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Condition	OMIM#	Gene/Locus	Location	Detection rate for deletion/duplication by microarray	Comments	References
<ul style="list-style-type: none"> 1p36 Microdeletion <p>Resources 1</p> <p>Resources 2</p>	607872	Multiple	1p36	~99% have a detectable deletion		<p>Heilstedt et al. 2003. Am J Hum Genet 72:1200-12. Medline</p> <p>Heilstedt et al. 2003. Clin Genet 64:310-16. Medline</p> <p>Yu et al. 2003. Hum Mol Genet 12:2145-52. Medline</p>
<ul style="list-style-type: none"> 1q21.1 Microdeletion with susceptibility for thrombocytopenia-absent radius (TAR) <p>Resources 1</p> <p>Resources 2</p>	274000	Multiple	1q21.1	~99% have a detectable deletion		<p>Klopocki et al. 2007. Am J Hum Genet 80:232-40. Medline</p>
<ul style="list-style-type: none"> 1q41-q42 Microdeletion 		Multiple	1q41	~99% have a detectable deletion	<p>Candidate gene DISP1 (607502)</p>	<p>Shaffer et al. 2007. Genet Med 9:607-616. Medline</p>

						Slavotinek et al. 2006. Eur J Hum Genet 14:999-1008. Medline
■ 2p15-2p16.1 Microdeletion		Multiple	2p15-p16.1	~99% have a detectable deletion		Racjan-Separovic et al. 2007. J Med Genet 44:269-76. Medline
■ 2q32.2-q33 Microdeletion	119540	Multiple	2q33.1	~99% have a detectable deletion	Candidate gene SATB2 (119540)	Van Buggenhout et al. 2005. Eur J Med Genet 48:276-89. Medline
■ 3q29 Microdeletion	609425	Multiple	3q29	~99% have a detectable deletion		Willatt et al. 2005. Am J Hum Genet 77:154-60. Medline
■ 6p25.3 Microdeletion		Multiple	6p25.3	~99% have a detectable deletion	Considerable phenotypic overlap with Craniocerebellar-cardiac	Descipio et al. 2005. Am J Med Genet 134:3-11. Medline
Resources						Lin et al. 2005. Am J Med Genet 136:162-68. Medline
■ 8p23.1 Microdeletion *		Multiple	8p23.1	~99% have a detectable deletion	Candidate gene GATA4 (600576). Phenotypic overlap with Congenital diaphragmatic hernia 2 (222400).	Slavotinek et al. 2006. Eur J Hum Genet 14:999-1008. Medline
Resources 1						Pehlivan et al. 1999. Am J Med Genet 83:201-6. Medline
Resources 2						Barber et al. 2008. Eur J Hum Genet 16:18-27. Medline
■ 9q22.32-q22.33 Microdeletion		Multiple	9q22.33	~99% have a detectable deletion	Candidate gene TGFBR1 (190181)	Redon et al. 2006. Eur J Hum Genet 14:759-67. Medline
■ 9q34 Microdeletion *	610253	Multiple	9q34.3	~99% have a detectable deletion	Candidate gene EHMT1 (610253). Rare mutations not detectable by array CGH.	Yatsenko et al. 2005. J Med Genet 42:328-35. Medline
Resources						Kleefstra et al. 2006. Am J Hum Genet 79:370-77. Medline
						Ruiter et al. 2007. Clin Genet 72:362-68. Medline

■ 10q22.3-q23.31 Microdeletion		Multiple	10q22.3-q23.31	~99% have a detectable deletion		Balciuniene et al. 2007. Am J Hum Genet 80:938-47. Medline Farrell et al. 1993. J Med Genet 30:248 50. Medline
■ 12q14.1-q15 Microdeletion *		Multiple	12q14.3	~99% have a detectable deletion	Candidate genes LEMD3 (607844) and GRIP1 (604597). Phenotypic overlap with Buschke-Ollendorff/Osteopoikilosis (166700).	Menten et al. 2007. J Med Genet 44:264-68. Medline
■ 12q24.21-12q24.23 Microduplication *		Multiple	12q24.21-q24.23	~99% have a detectable deletion		Doco-Fenzy et al. 2006. Am J Med Genet 140:212-21. Medline Ruiter et al. 2006. Clin Dysmorphol 15:133-37. Medline
■ 14q22-14q23 Microdeletion GeneReviews	600037	Multiple	14q22-q23	~99% have a detectable deletion		Nolen et al. 2006. Am J Med Genet 140:1711-1718. Medline
■ 15q24.1-q24.3 Microdeletion		Multiple	15q24.1-q24.3	~99% have a detectable deletion		Sharp et al. 2007. Hum Mol Genet 16:567-72. Medline Klopocki et al. 2007. Eur J Pediatr. Medline
■ 16p11.2-p12.2 Microdeletion *		Multiple	16p11.2-p12.2	~99% have a detectable deletion		Ballif et al. 2007. Nat Genet 39:1071-73. Medline

						Finelli et al. 2004. J Med Genet 41:e90. Medline
■ 16p13.1 Microdeletion predisposing to autism and/or mental retardation *		Multiple	16p13.1	~99% have a detectable deletion		Ullmann et al. 2007. Hum Mutat 28:674-82. Medline
■ 16p13.3 Microdeletion/Severe Rubinstein-Taybi	610543	CREBBP DNASE1	16p13.3	~99% have a detectable deletion	Phenotypic overlap with Rubenstein-Taybi (180849)	Bartsch et al. 2006. Hum Genet 120:179-86. Medline Bartsch et al. 1999. Eur J Hum Genet 7:748-56. Medline
■ 17q21.3 Microdeletion * Resources	610443	Multiple	17q21.3	~99% have a detectable deletion	Candidate gene MAPT (157140)	Shaw-Smith et al. 2006. Nat Genet 38:1032-37. Medline Sharp et al. 2006. Nat Genet 38:1038-42. Medline Kirkhoff et al. 2007. Eur J Med Genet 50:256-63. Medline
■ 22q13.3 Microdeletion* GeneReviews	606232	Multiple	22q13.3	~99% have a detectable deletion	Candidate genes ARSA (607574) and SHANK3 (606230)	Anderlid et al. 2002. Hum Genet 110:439-43. Medline Luciani et al. 2003. J Med Genet 40:690-96. Medline Phelan et al. 2001. Am J Med Genet 101:91-99. Medline Okamoto et al. 2007. Am J Med Genet 143:2804-09. Medline
■ Xp11.3 Microdeletion Resources	300578	Multiple	Xp11.3	~99% have a detectable deletion	Candidate genes RP2 (312600) and ZNF674 (300573)	Zhang et al. 2006. Am J Med Genet 140:349-57. Medline Lugtenberg et al. 2006. Am J Hum Genet 78:265-78. Medline

<ul style="list-style-type: none"> Adrenal hypoplasia congenita (AHC)* <p>GeneReviews</p>	300200	NR0B1	Xp21.2	~18% have a detectable deletion in isolated AHC; ~ 99% have a detectable deletion in AHC/GKD or AHC/GKD/DMD	~53% have mutations not detectable by array CGH	<p>Guo et al. 1995. JAMA 274:324-30. Medline</p> <p>Peter et al. 1998. J Clin Endocrinol Metab 83: 2666-74. Medline</p>
<ul style="list-style-type: none"> Adult-onset autosomal 	169500	LMNB1	5q23.2	Precise detection rate	Available as	Padiath et al. 2006. Nat Genet 38:1114
<ul style="list-style-type: none"> Alagille <p>GeneReviews</p>	118450	JAG1	20p12.2	3-7% have a detectable deletion	Majority have mutations not detectable by array CGH	<p>Krantz et al. 1998. Am J Hum Genet 62:1361-69. Medline</p> <p>Spinner et al. 2001. Hum Mutat 17:18-33. Medline</p>
<ul style="list-style-type: none"> Albright hereditary osteodystrophy-like syndrome/Brachydactyly MR <p>Resources 1</p> <p>Resources 2</p>	600430	Multiple	2q37.3	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	<p>Aldred et al. 2004. J Med Genet 41:433-39. Medline</p> <p>Phelan et al. 1995. Am J Med Genet 58:1-7. Medline</p> <p>Shrimpton et al. 2004. Clin Genet 66:537-44. Medline</p> <p>Wilson et al. 1995. Am J Hum Genet 56:400-407. Medline</p>
<ul style="list-style-type: none"> Alpha thalassemia mental retardation (ATR-16) <p>See SignatureChipOS page for additional information</p> <p>GeneReviews</p>	141750	Multiple	16p13.3	~99% have a detectable deletion	Deletion HBA1 (141800) and HBA2 (141850) responsible for alpha-thalassemia phenotype.	<p>Wilkie et al. 1990. Am J Hum Genet 46:1112-26. Medline</p> <p>Harteveld et al. 2007. Hum Genet. 122:283-92. Medline</p>
<ul style="list-style-type: none"> Alzheimer disease, early onset with cerebral amyloid angiopathy* 	104300	APP	21q21.3	~8% have a detectable duplication	Available as FISH test only. ~16% have mutations not detectable by array CGH	Rovelet-Lecrux et al. 2006. Nat Genet 38:24-26. Medline

GeneReviews					detectable by FISH. Not routinely tested by the	Raux et al. 2005. J Med Genet 42:793-93. Medline
<ul style="list-style-type: none"> ■ Angelman* GeneReviews	105830	UBE3A	15q11.2	~70% have a detectable deletion	~30% have either paternal UPD or mutations not detectable by array CGH	Magenis et al. 1987. Am J Med Genet 28:829-38. Medline Zacowski et al. 1993. Am J Med Genet 46:7-11. Medline
<ul style="list-style-type: none"> ■ Aniridia II GeneReviews	106210	PAX6	11p13	Rare deletions unless associated with contiguous gene syndrome	Majority have mutations not detectable by array CGH	Crolla et al. 2002. Am J Hum Genet 71:1138-49. Medline Gronskov et al. 2001. Hum Genet 109:11-18. Medline
<ul style="list-style-type: none"> ■ Atrial septal defect (ASD) with atrioventricular conduction defects Resources	108900	NKX2-5	5q35.2	Deletions uncommon	~10-27% have mutations not detectable by array CGH	Baekvad-Hansen et al. 2006. Am J Med Genet 140:427-33. Medline Sarkozy et al. 2005 J Med Genet 42:e16. Medline Benson et al. 1999. J Clin Invest 104:1567-73. Medline
<ul style="list-style-type: none"> ■ Bannayan-Riley-Ruvalcaba (BRRS) 	153480	PTEN	10q23.31	~2-11% have a detectable deletion	~60% have mutations not detectable by array CGH.	Marsh et al. 1998. Hum Mol Genet 7:507-15. Medline

<p>Signature Summary on PTEN Hamartoma Tumor Syndrome</p> <p>GeneReviews</p>					<p>Allelic with Cowden (158350)/ Macrocephaly/autism (605309)/ Proteus/Proteus-like (176920).</p>	<p>Marsh et al. 1999. Hum Mol Genet 8:1461-72.</p> <p>Medline</p> <p>Zhou et al. 2003. Am J Hum Genet 73:404-11. Medline</p>
<p>□ Bartter, antenatal 1</p> <p>Resources</p>	<p>601678</p>	<p>SLC12A1</p>	<p>15q21.1</p>	<p>Precise detection rate unknown</p>	<p>Recessive condition. Majority have mutations not detectable by array CGH</p>	<p>Vargas-Poussou et al. 1998. Am J Hum Genet 62:1332-40. Medline</p> <p>Simon et al. 1996. Nat Genet 13:183-88. Medline</p>
<p>□ Bartter, antenatal 2</p> <p>Resources</p>	<p>241200</p>	<p>KCNJ1</p>	<p>11q24.3</p>	<p>Precise detection rate unknown</p>	<p>Recessive condition. Majority have mutations not detectable by array CGH</p>	<p>Károlyi et al. 1997. Hum Mol Genet 6:17-26. Medline</p> <p>Feldmann et al. 1998. J Am Soc Nephrol 9:2357-59. Medline</p> <p>Jeck et al. 2001. Kidney Int 59:1803-11. Medline</p>
<p>□ Bartter 3 (classic)</p> <p>Resources</p>	<p>607364</p>	<p>CLCNKB</p>	<p>1p36.13</p>	<p>Precise detection rate unknown</p>	<p>Recessive condition. Majority of cases have at least one mutation not detectable by</p>	<p>Konrad et al. 2000. J Am Soc Nephrol 11:1449-59. Medline</p> <p>Simon et al. 1997. Nat Genet 17:171-78. Medline</p>
<p>□ Bartter 4 (infantile with sensorineural deafness)</p> <p>Resources</p>	<p>602522</p>	<p>BSND or</p>	<p>1p32.3</p>	<p>Unknown</p>	<p>Recessive condition. ~73% have mutations not detectable by array CGH</p>	<p>Birkenhäger et al. 2001. Nat Genet 29:310-14. Medline</p>
<p>CLCNKA & CLCNKB</p>	<p>1p36.13</p>					
<p>■ Basal cell nevus/Gorlin-Goltz</p>	<p>109400</p>	<p>PTCH1</p>	<p>9q22.32</p>	<p>Deletions uncommon</p>	<p>Allelic with Holoprosencephaly 7</p>	<p>Boonen et al. 2005. Am J Med Genet 132:324-28. Medline</p>

GeneReviews					(610828)	
<ul style="list-style-type: none"> ■ Beckwith-Wiedemann* GeneReviews 	130650	IGF2	11p15.5	Duplications uncommon	Majority have paternal isodisomy or mutations not detectable by array CGH	Henry et al. 1993. Eur J Hum Genet 1:19-29. Medline Li et al. 1998. Am J Med Genet 79:253-59. Medline Slavotinek et al. 1997. J Med Genet 34:819-26. Medline
<ul style="list-style-type: none"> □ Bilateral frontoparietal polymicrogyria (BFPP) GeneReviews 	606854	GPR56	16q13	Unknown	Recessive disorder. Majority have mutations not detectable by array CGH	Piao et al. 2004. Science 303:2033-36. Medline
<ul style="list-style-type: none"> ■ Blepharophimosis, ptosis epicanthus inversus (BPE) GeneReviews 	110100	FOXL2	3q22.3	Precise detection rate unknown		Crisponi et al. 2001. Nat Genet 27:159-66. Medline
<ul style="list-style-type: none"> ■ Branchio-Oto-Renal (BOR)/Melnick-Frasier GeneReviews 	113650	EYA1	8q13.3	7-11% have a detectable deletion	~40% have mutations not detectable by array CGH. Allelic with Oto-Facio-Cervical	Abdelhak et al. 1997. Hum Molec Genet 6:2247-55. Medline Chang et al. 2004. Hum Mutat 23:582-89. Medline
<ul style="list-style-type: none"> □ Buschke-Ollendorff 	166700	LEMD3	12q14.3	Unknown	Phenotypic overlap with 12q14.1-q15 Microdeletion	Hellemans et al. 2004. Nat Genet 36:1213-18. Medline
<ul style="list-style-type: none"> ■ Campomelic dysplasia (CMPD) 	114290	SOX9	17q24.3	Deletions uncommon	Majority have mutations not	Olney et al. 1999. Am J Med Genet 84:20-24. Medline

					detectable by array CGH	
Resources						
<ul style="list-style-type: none"> ■ Cat-eye* <p>< 1 \Resources></p> <p>Resources 2</p>	115470	Multiple	22q11.1	Precise detection rate unknown	The supernumary marker chromosome is detectable by array CGH	Bartsch et al. 2005. Eur J Hum Genet 13:592-98. Medline Johnson et al. 1999. Genomics 57:306-309. Medline Rosias et al. 2001. Genet Couns 12:273-82. Medline
<ul style="list-style-type: none"> ■ CHARGE <p>Resources</p>	214800	CHD7	8q12.2	~10% have a detectable deletion	Majority have mutations not detectable by array CGH	Vissers et al. 2004. Nat Genet 36:955-57. Medline
<ul style="list-style-type: none"> ■ Cleidocranial dysplasia (CCD) <p>GeneReviews</p>	119600	RUNX2	6p12.3	Deletions uncommon	Majority have mutations not detectable by array CGH	Mundlos et al. 1997. Cell 89:773-79. Medline Otto et al. 2002. Hum Mutat 19:209-16. Medline
<ul style="list-style-type: none"> ■ Congenital adrenal hyperplasia (CAH) <p>See SignatureChipOS for additional information</p> <p>GeneReviews</p>	201910	CYP21A2	6p21.32	Precise detection rate unknown	Recessive condition. ~95% have at least one mutation not detectable by array CGH	Speiser et al. 1992. J Clin Invest 90:584-95. Medline
<ul style="list-style-type: none"> ■ Congenital diaphragmatic hernia (CDH) <p>GeneReviews</p>	142340	CHD2	15q26.1	1-2% have a detectable deletion		Klaasens et al. 2005. Am J Hum Genet 76:877-82. Medline Schlembach et al. 2001. Prenat Diagn 21:289-92. Medline
		NR2F2	15q26.2			

<p>■ Congenital diaphragmatic hernia 2 (CDH2)*</p> <p>GeneReviews</p>	<p>222400</p>	<p>GATA4 candidate gene (600576)</p>	<p>8p23.1</p>	<p>~3% have a detectable deletion</p>	<p>Majority of reported deletions are detectable by array CGH. Phenotypic overlap with 8p23.1 Microdeletion.</p>	<p>Slavotinek et al. 2006. Eur J Hum Genet 14:999-1008. Medline</p> <p>Slavotinek et al. 2005. J Med Genet 42:730-36. Medline</p> <p>Barber et al. 2007. Eur J Hum Genet 16:18-27. Medline</p>
<p>□ Cornelia de Lange</p> <p>GeneReviews</p>	<p>122470</p>	<p>NIPBL</p>	<p>5p13.2</p>	<p>Rare deletions</p>	<p>~47% have mutations not detectable by array CGH</p>	<p>DeScipio et al. 2005. Am J Med Genet 137:276-82. Medline</p> <p>Gillis et al. 2004. Am J Hum Genet 75:610-23. Medline</p> <p>Krantz et al. 2004. Nat Genet 36:631-35. Medline</p>
<p>■ Cowden</p> <p>Signature Summary on PTEN Hamartoma Tumor Syndrome</p> <p>GeneReviews</p>	<p>158350</p>	<p>PTEN</p>	<p>10q23.31</p>	<p>~1% have a detectable deletion</p>	<p>~80% have mutations not detectable by array CGH. Allelic with Bannayan-Riley-Ruvalcaba (153480)/ Macrocephaly/autism (605309)/ Proteus/Proteus-</p>	<p>Marsh et al. 1998. Hum Mol Genet 7:507-15. Medline</p> <p>Zhou et al. 2003. Am J Hum Genet 73:404-11. Medline</p>
<p>■ Cri-du-Chat</p> <p>Resources</p>	<p>123450</p>	<p>Multiple</p>	<p>5p15.2</p>	<p>~ 99% have a detectable deletion</p>		<p>Church et al. 1997. Genome Res 7:787-801. Medline</p> <p>Mainardi et al. 2001. J Med Genet. 38:151-58. Medline</p>

						Zhang et al. 2005. Am J Hum Genet 76:312-26. Medline
<ul style="list-style-type: none"> ■ Currarino <p>Resources</p>	176450	HLXB9	7q36.3	2-3% have a detectable deletion	26-75% have mutations not detectable by array CGH	Hagan et al. 2000. Am J Hum Genet Belloni et al. 2000. Am J Hum Genet 66:312-19. Medline
<ul style="list-style-type: none"> ■ Dandy-Walker malformation (DWM) <p>Resources 1</p> <p>Resources 2</p>	220200	ZIC1 ZIC4	3q24	Deletions uncommon		Grinberg et al. 2004. Nat Genet 36:1053-55. Medline
<ul style="list-style-type: none"> ■ DiGeorge/Velocardiofacial (VCF)* <p>GeneReviews</p>	188400	HIRA TBX1	22q11.21	>95% have a detectable deletion		Mantripragada et al. 2004. Int J Mol Med 13:273-79. Medline Shaikh et al. 2000. Hum Mol Genet. 9:489-501. Medline Yagi et al. 2003. Lancet 362:1366-73. Medline
<ul style="list-style-type: none"> ■ DiGeorge 2 <p>Resources</p>	601362	Multiple	10p14	<1% have a detectable deletion		Berend et al. 2000. Am J Med Genet 91:313-17. Medline Van Esch et al. 1999. Clin Genet 55:269-76. Medline
<ul style="list-style-type: none"> ■ Dosage-sensitive sex reversal* <p>Resources</p>	300018	NR0B1	Xp21.2	Precise detection rate unknown		Bardoni et al. 1994. Nat Genet 7:497-501. Medline Sanlaville et al. 2004. Am J Med Genet 128:325-30. Medline

<p>■ Down syndrome critical region (DSCR)*</p> <p>Resources</p>	<p>602917</p>	<p>Multiple</p>	<p>21q22.13</p>	<p>Precise detection rate unknown</p>	<p>Majority of reported duplications are detectable by array CGH</p>	<p>Korenberg et al. 1990. Am J Hum Genet 47:236-46. Medline</p> <p>Delabar et al. 1993. Eur J Hum Genet 1:114-24. Medline</p> <p>Barlow et al. 2001. Genet Med 3:91-101. Medline</p> <p>Ronan et al. 2007. J Med Genet 44:448-51. Medline</p>
<p>■ Familial adenomatous polyposis (FAP)/Gardner/MR</p> <p>GeneReviews</p>	<p>175100</p>	<p>APC</p>	<p>5q22.2</p>	<p>>98% have a detectable deletion</p>	<p>Majority of isolated FAP cases have mutations not detectable by array CGH</p>	<p>Pilarski et al. 1999. Am J Med Genet 86:321-24. Medline</p> <p>Raedle et al. 2001. Am J Gastroent 96:3016-20. Medline</p>
<p>□ Familial hypocalciuric hypercalcemia 1 (HHC1)</p> <p>Resources 1</p>	<p>145980</p>	<p>CASR</p>	<p>3q21.1</p>	<p>Unknown</p>	<p>~40-67% have mutations not detectable by array CGH. Allelic with</p>	<p>Chou et al. 1995. Am J Hum Genet 56:1075-79. Medline</p> <p>Pearce et al. 1995. J Clin Invest 96:2683-92. Medline</p>
<p>■ Feingold</p> <p>Resources</p>	<p>164280</p>	<p>MYCN</p>	<p>2p24.3</p>	<p>~4% have a detectable deletion</p>	<p>~63% have deletions not detectable by array CGH</p>	<p>Celli et al. 2000. Am J Hum Genet 66:436-44. Medline</p> <p>van Bokhoven et al. 2005. Nat Genet 37:465-67. Medline</p>
<p>□ FG 5*</p>	<p>300581</p>	<p>MID2</p>	<p>Xq22.3</p>	<p>Rare duplications</p>	<p>Majority of reported duplications are detectable by array CGH</p>	<p>Jehee et al. 2005. Am J Med Genet 139:221-26. Medline</p>

Resources						
■	FMR1 microdeletion	300624	FMR1	Xq27.3	<1% of individuals with Fragile X have a detectable deletion	>99% of individuals with Fragile X have CGG triplet expansions or other mutations Quan et al. 1995. Am J Hum Genet 56:1042-51. Medline Hammond et al. 2007. Am J Med Genet 72:430-34. Medline
	GeneReviews					
■	Fryns	229850	DISP1 candidate gene (607502)	1q41	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH Shaffer et al. 2007. Genet Med 9:607-616. Medline Slavotinek et al. 2006. Eur J Hum Genet 14:999-1008. Medline
	GeneReviews					
□	Generalized epilepsy with febrile seizures plus 2 (GEFS+2)	604233	SCN1A	2q24.4	Unknown	~6% have mutations not detectable by array CGH. Allelic with severe myoclonic epilepsy of infancy Wallace et al. 2001. Am J Hum Genet 68:859-65. Medline
	GeneReviews					
□	Gitelman	263800	SLC12A3	16q13	Precise detection rate unknown	Recessive condition. Majority have at least one mutation not detectable by Mastroianni et al. 1996. Am J Hum Genet 59:1019-26. Medline Syrén et al. 2002. Hum Mutat 20:78. Medline
	Resources					
■	Glycerol kinase deficiency	300474	GK	Xp21.2	Rare deletions	Majority have mutations not detectable by array CGH Sargent et al. 2000 J Med Genet 37:434-41. Medline
	Resources					
■	Greig cephalopolysyndactyly	175700	GLI3	7p14.1	~30% have a detectable deletion	Johnston et al. 2003. Am J Med Genet 123:236-42. Medline

[GeneReviews](#)

Holoprosencephaly

25-50% of cases with holoprosencephaly (HPE) have abnormal karyotypes, the vast majority of which are detectable by array CGH.

15-20% of HPE cases with normal chromosomes will have sequence mutations in SHH, ZIC2, SIX3, or TGIF. Sequence mutations are not detectable by array CGH. A negative microarray test result does not exclude the possibility that one or more of these genes may play a role in the patient's phenotype.

<p>SignatureChip® Detection Rates for Holoprosencephaly</p>	<p>4.7% of chromosomally normal and mutation-analysis normal HPE cases have microdeletions in SHH, ZIC2, SIX3 or TGIF (Bendavid et al. 2006. Hum Genet 119:1-8. Medline). The majority of reported microdeletions are detectable by array CGH.</p>				
<p>□ Holoprosencephaly 1</p> <p>Signature Summary on Holoprosencephaly</p> <p>GeneReviews</p>	<p>236100</p>	<p>TMEM1</p>	<p>21q22.3</p>	<p>Unknown</p>	<p>Muenke et al. 1995. Am J Hum Genet 57:1074-9. Medline</p> <p>Nagamine et al. 1997. Biochem Biophys Res Commun 235:185-90. Medline</p>

<p>■ Holoprosencephaly 2</p> <p>Signature Summary on Holoprosencephaly</p> <p>GeneReviews</p>	<p>157170</p>	<p>SIX3</p>	<p>2p21</p>	<p>~1% have a detectable deletion</p>	<p>~4% have mutations not detectable by array CGH</p>	<p>Bendavid et al. 2006. Hum Genet 119:1-8. Medline</p> <p>Dubourg et al. 2004. Hum Mutat 24:43-51. Medline</p> <p>Ming et al. 2002. Am J Hum Genet 71:1017-32. Medline</p>
<p>■ Holoprosencephaly 3</p> <p>Signature Summary on Holoprosencephaly</p> <p>GeneReviews</p>	<p>142945</p>	<p>SHH</p>	<p>7q36.3</p>	<p>1-2% have a detectable deletion</p>	<p>6-8% have mutations not detectable by array CGH</p>	<p>Bendavid et al. 2006. Hum Genet 119:1-8. Medline</p> <p>Ming et al. 2002. Am J Hum Genet 71:1017-32. Medline</p> <p>Nanni et al. 1999. Hum Mol Genet 8:2479-88. Medline</p>
<p>■ Holoprosencephaly 4</p> <p>Signature Summary on Holoprosencephaly</p> <p>GeneReviews</p>	<p>142946</p>	<p>TGIF</p>	<p>18p11.31</p>	<p><1% have a detectable deletion</p>	<p>~1% have mutations not detectable by array CGH</p>	<p>Bendavid et al. 2006. Hum Genet 119:1-8. Medline</p> <p>Dubourg et al. 2004. Hum Mutat 24:43-51. Medline</p> <p>Gripp et al. 2000. Nat Genet 25:205-208. Medline</p> <p>Ming et al. 2002. Am J Hum Genet 71:1017-32. Medline</p>
<p>■ Holoprosencephaly 5</p> <p>Signature Summary on Holoprosencephaly</p>	<p>609637</p>	<p>ZIC2</p>	<p>13q32.3</p>	<p><1% have a detectable deletion</p>	<p>~3% have mutations not detectable by array CGH</p>	<p>Bendavid et al. 2006. Hum Genet 119:1-8. Medline</p> <p>Brown et al. 2001. Hum Molec Genet 10:791-96. Medline</p>

GeneReviews						Dubourg et al. 2004. Hum Mutat 24:43-51. Medline
<input type="checkbox"/> Holoprosencephaly 6 Signature Summary on Holoprosencephaly GeneReviews	605934	HPE6	2q37.1 -q37.3	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Lehman et al. 2001. Am J Med Genet 100:179-81. Medline
<input type="checkbox"/> Holoprosencephaly 7 Signature Summary on Holoprosencephaly GeneReviews	601309	PTCH1	9q22.32	Unknown	Allelic with Basal cell nevus/Gorlin-Goltz (109400)	Ming et al. 2002. Hum Genet 110:297-301. Medline
<input checked="" type="checkbox"/> Holoprosencephaly 8 Signature Summary on Holoprosencephaly GeneReviews	609408	Multiple	14q13.1-q13.2	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Kamnasaran et al. 2005. Genomics 85:608-21. Medline
<input type="checkbox"/> Holoprosencephaly and preaxial polydactyly* Signature Summary on Holoprosencephaly	605651	FBXW11	5q35.1	Precise detection rate unknown	Majority of reported duplications are detectable by array CGH	Koolen et al. 2006. J Hum Genet 51:721-26. Medline

GeneReviews						
<ul style="list-style-type: none"> □ Holt-Oram* GeneReviews	142900	TBX5	12q24.1	Rare deletions	30-35% have mutations not detectable by array CGH	Borozdin et al. 2006. Am J Med Genet 140:1880-86. Medline Brassington et al. 2003. Am J Hum Genet 73:74-85. Medline Cross et al. 2000. J Med Genet 37:785-87. Medline Doco-Fenzy et al. 2006. Am J Med Genet 140:212-21. Medline
<ul style="list-style-type: none"> ■ Hypoparathyroidism, sensorineural deafness, renal disease (HDR) Resources	146255	GATA3	10p14	~40% have a detectable deletion	10-20% have mutations not detectable by array CGH	Muroya et al. 2001. J Med Genet 38:374-80. Medline Van Esch et al. 2000. Nature 406:419-22. Medline
<ul style="list-style-type: none"> ■ Jacobsen/11q terminal deletion disorder Resources 1 Resources 2	147791	Multiple	11q23 -11qter	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	De Pater et al. 1997. Genet Couns 8:335-39. Medline Grossfeld et al. 2004. Am J Med Genet 129:51-61. Medline Tunnacliffe et al. 1999. Genome Res 9:44-52. Medline
<ul style="list-style-type: none"> □ Joubert 3 GeneReviews	608629	AHI1	6q23.3	Unknown	Recessive condition. ~11% have at least one mutation not detectable by array CGH	Parisi et al. 2006. J Med Genet 43:334-39. Medline

<p>■ Joubert 4</p> <p>GeneReviews</p>	<p>609583</p>	<p>NPHP1</p>	<p>2q13</p>	<p>Precise detection rate unknown</p>	<p>Recessive condition. Allelic with Nephronophthisis 1 (256100).</p>	<p>Parisi et al. 2004. Am J Hum Genet 75:82-91. Medline</p>
<p>□ Joubert 5</p> <p>GeneReviews</p>	<p>610188</p>	<p>CEP290</p>	<p>12q21.32</p>	<p>Unknown</p>	<p>Recessive condition. ~7% have at least one mutation not detectable by array CGH. Allelic with Leber Congenital Amaurosis X (610142)/ Meckel 4 (611134)/ Senior-Loken 6 (610189).</p>	<p>Helou et al. 2007. J Med Genet 44:657-63. Medline</p>
<p>■ Juvenile polyposis (JPS), BMPR1A-related</p> <p>GeneReviews</p>	<p>174900</p>	<p>BMPR1A</p>	<p>10q23.2</p>	<p>~1-7% have a detectable deletion</p>	<p>~11-21% have mutations not detectable by array CGH</p>	<p>Sweet et al. 2005. JAMA 19:2465-73. Medline</p> <p>Pyatt et al. 2006. J Molec Diagn 8:84-88. Medline</p> <p>Aretz et al. 2007. J Med Genet. 44:702-9. Medline</p> <p>Howe et al. 2004. J Med Genet 41:484-91. Medline</p>
<p>■ Juvenile polyposis (JPS), MADH4-related</p> <p>GeneReviews</p>	<p>174900</p>	<p>MADH4 (SMAD4)</p>	<p>18q21.2</p>	<p>~4-6% have a detectable deletion</p>	<p>~19-22% have mutations not detectable by array CGH</p>	<p>van Hattem et al. 2008. Gut. Medline</p> <p>Aretz et al. 2007. J Med Genet. 44:702-9. Medline</p>

						Howe et al. 2004. J Med Genet 41:484-91. Medline Pyatt et al. 2006. J Molec Diagn 8:84-88. Medline
<ul style="list-style-type: none"> Kallmann 1 Resources 	308700	KAL1	Xp22.31	10-12% have a detectable deletion		Ballabio et al. 1986. Hum Genet 72:237-40. Medline Hardelin et al. 1993. J Clin Endocrinol Metab 76:827-31. Medline Sato et al. 2004. J Clin Endocrinol Metab 89:1079-88. Medline
<ul style="list-style-type: none"> Langer-Giedion Resources 	150230	TRPS1 EXT1	8q23.3 8q24.11	~75% have a detectable deletion		Ahn et al. 1995. Nat Genet 11:137-43. Medline Ludecke et al. 1995. Hum Mol Genet 4:31-36. Medline Nardmann et al. 1997. Hum Genet 99:638-43. Medline
<ul style="list-style-type: none"> Langer mesomelic dysplasia (LMD) See SignatureChipOS page for additional information Resources 	249700	SHOX	Xpter-Xp22.3 & Ypter-Yp11.32	Precise detection rate unknown	Recessive condition. Many reported deletions are detectable by array CGH. Allelic with X-linked idiopathic short stature(300582)/Leri-Weill	>Thomas et al. 2004. Am J Med Genet 128:179-84. Medline Robertson et al. 2000. J Med Genet 37:959-64. Medline

<p>□ Leber Congenital Amaurosis X (LCAX)</p> <p>GeneReviews</p>	<p>610142</p>	<p>CEP290</p>	<p>12q21.32</p>	<p>Unknown</p>	<p>Recessive condition. 21% have at least one mutation not detectable by microarray. Allelic with Joubert 5 (610188)/ Meckel 4 (611134)/ Senior-Lakes C</p>	<p>den Hollander et al. 2006. Am J Hum Genet 79:556-61. Medline</p>
<p>■ Leri-Weill dyschondrosteosis</p> <p>GeneReviews</p>	<p>127300</p>	<p>SHOX</p>	<p>Xpter-Xp22.3 & Ypter-Yp11.32</p>	<p>~34-41% have detectable deletions</p>	<p>~23% have mutations not detectable by microarray. Allelic with X-</p>	<p>Huber et al. 2006. J Med Genet 43:735-39. Medline</p> <p>Benito-Sans et al. 2006. Am J Hum Genet 79:409</p>
<p>□ Li-Fraumeni 1 (LFS)</p> <p>GeneReviews</p>	<p>151623</p>	<p>TP53</p>	<p>17p13.1</p>	<p>Rare deletions</p>	<p>~71-79% have mutations not detectable by array CGH</p>	<p>Bougeard et al. 2003. Oncogene 22:840-46. Medline</p> <p>Varley et al. 2003. Hum Mutat 21:313-20. Medline</p> <p>Varley et al. 1997. Cancer Res 57:3245-52. Medline</p>
<p>■ Lissencephaly 1</p> <p>Resources</p>	<p>607432</p>	<p>PAFAH1B1 (LIS1)</p>	<p>17p13.3</p>	<p>>13% have detectable deletions</p>		<p>Pilz et al. 1998. Genet Med 1:29-33. Medline</p>
<p>□ Lissencephaly with cerebellar hypoplasia</p> <p>Resources</p>	<p>257320</p>	<p>RELN</p>	<p>7q22.1</p>	<p>Unknown</p>		<p>Hong et al. 2000. Nat Genet 26:93-96. Medline</p>
<p>□ Loeys-Dietz (LDS), TGFBR1-related</p> <p>Resources</p>	<p>609192</p>	<p>TGFBR1</p>	<p>9q22.33</p>	<p>Unknown</p>	<p>~25% have mutations not detectable by array CGH</p>	<p>Loeys et al. 2006. NEJM 355:788-98. Medline</p> <p>Loeys et al. 2005. Nat Genet 37:275-281. Medline</p>

<p>□ Loeys-Dietz (LDS), TGFBR2-related</p> <p>Resources</p>	<p>609192</p>	<p>TGFBR2</p>	<p>3p24.1</p>	<p>Unknown</p>	<p>~56% have mutations not detectable by array CGH. Allelic with Marfan 2 (154705).</p>	<p>Loeys et al. 2006. NEJM 355:788-98. Medline</p>
<p>■ Lowie</p> <p>GeneReviews</p>	<p>309000</p>	<p>OCRL</p>	<p>Xq25</p>	<p>Large deletions uncommon</p>	<p>Majority have mutations not detectable by array CGH</p>	<p>Addis et al. 2007. Eur J Med Genet 50:79-84. Medline</p> <p>Lin et al. 1997. Am J Hum Genet 60:1384-88. Medline</p>
<p>□ Macrocephaly/autism</p> <p>Signature Summary on PTEN Hamartoma Tumor Syndrome</p>	<p>605309</p>	<p>PTEN</p>	<p>10q23.31</p>	<p>Unknown</p>	<p>~4% have mutations not detectable by array CGH. Allelic with Bannayan-Riley-Ruvalcaba (153480)/Cowden (158350)/Proteus/Proteus-like (176920).</p>	<p>Butler et al. 2005. J Med Genet 42:318-21. Medline</p> <p>Buxbaum et al. 2007. Am J Med Genet B 144:484-91. Medline</p>
<p>■ Marfan 1 (MFS1)</p> <p>GeneReviews</p>	<p>154700</p>	<p>FBN1</p>	<p>15q21.1</p>	<p><1% have a detectable deletion</p>	<p>~60-93% have mutations not detectable by array CGH</p>	<p>Mátyás et al. 2007. Hum Genet 122:23-32. Medline</p> <p>Halliday et al. 2002. J Med Genet 39:589-93. Medline</p> <p>Loeys et al. 2004. Hum Mutat 24:140-146. Medline</p>
<p>□ Marfan 2 (MFS2)</p>	<p>154705</p>	<p>TGFBR2</p>	<p>3p24.1</p>	<p>Unknown</p>	<p>~12% have mutations not detectable by array CGH. Allelic with Loeys-Dietz (609192).</p>	<p>Singh et al. 2006. Hum Mutat 27:770-77. Medline</p>

Resources						
<ul style="list-style-type: none"> □ Meckel 4 	611134	CEP290	12q21.32	Unknown	Recessive condition. ~10% have at least one mutation not detectable by array CGH. Allelic with Joubert 5 (610188)/ Leber congenital amaurosis X (610142)/Senior-Loken 6 (610189).	Baala et al. 2007. Am J Hum Genet 81:170-79. Medline
Resources						
<ul style="list-style-type: none"> ■ Microphthalmia 3 	206900	SOX2	3q26.33	~2% have a detectable deletion	~8% have mutations not detectable by array CGH	Bakrania et al. 2007. Br J Ophthalmol 91:1471-76. Medline
GeneReviews						
<ul style="list-style-type: none"> ■ Microphthalmia with linear skin defects 	309801	Multiple	Xp22.2	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Kayserili et al. 2001. J Med Genet 38:411-17. Medline Prakash et al. 2002. Hum Mol Genet 11:3237-48. Medline Zvulunov et al. 1998. Br J Dermatol 138:1046-52. Medline
Resources						
<ul style="list-style-type: none"> ■ Miller-Dieker 	247200	PAFAH1B1 (LIS1)	17p13.3	85-90% have a detectable deletion		Cardoso et al. 2003. Am J Hum Genet 72:918-30. Medline Dobyns et al. 1991. Am J Hum Genet 48:584-94. Medline Ledbetter et al. 1992. Am J Hum Genet 50:182-89. Medline
Resources						

						Pilz et al. 1998. Genet Med 1:29-33. Medline
■ Mohr-Tranebjaerg	304700	TIMM8A	Xq22.1	Rare deletions unless associated with contiguous gene deletion syndrome involving X-linked agammaglobulinemia (300300).	Majority have mutations not detectable by array CGH	Sediva et al. 2007. J Clin Immunol 27:640-46. Medline
GeneReviews						
■ Mowat-Wilson*	235730	ZFXH1B	2q22.3	~15-21% have a detectable deletion	~21-28% have mutations not detectable by array CGH	Ishihara et al. 2004. J Med Genet 41:387-93. Medline Dastot-Le Moal et al. 2006. Hum Mutat 28:313-21. Medline Amiel et al. 2001. Am J Hum Genet 69:1370-77. Medline
GeneReviews						
■ Nablus mask-like facial	608156	Multiple	8q21.3-q22.1	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Shieh et al. 2006. Am J Med Genet 140:1267-73. Medline
■ Nail-patella (NPS)	161200	LMX1B	9q33.3	~1-5% have a detectable deletion	~85% have mutations not detectable by array CGH	Dunston et al. 2004. Genomics 84:565-76. Medline
GeneReviews						
■ Nephronophthisis 1	256100	NPHP1	2q13	80% have detectable homozygous deletions	Recessive condition. Allelic with Joubert 4 (609583)	Saunier et al. 2000. Am J Hum Genet 66:778-89. Medline
Resources						
□ Neonatal severe primary hypoparathyroidism (NSHPT)	239200	CASR	3q21.1	Unknown	Recessive condition. Allelic with Familial hypocalciuric	Pollak et al. 1994. J Clin Invest 93:1108-12. Medline

Resources 1					hypercalcemia 1 (145980).	Ward et al. 2004. J Clin Endocr Metab 89:3721-30. Medline
<ul style="list-style-type: none"> ■ Neurofibromatosis 1 (NF1)/MR <p>GeneReviews</p>	162200	NF1	17q11.2	5-20% have a detectable deletion		Crossen et al. 1997. Hum Mutat 9:458-64. Medline Jenne et al. 2003. Genes Chrom & Cancer 37:111-20. Medline Upadhyaya et al. 1998. Hum Genet 102:591-97. Medline
<ul style="list-style-type: none"> ■ Neurofibromatosis 2 (NF2) <p>GeneReviews</p>	101000	NF2	22q12.2	~15-21% have a detectable deletion	34-66% have mutations not detectable by array CGH	Bruder et al. 2001. Hum Mol Genet 10:271-82. Medline Zucman-Rossi et al. 1998. Hum Mol Genet 7:2095-101. Medline Evans et al. 2000. J Med Genet 37:897-904. Medline
<ul style="list-style-type: none"> ■ NFIA haploinsufficiency 	600727	NFIA	1p31.3	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Lu et al. 2007. PLoS Genet 3:0830-43. Medline
<ul style="list-style-type: none"> □ Noonan 1 <p>GeneReviews</p>	163950	PTPN11	12q24.13	Precise detection rate unknown	Majority have mutations not detectable by array CGH	Tartaglia et al. 2001. Nat Genet 29:465-68. Medline
<ul style="list-style-type: none"> □ Noonan 4 <p>GeneReviews</p>	610733	SOS1	2p22.1	Precise detection rate unknown	~9-15% have mutations not detectable by array CGH	Roberts et al. 2007. Nat Genet 39:70-74. Medline Tartaglia et al. 2007. Nat Genet 39:75-79. Medline
<ul style="list-style-type: none"> ■ Oculocutaneous Albinism 2 (OCA2)* 	203200	OCA2	15q13.1	Rare homozygous deletions in most ethnicities; ~99% in Navaio population	Recessive condition. ~0-91% have at least one	Stevens et al. 1995. Am J Hum Genet 56:586-91. Medline

<p>See SignatureChipOS page for additional information</p> <p>GeneReviews</p>				average population	most are mutation not detectable by array CGH depending on ethnicity	<p>Yi et al. 2003. Am J Hum Genet 72:62-72. Medline</p> <p>Suzuki et al. 2003. J Invest Derm 120:781-3. Medline</p> <p>Akahoshi et al. 2001. Am J Med Genet 104:299-302. Medline</p>
<p>■ Okhiro</p> <p>GeneReviews</p>	607323	SALL4	20q13.2	~6% have a detectable deletion	63-90% have mutations not detectable by array CGH.	<p>Borozdin et al. 2007. Hum Mutat 28:830. Medline</p> <p>Borozdin et al. 2004. J Med Genet 41:e113. Medline</p> <p>Kohlhase et al. 2002. Hum Mol Genet 11:2979-87. Medline</p>
<p>■ Ornithine transcarbamylase deficiency (OTC)</p> <p>GeneReviews</p>	311250	OTC	Xp11.4	3-12% have a detectable deletion	~62-92% have mutations not detectable by array CGH	<p>Genet et al. 2000. J Inherit Metab Dis 23:669-76. Medline</p> <p>Tuchman et al. 1996. Hum Genet 97:274-76. Medline</p>
<p>□ Oro-facio-digital 1 (OFD1)</p> <p>GeneReviews</p>	311200	OFD1	Xp22.2	Unknown	Majority have mutations not detectable by array CGH	<p>Thauvin-Robinet et al. 2006. J Med Genet 43:54-61. Medline</p> <p>Morisawa et al. 2004. Hum Genet 115:97-103. Medline</p>
<p>□ Oto-Facio-Cervical (OFC)</p> <p>Resources 1</p> <p>Resources 2</p>	166780	EYA1	8q13.3	Precise detection rate unknown	Allelic with Branchio-Oto-Renal (BOR)/Melnick-Fraser (113650)	Rickard et al. 2001. Hum Genet 108:398-403. Medline
<p>■ Pallister-Killian *</p>	601803	Multiple	12p	Precise detection rate unknown	Tetrasomy 12p is detectable by array CGH	Van den Veyver et al. 1993. Am J Med Genet 47:1171-74. Medline

Resources					array CGH	
<ul style="list-style-type: none"> ■ Pelizaeus-Merzbacher* GeneReviews 	312080	PLP1	Xq22.2	60-70% have a detectable duplication	~30% have mutations not detectable by array CGH	Inoue et al. 1999. Ann Neuro 45:624-32. Medline Woodward et al. 1998. Am J Hum Genet 63:207-17. Medline
<ul style="list-style-type: none"> ■ Polycystic kidney disease 1 See SignatureChipOS page for additional information GeneReviews 	601313	PKD1	16p13.3	Rare deletions unless associated with contiguous gene syndrome	Majority have mutations not detectable by array CGH	Ariyurek et al. 2004. Hum Mutat 23:99-105. Medline Brook-Carter et al. 1994. Nat Genet 8:328-32. Medline Torra et al. 1998. Am J of Kidney Dis 31:1038-43. Medline
<ul style="list-style-type: none"> ■ Potocki-Shaffer Resources 	601224	EXT2 ALX4	11p11.2	~ 99% have a detectable deletion		Potocki et al. 1996. Am J Med Genet 62:319-25. Medline Wakui et al. 2005. Eur J Hum Genet 13:528-40. Medline
<ul style="list-style-type: none"> ■ Prader-Willi* GeneReviews 	176270	SNRPN	15q11.2	~70% have a detectable deletion	~30% have either maternal UPD or mutations not detectable by array CGH	Kuwano et al. 1992. Hum Mol Genet 1:417-25. Medline Magenis et al. 1990. Am J Med Genet 35:333-49. Medline
<ul style="list-style-type: none"> ■ Prader-Willi-like phenotype Resources 	176270	SIM1	6q16.3	Deletions uncommon		Faivre et al. 2002. J Med Genet 39:594-96. Medline
<ul style="list-style-type: none"> □ Proteus/Proteus-like Signature Summary on PTEN Hamartoma Tumor Syndrome 	176920	PTEN	10q23.31	Unknown	Allelic with Bannayan-Riley-Ruvalcaba (153480)/ Cowden (158350)/ Macrocephaly/autism (605309).	Smith et al. 2002. J Med Genet 39:937-40. Medline Zhou et al. 2000. Hum Molec Genet 9:765-68. Medline

GeneReviews						
PTEN Hamartoma Tumor syndrome SignatureChip® Detection Rates for PTEN Hamartoma Tumor Syndrome and Allelic Disorders	Hamartoma Tumor					
	Bannayan-					
	~1% of Cowden syndrome (CS) is caused by deletions of the PTEN gene, the majority of which are detectable by array CGH technology. Approximately 80% have identifiable PTEN point mutations that are not detectable by array CGH.					
<ul style="list-style-type: none"> Renal cysts and diabetes (RCAD)* Resources 	137920	TCF2	17q12	22% have a detectable deletion	~45% have mutations not detectable by array CGH	Bellanné-Chantelot et al. 2005. Diabetes 54:3126-32. Medline
<ul style="list-style-type: none"> Retinoblastoma/MR GeneReviews 	180200	RB1	13q14.2	80% have a detectable deletion	3-5% of bilateral and unilateral isolated RB cases have deletions	Cowell et al. 1989. Ophthalmic Paediatr Genet 10:117-27. Medline Richter et al. 2003. Am J Hum Genet 72:253-69. Medline
<ul style="list-style-type: none"> Rieger 1 (RIEG1) 	180500	PITX2	4q25	Unknown	~40% have mutations not detectable by array CGH	Amendt et al. 2000. Cell Mol Life Sci 57:1652-66. Medline

<p>□ Senior-Loken 6</p> <p>Resources</p>	<p>610189</p>	<p>CEP290</p>	<p>12q21.32</p>	<p>Unknown</p>	<p>Recessive condition. ~3% have at least one mutation not detectable by array CGH. Allelic with Joubert 5 (610188)/ Leber congenital amaurosis X (610142)/Meckel 4 (611134).</p>	<p>Helou et al. 2007. J Med Genet 44:657-63. Medline</p>
<p>■ Severe myoclonic epilepsy of infancy (SMEI)</p> <p>GeneReviews</p>	<p>607208</p>	<p>SCN1A</p>	<p>2q24.3</p>	<p>2% have a detectable deletion</p>	<p>~33-35% have mutations not detectable by array CGH. Allelic with generalized epilepsy with febrile seizures plus 2 (604233<).</p>	<p>Suls et al. 2006. Hum Mutat 27:914-20. Medline</p> <p>Nabbout et al. 2003. Neurology 60:1961-67. Medline</p>
<p>□ Short stature, pituitary and cerebellar defects, small sella turcica</p> <p>Resources</p>	<p>606606</p>	<p>LHX4</p>	<p>1q25.2</p>	<p>Unknown</p>		<p>Machinis et al. 2001. Am J Hum Genet 69:961-68. Medline</p> <p>Tajima et al. 2007. Endocr J 54:637-41. Medline</p>
<p>□ Smith-Lemli-Opitz (SLOS)</p>	<p>270400</p>	<p>DHCR7</p>	<p>11q13.4</p>	<p>Unknown</p>	<p>Recessive condition. ~88-93% have at least one mutation not</p>	<p>Witsch-Baumgartner et al. 2000. Am J Hum Genet 66:402-12. Medline</p>

GeneReviews					detectable by array CGH	Yu et al. 2000. Hum Mol Genet 9:1385-91. Medline
<ul style="list-style-type: none"> ■ Smith-Magenis GeneReviews	182290	RAI1	17p11.2	90-99% have a detectable deletion	Very few have mutations not detectable by array CGH	Greenberg et al. 1991. Am J Hum Genet 49:1207-18. Medline Seranski et al. 1999. Genomics 56:1-11. Medline Slager et al. 2003. Nature Genet. 33:466-68. Medline Vlangos et al. 2003. Mol Genet Metab 79:131-41. Medline
<ul style="list-style-type: none"> ■ Sotos GeneReviews	117550	NSD1	5q35.3	10-40% have a detectable deletion depending upon ethnicity	14-90% have mutations not detectable by array CGH depending upon ethnicity	Kurotaki et al. 2003. Hum Mutat 22:378-87. Medline Tatton-Brown et al. 2005. J Med Genet 42:307-13. Medline Turkmen et al. 2003. Europ J Hum Genet 11:858-65. Medline Waggoner et al. 2005. Genet Med 7:524-33. Medline
<ul style="list-style-type: none"> ■ Split-Hand/Foot Malformation 1 (SHFM1) Resources	183600	SHFM1	7q21.3	Precise detection rate unknown	Majority of reported deletions are detectable by array CGH	Crackower et al. 1996. Hum Molec Genet 5:571-79. Medline Elliott et al. 2005. Clin Genet 68:408-23. Medline Scherer et al. 1994. Am J Hum Genet 55:12-20. Medline Wieland et al. 2004. J Med Genet 41:e54. Medline

<p>■ Split-Hand/Foot Malformation 3 (SHFM3)*</p> <p>Resources</p>	<p>600095</p>	<p>FBXW4</p>	<p>10q24.32</p>	<p>Precise detection rate unknown</p>	<p>Majority of reported duplications are detectable by array CGH</p>	<p>deMollerat et al. 2003. Hum Mol Genet 12:1959-71. Medline</p> <p>Elliott et al. 2005. Clin Genet 68:408-23. Medline</p> <p>Kano et al. 2005. Hum Genet 118:477-83. Medline</p>
<p>□ Split-Hand/Foot Malformation 4 (SHFM 4)</p> <p>Resources</p>	<p>605289</p>	<p>TP73L</p>	<p>3q28</p>	<p>Unknown</p>	<p>~99% have mutations not detectable by array CGH</p>	<p>Iankiev et al. 2000. Am J Hum Genet 67:59-66. Medline</p> <p>Van Bokhoven et al. 2001. Am J Hum Genet 69:481-92. Medline</p>
<p>■ Split-Hand/Foot Malformation 5 (SHFM 5)</p> <p>Resources</p>	<p>606708</p>	<p>DLX1</p> <hr/> <p>DLX2</p> <hr/>	<p>2q31.1</p>	<p>Unknown</p>		<p>Bijlsma et al. 2005. Prenat Diag 25:39-44. Medline</p> <p>Boles et al. 1995. Am J Med Genet 55:155-60. Medline</p> <p>Duijf et al. 2003. Hum Molec Genet 12:R51-60. Medline</p>
<p>SRY Dosage Abnormalities</p>	<p>The SRY (Sex Determining Region Y) gene is located on Yp11.31. Dosage abnormalities of SRY (i.e. loss of SRY on the Y chromosome or presence of SRY on other chromosomes) are responsible for disorders of sexual differentiation.</p>					

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[Abnormalities](#)

XX male syndrome: XX karyotype with male phenotype (external genitalia normal to ambiguous, normal testicles, azoospermia, lacking internal female structures).

~80% of XX males have SRY. Typically, XX males with SRY have normal external genitalia and develop gynecomastia around the time of puberty. Presence of SRY on an X chromosome is typically due to interchange between pseudoautosomal regions on the p-arms of X and Y.

~20% of XX males have no SRY. Typically, XX males with no SRY have some level of genital ambiguity and are more likely to have gynecomastia a prior to puberty. The cause of masculinization in these individuals is not well understood. Explanations for some cases may include: low level XX/XY or XX/XXY mosaicism which is known to cause overlapping features, SOX9 duplication on chromosome 17q (one

XY females: XY karyotype with female phenotype (range of normal primary and secondary sexual characteristics, defined by individual syndrome).

		<p>Loss of SRY on the Y chromosome causes XY gonadal dysgenesis, also called Swyer syndrome, causing failure of pubertal development, lack of external secondary sexual characteristics, and streak gonads internally with an increased risk for gonadoblastoma. Expressivity in families is variable.</p>				
<p>■ Steroid sulfatase deficiency</p> <p>Resources</p>	<p>308100</p>	<p>STS</p>	<p>Xp22.31</p>	<p>80-90% have a detectable deletion</p>	<p>10-20% have mutations not detectable by array CGH</p>	<p>Ballabio et al. 1989. Genomics 4:36-40. Medline</p> <p>Conary et al. 1987. Biochem Biophys Res Commun 144:1010-17. Medline</p> <p>Kashork et al. 2002. Prenat Diag 22:1028-32. Medline</p>

						Shapiro et al. 1989. Proc Nat Acad Sci USA 86:8477-81. Medline
□ Stickler I	108300	COL2A1	12q13.11	Rare deletions		Miyake et al. 2004. J Hum Genet 49:282-84. Medline Richards et al. 2007. Hum Mutat 28:639. Medline
GeneReviews						
■ Synpolydactyly/Syndactyly II	186000	HOXD gene cluster		Deletions uncommon	Majority have mutations not detectable by array CGH	Goodman. 2002. Am J Med Genet 112:256-65. Medline Goodman et al. 2002. Am J Hum Genet 70:547-55. Medline
Resources 1						
Resources 2						
■ Townes-Brocks 1	107480	SALL1	16q12.1	~1% have a detectable deletion		Borozdin et al. 2006. Hum Mutat 27:211-12. Medline Marlin et al. 1999. Hum Mutat 14:377-86. Medline Botzenhart et al. 2005. Hum Mutat 26:282. Medline
GeneReviews						
■ Trichorhinophalangeal 1	190350	TRPS1	8q23.3	<20% have a detectable deletion	>80% have mutations not detectable by array CGH	Ludecke et al. 2001. Am J Hum Genet 68: 81-91. Medline Momeni et al. 2000. Nat Genet 24:71-74. Medline
Resources						
■ Tuberous Sclerosis 2 (TSC2)	191100	TSC2	16p13.3	10-30% have a detectable deletion	~60% have mutations not detectable by array CGH	Sampson et al. 1997. Am J Hum Genet 61:843-51. Medline van Bakel et al. 1997. Hum Mol Genet 6:1409-14. Medline
See SignatureChipOS page for additional information						
GeneReviews						

<ul style="list-style-type: none"> ■ Ulnar-mammary <p style="text-align: center;">Resources</p>	181450	TBX3	12q24.21	Deletions uncommon	Majority have mutations not detectable by array CGH	Klopocki et al. 2006. Eur J Hum Genet 14:1274-79. Medline Borozdin et al. 2006. Am J Med Genet 140:1880-86. Medline Bamshad et al. 1999. Am J Hum Genet 64:1550-62. Medline
<ul style="list-style-type: none"> ■ Van der Woude <p style="text-align: center;">GeneReviews</p>	119300	IRF6	1q32.2	~2-3% have a detectable deletion	~43% have mutations not detectable by array CGH	Schutte et al. 1999. Am J Med Genet 84:145-50. Medline Kondo et al. 2002. Nat Genet 32:285-89. Medline
<ul style="list-style-type: none"> □ Vascular endothelial growth factor (VEGFA)-related disorders 	192240	VEGFA	6p21.1	Rare deletions		Izumi et al. 2006. Am J Med Genet 140:398-401. Medline
<ul style="list-style-type: none"> ■ Waardenburg IIA <p style="text-align: center;">Resources</p>	193510	MITF	3p14.1	Precise detection rate unknown	~22% have mutations not detectable by array CGH	Schwarzbraun et al. 2007. Am J Med Genet 143:619-24. Medline Tassabehji et al. 1995. Hum Mol Genet 4:2131-37. Medline
<ul style="list-style-type: none"> ■ WAGR <p style="text-align: center;">GeneReviews</p>	194072	PAX6 WT1	11p13	~66% have a detectable deletion		Crolla et al. 2002. Am J Hum Genet 71:1138-49. Medline
<ul style="list-style-type: none"> ■ Williams-Beuren* <p style="text-align: center;">GeneReviews</p>	194050	ELN	7q11.23	>95% have a detectable deletion		Lowery et al. 1995. Am J Hum Genet 57:49-53. Medline Nickerson et al. 1995. Am J Hum Genet 56:1156-61. Medline
<ul style="list-style-type: none"> ■ Wilms Tumor 1 <p style="text-align: center;">GeneReviews</p>	194070	WT1	11p13	Rare deletions unless associated with contiguous gene syndrome	Majority have mutations not detectable by array CGH	Royer-Pokora et al. 2004. Am J Med Genet 127:249-57. Medline
<ul style="list-style-type: none"> ■ Wolf-Hirschhorn 	194190	Multiple	4p16.3	>95% have a detectable deletion		Altherr et al. 1997. Am J Med Genet 71:47-53. Medline

GeneReviews						Battaglia et al. 2001. Adv Pediatr 48:75-113. Medline
<ul style="list-style-type: none"> ■ X-linked agammaglobulinemia GeneReviews	300300	BTK	Xq22.1	Precise detection rate unknown	~93% have mutations not detectable by array CGH	Van Buggenhout et al. 2004. J Med Genet 41:691-98. Medline Conley et al. 1998 Am J Hum Genet 62:1034-43. Medline Šedivá et al. 2007. J Clin Immunol 27:640-46. Medline Richter et al. 2001. Pediatr Allergy Immunol 12:107-11. Medline
<ul style="list-style-type: none"> ■ X-linked heterotaxy Resources	306955	ZIC3	Xq26.3	Deletions uncommon	~4% have mutations not detectable by array CGH	Ferrero et al. 1997. Am J Hum Genet 61:395-401. Medline Ware et al. 2004. Am J Hum Genet 74:93-105. Medline
<ul style="list-style-type: none"> ■ X-linked idiopathic short stature (ISS) See SignatureChipOS page for additional information GeneReviews	300582	SHOX	Xpter-Xp22.3 & Ypter-Yp11.32	~2-14% have a detectable deletion	~0.4-12% have mutations not detectable by array CGH. Allelic with Langer mesomelic dysplasia (249700)/ Leri-Weill dyschondrosteosis (127300).	Rappold et al. 2002. J Clin Endocrinol Metab 87:1402-06. Medline Huber et al. 2006. J Med Genet 43:735-39. Medline Schneider et al. 2005. Am J Hum Genet 77:89-96. Medline

<p>□ X-linked infantile spasms, ARX-related</p> <p>Resources</p>	<p>308350</p>	<p>ARX</p>	<p>Xp21.3</p>	<p>Unknown</p>	<p>~80% have mutations not detectable by array CGH. Allelic with X-linked mental retardation 54 (300419)/ X-linked lissencephaly with ambiguous genitalia (300215).</p>	<p>Strømme et al. 2002. Nat Genet 30:441-5. Medline</p>
<p>■ X-linked infantile spasms, CDKL5-related</p> <p>Resources</p>	<p>300203</p>	<p>CDKL5</p>	<p>Xp22.13</p>	<p>Deletions uncommon</p>	<p>~5-7% have mutations not detectable by array CGH</p>	<p>Van Esch et al. 2007. Am J Med Genet 143:364-69. Medline</p> <p>Scala et al. 2005. J Med Genet 42:103-7. Medline</p> <p>Archer et al. 2006. J Med Genet 43:729-34. Medline</p>
<p>□ X-linked juvenile retinoschisis</p> <p>GeneReviews</p>	<p>312700</p>	<p>RS1</p>	<p>Xp22.13</p>	<p>Rare deletions</p>	<p>~91% have mutations not detectable by array CGH</p>	<p>den Dunnen et al. 1998. Hum Mol Genet 7:1185-92. Medline</p> <p>Huopaniemi et al. 2000. Hum Mutat 16:307-14. Medline</p>
<p>■ X-linked lissencephaly</p> <p>Resources</p>	<p>300067</p>	<p>DCX</p>	<p>Xq22.3</p>	<p>Unknown</p>	<p>20-38% have mutations not detectable by array CGH</p>	<p>Dobyns et al. 1996. Neurology 47:331-39. Medline</p> <p>Pilz et al. 1998. Hum Molec Genet 7:2029-37. Medline</p>

<p>□ X-linked lissencephaly with ambiguous genitalia</p> <p>Resources</p>	<p>300215</p>	<p>ARX</p>	<p>Xp21.3</p>	<p>Unknown</p>	<p>~87.5% have mutations not detectable by array CGH. Allelic with X-linked mental retardation 54 (300419)/ X-linked infantile spasms, ARX-related (308350).</p>	<p>Kato et al. 2004. Hum Mutat 23:147-59. Medline</p>
<p>■ X-linked lymphoproliferative (XLP)</p> <p>GeneReviews</p>	<p>308240</p>	<p>SH2D1A</p>	<p>Xq25</p>	<p>~4-9% have a detectable deletion</p>	<p>16-89% have mutations not detectable by array CGH depending on features</p>	<p>Sumegi et al. 2000. Blood 96:3118-25. Medline</p> <p>Arico et al. 2001. Blood 97:1131-33. Medline</p>
<p>■ X-linked mental retardation 21</p> <p>Resources</p>	<p>300143</p>	<p>IL1RAPL1</p>	<p>Xp21.3</p>	<p>Precise detection rate unknown</p>	<p>Majority of reported deletions are detectable by array CGH</p>	<p>Zhang et al. 2004. Hum Mutat 24:273. Medline</p> <p>Jin et al. 2000. Eur J Hum Genet 8:87-97. Medline</p>
<p>□ X-linked mental retardation 30</p> <p>Resources</p>	<p>300558</p>	<p>PAK3</p>	<p>Xq22.3</p>	<p>Unknown</p>	<p>Rare mutations not detectable by array CGH</p>	<p>Allen et al. 1998. Nat Genet 20:25-30. Medline</p> <p>Rifé et al. 2000. Am J Med Genet 94:389-91. Medline</p>
<p>□ X-linked mental retardation 54</p>	<p>300419</p>	<p>ARX</p>	<p>Xp21.3</p>	<p>Unknown</p>	<p>~2% have mutations not detectable by array CGH. Allelic with X-linked infantile spasms, ARX-related (308350)/X-linked lissencephaly with ambiguous genitalia (300215).</p>	<p>Bienvenu et al. 2002. Hum Mol Genet 11:981-91. Medline</p>

Resources						
<ul style="list-style-type: none"> ■ X-linked mental retardation with isolated growth hormone deficiency* Resources 	300123	SOX3	Xq27.1	Precise detection rate unknown	Many reported deletions and duplications are detectable by array CGH	Laumonier et al. 2002. Am J Hum Genet 71:1450-55. Medline Raynaud et al. 1998. Am J Med Genet 76:255-61. Medline Woods et al. 2005. Am J Hum Genet 76:833-49. Medline
<ul style="list-style-type: none"> ■ XX male Signature Summary on SRY Dosage Abnormalities GeneReviews 	278850	SRY	Yp11.31	20% have absent SRY		Muller et al. 1987. Development 101 Suppl:51-58. Medline McElreavey et al. 2001. Semin Reprod Med 19:133-39. Medline
<ul style="list-style-type: none"> ■ XY gonadal dysgenesis Signature Summary on SRY Dosage Abnormalities Resources 	306100	SRY	Yp11.31	Large deletions uncommon	20-30% have small deletions or mutations not detectable by array CGH	Scherer et al. 1998. Cytogenet Cell Genet 80:188-92. Medline McElreavey et al. 1992. Proc Natl Acad Sci USA 89:11016-20. Medline
<ul style="list-style-type: none"> □ XY sex-reversal, +/- adrenal failure Resources 	184757	NR5A1	9q33.3	Precise detection rate unknown	~13% have mutations not detectable by array CGH	Schlaubitz et al. 2007. Am J Med Genet 143:1071-81. Medline Lin et al. 2007. J Clin Endocrinol Metab 92:991-99. Medline
All 43 unique pericentromeric regions		Multiple	43 sites	Detection rate variable depending upon the marker chromosome		
All 41 unique subtelomeric regions		Multiple	41 sites	0.5-7% have a detectable deletion		Knight et al. 2000. Am J Hum Genet. 67:320-32. Medline

						Ravnan et al. 2005. J Med Genet. Medline Veltman et al. 2002. Am J Hum Genet 5:1269-76. Medline Wong et al. 2005. Genet Med 7:264-71. Medline
Aneuploidy		Multiple	24 chromosomes	> 99% detectable by microarray		Ballif et al. 2006. Prenat Diagn 26:333-39. Medline Schaeffer et al. 2004. Am J Hum Genet 74:1168-74. Medline

* Duplication of these regions are associated with a syndrome/clinical phenotype.

■ Microdeletions or microduplications have been associated with this condition.

□ Microdeletions or microduplications are rare or not yet associated with this condition