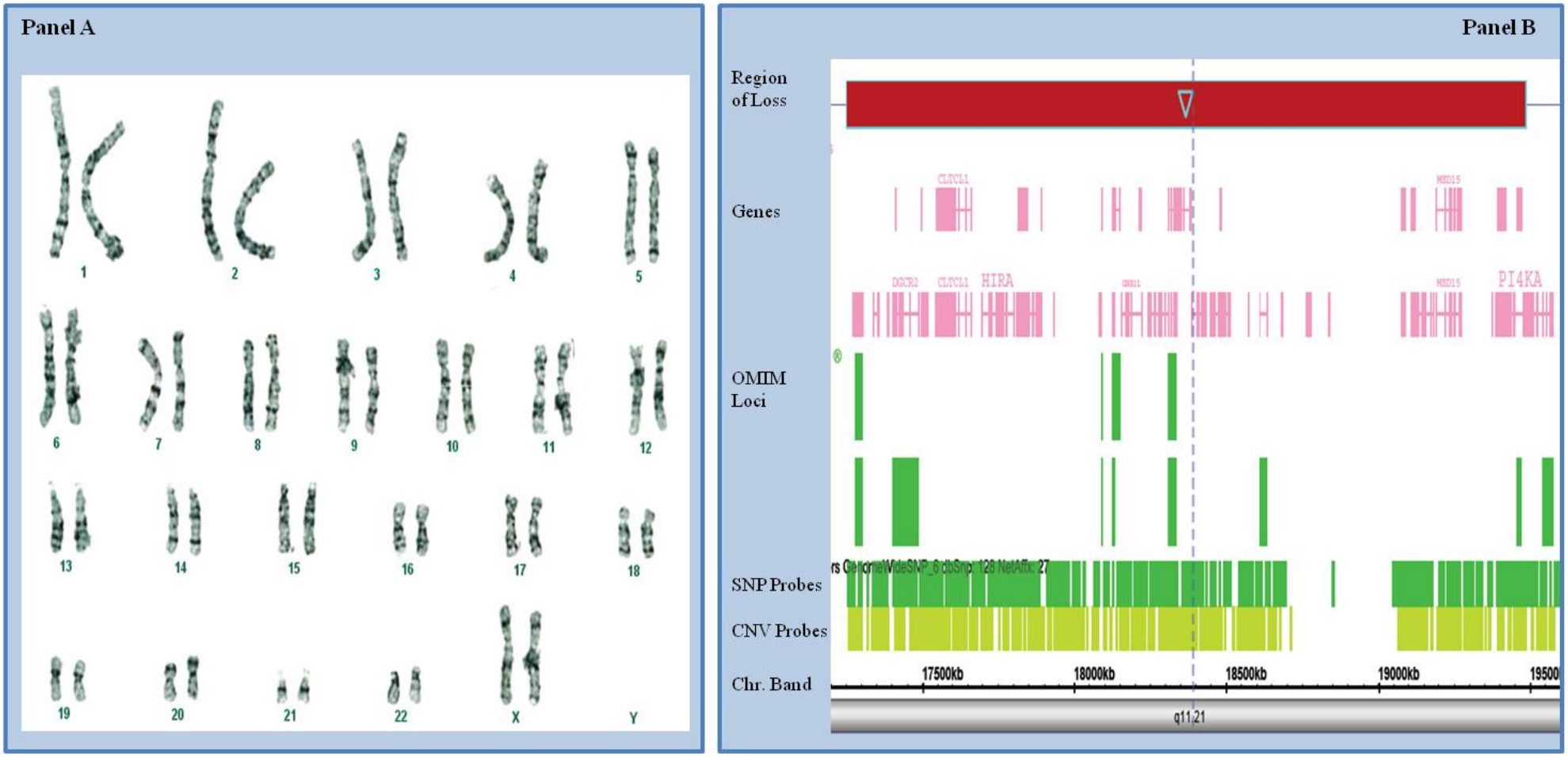
***Panel A*. Normal 46, XY karyotype of a 27 week stillbirth with multiple congenital malformations: limb deficiencies, cranio-facial dysmorphism, cleft soft palate, multiple cardiac defects.**

***Panel B1*. Microarray analysis reveals a 25 Mb deletion of chromosome 4q32.3→4qtel. The red bar represents the deletion. The pink bars represent known genes. This deletion affects at least 50 genes. The green bars are known OMIM loci. 7 OMIM loci are deleted including those associated with digital clubbing, asparylglucosemia, cardiomyopathy, and factor XI deficiency. The bottom dark and light green lines represent the location of Single Nucleotide Polymorphism (SNP) and Copy Number Variant (CNV) probes. The numbered line indicates the physical genomic position and the grey and black bars show the chromosome band location.**

***Panel B2*. There is also a 2.5 Mb gain of chromosome 17pter→17p13.3 identified by microarray. The blue bar represents the gain. Other data lines are as described above. This gain encompasses over 20 genes and 6 OMIM loci including Miller-Dieker Lissencephaly and subcortical laminar heterotopia. These large genomic imbalances are consistent with a fetal unbalanced translocation rather than two separate unrelated events.**

***Panel C1 to C3.* Multiple limb defects are visualized.**

Figure S3. Case 2



Panel A. **Normal 46,XX karyotype from a 37 week female stillbirth with abnormal facies, multiple cardiopulmonary anomalies, skeletal anomalies, urogenital anomaly, hypoplastic thymus as well as severe chronic villitis of the placenta.**

Panel B. **Microarray analysis reveals a 2.5 Mb deletion of chromosome 22 from 17.3 to 19.8 Mb on chromosome 22q11.21. The figure shows a zoomed view of chromosome 22q11.21. The red bar represents the deletion. Other data lines are as described in figure 3a. This deletion involves >35 genes and 7 OMIM loci including the DiGeorge/velocardiofacial syndrome (DGS/VCFS) locus.**

Table S1. Comparison of subgroups of eligible women with stillbirth

Characteristic – n (%)	Data Available for Screening			Data from All Sources on Enrolled		
	Enrolled to the SCRN			Postnatal Karyotype and Microarray Results		
	No (N=290)	Yes (N=663)	p-value	No (N=139)	Yes (N=524)	p-value
Maternal age at delivery in years						
<20	40 (13.8)	85 (12.8)	0.64	25 (18.0)	60 (11.5)	0.19
20-34	196 (67.6)	470 (70.9)		90 (64.7)	380 (72.5)	
35-39	37 (12.8)	80 (12.1)		18 (12.9)	62 (11.8)	
40+	17 (5.9)	28 (4.2)		6 (4.3)	22 (4.2)	
Maternal race/ethnicity						
White, non-Hispanic	95 (33.6)	259 (39.2)	0.39	34 (24.5)	200 (38.2)	0.01
African American, non-Hispanic	79 (27.9)	160 (24.2)		30 (21.6)	112 (21.4)	
Hispanic	98 (34.6)	218 (33.0)		62 (44.6)	175 (33.5)	
Other	11 (3.9)	23 (3.5)		13 (9.4)	36 (6.9)	
Marital status/cohabitating						
Not married or cohabitating				33 (26.6)	117 (23.8)	0.23
Cohabitating				38 (30.6)	123 (25.1)	
Married				53 (42.7)	251 (51.1)	
Maternal education						
0-11(none/primary/some secondary)				39 (31.7)	106 (21.7)	0.01
12 (completed secondary)				43 (35.0)	134 (27.4)	
13+ (college)				41 (33.3)	249 (50.9)	
Insurance/method of payment						
No insurance	10 (4.0)	52 (8.0)	0.06	9 (6.6)	31 (5.9)	0.18
Any public/private assistance	137 (54.4)	317 (48.5)		81 (59.1)	266 (51.0)	
VA/commercial health ins/HMO	105 (41.7)	285 (43.6)		47 (34.3)	225 (43.1)	
Income						
Only public/private assistance				10 (8.2)	41 (8.4)	0.10
Assistance & personal income				56 (45.9)	172 (35.4)	
Only personal income				56 (45.9)	273 (56.2)	
1st or 2nd Trimester Prenatal Care						
Yes				124 (89.2)	490 (93.5)	0.08
No				15 (10.8)	34 (6.5)	
Gestational age in months						
18-19	9 (3.1)	15 (2.3)	0.15	3 (2.2)	12 (2.3)	0.37
20-23	105 (36.2)	216 (32.6)		55 (39.6)	161 (30.7)	
24-27	43 (14.8)	108 (16.3)		22 (15.8)	86 (16.4)	
28-31	25 (8.6)	95 (14.3)		20 (14.4)	75 (14.3)	
32-36	62 (21.4)	119 (17.9)		18 (12.9)	101 (19.3)	
37+	46 (15.9)	110 (16.6)		21 (15.1)	89 (17.0)	
Parity						
Nulliparous				69 (50.0)	231 (44.2)	0.22
Multiparous				69 (50.0)	292 (55.8)	
Plurality of Index Pregnancy						
Singleton				128 (92.1)	492 (93.9)	0.44
Twins or Triplets				11 (7.9)	32 (6.1)	

Limited data were available at the time of screening on all 956 women with stillbirth who were eligible for the study. These data are shown above by enrollment status. For the women enrolled, more information were collected. Using information available from all sources, various characteristics are provided above for the enrolled women without versus with postnatal karyotype and microarray results on one or more stillborn babies from the pregnancy.

Table S2. Detailed information used to classify pathogenic, VOUS and probably benign cases with CNVs meeting the criteria of ≥ 500 kb and not in the 3 databases of normal individuals

[This document is formatted to print landscape on legal paper (8 1/2" by 14").]

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
Pathogenic	4037 (del)	arr 1q21.1(143,845,772-146,838,707)x1	Atrial_fibrillation(608583) (GJA5) Hemochromatosis_juvenile_digenic(602390) (HFE2) Cataract_zonular_pulverulent-1(116200)(GJA8) Cataract-microcornea_syndrome(116150)(GJA8)	LOC645166, LOC645166, NUDT17, HFE2, GPR89C, FMO5, FMO5, GNRHR2, NBPF11, PDE4DIP, CHD1L, POLR3GL, ANKRD35, LOC200030, HFE2, CD160, ITGA10, NOTCH2NL, PDZK1P1, PEX11B, HFE2, PDE4DIP, PDE4DIP, NBPF14, GPR89A, GPR89C, PRKAB2, BCL9, RBM8A, PPIAL4A, NBPF10, PPIAL4E, SEC22B, ACP6, LOC728989, LIX1L, RNF115, NBPF20, LOC728875, PDZK1P1, LOC200030, PPIAL4E, TXNIP, PDE4DIP, C1orf152, GPR89A, GJA5, GJA8, POLR3C, FMO5, ANKRD34A, FLJ39739, PDZK1, HFE2, PIAS3, PDIA3P, PDE4DIP, LOC645166, GJA5, NBPF16, GPR89B, NBPF16, NBPF11, NBPF15	37 week male; Congenital anomalies of the kidney and urinary tract; extremity malformations
Pathogenic	25351 (del); 2811 (dup)	arr 4q32.3q35.2(165,903,367-191,254,120)x1, 17p13.3(514-2,811,647)X3	Chromosome 4: Digital_clubbing_isolated_congenital(119900)(HPGD) Factor_XI_deficiency_autosomal_recessive(612416)(F11) Herpes_simplex_encephalitis_TLR3-deficient(0)(TLR3) Bietti_crystalline_corneoretinal_dystrophy(210370) (CYP4V2) Aspartylglucosaminuria___(0)(AGA) Progressive_external_ophthalmoplegia_with_mitochondrial_DNA_deletions(157640) (SLC25A4) Fletcher_factor_deficiency(612423) (KLKB1) Cardiomyopathy_familial_hypertrophic(192600)(SLC25A4) Hypertrophic_osteoarthropathy_primary_autosomal_recessive(259100)(HPGD) Pancreatic_cancer_susceptibility_to_1(606856)(PALLD) Cranioosteoarthropathy(259100)(HPGD) Digital_clubbing_isolated_congenital(119900)(HPGD) Chromosome 17: Miller-Dieker_lissencephaly(247200) (YWHAE) Plasmin_inhibitor_deficiency___(0)(SERPINF2) Lissencephaly-1(607432)(PAFAH1B1) Retinitis_pigmentosa-13(600059)(PRPF8) Epilepsy_progressive_myoclonic_1B(612437)(RILP) Subcortical_laminar_heterotopia___(0)(PAFAH1B1)	Chromsome 4: SH3RF1, LOC653544, MLF1IP, KIAA1430, STOX2, SPOCK3, SAP30, SNX25, TUBB4Q, IRF2, GALNTL6, ACSL1, CYP4V2, MORF4, LOC653545, C4orf38, DUX4, LOC653545, SCRG1, ANXA10, LOC653545, LOC653544, AADAT, LOC653545, HAND2, TLL1, DUX4, AADAT, LOC728410, ADAM29, PALLD, DCTD, KIAA1712, MGC45800, MFAP3L, TRIM75, C4orf39, KLHL2, SPOCK3, KLHL2, ZFP42, FAM149A, SORBS2, C4orf27, LOC653543, SORBS2, HPGD, FAM149A, TRIML2, HPGD, CLCN3, CCDC110, RWDD4A, LOC728410, SLC25A4, LOC653544, KIAA1712, HMGB2, CASP3, MFAP3L, LOC653544, GPM6A, VEGFC, LOC728410, ADAM29, LRP2BP, KLKB1, LOC653545, LOC285501, GPM6A, PDLIM3, WWC2, C4orf47, SPCS3, HMGB2, FAT1, SLED1, UFSP2, HPGD, FAM92A3, HELT, SORBS2, ADAM29, SORBS2, PDLIM3, NBLA00301, NEK1, SC4MOL, ASB5, CDKN2AIP, MTNR1A, ADAM29, SORBS2, TRIM61, LOC653543, DUX4, CPE, KLHL2, C4orf41, WDR17, SORBS2, LOC653544, GK3P, LOC653544, CASP3, SORBS2, LOC728410, FRG2, GLRA3, SORBS2, WDR17, DDX60, DUX4, CBR4, SPATA4, TRIML1, DCTD, TMEM192, FBXO8, FRG1, HMGB2, SC4MOL, TLR3, CLDN22, ODZ3, TRIM60, AGA, ANKRD37, LOC728410, NEIL3, CCDC111, GALNT7, ENPP6, CCDC110, LOC653545, GLRA3, C4orf41, ING2, GPM6A, DDX60L, DUX4, CLCN3, LOC653543, F11 Chromosome 17: TSR1, YWHAE, YWHAE, NXN, SERPINF1, RPH3AL, GLOD4, SLC43A2, SRR, HIC1, SNORD91A, MNT, ABR, INPP5K, INPP5K, TIMM22, METT10D, PAFAH1B1, MYO1C, TUSC5, RNMTL1, ELP2P, PRPF8, MYO1C, SCARF1, SMYD4, RTN4RL1, SCARF1, KIAA0664, C17orf91, SMG6, PITPNA, ABR, INPP5K, SERPINF2, FAM57A, HIC1, SGSM2, OVCA2, SNORD91B, SGSM2, GEMIN4, VPS53, VPS53, MYO1C, C17orf91, CRK, SCARF1, SCARF1, C17orf97, ABR, RILP, CRK, SCARF1, LOC284009, FAM101B, DPH1, RPA1, GARNL4, GARNL4	27 week male; Cardiovascular anomalies, limb deficiencies, craniofacial dysmorphism
Pathogenic	506 (del)	arr 7q11.23(73,247,250-73,753,322)x1		RFC2, LAT2, CLIP2, CLIP2, GTF2IRD1, LAT2, LAT2, RFC2, GTF2IRD1, GTF2I, EIF4H	23 week female; No anomalies. Placenta-abruption

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
Pathogenic	3062 (dup)	arr 16p13.11p12.3(15,224,214-18,286,344)x3	Aortic_aneurysm_familial_thoracic_4(132900)(MYH11) Pseudoxanthoma_elasticum_modifier_of_severity_of(264800)(XYLT1) Pseudoxanthoma_elasticum_forme_fruste(177850)(ABCC6)	NDE1, ABCC6, LOC339047, MYH11, NDE1, MYH11, MPV17L, MYH11, MYH11, NOMO3, ABCC1, ABCC1, C16orf45, C16orf45, KIAA0430, C16orf63, MPV17L, ABCC6, ABCC1, ABCC1, XYLT1, ABCC1	34 week male; No anomalies. Asymmetric fetal growth restriction
Pathogenic	3075 (dup)	arr 16p13.11p12.3(15,389,423-18,464,701)x3	Aortic_aneurysm_familial_thoracic_4(132900)(MYH11) Pseudoxanthoma_elasticum(264800) (ABCC6) Pseudoxanthoma_elasticum_forme_fruste(177850)(ABCC6) Pseudoxanthoma_elasticum_modifier_of_severity_of(264800)(XYLT1)	LOC339047, ABCC1, ABCC1, NDE1, ABCC6, XYLT1, ABCC6, C16orf45, ABCC1, C16orf63, MYH11, MPV17L, LOC339047, KIAA0430, NDE1, C16orf45, MYH11, MPV17L, MYH11, MYH11, ABCC1, ABCC1, NOMO3, NOMO2, NOMO2	23 week male; Absent thymus. Feature of many immunodeficiency syndromes.
Pathogenic	1662 (dup)	arr 17q12(31,890,369-33,552,890)x3;	Acetyl-CoA_carboxylase_deficiency___(0)(ACACA) Renal_cell_carcinoma(144700) (HNF1B) Renal_cysts_and_diabetes_syndrome(137920)(HNF1B)	TBC1D3, ACACA, AATF, AP1GBP1, DDX52, DUSP14, MRM1, MYO19, ACACA, TBC1D3E, ACACA, TADA2L, TBC1D3F, TADA2L, TBC1D3F, ACACA, GGNBP2, TBC1D3D, ZNHIT3, HNF1B, TBC1D3, DHRS11, TBC1D3E, LHX1, TBC1D3E, PIGW, AP1GBP1, ACACA, MYO19, C17orf78, LOC284100, DDX52	20 week male; No anomalies. Features of oligohydramnios-micrognathia, left rocker bottom feet
Pathogenic	1186 (dup)	arr 18p11.21(13,574,399-14,760,946)x3	Glucocorticoid_deficiency_due_to_ACTH_unresponsiveness(202200) (MC2R)	CXADRP3, C18orf19, ZNF519, C18orf1, MC5R, C18orf19, POTEC, C18orf1, RNMT, LOC284233, MC2R, C18orf1, C18orf1, ANKRD30B, C18orf1, C18orf1	27 week male; Ventricular Septal Defect
Pathogenic	11658 (del)	arr 18q22.1q23(59,768,718-76,116,030)x1	Methemoglobinemia_due_to_cytochrome_b5_deficiency___(0)(CYB5A) Congenital_cataracts_facial_dysmorphism_and_neuropathy(604168)(CTDP1)	LOC284276, C18orf55, FBXO15, CD226, C18orf22, KCNG2, CYB5A, TXNL4A, ZNF407, MBP, RTTN, CYB5A, CBLN2, ZNF407, C18orf62, LOC100130522, PQLC1, NETO1, GALR1, NFATC1, FBXO15, ZADH2, ZNF236, PQLC1, DOK6, SOCS6, ADNP2, MBP, ZNF516, LOC400657, TSHZ1, C18orf51, CTDP1, CTDP1, MBP, NFATC1, CNDP1, LOC100130522, MBP, LOC100130522, SALL3, NFATC1, NETO1, ATP9B, PQLC1, NETO1, NFATC1, LOC440498, NFATC1, CNDP2, MBP, CCDC102B, TMX3, MBP, PARD6G, ZNF407, CCDC102B	23 week male; External midline anomalies- Cleft uvula. Short sterum. Flat nose. Severe flexion deformities of hands, bilateral clubbed feet, severe maceration.
Pathogenic	1519 (dup)	arr 22q11.21(17,128,427-18,647,705)x3	Schizophrenia_susceptibility_to(181500)(COMT) DiGeorge_syndrome(188400) (TBX1) DiGeorge_syndrome_velocardiofacial_syndrome_complex-2___(0)(DGCR2) Bernard-Soulier_syndrome_type_B(231200)(GP1BB) Panic_disorder_susceptibility_to(167870) (COMT) Velocardiofacial_syndrome(192430) (TBX1) Conotruncal_anomaly_face_syndrome(217095)(TBX1) Hyperprolinemia_type_I(239500)(PRODH) Giant_platelet_disorder(0)(GP1BB)	GSC2, RANBP1, LOC150185, COMT, HIRA, SEPT5, TBX1, COMT, RTN4R, ZDHHC8, UFD1L, CDC45L, CLTCL1, TRMT2A, DGCR2, DGCR11, TRMT2A, COMT, C22orf39, ARVCF, MRPL40, TBX1, CLTCL1, CLDN5, GNB1L, DGCR5, C22orf29, C22orf25, LOC150197, DGCR9, COMT, GGT3P, TXNRD2, PRODH, DGCR10, TSSK2, DGCR14, CLDN5, DGCR8, GP1BB, TBX1, SLC25A1, DGCR6, UFD1L	33 week male; No anomalies. Small placenta- terminal villous hypoplasia
Pathogenic	2227 (del)	arr 22q11.21(17,256,416-19,795,836)x1	Schizophrenia_susceptibility_to(181500)(COMT) DiGeorge_syndrome(188400) (TBX1) DiGeorge_syndrome_velocardiofacial_syndrome_complex-2___(0)(DGCR2) Bernard-Soulier_syndrome_type_B(231200)(GP1BB) Panic_disorder_susceptibility_to(167870) (COMT) Velocardiofacial_syndrome(192430) (TBX1) Conotruncal_anomaly_face_syndrome(217095)(TBX1) Hyperprolinemia_type_I(239500)(PRODH) Giant_platelet_disorder(0)(GP1BB)	PI4KA, TBX1, COMT, CLTCL1, C22orf25, TMEM191A, DGCR14, TRMT2A, UFD1L, PRODH, ZDHHC8, TBX1, CLDN5, PI4KAP1, SERPIND1, COMT, COMT, CLTCL1, DGCR9, LOC150197, RANBP1, POM121L4P, DGCR10, SCARF2, DGCR5, DGCR8, MED15, HIRA, RTN4R, TBX1, ZNF74, GSC2, DGCR2, GNB1L, ZNF74, LOC150185, TSSK2, DGCR6L, DGCR6, KLHL22, COMT, GP1BB, C22orf29, CLDN5, CDC45L, TXNRD2, MED15, SEPT5, SLC25A1, RIMBP3, ARVCF, TRMT2A, C22orf39, DGCR11, SCARF2, UFD1L, MRPL40, PI4KA	37 week female; Declined autopsy. Minor external anomalies- flattened tip of nose, crowding of toes with ventral positioning of third toes bilaterally.

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
Pathogenic	4883 (del)	arr 22q11.21q11.23(17,256,416-22,140,054)x1	Leukemia(0)(BCR) Hyperprolinemia_type_I(239500)(PRODH) Conotruncal_anomaly_face_syndrome(217095)(TBX1) Cerebral_dysgenesis_neuropathy_ichthyosis_and_palmoplantar_keratoderma_syndrome (609528)(SNAP29) DiGeorge_syndrome(188400)(TBX1) Bernard-Soulier_syndrome_type_B(231200)(GP1BB) Leukemia_chronic_myeloid(608232)(BCR) Thrombophilia_due_to_heparin_cofactor_II_deficiency(612356)(SERPIND1) Giant_platelet_disorder(0)(GP1BB) Panic_disorder_susceptibility_to(167870)(COMT) Schizophrenia_susceptibility_to_4(600850)(PRODH) Conotruncal_anomaly_face_syndrome(217095)(TBX1) DiGeorge_syndrome_velocardiofacial_syndrome_complex-2___(0)(DGCR2)	SLC7A4, RANBP1, P2RX6, COMT, PRODH, SEPT5, FLJ39582, YPEL1, COMT, RTDR1, TMEM191A, KLHL22, PRAME, C22orf39, RAB36, TRMT2A, MAPK1, MED15, DGCR14, POM121L1P, PRAME, HIC2, GP1BB, RIMBP3C, PPM1F, LOC150197, FLJ39582, GSC2, PRAME, THAP7, P2RX6P, RIMBP3C, P2RX6, TOP3B, TBX1, DGCR10, CLDN5, CDC45L, TRMT2A, THAP7, POM121L8P, CLTCL1, DGCR11, DGCR6, GNAZ, SCARF2, SERPIND1, SDF2L1, ZNF74, RIMBP3, PI4KAP2, RTN4R, COMT, SCARF2, TBX1, UBE2L3, DGCR6L, PI4KAP1, PI4KA, UFD1L, UFD1L, ARVCF, GGTLC2, DGCR5, C22orf25, AIFM3, RIMBP3B, MED15, ZDHHC8P, TSSK2, ZDHHC8, BCR, CRKL, BCR, AIFM3, VPREB1, RIMBP3B, MAPK1, LOC648691, MRPL40, PPIL2, CLTCL1, POM121L4P, SNAP29, AIFM3, LOC400891, YDJC, ZNF280B, HIRA, AIFM3, CCDC116, PPIL2, C22orf29, COMT, PRAME, UBE2L3, DGCR9, SLC25A1, ZNF280A, DGCR2, LOC150185, LZTR1, PI4KA, CLDN5, DGCR8, LOC96610, ZNF74, GNB1L, MGC16703, TBX1, PPIL2, TXNRD2, PRAME	36 week male; DiGeorge syndrome- multiple cardiopulmonary anomalies, abnormal facies, skeletal anomalies, urogenital anomaly, hypoplastic thymus
Pathogenic	869 (del)	arr Xp22.31(6,903,881-7,774,557)x0	Ichthyosis_X-linked(308100)(STS)	STS, HDHD1A, VCX, HDHD1A	22 week male; No anomalies. Epidermal sloughing
VOUS	507 (del)	arr 1p35.3(28,444,904-28,952,754)x1		MED18, SNHG12, RNU11, TRNAU1AP, RCC1, SNHG3, SNHG3-RCC1, RAB42, SNORA44, PHACTR4, MED18, RCC1, RCC1, GMEB1, SNORD99, TAF12, GMEB1, SNORA16A, SESN2, TRNAU1AP, PHACTR4, SNORA61, TAF12, SNHG3-RCC1, SNHG3-RCC1, YTHDF2	27 week female; Non-immune hydrops- skin edema, ascites, pleural effusions. No structural anomalies.
VOUS	649 (dup)	arr 3p21.31(45,806,446-46,455,963)x3	HIV_infection(0)(CCR2) Diabetes_mellitus_insulin-dependent_22(612522)(CCR5) West_nile_virus_susceptibility_to(610379)(CCR5) Hepatitis_C_virus_resistance_to(609532)(CCR5)	CCR9, CCR1, CCR3, CCRL2, LZTFL1, CCR2, CCR9, CCR3, XCR1, XCR1, FYCO1, CCR5, CCR2, CCRL2, CXCR6, CCR5, SLC6A20, SLC6A20, LTF	24 week female; No major anomalies. Posterior nuchal and scalp lymphedema. Minor morphologic anomalies. Small placenta.
VOUS	551 (dup)	arr 5p15.2(10,908,334 - 11,459,739)X3	Mental_retardation_in_cri-du-chat_syndrome(123450)(CTNND2)	CTNND2	23 week male; No anomalies.
VOUS	613 (dup)	arr 6p25.1p24.3(6,844,061-7,457,081)x3		RREB1, CAGE1, SSR1, RREB1, RIOK1, RIOK1	24 week female; No anomalies.
VOUS	650 (dup)	arr 7p12.3(48,008,179-48,659,125)x3		UPP1, ABCA13, C7orf57, UPP1, SUNC1, SUNC1	35 week male; No anomalies, placental insufficiency
VOUS	2204 (dup)	arr 8q24.23(137,042,624-139,247,552)x3		FAM135B	37 week male; Double ureter, right kidney

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
VOUS	549 (dup)	arr 10q23.31(90,658,193-91,207,964)x3	Cholesteryl_ester_storage_disease___(0)(LIPA) Autoimmune_lymphoproliferative_syndrome_type_IA(601859)(FAS) Squamous_cell_carcinoma_burn_scar-related(0)(FAS) Wolman_disease___(0)(LIPA) Aortic_aneurysm_familial_thoracic_6(611788)(ACTA2) Autoimmune_lymphoproliferative_syndrome(601859)(FAS) Cataract_juvenile_with_microcornea_and_glucosuria(612018)(SLC16A12)	ACTA2, FAS, FAS, FAS, FAS, IFIT5, FAS, FAS, IFIT2, LIPA, FAS, FAS, IFIT1, CH25H, ACTA2, IFIT1L, IFIT3, IFIT3, LIPA, STAMBPL1, SLC16A12	24 week male; No autopsy done. Placental abruption
VOUS	587 (dup)	arr 11p13(33,005,102-33,592,112)x3		CSTF3, LOC283267, CSTF3, TCP11L1, CSTF3, HIPK3, HIPK3, TCP11L1, C11orf41, DEPDC7, DEPDC7	24 week female; No anomalies. Uteroplacental insufficiency
VOUS	721 (dup)	arr 15q12q13.1(25,366,691-26,087,702)x3	Skin_hair_eye_pigmentation_1_blue_nonblue_eyes(227220)(OCA2) Skin_hair_eye_pigmentation_1_blond_brown_hair(227220)(OCA2) Albinism_brown_oculocutaneous(203200)(OCA2) Albinism_oculocutaneous_type_II(203200)(OCA2)	OCA2, HERC2, GABRG3	38 week male; No anomalies. Placenta-multifocal thrombosis of fetal vessels
VOUS	704 (del)	arr 16p11.2(29333900 - 30038055)x1	Glycogen_storage_disease_XII(611881)(ALDOA) Mitral_valve_prolapse(0)(MVP)	ALDOA, TAOK2, GIYD1, CDIPT, QPRT, SPN, C16orf53, C16orf92, SPN, SLC7A5P1, C16orf54, LOC440356, GIYD1, MAZ, SULT1A4, TMEM219, ALDOA, GDPD3, INO80E, LOC440356, GIYD2, YPEL3, GIYD2, SEZ6L2, LOC613038, C16orf92, MVP, SEZ6L2, HIRIP3, LOC100271831, PPP4C, LOC606724, LOC440354, SEZ6L2, ALDOA, MVP, TBX6, LOC388242, YPEL3, ASPHD1, SULT1A3, PRRT2, TAOK2, BOLA2B, TMEM219, SULT1A3, DOC2A, ALDOA, BOLA2, KCTD13, SULT1A4, MAZ, FAM57B, SEZ6L2, MAPK3, MAPK3, MAPK3	26 week male; No anomalies. Features of oligohydramnios- flattened nose, mild micrognathia, flattened ears
VOUS	775 (dup)	19p12(23,613,361-24,388,578)x3		RPSAP58, ZNF681, LOC100101266, ZNF675, ZNF254	20 week female; No anomalies. Placenta-abruption
VOUS	930 (dup)	19p13.3(339937 - 1270320)x3	Precocious_puberty_central(176400)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Testicular_tumor_sporadic(273300)(STK11) Blood_group_OK(111380)(BSG) Melanoma(0)(STK11) Complement_factor_D_deficiency___(0)(CFD) Peutz-Jeghers_syndrome(175200)(STK11) Pancreatic_cancer(0)(STK11)	RNF126, C19orf6, ARID3A, PTBP1, ELANE, ABCA7, PALM, ATP5D, C19orf23, C19orf26, CIRBP, CDC34, GZMM, FAM148C, WDR18, HCN2, POLRMT, PRG2, PTBP1, BSG, PTBP1, CFD, C19orf22, BSG, KISS1R, AZU1, PRTN3, PTBP1, EFNA2, FGF22, HMHA1, PALM, C19orf20, BSG, CIRBP, CNN2, ATP5D, C19orf24, CNN2, ODF3L2, CIRBP, MADCAM1, FSTL3, GPX4, STK11, SBNO2, GPX4, GRIN3B, C19orf6, MED16, MADCAM1, POLR2E, SBNO2, PRSSL1, MIDN, GPX4, SHC2, C19orf21	36 week male; No anomalies. Placenta-chronic abruption
VOUS	601 (dup)	19p13.3(363729 - 965377)x3	Blood_group_OK(111380)(BSG) Precocious_puberty_central(176400)(KISS1R) Complement_factor_D_deficiency___(0)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD)	MADCAM1, SHC2, ODF3L2, BSG, BSG, ARID3A, C19orf21, WDR18, PTBP1, AZU1, BSG, GZMM, MADCAM1, PRSSL1, PTBP1, KISS1R, PTBP1, HCN2, GRIN3B, PALM, PALM, RNF126, PTBP1, CDC34, FSTL3, PRG2, C19orf22, PRTN3, POLRMT, C19orf20, ELANE, CFD, FGF22, MED16, C19orf6, C19orf6	24 week female; No anomalies. Placenta-decidual vasculopathy, villous infarction

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
VOUS	888 (dup)	19p13.3(373,237 - 1,261.136)x3	Precocious_puberty_central(176400)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Testicular_tumor_sporadic(273300)(STK11) Blood_group_OK(111380)(BSG) Melanoma(0)(STK11) Complement_factor_D_deficiency___(0)(CFD) Peutz-Jeghers_syndrome(175200)(STK11) Pancreatic_cancer(0)(STK11)	RNF126, C19orf6, ARID3A, PTBP1, ELANE, ABCA7, PALM, ATP5D, C19orf23, C19orf26, CIRBP, CDC34, GZMM, WDR18, HCN2, POLRMT, PRG2, PTBP1, BSG, PTBP1, CFD, C19orf22, BSG, KISS1R, AZU1, PRTN3, PTBP1, EFNA2, FGF22, HMHA1, PALM, C19orf20, BSG, CIRBP, CNN2, ATP5D, C19orf24, CNN2, ODF3L2, CIRBP, MADCAM1, FSTL3, GPX4, STK11, SBNO2, GPX4, GRIN3B, C19orf6, MED16, MADCAM1, POLR2E, SBNO2, PRSSL1, MIDN, GPX4, C19orf21, SHC2	29 week female; No anomalies
VOUS	882 (dup)	19p13.3(388,808 - 1,270,320)x3	Precocious_puberty_central(176400)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Testicular_tumor_sporadic(273300)(STK11) Blood_group_OK(111380)(BSG) Melanoma(0)(STK11) Complement_factor_D_deficiency___(0)(CFD) Peutz-Jeghers_syndrome(175200)(STK11) Pancreatic_cancer(0)(STK11)	KISS1R, FGF22, C19orf20, FSTL3, AZU1, BSG, GRIN3B, GPX4, BSG, MADCAM1, PRSSL1, HCN2, C19orf21, POLRMT, ATP5D, RNF126, MIDN, CNN2, GPX4, C19orf26, C19orf24, PALM, MADCAM1, CNN2, PTBP1, ATP5D, WDR18, PALM, CIRBP, CFD, GPX4, STK11, ABCA7, C19orf6, CIRBP, BSG, C19orf23, PTBP1, SBNO2, CIRBP, EFNA2, ELANE, MED16, C19orf22, CDC34, C19orf6, PRTN3, ODF3L2, POLR2E, PTBP1, SBNO2, PRG2, HMHA1, PTBP1, ARID3A, GZMM, SHC2	23 week male; No anomalies
VOUS	581 (dup)	19p13.3(392,194 - 972,725)x3	Blood_group_OK(111380)(BSG) Precocious_puberty_central(176400)(KISS1R) Complement_factor_D_deficiency___(0)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD)	ODF3L2, MADCAM1, C19orf20, GZMM, BSG, AZU1, PRG2, CDC34, PALM, PALM, WDR18, C19orf21, BSG, C19orf6, POLRMT, KISS1R, GRIN3B, MED16, PTBP1, RNF126, C19orf6, HCN2, PTBP1, PTBP1, C19orf22, PRTN3, ARID3A, PTBP1, FGF22, ELANE, CFD, FSTL3, MADCAM1, PRSSL1, BSG, SHC2	21 week male; Congenital Cytomegalovirus
VOUS	820 (dup)	19p13.3(441,414 - 1,261,136)x3	Precocious_puberty_central(176400)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Testicular_tumor_sporadic(273300)(STK11) Blood_group_OK(111380)(BSG) Melanoma(0)(STK11) Complement_factor_D_deficiency___(0)(CFD) Peutz-Jeghers_syndrome(175200)(STK11) Pancreatic_cancer(0)(STK11)	GRIN3B, C19orf23, ARID3A, BSG, MADCAM1, WDR18, POLRMT, CIRBP, FGF22, ELANE, C19orf22, CIRBP, C19orf6, CDC34, C19orf24, BSG, PTBP1, SBNO2, C19orf21, ABCA7, MADCAM1, RNF126, GZMM, HMHA1, AZU1, GPX4, PTBP1, PRSSL1, EFNA2, MED16, FSTL3, PRTN3, CIRBP, C19orf26, PALM, ATP5D, PALM, CNN2, HCN2, SBNO2, CFD, PRG2, KISS1R, C19orf20, ATP5D, BSG, POLR2E, MIDN, C19orf6, GPX4, PTBP1, GPX4, PTBP1, STK11, CNN2	40 week male; No anomalies
VOUS	524 (dup)	19p13.3(441,414 - 965,377)x3	Blood_group_OK(111380)(BSG) Precocious_puberty_central(176400)(KISS1R) Complement_factor_D_deficiency___(0)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD)	MADCAM1, BSG, BSG, ARID3A, C19orf21, WDR18, PTBP1, AZU1, BSG, GZMM, MADCAM1, PRSSL1, PTBP1, KISS1R, PTBP1, HCN2, GRIN3B, PALM, PALM, RNF126, PTBP1, CDC34, FSTL3, PRG2, C19orf22, PRTN3, POLRMT, C19orf20, ELANE, CFD, FGF22, MED16, C19orf6, C19orf6	18 week of ambiguous gender; No anomalies. Placenta- diffuse avascular villi, chronic decuiditis. Severe utero-placental deficiency
VOUS	524 (dup)	19p13.3(441,414 - 965,377)x3	Blood_group_OK(111380)(BSG) Precocious_puberty_central(176400)(KISS1R) Complement_factor_D_deficiency___(0)(CFD) Hypogonadotropic_hypogonadism(146110)(KISS1R) Corneal_fleck_dystrophy(121850)(CFD)	KISS1R, CFD, AZU1, PRTN3, PTBP1, ARID3A, PRG2, MED16, GZMM, PTBP1, PTBP1, FGF22, FSTL3, C19orf21, RNF126, HCN2, BSG, C19orf20, GRIN3B, PALM, ELANE, POLRMT, BSG, MADCAM1, WDR18, PALM, MADCAM1, PRSSL1, C19orf22, BSG, PTBP1, CDC34, C19orf6, C19orf6	22 week male; No anomalies

CNV classification	CNV size (kilobases) and type	Array call	OMIM loci	Genes	Postmortem Exam Findings
VOUS	526 (dup)	19q13.11-q13.12(41,961,955 - 42,487,630)x3		ZNF567, ZNF529, ZNF529, ZNF461, ZNF382, ZNF566, ZNF566, ZNF566, ZNF529, ZNF529, ZNF260, ZFP82, ZNF566, ZNF420, ZNF585B, ZNF585A, ZNF585A, ZNF383, ZNF568	31 week female; No anomalies
VOUS	524 (dup)	19q13.12(57,198,183 - 57,722,222)x3		ZNF610, ZNF528, LOC400713, ZNF616, ZNF610, PPP2R1A, ZNF614, ZNF836, ZNF841, ZNF432, ZNF534, ZNF610, ZNF534, ZNF578, ZNF766, ZNF480, ZNF610, ZNF615	28 week male; No anomalies. Placenta-abruption
VOUS	500 (dup)	arr 21q22.13(36,685,848-37,185,921)x3	Deafness(0)(CLDN14) Holocarboxylase_synthetase_deficiency(253270)(HLCS)	CLDN14, SIM2, CLDN14, CLDN14, CLDN14, SIM2, CLDN14, CHAF1B, HLCS	22 week male; No anomalies
VOUS	1178 (dup)	arr 21q21.3(27,162,033-28,340,061)x3		C21orf94, ADAMTS5, NCRNA00113	21 week female; No anomalies
VOUS	635 (dup)	arr Xq27.1(138,676,821-139,311,901)x3		CXorf66, ATP11C, ATP11C	24 week female; No anomalies
VOUS	851 (del)	arr Yq11.221(18,148,539-18,999,761)x0		LOC401630, XKRY2, CDY2B, LOC401629, XKRY, CDY2A	25 week male. Fetal growth restriction. Features suggestive of Trisomy 21- bilateral hypoplasia of 1st metacarpals, middle phalanx of 2nd and 5th digits, bilateral 12th rib aplasia, prominent nuchal lymphedema
Probably Benign	584 (del)	arr 1p21.1 (105,176,871-105,760,540)x1			32 week male; No anomalies. Placental abruption.
Probably Benign	682 (dup)	arr 6p11.2(57,508,637 - 58,190,898)X4		PRIM2	20 week female; No anomalies.
Probably Benign	575 (dup)	arr 6p11.2(57,604,034 - 58,179,324)X3		PRIM2	28 week female; No autopsy done. Placenta-large chorangioma.
Probably Benign	1675 (dup)	arr Xp22.31(6,465,151-8,140,292)x3	Ichthyosis_X-linked(308100)(STS)	STS, PNPLA4, VCX2, PNPLA4, VCX, HDHD1A, HDHD1A	37 week male; No anomalies. Placenta-abruption

Table S3. Comparison of the results from karyotype and array when the karyotype found an abnormal result and the array did not find the change or identified a different one

Case number	Karyotype result	Array Result
1	46,XX,i(22)(q10)[2]/46,XX[38] Low level Mosaicism (2 of 40 cells abnormal)	arr(1-22,X)x2 Normal Female
2	46,XY,i(5)(p11.2),der(19)t(5;19)(q11.2;p13.3)[2]/47,XY,+17[2]/46,XY[17] Complex low level Mosaicism that may be due to culture artifacts (4 of 21 cells abnormal with 2 different abnormalities)	arr(1-22)x2,(XY)x1 Normal Male
3	46,XY,del(1)(q12)[3]/46,XY[17] Low level Mosaicism (3 of 20 cells abnormal)	arr 7p12.3(48,008,179-48,659,125)x3 651 Kb Duplication VOUS
4	45,X Monosomy X	arr Yq11.222(10,668,731-27,209,311)x0 Partial deletion of Y; SRY present
5	47,XY,+21 Trisomy 21	NO RESULT *
6	46,XY,dup(2)(q37) Duplication	NO RESULT *

* DNA degraded, microarray analysis not performed