Disorder	Causative Gene or Region (OMIM#)
Imprinting and Trinucleotide Repeat Disorders	
Angelman syndrome (AS)	15q11.2-q13 (*SNRPN* promoter, SNURF) (105830)
Beckwith-Wiedemann syndrome (BWS)	11p15 (IC1 and IC2) (130650)
Diabetes mellitus, transient neonatal 1 (TNDM1)	6q24 (*PLAG1*) (601410)
Fragile X syndrome (FXS)	*FMR1* promoter (300624)
Kagami-Ogata syndrome	14q32 (*MEG3* promoter) (608149)
Mulchandani-Bhoj-Conlin syndrome (MBCS)	20q11-q13 (*GNAS*) (617352)
Prader-Willi syndrome (PWS)	15q11.2 (*SNRPN* promoter, SNURF) (176270)
Pseudohypoparathyroidism, Type IA, IB (PHP1A, PHP1B)	20q13.32 (*GNAS*) (139320/603233)
Silver-Russel syndrome 1 (SRS1)	11p15 (IC1 and IC2) (180860)
Silver-Russel syndrome 2 (SRS2)	7p13-q32 (618905)
Temple syndrome	14q32 (*MEG3* promoter) (616222)
Episignature Disorders	
Alpha-thalassemia/Impaired intellectual development syndrome, X-linked[1]	*ATRX* (301040)
Arboleda-Tham syndrome (ARTHS)[2]	*KAT6A* (616268)
ARID1A duplication-related syndrome[2,3]*	*ARID1A* (603024)
BAFopathies: Coffin-Siris 1-4 (CSS1, CSS2, CSS3, CSS4) & Nicolaides-Baraitser (NCBRS) syndromes[4]	*ARID1B, ARID1A, SMARCB1, SMARCA4, SMARCA2* (135900, 614607, 614608, 614609, 601358)
BAFopathies: Coffin-Siris syndrome 1 and 2 (CSS1, CSS2)[5]	*ARID1B, ARID1A*(135900, 614607)
Beck-Fahrner syndrome (BEFAHRS)[6,7]	*TET3* (618798)
Blepharophimosis-impaired intellectual development syndrome (BIS)	*SMARCA2* (619293)
Börjeson-Forssman-Lehmann syndrome (BFLS)[1,2,8]	*PHF6* (301900)
Branchial arch abnormalities, choanal atresia, athelia, hearing loss, and hypothyroidism syndrome (BCAHH) [2,9]*	*KMT2D* (620186)
Cerebellar ataxia, deafness, and narcolepsy, autosomal dominant (ADCADN)[2]	*DNMT1* (604121)
CHARGE syndrome	*CHD7* (214800)
Chr1p36 deletion syndrome [2,10]	Chr1p36 deletion (607872)
Chromosome 19p13.13 Deletion Syndrome[11]*	Chr19p13.13del (613638)
Chromosome Xp11.22 duplication syndrome[1,2,12]*	ChrXp11.22 duplication (300705)
Chung-Jansen syndrome, White-Kernohan syndrome and Börjeson-Forssman-Lehmann syndrome*	*PHIP, DDB1, PHF6* (617991, 619426, 301900)
Chung-Jansen syndrome[2,8]**Error! Bookmark not defined.***	*PHIP* (617991)
Clark-Baraitser syndrome*	*TRIP12* (617752)
Coffin-Siris syndrome-1 (CSS1)[2,13]	*ARID1B* (135900)
Coffin-Siris syndrome-2 (CSS2)[2,13]	*ARID1A* (614607)
Coffin-Siris syndrome-3 (CSS3)[2,13]	*SMARCB1* (614608)
Coffin-Siris syndrome-4 (CSS4)[2,13]	*SMARCA4* (614609)
Coffin-Siris syndrome-4 (CSS4)[2,13,14]	*SMARCA4* c.2656 (614609)
Coffin-Siris syndrome-6 (CSS6)*	*ARID2* (617808)
Congenital heart defects, dysmorphic facial features, and intellectual developmental disorder (CHDFIDD)[2]	*CDK13, CCNK* (617360)

Cornelia de Lange syndromes 1-4 (CDLS1, CDLS2, CDLS3, CDLS4)[15]	*NIPBL, SMC1A, SMC3, RAD21* (122470, 300590, 610759, 614701)
DEGCAGS syndrome[16]*	*ZNF699* (619488)
Desanto-Shinawi syndrome (DESSH)†	*WAC* (616708)
Developmental and epileptic encephalopathy 54 (DEE54)*	*HNRNPU* (617391)
Developmental and epileptic encephalopathy 94 (DEE94)	*CHD2* (615369)
Developmental delay with or without dysmorphic facies and autism (DEDDFA)[17]†	*TRRAP* (618454)
Developmental delay with variable intellectual disability and dysmorphic facies*	*JARID2* (601594)
Diamond-Blackfan anemia 1 (DBA1)[18]†	*RPS19* (105650)
Diamond-Blackfan anemia 5 (DBA5)[18]†	*RPL35A* (612528)
Diets-Jongmans syndrome (DIJOS)*	*KDM3B* (618846)
Down syndrome	*Chr21 trisomy* (190685)
Dystonia 28, Childhood-onset (DYT28)	*KMT2B* (617284)
Fanconi Anemia (FANCA, FANCC, FANCD2, FANCG, FANCI, FANCL)[16,19]*	*FANCA, FANCC, FANCD2, FANCG, FANCI, FANCL* (227650, 613899, 613984, 602956, 611360, 608111)
Fetal valproate syndrome (FVS)[20]*	Not applicable (609442)
Floating-Harbor syndrome (FLHS)	*SRCAP* (136140)
Gabriele-de Vries syndrome (GADEVS)[2]	*YY1* (617557)
Genitopatellar syndrome (see also Ohdo syndrome) (GTPTS)[2,21]	*KAT6B* (606170)
Hao-Fountain syndrome (HAFOUS)*	*USP7* (616863)
Helsmoortel-van der Aa syndrome (HVDAS)[22]	*ADNP* (615873)
Hunter-McAlpine craniosynostosis syndrome[23]	Chr5q35-qter duplication including *NSD1* (601379)
Hypercholesterolemia, familial, 1 (FHCL1)[24]†	*LDLR* (143890)
Hypermethioninemia with deficiency of S-adenosylhomocysteine hydrolase†	*AHCY* (613752)
Immunodeficiency-centromeric instability-facial anomalies syndromes 1-4 (ICF1, ICF2, ICF3, ICF4)[2,25]	*DNMT3B, CDCA7, ZBTB24, HELLS* (242860, 614069, 616910, 616911)
Intellectual developmental disorder with autism and macrocephaly (IDDAM)[2]	*CHD8* (615032)
Intellectual developmental disorder with dysmorphic facies and behavioral abnormalities (IDDFBA)†	*FBXO11* (618089)
Intellectual developmental disorder with microcephaly and with or without ocular malformations or hypogonadotropic hypogonadism (IDDMOH)[2]	*SOX11* (615866)
Intellectual developmental disorder with seizures and language delay (IDDSELD)	*SETD1B* (619000)
Intellectual Developmental Disorder with Speech Delay, Dysmorphic Facies, and T-cell abnormalities (IDDSFTA)[2]*	*BCL11B* (618092)
Intellectual developmental disorder, autosomal dominant 21 (MRD21)*	*CTCF* (615502)
Intellectual developmental disorder, autosomal dominant 23 (MRD23)[2,26]	*SETD5* (615761)
Intellectual developmental disorder, autosomal dominant 51 (MRD51)[2,6]	*KMT5B* (617788)
Intellectual developmental disorder, autosomal dominant 7 (MRD7)*	*DYRK1A* (600855)
Intellectual developmental disorder, X-linked 93 (XLID93)[2,6]	*BRWD3* (300659)

Intellectual developmental disorder, X-linked 97 (XLID97)[2,27]	*ZNF711* (300803)
Intellectual developmental disorder, X-linked 112 (XLID112)†	*ZMYM3* (301111)
Intellectual developmental disorder, X-linked syndromic, Nascimento-type (MRXSN)[1,2]	*UBE2A* (300860)
Intellectual developmental disorder, X-linked, syndromic, Armfield type (MRXSA)[1,2]	*FAM50A* (300261)
Intellectual developmental disorder, X-linked, syndromic, Claes-Jensen type (MRXSCJ)[6,28]	*KDM5C* (300534)
Intellectual developmental disorder, X-linked, syndromic, Snyder-Robinson type (MRXSSR)[1,2]	*SMS* (309583)
Kabuki syndrome 1 (KABUK1)[29]	*KMT2D* (147920)
Kabuki syndrome 1 and 2 (KABUK1, KABUK2)	*KMT2D, KDM6A* (147920, 300867)
Kabuki syndrome 2 (KABUK2)[29]	*KDM6A* (300867)
KBG Syndrome (KBGS)[26]	*ANKRD11* (148050)
KDM2B-related syndrome	*KDM2B* (609078)
Kleefstra syndrome 1 (KLEFS1)	*EHMT1* (610253)
Klinefelter Syndrome[30]	ChrX duplication; 47,XXY
KMT2C-related syndrome†	*KMT2C* (606833)
Koolen-De Vries syndrome (KDVS)	*KANSL1* (610443)
Luscan-Lumish syndrome (LLS)	*SETD2* (616831)
Menke-Hennekam syndrome 1 and 2 (MKHK1, MKHK2)[31]	*CREBBP, EP300* (618332, 618333)
Mowat-Wilson Syndrome (MOWS)*	*ZEB2* (235730)
MSL2 associated syndrome[2]*	*MSL2* (614802)
Neurodevelopmental-craniofacial syndrome with variable renal and cardiac abnormalities (NECRC)†	*ZMYM2* (619522)
Neurodevelopmental disorder with dysmorphic facies and behavioral abnormalities (NEDFBA)*	*SRSF1* (620489)
Neurodevelopmental disorder with hypotonia, stereotypic hand movements, and impaired language (NEDHSIL)*	*MEF2C* (613443)
Neuroocular syndrome[2,32]*	*PRR12* (619539)
Nicolaides-Baraitser syndrome (NCBRS)[13]	*SMARCA2* (601358)
NSD2 duplication syndrome[33]*	*NSD2* (602952)
Ohdo syndrome, SBBYSS variant (see also Genitopatellar syndrome) (SBBYSS)[2,21]	*KAT6B* (603736)
Phelan-McDermid syndrome (PHMDS)[34]	Chr22q13.3 deletion (606232)
PHF12-related syndrome†	*PHF12* (618645)
Pitt-Hopkins Syndrome (PTHS)*	*TCF4* (610954)
Potocki-Lupski syndrome (PTLS)[35]	Chr17p11.2 duplication (610883)
PRC2 Complex ((Weaver syndrome (WVS) and Cohen-Gibson syndrome (COGIS))[36]	*EED, EZH2* (617561, 277590)
Rahman syndrome (RMNS)	*HIST1H1E* (617537)
Recurrent constellations of embryonic malformations[37]†	Not applicable
Renpenning syndrome (RENS1)[1,2]	*PQBP1* (309500)
Rubinstein-Taybi syndrome 1 (RSTS1)[38]	*CREBBP* (180849)
Rubinstein-Taybi syndrome 1 and 2 (RSTS1, RSTS2)	*CREBBP, EP300* (180849, 613684)

Rubinstein-Taybi syndrome 2 (RSTS2)[38]	*EP300* (613684)
Schuurs-Hoeijmakers syndrome (SHMS)†	*PACS1* (615009)
SETD1A-related syndrome†	*SETD1A* (611052)
Sifrim-Hitz-Weiss syndrome (SIHIWES)	*CHD4* (617159)
SLC32A1 related disorder[2]	*SLC32A1* (616440)
Smith-Magenis syndrome (SMS)[39]	Chr17p11.2 deletion (182290)
Sotos syndrome (SOTOS)	*NSD1* (117550)
Tatton-Brown-Rahman syndrome (TBRS)[2]	*DNMT3A* (615879)
Turner Syndrome*	Monosomy X
Velocardiofacial syndrome (VCFS)[40]	Chr22q11.2 deletion (192430)
White-Kernohan syndrome[8]*	*DDB1* (619426)
White-Sutton syndrome (WHSUS)	*POGZ* (616364)
Wieacker-Wolff Syndrome (WRWF)[1,2]	*ZC4H2* (314580)
Wiedemann-Steiner syndrome (WDSTS)	*KMT2A* (605130)
Williams-Beuren region duplication syndrome[41]	Chr7q11.23 duplication (609757)
Williams-Beuren syndrome (WBS)[42]	Chr7q11.23 deletion (194050)
Witteveen-Kolk syndrome (WITKOS)[2]	*SIN3A* (613406)
Wolf-Hirschhorn syndrome (WHS) & Rauch-Steindl Syndrome (RAUST)[43]	Chr4p16.13 deletion, *NSD2* (194190, 602952)

**These disorders are new for V5 of EpiSign™.*

†These episignatures are available for EpiSign™ Single requests only.

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[1] Defined with male cases only. Heterozygotes have been shown to not match the episignature.
[2] Reduced sensitivity may be observed.
[3] The range of validated coordinates is 1p36.11(26,964,202-27,099,490). CNVs overlapping or expanding this region may also be detected.
[4] Patients with other BAFopathy genes may be detected, but not confirmed in our experiments.
[5] Only for variants near c.6200. No separate episignature due small cohort size, however these samples cluster separately from other BAFopathy/CSS1&2 samples.
[6] Healthy carriers and those with incomplete penetrance are detectable.
[7] Patients with biallelic variants are distinguishable from those with monoallelic variants.
[8] This is a secondary episignature; sample must also be positive for CHU_BFL_WHI.
[9] Only for variants within the amino acid range of 3400-3700.
[10] The range of validated coordinates is 1p36.33p36.32(1,019,753-2,867,961). CNVs overlapping or expanding this region may also be detected.
[11] The range of validated coordinates is 19p13.13p13.2(13,201,983-13,213,144). CNVs overlapping or expanding this region may also be detected. Only for copy number variants. NFIX sequence variants have been shown to not match the episignature.
[12] The range of validated coordinates is Xp11.22(53,559,057-53,654,518). CNVs overlapping or expanding this region may also be detected.
[13] This is a secondary episignature; sample must also be positive for BAFopathy.
[14] Only for variants near c.2656. No separate episignature due small cohort size however these samples cluster separately from other BAFopathy/CSS4 samples.
[15] Male CdLS5 patients (HDAC8 mutations) may be detected, but not confirmed in our experiments.
[16] Heterozygotes have been shown to not match the episignature.
[17] Only for variants within the amino acid range of 960-1159.
[18] Reduced sensitivity against other Diamon-Blackfan anemia disorders may be observed.
[19] Patients with other FANC genes may be detected, but not confirmed in our experiments.
[20] Available as a targeted request only.

[21] GTPTS and SBBYSS are both caused by KAT6B mutations. We will report both regardless of which one is requested.
[22] ADNP consists of two distinct episignatures dependent on variant location. HVDAS_T includes variants within the N- and C-terminus while HVDAS_C includes variants within the central region (approximately c.2054-2340).
[23] The range of validated coordinates is 5q35.2q35.3(175,839,681-176,904,798). CNVs overlapping or expanding this region may also be detected.
[24] Sensitivity against other hereditary hypercholesterolemia disorders has not been evaluated. Both monoallelic and biallelic cases are detected.
[25] ICF1 exhibits a unique episignature while ICF 2, 3 and 4 exhibit a distinct, shared episignature
[26] This is a secondary episignature; sample must also be positive for KBGS_MRD23.
[27] Heterozygotes have been shown to match the episignature.
[28] Heterozygotes have a distinct profile from hemizygotes.
[29] This is a secondary signature; sample must also be positive for combined Kabuki signature.
[30] XXX and XYY cases may also be detected.
[31] Only for domain ID4. MKHK1/2 exhibit a shared ID4 domain episignature and therefore cannot distinguish between MKHK1 and MKHK2. Other domains of MKHK1/2 are not available for assessment.
[32] Healthy carriers and those with incomplete penetrance are detectable. Reduced sensitivity may be observed.
[33] The range of validated coordinates is 4p16.3(1,832,733-1,975,031). CNVs overlapping or expanding this region may also be detected.
[34] The range of validated coordinates is 22q13.3(49,238,268-50,248,907). CNVs overlapping or expanding this region may also be detected. Only for copy number variants. *SHANK3* sequence variants have been shown to not match the episignature.
[35] The range of validated coordinates is 17p11.2(16,779,412-20,231,379). CNVs overlapping or expanding this region may also be detected. Reduced sensitivity may be observed.
[36] Shared episignatures between PRC2 complex syndromes WVS and COGIS. IMMAS (Imagawa-Matsumoto syndrome) cases with variants in SUZ12 have also been detected.
[37] Includes cases with phenotypic presentation of OAV, OAVV, VACTERL and VATER.
[38] This is a secondary signature; sample must also be positive for combined RSTS signature.
[39] The range of validated coordinates is 17p11.2(17,322,913-18,515,769). CNVs overlapping or expanding this region may also be detected. Only for copy number variants. *RAI1* sequence variants have been shown to not match the episignature.
[40] The range of validated coordinates is 22q11.21(19,510,547-20,285,090). CNVs overlapping or expanding these regions may be detected.
[41] The range of validated coordinates is 7q11.23(73,953,518-74,138,459). CNVs overlapping or expanding this region may also be detected.
[42] CNVs overlapping or expanding 7q11.23 may also be detected.
[43] The range of validated coordinates is 4p16.3(679,715-2,169,001). CNVs overlapping or expanding this region may also be detected. *NSD2* sequence variants have been shown to match the episignature.