Mount Sinai

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Genetic Testing Laboratory

Chromosome Microarray
aCGH+SNP Testing

Illustration by Viktor Koen

Chromosome Microarray

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Chromosome microarray using array comparative genomic hybridization with single nucleotide polymorphism (array CGH+SNP) testing is a comprehensive analysis to examine the entire genome for deletions and duplications as well as copy neutral changes that may be clinically significant. This cutting-edge technology can be used in the aid of diagnosing prenatal and postnatal cases, including products of conception (POC). The array CGH technology uses dosage analysis of your patient's DNA in comparison to a standardized reference DNA at loci all across the genome. Our comprehensive platform coupled with the expertise of our ABMG certified laboratory directors will give you the most accurate results possible.

The high resolution array CGH microarray that we offer utilizes **~180,000 CGH+SNP probes** covering the entire genome with enriched coverage in regions known to be involved in submicroscopic chromosome abnormalities. This array yields high resolution detection of deletions and duplications with aberrations < 1kb possible in known genomic loci. The additional SNP probes allow for the simultaneous detection of regions of homozygosity for detection of uniparental disomy (UPD) and large regions with copy neutral absence of heterozygosity (AOH).

What are the benefits of array CGH+SNP technology?

- Diagnose children with developmental delay, intellectual disability, and/or multiple congenital anomalies
- Identify a specific genetic etiology in children diagnosed with Autism Spectrum Disorder
- Aid in diagnosing a child or adult that presents with non-classical features of a genetic syndrome
- Aid in diagnosing a fetus presenting with ultrasound abnormalities
- Higher resolution than conventional karyotyping to identify pathogenic deletions and duplications
- Detect chromosomal aneuploidies (e.g., trisomy 21 and 45,X)
- Detect unbalanced rearrangements that are *de novo* or associated with parental balanced structural aberrations
- Diagnose UPD
- Identify copy neutral AOH indicative of autosomal recessive disorders

Note: All abnormal results are confirmed in-house using fluorescence *in situ* hybridization (FISH)

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How are array CGH+SNP results reported?

Results are reported to the referring physician within 5-14 days from the receipt of the specimen (please allow additional time for specimens that require culturing).

Pathogenic

A deletion or duplication known to cause a specific genetic syndrome was identified, giving the patient a definitive diagnosis

Variant of Uncertain Significance (VUS)

A deletion or duplication was identified; however, clinical interpretation is currently not clear so it is classified as a VUS. Parental studies are strongly recommended to determine if the VUS is *de novo* or inherited. Based on parental follow-up testing, this VUS could then be sub-classified as VUS-likely pathogenic or VUS-likely benign

Normal

No deletions or duplications were identified that are known to cause genetic disease

Regions of homozygosity are reported when a single region of AOH is >10Mb or when the total autosomal AOH proportion is greater than 3% (>90Mb) (AOH regions >2Mb will be considered for this estimate). When common descent is suspected, identified regions of AOH >2Mb will be reported to allow for the possible identification of recessive risk alleles.

What specimens are accepted for testing?

Prenatal

Chorionic Villi (5-10 mg), Amniotic Fluid (10-15 ml), Confluent T-25 flasks (2)

- *SNPs may be omitted during prenatal testing if desired*
- *Parental blood specimens (in EDTA lavender-top tubes) should also be submitted for maternal cell contamination studies and in the event that they are needed for testing and result interpretation.*

Peripheral Blood

5-10 ml in EDTA lavender-top tube

POC

Chorionic villi, skin biopsy or umbilical cord

It is recommended to submit a maternal blood specimen in an EDTA lavender-top tube at the time of POC submission to rule out maternal cell contamination

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The following is a list of genetic syndromes that can be detected using our 180K CGH+SNP platform. Please contact the Mount Sinai Genetic Testing Laboratory for questions regarding coverage of a specific locus not listed below.

Syndrome	Gene	Locus	OMIM#
• Aneuploidy for 24 chromosomes	-----	-----	-----
• All 41 unique subtelomeric regions	-----	-----	-----
• All 48 unique pericentromeric regions	-----	-----	-----
• 1p36 deletion syndrome	multiple	1p36	607872
• 1q21.1 microdeletion syndrome with susceptibility to mental retardation, autism, or congenital anomalies	multiple	1q21.2	612474
• 1q21.1 microdeletion syndrome with susceptibility to thrombocytopenia-absent radius (TAR)	multiple	1q21.1	274000
• 1q41-q42 microdeletion syndrome	multiple/DISP1 (candidate)	1q41	-----
• 1q43-q44 microdeletion syndrome	multiple/AKT3 (candidate)	1q43-q44	612337
• 2p15-p16.1 deletion syndrome	multiple	2p16.1-p15	612513
• 2p21 microdeletion, homozygous	multiple	2p21	606407
• 2q32.2-q33 microdeletion syndrome	SATB2/multiple	2q33.1	119540
• 3q29 microdeletion syndrome	PAK2, DLG1	3q29	609425
• 8p23.1 microdeletion syndrome	GATA4/multiple	8p23.1-p23.3	-----
• 9p24.3 deletion syndrome	multiple	9p24.3	154230
• (46,XY gonadal dysgenesis, with 9p24.3 deletion)			
• 9q22.32-q22.33 microdeletion syndorme TGFBR1/multiple 9q22.33 Loss	TGFBR1 /multiple	9q22.33	-----
• 9q34.3 deletion syndrome	EHMT1 (candidate)	9q34.3	610253
• 10q22.3-q23.31 microdeletion syndrome	multiple	10q22.3-q23.31	
• 10q26 deletion syndrome	ADRB1, CTBP2 candidates	10q26.2	609625
• 12q14.1-q15 microdeletion	LEMD3, GRIP1 (candidate)	12q14.3	-----
• 12q24.21-12q24.23 microduplication	THRAP2, NOS1, RFC5	12q24.21-q24.23	-----
• 13q33q34 deletion syndrome	EFNB2, ARHGEF7	13q33.3-q34	-----
• 14q11.2 deletion syndrome	SUPT16H, CHD8	14q11.2	-----
• 14q22-q23 microdeletion syndrome	multiple	14q22-q23	-----
• 15q11-q13 duplication syndrome	UBE3A, GABRB3, GABRB4, GABRG3	15q11.2-q14	608636
• 15q13.3 microdeletion syndrome	multiple/CHRNA7	15q13.3	612001
• 15q24 deletion Syndrome	PML	15q24.1	-----
• 15q26.3 deletion syndrome/severe intrauterine growth retardation (IUGR)	IGF1R	15q26.2-qter	-----
• 16p11.2 microdeletion , susceptible to Autism	multiple	16p11.2	611913
• 16p11.2-p12.2 microdeletion syndrome	SALL1, ZNF423	16p11.2-p12.2	-----
• 16p13.1 microdeletion/microduplication predisposing to autism and /or mental retardation	multiple	16p13.1	-----
• 17q21.31 microdeletion syndrome	MAPT,CRHR1	17q21.31	610443
• 18q deletion syndrome	MBP, DCC	18q21.2-qter	601808
• 22q11 duplication syndrome	multiple	22q11.2	608363
• 22q11.2 distal microdeletion syndrome	multiple	22q11.2	611867
• 22q13.3 deletion syndrome	SHANK3 candidate	22q13.33	606232
• Xp11.3 deletion syndrome (XMR, with retinitis pigmentosa)	RP2	Xp11.3	300578
• Xp11.4-p21.2 Contiguous gene deletion	multiple, L1RAPL1 (OTC candidate)	Xp11.4-p21.2	-----
• XY sex-reversal, +/- adrenal failure	NR5A1	9q33.3	184757
• Adrenal hypoplasia congenita (AHC)	NR0B1	Xp21.2	300200
• Alagille syndrome 1 (ALGS1)	JAG1	20p12.2	118450

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Syndrome	Gene	Locus	OMIM#
• Albright hereditary osteodystrophy-like/brachydactyly/mental retardation	CENTG2, GPC1, GRP35, ATSV/KIF1A, STK25	2q37.3	600430
• Alpha thalassemia mental retardation (ATR-16)	HBA1, HBA2	16p13.3-pter	141750
• Androgen insensitivity syndrome	AR	Xq12	300068
• Angelman syndrome (AS)	UBE3A, AS-SRO	15q11.2-q12	105830
• Aniridia (AN)	PAX6	11p13	106210
• Atrial septal defect (ASD) with atrioventricular conduction defects	NKX2-5	5q35.2	108900
• Bannayan-Riley-Ruvalcaba Syndrome (BRRS)	PTEN	10q23.31	153480
• Basal cell nevus syndrome (BCNS)/Gorlin Syndrome	PTCH1	9q22.3	109400
• Becker muscular dystrophy	DMD	Xp21.2-p21.1	300376
• Beckwith-Wiedemann syndrome	H19, IGF2, KCNQ1, KCNQ1OT1 (LIT1), CDKN1C	11p15.5-p15.4	130650
• Blepharophimosis, ptosis and epicanthus inversus (BPES)	FOXL2	3q22.3	110100
• Branchiootorenal syndrome 1 (BOR1)	EYA1	8q13.3	113650
• Buschke-Ollendorff syndrome/osteopoikilosis, short stature and mental retardation	LEMD3	12q14.3	166700
• Campomelic dysplasia/sex reversal	SOX9	17q24.3	114290
• Cat eye syndrome	CECR1, CECR5, CECR6	inv dup(22)(q11)	115470
• Cerebellar hypoplasia, VLDLR-related, Hutterite dysequilibrium	VLDLR	9p24.2	224050
• Cerebral cavernous malformations, type 1 (CCM1)	KRIT1	7q21.2	116860
• Cerebral cavernous malformations, type 2 (CCM2)	CCM2	7p13	603284
• Cerebral cavernous malformations, type 3 (CCM3)	PDCD10	3q26.1	603285
• CHARGE	CHD7	8q12.2	214800
• Choroideremia	CHM	Xq21.2	303100
• Cleidocranial dysplasia (CCD)	RUNX2	6p21.1	119600
• Complex glycerol kinase deficiency (Xp21 contiguous gene syndrome)	NR0B1, GK, DMD	Xp21.2-p21.3	307030
• Congenital diaphragmatic hernia 1 (CDH 1)	CHD2, NR2F2	15q26.1-q26.2	142340
• Congenital diaphragmatic hernia 2 (CDH2)	GATA4 (candidate)	8p23.1	222400
• Cornelia de Lange syndrome 1 (CDLS1)	NIPBL	5p13.2	122470
• Cowden Syndrome	PTEN	10q23.31	158350
• Craniofrontonasal syndrome	EFNB1	Xq13.1	304110
• Craniosynostosis, type 2 (CRS2)	MSX2	5q35.2	604757
• Cri-du-chat syndrome	multiple (TERT, EGR1)	5p15.31-p15.2	123450
• Currarino syndrome	MNX1	7q36.3	176450
• Dandy-Walker malformation (DWM)	ZIC1, ZIC4	3q24	220200
• DiGeorge syndrome 2 (DGS2)	multiple	10p14-p13	601362
• DiGeorge/velocardiofacial syndrome (DGS1)	TBX1, GNB1L	22q11.2	188400
• Dosage-sensitive sex reversal Xp11.4-p21.2 Contiguous gene deletion	NR0B1	Xp21.2	300018
• Down syndrome critical region (DSCR)	multiple	21q22.13-q22.2	190685
• Duchennemuscular dystrophy	DMD	Xp21.2-p21.1	310200
• Familial adenomatous polyposis w/ mental retardation	APC	5q22.2	175100
• Feingold syndrome	MYCN	2p24.3	164280
• Focal Dermal Hypoplasia; FDH (GOLTZ Syndrome)	PORCN	Xp11.23	305600
• Fragile X mental retardation syndrome	FMR1	Xq27.3	300624
• Fryns syndorme	DISP1 candidate	1q41	229850
• Gonadal Dysgenesis, XY female type (GDXY)/SRY dosage abnormalities	SRY	Yp11.3	400044
• Greig cephalo-polysyndactyly syndrome (GCPS)	GLI3	7p13	175700

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Syndrome	Gene	Locus	OMIM#
• Hemophilia A	F8	Xq28	306700
• Hemophilia B	F9	Xq27.1	306900
• Hereditary hemorrhagic telangiectasia, type 2	ACVRL1	12q13.13	600376
• Holoprosencephaly 1 (HPE1)	TMEM1 (TRAPPC10)	21q22.3	236100
• Holoprosencephaly 2 (HPE2)	SIX3	2p21	157170
• Holoprosencephaly 3 (HPE3)	SHH	7q36	142945
• Holoprosencephaly 4 (HPE4)	TGIF	18p11.3	142946
• Holoprosencephaly 5 (HPE5)	ZIC2	13q32.3	609637
• Holoprosencephaly 6 (HPE6)	multiple	2q37.1-q37.3	605934
• Holoprosencephaly 7 (HPE7)	PTCH1	9q22.3	610828
• Holoprosencephaly 8 (HPE8)	multiple	14q13.1-q13.2	609408
• Holt-Oram	TBX5	12q24.1	142900
• Hypoparathyroidism, sensorineural deafness and renal disease (HDR)	GATA3	10p14	146255
• Hypotonia-cystinuria	SLC3A1, PREPL	2p21	606407
• Infantile hyperinsulinism with enteropathy & deafness	USH1C, ABCC8	11p15.1	606528
• Infantile spasms, MAGI2-related	MAGI2	7q21.11	606382
• Myoclonus dystonia	SGCE	7q21.3	159900
• Jacobsen syndrome/11q terminal deletion disorder	multiple	11q23.3-11qter	147791
• Joubert syndrome 4	NPHP1	2q13	609583
• Juvenile polyposis (JPS), BMPR1A-related	BMPR1A	10q23.2	174900
• Juvenile polyposis (JPS), SMAD4-related	SMAD4	18q21.2	174900
• Kallmann syndrome 1 (KS1)	KAL1	Xp22.31	308700
• Langer mesomelic dysplasia (LMD)	SHOX	Xp22.13-Xpter/ Yp11.32 - Ypter	249700
• Langer-Giedion syndrome (LGS) /TRPS2	TRPS1, EXT1	8q23.3-8q24.1	150230
• Leri-Weill dyschondrosteosis (LWD)	SHOX	Xp22.13-Xpter/ Yp11.32 - Ypter	127300
• Li-Fraumeni syndrome 1 (LFS)	TP53	17p13.1	151623
• Lissencephaly 1	PAFAH1B1 (LIS1)	17p13.3	607432
• Loeys-Dietz syndrome, type 1A (LDS1A) (aortic aneurysm syndrome)	TGFBR1	9q22.33	609192
• Loeys-Dietz syndrome, type 2B (LDS2B)	TGFBR2	3p24.1	610168
• Lowe syndrome	OCRL	Xq25	309000
• LUBS XLMR Syndrome; MRXSL/(MECP2 duplication Syndrome)	MECP2	Xq28	300260
• Marfan syndrome 1 (MFS1)	FBN1	15q21.1	154700
• McLeod syndrome	XK	Xp21.1	314850
• Menkes syndrome	ATP7A	Xq21.1	309400
• Microphthalmia 7 with linear skin defects	multiple	Xp22.2	309801
• Microphthalmia syndrome 6 (MCOPS6)/pituitary hypoplasia, anophthalmia, brain/digital anomalies	BMP4	14q22.2	607932
• Microphthalmia, syndrome 3 (MCOPS3)	SOX2, CHRD	3q26.33	206900
• Miller-Dieker syndrome (MDLS)	LIS1, YWHAE	17p13.3	247200
• Mohr-Tranebjaerg syndrome	TIMM8A	Xq22.1	304700
• Monosomy 9p deletion syndrome	CER1, TYP1, ZDHHC21/ multiple	9p23-p22.3	158170
• Mowat-Wilson syndrome (MWS)	ZEB2 (ZFHX1B)	2q22.3	235730
• Nablus mask-like facial syndrome	multiple	8q21.3-q22.1	608156
• Nail-patella syndrome	LMX1B	9q33.3	161200
• Nephronophthisis 1 (NPH)	NPHP1, MALL	2q13	256100

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Syndrome	Gene	Locus	OMIM#
• Nephropathic cystinosis	CTNS	17p13.3	219800
• Neurosensory deafness, autosomal recessive (DFNB1)	GJB6	13q12.11	220290
• NF1 Microdeletion syndrome	NF1	17q11.2	162200
• NFIA haploinsufficiency	NFIA	1p31.3	600727
• Noonan syndrome 1 (NS1)	PTPN11	12q24.13	163950
• Okihiro syndrome	SALL4	20q13.2	607323
• Ornithine transcarbamylase deficiency	OTC	Xp21.1	311250
• Oto-dental	FGF3	11q13.3	166750
• Oto-facio-cervical syndrome (OFC)	EYA1	8q13.3	166780
• Pallister-Killian Syndrome	multiple	i(12)(p10)	601803
• Pelizaeus-Merzbacher disease (PMD)	PLP1	Xq22.2	312080
• Peutz-Jeghers syndrome (PJS)	STK11	19p13.3	175200
• Pitt-Hopkins syndrome	TCF4	18q21.1	610954
• Polycystic kidney disease 1 (PKD1)	PKD1	16p13.3	601313
• Potocki-Lupski syndrome (PTLS)	RAI1	17p11.2	610883
• Potocki-Shaffer Syndrome	ALX4, EXT2 candidates	11p11.2	601224
• Prader-Willi syndrome (PWS)	PWS-SRO, SNRPN, snoRNAs cluster	15q11.2-q12	176270
• Prader-Willi syndrome-like with obesity	SIM1 candidate	6q16.2	176270
• PTEN hamartoma tumor	PTEN	10q23.31	158350
• Renal cysts and diabetes syndrome (RCAD, MODY5)	TCF2 (aka HNF1B)	17q12	137920
• Retinoblastoma with mental retardation syndrome	RB1	13q14.2	180200
• Rieger syndrome type 1 (RIEG1)	PITX2	4q25	180500
• Rubinstein-Taybi syndrome	CREBBP	16p13.3	180849
• Saethre-Chotzen syndrome	TWIST	7p21.3-p21.2	101400
• Sensorineural deafness and male infertility	STRC, CATSPER2	15q15.3	611102
• Severe myoclonic epilepsy of infancy (SMEI)	SCN1A	2q24.3	607208
• Simpson-Golabi-Behmel syndrome (SGBS)	GPC3	Xq26.2	312870
• Smith-Lemli-Opitz (SLOS)	DHCR7	11q13.4	270400
• Smith-Magenis syndrome (SMS)	RAI1	17p11.2	182290
• Sotos syndrome	NSD1	5q35.3	117550
• Speech-language disorder 1	FOXP2 (candidate)	7q31	602081
• Split-hand/split-foot malformation (SHFM1)	DLX5, DLX6, DSS1	7q21.2-p21.3	183600
• Split-hand/split-foot malformation (SHFM3)	FBXW4	10q24.3	600095
• Split-hand/split-foot malformation 5 (SHFM5)	DLX1, DLX2	2q31.1	606708
• Steroid sulfatase deficiency	STS	Xp22.31	308100
• Stickler syndrome, Type 1 (STL1)	COL2A1	12q13.11-q13.2	108300
• Synpolydactyly 1 (with foot anomalies)	HOXD9, 10,11, 12,13; EVX2	2q31.1-q32	186000
• Townes-Brocks syndrome 1	SALL1	16q12.1	107480
• Trichorhinophalangeal syndrome 1 (TRPS1)	TRPS1	8q24.12	190350
• Tuberous sclerosis 1	TSC1	9q34.13	191100
• Tuberous sclerosis 2	TSC2	16p13.3	191092
• Ulnar-mammary	TBX3	12q24.21	181450
• Van der Woude syndrome	IRF6	1q32.2	119300
• Von Hippel-Lindau syndrome	VHL	3p25.3	193300
• Waardenburg syndrome type 2A (WS2A)	MITF	3p14.1	193510

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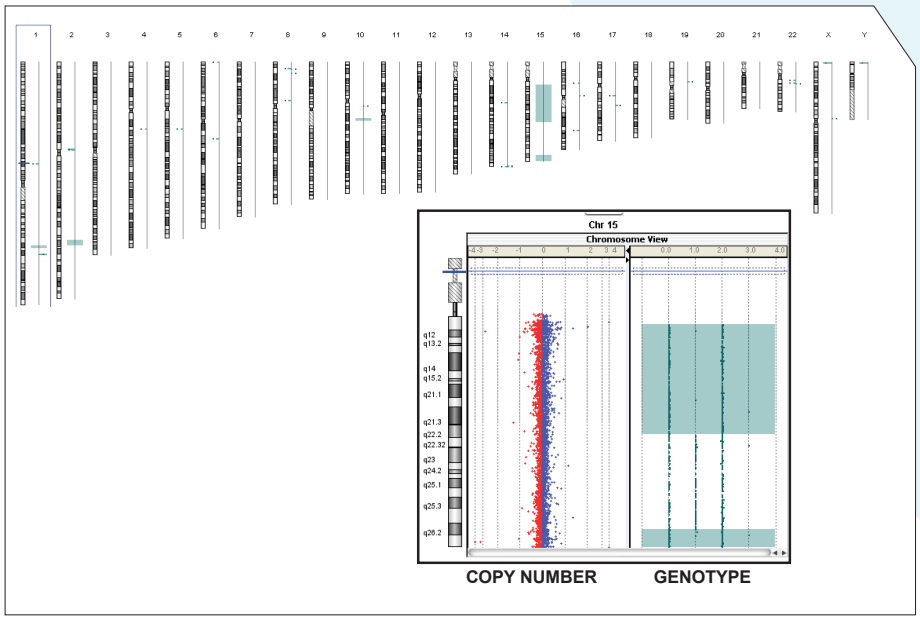
Syndrome	Gene	Locus	OMIM#
• Waardenburg syndrome, type 1 (WS1)	PAX3	2q35	193500
• Williams-Beuren region duplication syndrome	GTF2I, LIMK1, WBSCR1	7q11.23	609757
• Williams-Beuren syndrome (WBS)	multiple (ELN, RFC2, LIMK1, WSCR1)	7q11.23	194050
• Wilms tumor 1 (WT1, Nephroblastoma)	WT1	11p13	194070
• Wilms tumor, aniridia, genitourinary anomalies and mental retardation syndrome (WAGR)	PAX6, WT1	11p14.2-p13	194072
• Wolf-Hirschhorn syndrome	multiple (LETM1, WFS1, WHCR1/2)	4p16.3	194190
• X-linked agammaglobulinemia	BTK	Xq22.1	300750
• X-linked Alport plus diffuse leiomyomatosis (ATS-DL)	COL4A5, COL4A6	Xq22.3	301050
• X-linked Alport syndrome	COL4A5	Xq22.3	301050
• X-linked chronic granulomatous disease	CYBB	Xp11.4	306400
• X-linked heterotaxy, visceral, 1 (HTX1)	ZIC3	Xq26.3	306955
• X-linked hydrocephalus and nephrogenic diabetes	L1CAM, AVPR2	Xq28	----
• X-linked idiopathic short stature (ISSX)	SHOX	Xp22.13-Xpter/ Yp11.32 - Ypter	300582
• X-linked lissencephaly syndrome (LISX)	DCX	Xq22.3	300067
• X-linked lymphoproliferative syndrome (XLP1)	SH2D1A	Xq25	308240
• X-linked mental retardation (XLMR), microcephaly with pontine and cerebellar hypoplasia	CASK	Xp11.4	300749
• X-linked mental retardation with isolated growth hormone deficiency	SOX3	Xq27.1	300123
• XLMR; MRX92	ZNF674	Xp11.3	300573
• XLMR; MRX17, MRX31	HSD17B10, HUWE1	Xp11.2	300705
• XLMR; MRX21 , MRX34	IL1RAPL1	Xp21.3-p22.1	300143



CGH+SNP Array detects both copy number gains/losses and AOH.

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