マイクロアレイ染色体検査普及のための産学連携コンソーシアム主催
マイクロアレイ染色体検査解釈ハンズオンウェビナー 2023.9.19

マイクロアレイ染色体検査解釈 ハンズオンウェビナー

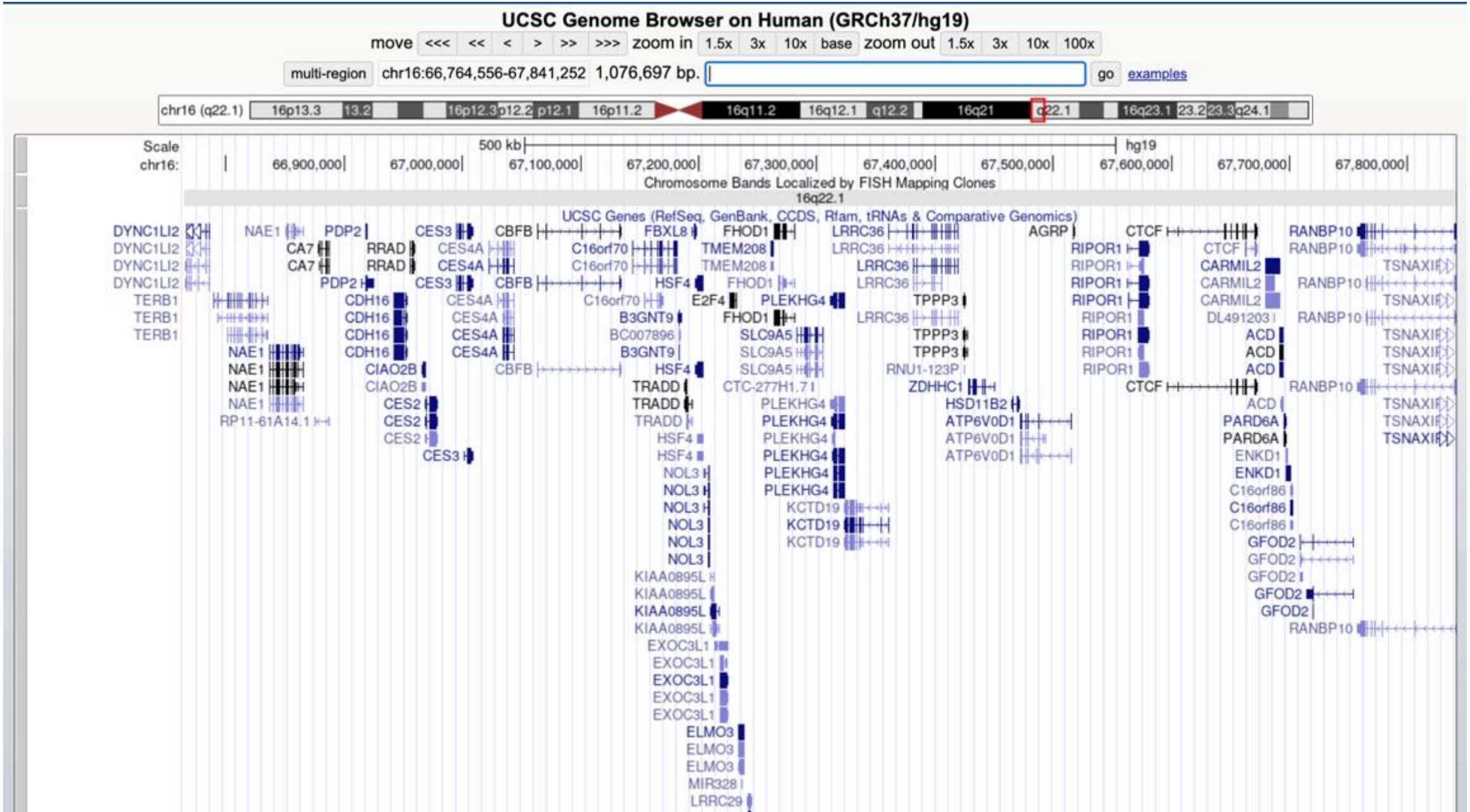
初級編　解説資料 症例２

神奈川県立こども医療センター遺伝科
黒田　友紀子

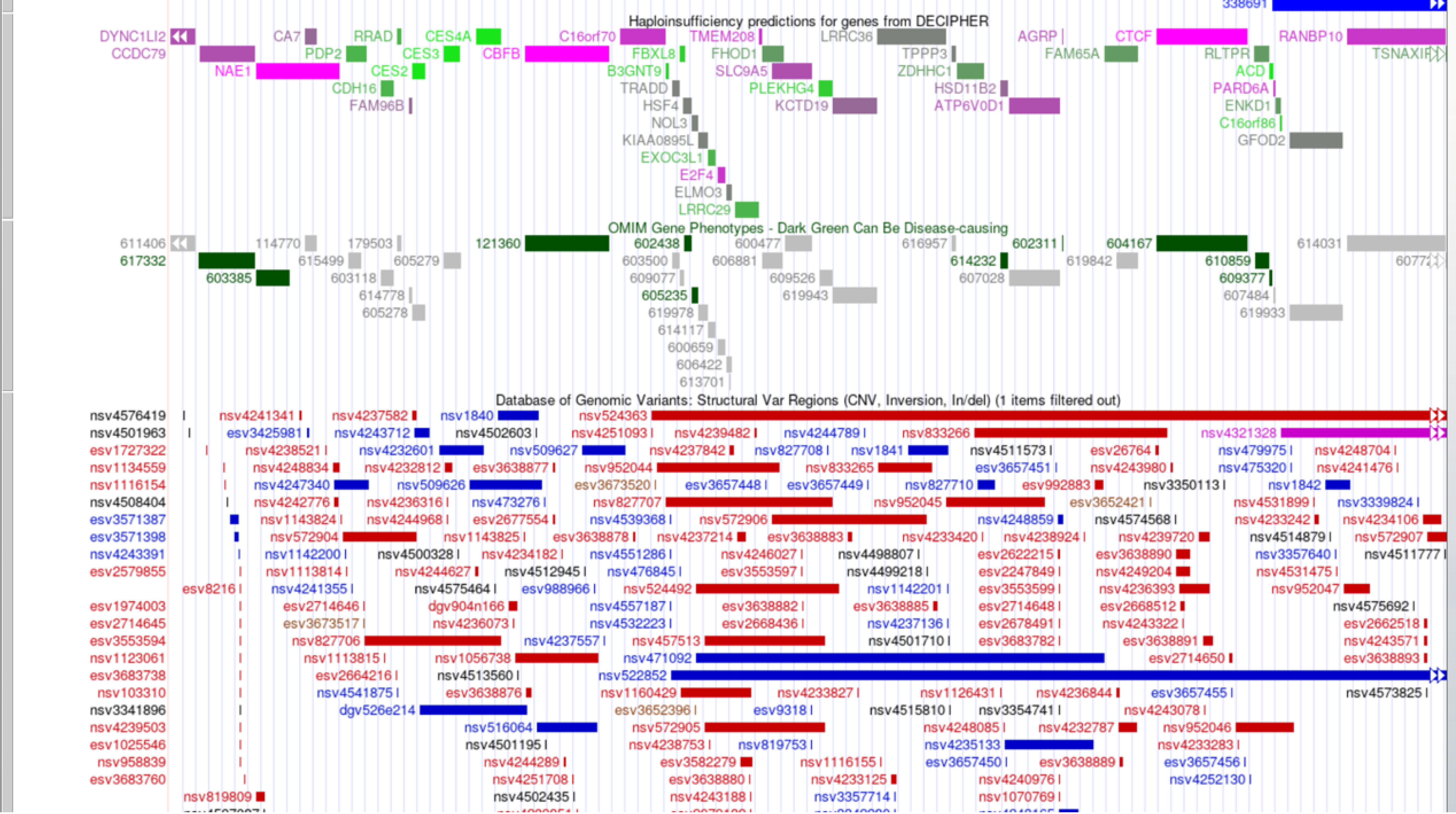
症例2

- 10歳男児：発達遅滞、てんかん
- 【CNV】chr16: 66,764,556-67,841,252
  16q22.1 1.08Mb deletion
  log2ratio=-0.87 [Loss]

chr16: 66,764,556-67,841,252 16q22.1 1.08Mb deletion




LRRC29
ClinGen Dosage Sensitivity Map - Haploinsufficiency
CBFB
CTCF
ACD
ClinGen Dosage Sensitivity Map - Triplosensitivity
CBFB
CTCF
ACD
ClinGen Gene-Disease Validity Classification
syndromic intellectual disability
ClinGen CNVs: Benign Gain Coverage
ClinGen CNVs: Benign Loss Coverage
ClinGen CNVs: Pathogenic
nssv13643930_unk
nssv13652052_unk
nssv13645004_unk
nssv13651804_unk
nssv13645588_unk
nssv583801_unk
nssv578713_unk
nssv578715_unk
nssv578716_unk
nssv577557_dnovo
nssv577561_unk
nssv577562_dnovo
nssv582684_unk
nssv582250_unk
nssv1604001_unk
nssv3396910_dnovo
nssv3395354_unk
nssv3395390_unk
ClinGen CNVs: Pathogenic Gain Coverage
ClinGen CNVs: Pathogenic Loss Coverage
DECIPHER CNVs (Merged 22 items)
4595
249502
Merged 22 items
356379
301106
289758
271207
289694
331173
2150
Position: chr16:67672432-68090443, S
418012, Type: Deletion, Significance: Li
pathogenic, Phenotypes: Abnormality o
upper respiratory tract, Anteverted nare



338691
Haploinsufficiency predictions for genes from DECIPHER
DYNC1LI2
CA7
RRAD
CES4A
C16orf70
TMEM208
LRRC36
AGRP
CTCF
RANBP10
CCDC79
PDP2
CES3
CBFB
FBXL8
FHOD1
TPPP3
FAM65A
RLTPR
TSNAXIP1
NAE1
CES2
B3GNT9
SLC9A5
ZDHHC1
ACD
CDH16
TRADD
PLEKHG4
HSD11B2
PARD6A
FAM96B
HSF4
KCTD19
ATP6V0D1
ENKD1
NOL3
C16orf86
KIAA0895L
GFOD2
EXOC3L1
E2F4
ELMO3
LRRC29
OMIM Gene Phenotypes - Dark Green Can Be Disease-causing
611406 114770 179503 121360 602438 600477 616957 602311 604167 614031
617332 615499 605279 603500 606881 614232 619842 610859
603385 603118 609077 609526 607028 609377
614778 605235 619943 607484
605278 619978 619933
614117
600659
606422
613701
Database of Genomic Variants: Structural Var Regions (CNV, Inversion, In/del) (1 items filtered out)
nsv4576419 nsv4241341 nsv4237582 nsv1840 nsv524363
nsv4501963 esv3425981 nsv4243712 nsv4502603 nsv4251093 nsv4239482 nsv4244789 nsv833266 nsv4321328
esv1727322 nsv4238521 nsv4232601 nsv509627 nsv4237842 nsv827708 nsv1841 nsv4511573 esv26764 nsv479975 nsv4248704
nsv1134559 nsv4248834 nsv4232812 esv3638877 nsv952044 nsv833265 esv3657451 nsv4243980 nsv475320 nsv4241476
nsv1116154 nsv4247340 nsv509626 esv3673520 esv3657448 esv3657449 nsv827710 esv992883 nsv3350113 nsv1842
nsv4508404 nsv4242776 nsv4236316 nsv473276 nsv827707 nsv952045 esv3652421 nsv4531899 nsv3339824
esv3571387 nsv1143824 nsv4244968 esv2677554 nsv4539368 nsv572906 nsv4248859 nsv4574568 nsv4233242 nsv4234106
esv3571398 nsv572904 nsv1143825 esv3638878 nsv4237214 esv3638883 nsv4233420 nsv4238924 nsv4239720 nsv4514879 nsv572907
nsv4243391 nsv1142200 nsv4500328 nsv4234182 nsv4551286 nsv4246027 nsv4498807 esv2622215 esv3638890 nsv3357640 nsv4511777
esv2579855 nsv1113814 nsv4244627 nsv4512945 nsv476845 esv3553597 nsv4499218 esv2247849 nsv4249204 nsv4531475
esv8216 nsv4241355 nsv4575464 esv988966 nsv524492 nsv1142201 esv3553599 nsv4236393 nsv952047
esv1974003 esv2714646 dgv904n166 nsv4557187 esv3638882 esv3638885 esv2714648 esv2668512 nsv4575692
esv2714645 esv3673517 nsv4236073 nsv4532223 esv2668436 nsv4237136 esv2678491 nsv4243322 esv2662518
esv3553594 nsv827706 nsv4237557 nsv457513 nsv4501710 esv3683782 esv3638891 nsv4243571
nsv1123061 nsv1113815 nsv1056738 nsv471092 esv2714650 esv3638893
esv3683738 esv2664216 nsv4513560 nsv522852
nsv103310 nsv4541875 esv3638876 nsv1160429 nsv4233827 nsv1126431 nsv4236844 esv3657455 nsv4573825
nsv3341896 dgv526e214 esv3652396 esv9318 nsv4515810 nsv3354741 nsv4243078
nsv4239503 nsv516064 nsv572905 nsv4248085 nsv4232787 nsv952046
esv1025546 nsv4501195 nsv4238753 nsv819753 nsv4235133 nsv4233283
nsv958839 nsv4244289 esv3582279 nsv1116155 esv3657450 esv3638889 esv3657456
esv3683760 nsv4251708 esv3638880 nsv4233125 nsv4240976 nsv4252130
nsv819809 nsv4502435 nsv4243188 nsv3357714 nsv1070769

* 604167

CCCTC-BINDING FACTOR; CTCF

Alternative titles; symbols

TRANSCRIPTIONAL REPRESSOR CTCF

HGNC Approved Gene Symbol: CTCF

Cytogenetic location: 16q22.1 Genomic coordinates (GRCh38): 16:67,562,526-67,639,185 (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key
16q22.1	Intellectual developmental disorder, autosomal dominant 21	615502	AD	3

PheneGene Graphics

TEXT

▼ External Links
▶ Genome
▶ DNA
▶ Protein
▶ Gene Info
▶ Clinical Resources
▼ Variation
ClinVar
DECIPHER
gnomAD
GWAS Catalog
GWAS Central
HGMD
NHLBI EVS
PharmGKB
▶ Animal Models
▶ Cellular Pathways

ClinGen Dosage Sensitivity Map - Haploinsufficiency (CTCF)

Item: CTCF
Score: 0
Position: chr16:67596310-67673088
Band: 16q22.1
Genomic Size: 76779
View DNA for this feature (hg19/Human)

ClinGen URL	https://search.clinicalgenome.org/kb/gene-dosage/CTCF
Gene Symbol or ISCA Region Name	CTCF
Gene ID or ISCA ID	10664
Cytoband	16q22.1
Last evaluation date	2021-09-22
Haploinsufficiency score	3
Haploinsufficiency phenotype description	Sufficient evidence for dosage pathogenicity
Associated PubMed ID 1	23746550
Associated PubMed ID 2	30893510
Associated PubMed ID 3	31239556
Associated PubMed ID 4	25363768
Associated PubMed ID 5	33004838
Associated PubMed ID 6	
Mondo disease ontology ID	MONDO:0000508

Haploinsufficiency (HI) Score Details

HI Score: 3

HI Evidence Strength: **Sufficient Evidence for Haploinsufficiency** (Disclaimer)

HI Disease: Syndromic Intellectual Disability Monarch

HI Evidence: PUBMED: 23746550

Gregor et al. (2013) performed exome sequencing in an individual with mild intellectual disability, short stature, microcephaly, cleft palate and congenital heart defects and identified two de novo variants: one missense in POLR2A and one frameshift in CTCF. The CTCF variant was a single base duplication (c.375dupT) not observed in control databases.

The authors then performed mutational screening of an additional 399 individuals with intellectual disability and identified CTCF variants in an additional two boys. Both variants were de novo: one frameshift variant (c.1186dupA) and the other a missense variant (c.1699C>T, p.Arg567Trp). The authors confirmed reduced mRNA expression and protein levels in both patients with frameshift variants and sequencing of the cDNA showed almost complete absence of the mutated allele suggesting loss of function or haploinsufficiency as possible disease mechanism. The missense variant did not impact CTCF mRNA expression or protein levels and at this time there is insufficient evidence to determine whether this variant leads to loss of function.

Clinical phenotypes shared among all three patients include variable intellectual disability, lower head circumference and/or body height, and feeding difficulties.

CTCF遺伝子の**機能喪失**により
知的障害を発症する

回答	症例2
CNV病原性(5段階評価)	Pathogenic
遺伝学的診断	CTCF関連知的障害
判断根拠 -使用したデータベースの結果や文献情報等より病原性や遺伝学的診断の判断　根拠を明確に（自由記載）	ハプロ不全遺伝子*CTCF*全体を含む欠失 ClinGen Haploinsufficiency score 3 Sufficient Evidence for Haploinsufficiency (3) *CTCF*遺伝子は機能喪失バリアントや欠失により知的障害、てんかんをおこすことが報告されている。