

2021/12/16

AJACS統合データベース講習会  
「疾患に関する多型データを解析する」

表現型と遺伝子型のデータを  
共有および比較する

東京女子医科大学大学院医学研究科先端生命医科学系専攻遺伝子医学分野／  
東京女子医科大学ゲノム診療科

山本俊至

発表に関するCOI開示  
開示すべきCOIなし



# この講義のねらい

- ・ 関心対象の表現型が、解析によって明らかになった遺伝子型（主にゲノムコピー数変化）によって説明できるかどうかを検証できるようになること

# マイクロアレイ染色体検査の保険適用

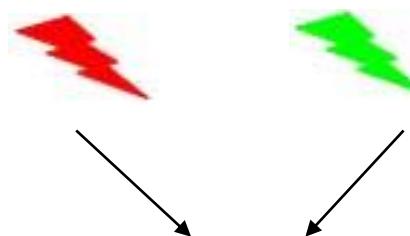
2020年夏：アジレント社のマイクロアレイ染色体検査機器が薬事承認

2021年10月：保険収載



# Comparative Genome Hybridization (CGH) 法の原理

患者ゲノムを  
Cy5という蛍光色素(赤)で  
ラベル化する



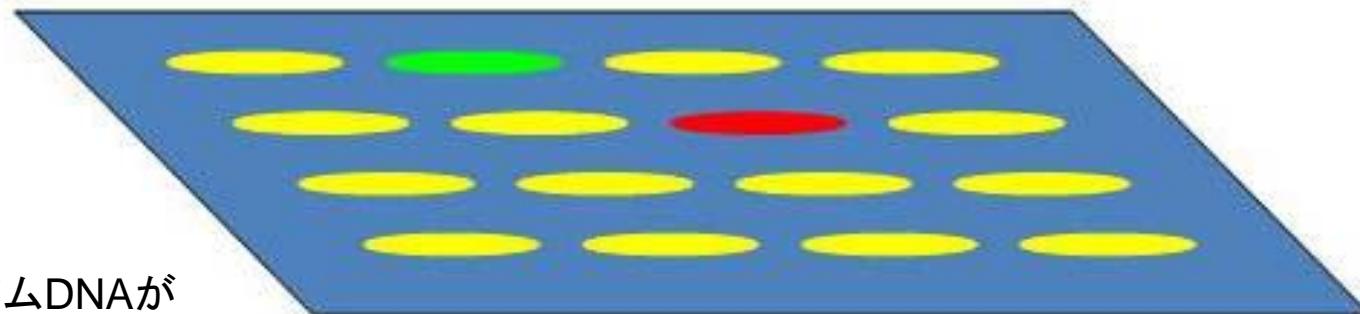
コントロールゲノムを  
Cy3という蛍光色素(緑)で  
ラベル化する



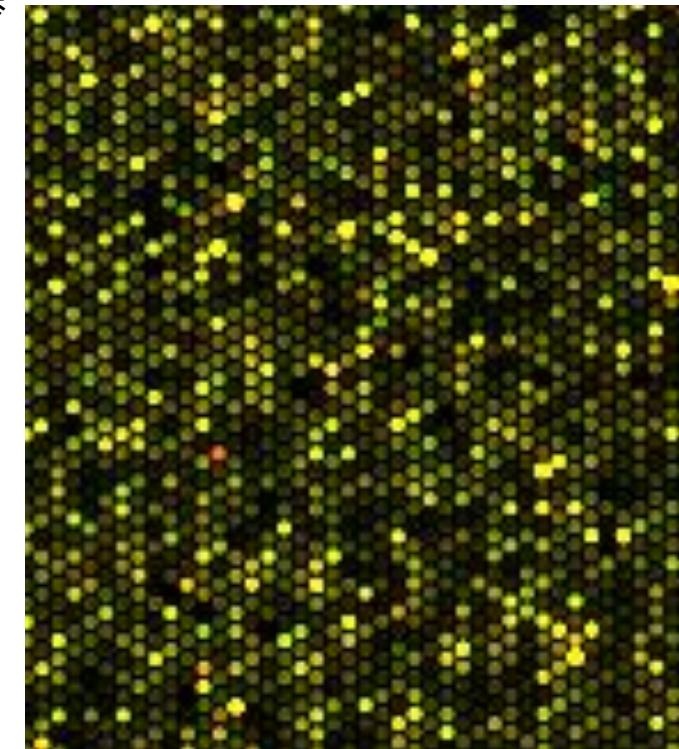
マイクロアレイスライド上で競合ハイブリダイゼーション  
(一緒にしてスライド上にふりかける)



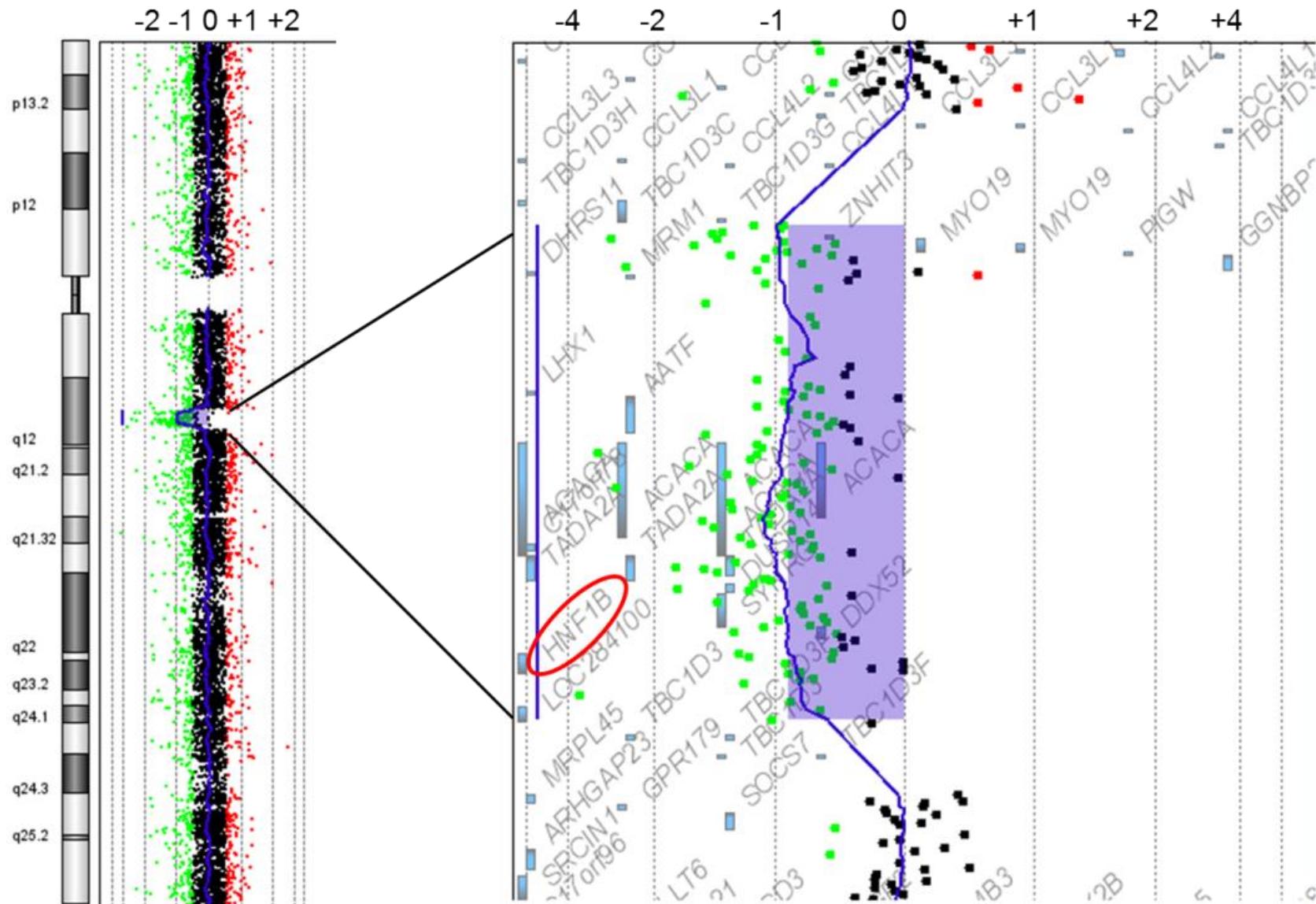
スキャナで読み取る  
↓  
患者さんのコピー数が少ない(欠失)と緑に、  
患者さんのコピー数が多い(重複)と赤に傾く

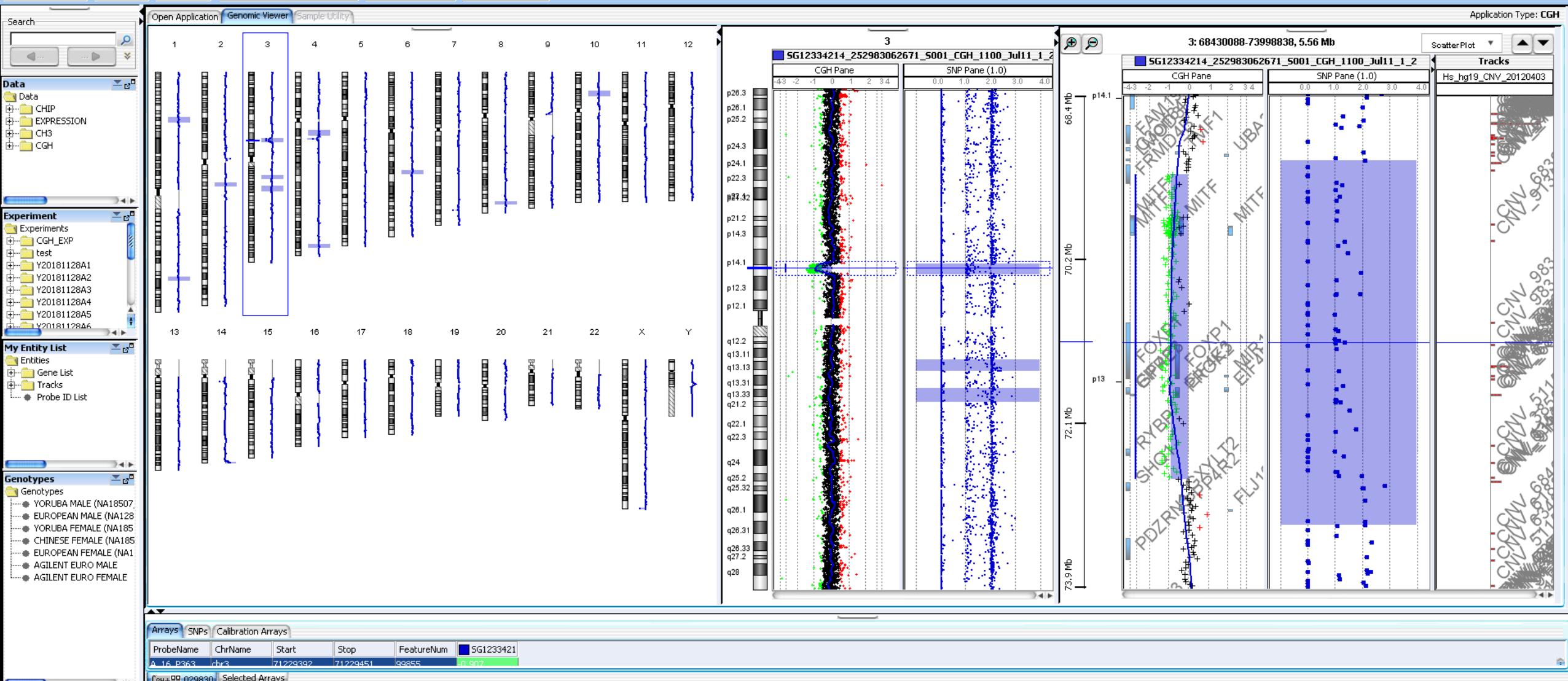


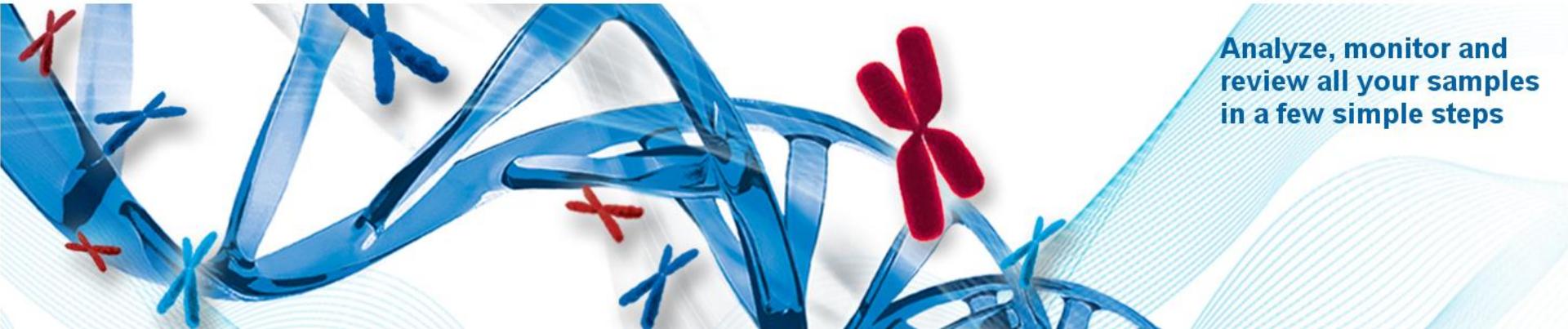
細かく切断されたゲノムDNAが  
スライドにはりつけられているスライド



# マイクロアレイ染色体検査結果の表示方法







Analyze, monitor and review all your samples in a few simple steps

#### Introduction

CytoGenomics is a workflow-based application that helps you analyze, review, and report on CGH and CGH+SNP microarray data in a few simple steps. You import your samples and run an analysis, then return to CytoGenomics to review the QC metrics, review and classify aberration calls in the triage view, and finally create reports.

You can use CytoGenomics as a standalone program, or you can share data by connecting to a central database.

#### Setting up for analysis and review

#### Automated processing

CytoGenomics can run a background process to automatically feature extract and analyze data as microarrays are scanned, using preconfigured design files and analysis workflow settings. Use Settings on the Auto-Processing tab to set up the input and archive folders, then start automated processing using the controls. You can then exit from CytoGenomics and return when you wish to review your samples.

#### Manual processing

#### Sample review

#### CytoGenomics News and Updates

Agilent recently released a software patch v5.1.2 for CytoGenomics software to address some bug fixes found in an earlier version of CytoGenomics, v5.1.1. All CytoGenomics users are strongly encouraged to perform the upgrade to take advantage of the bug fixes.

#### Watch Demo Videos

Running workflows using Auto-Processing

Running workflows manually

Running a single cell analysis workflow

Configuring an analysis method

Reviewing aberration calls and signing off results

#### Launch Pad



SureFISH

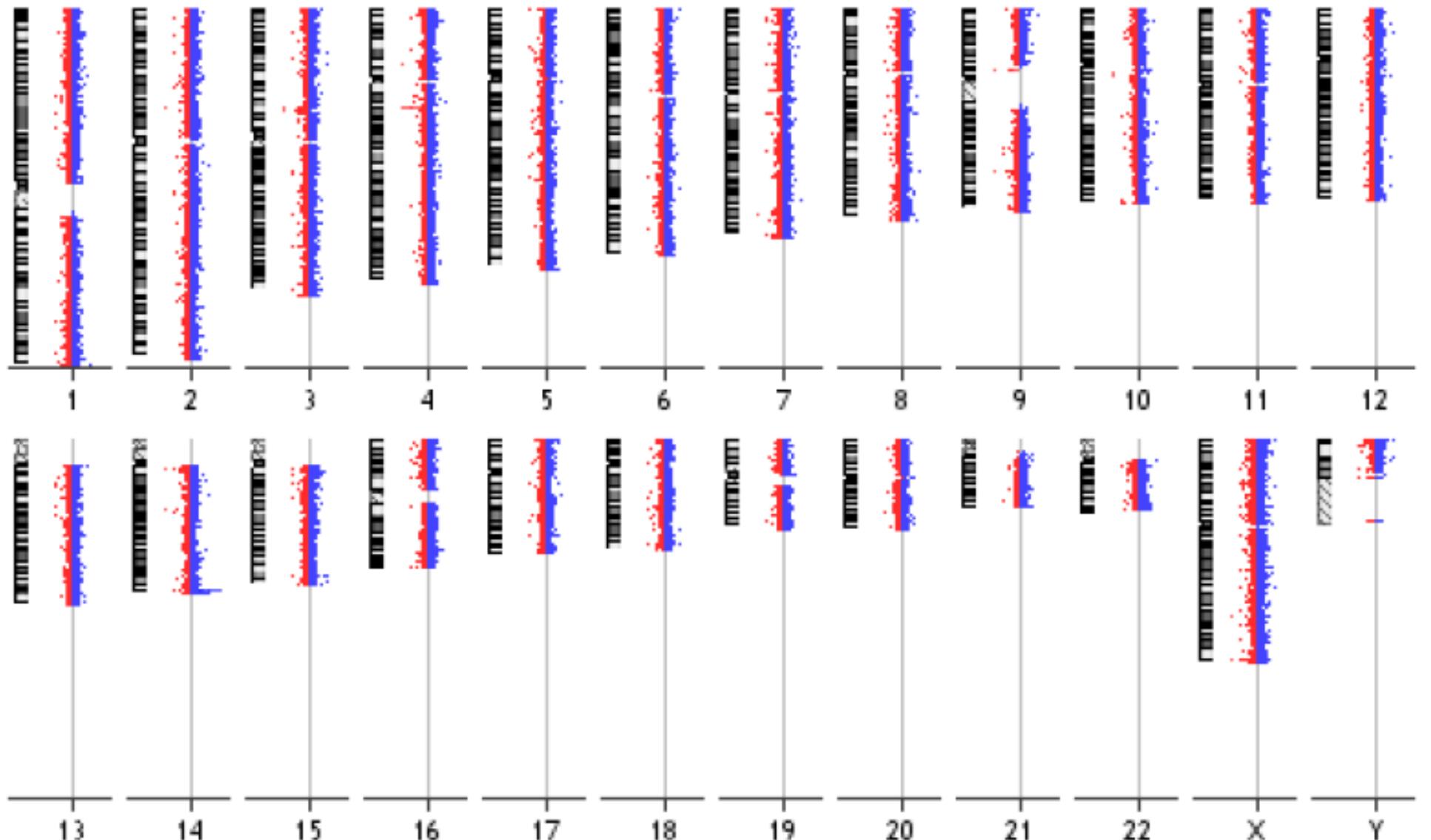


SureCall

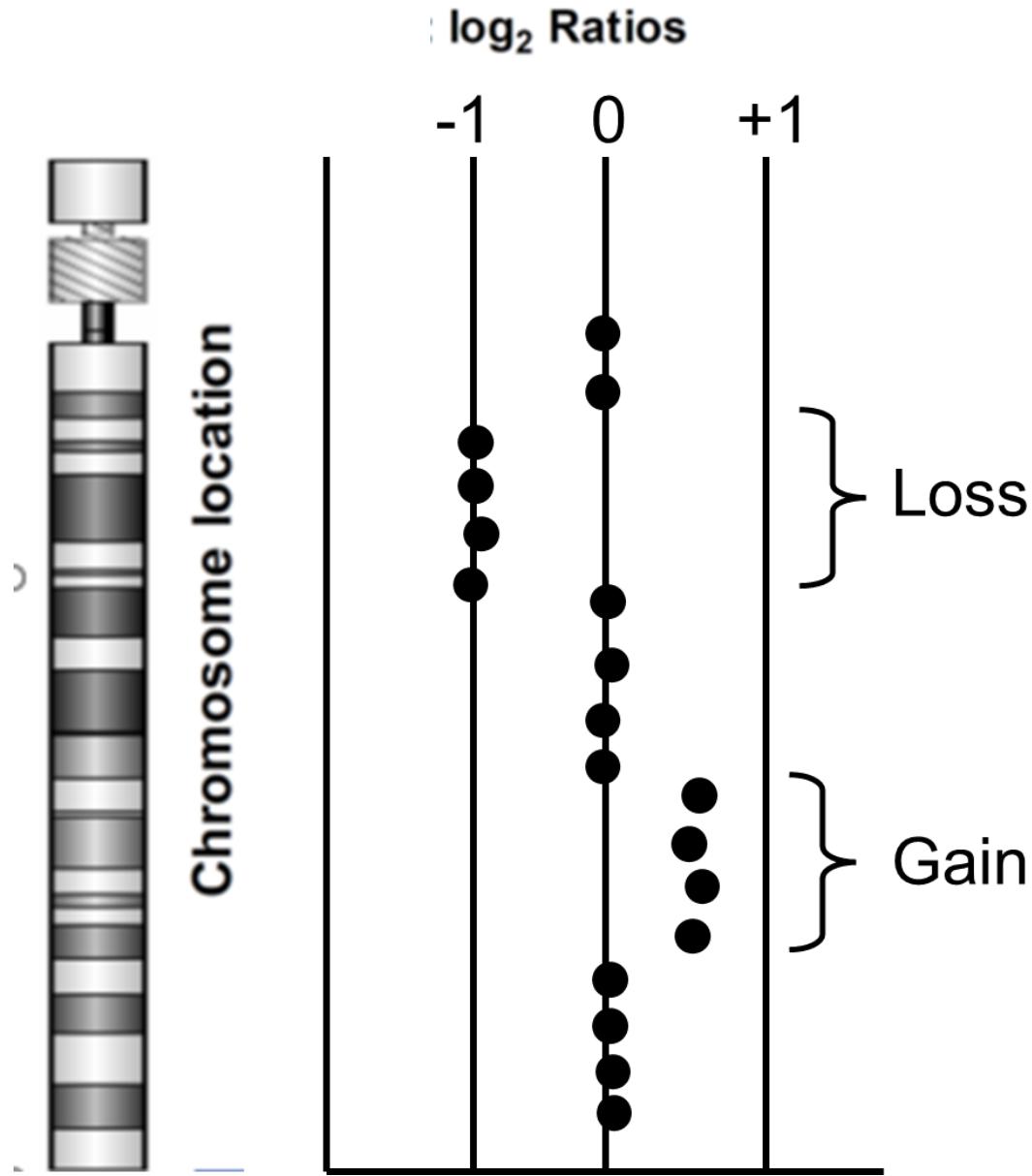


SureDesign

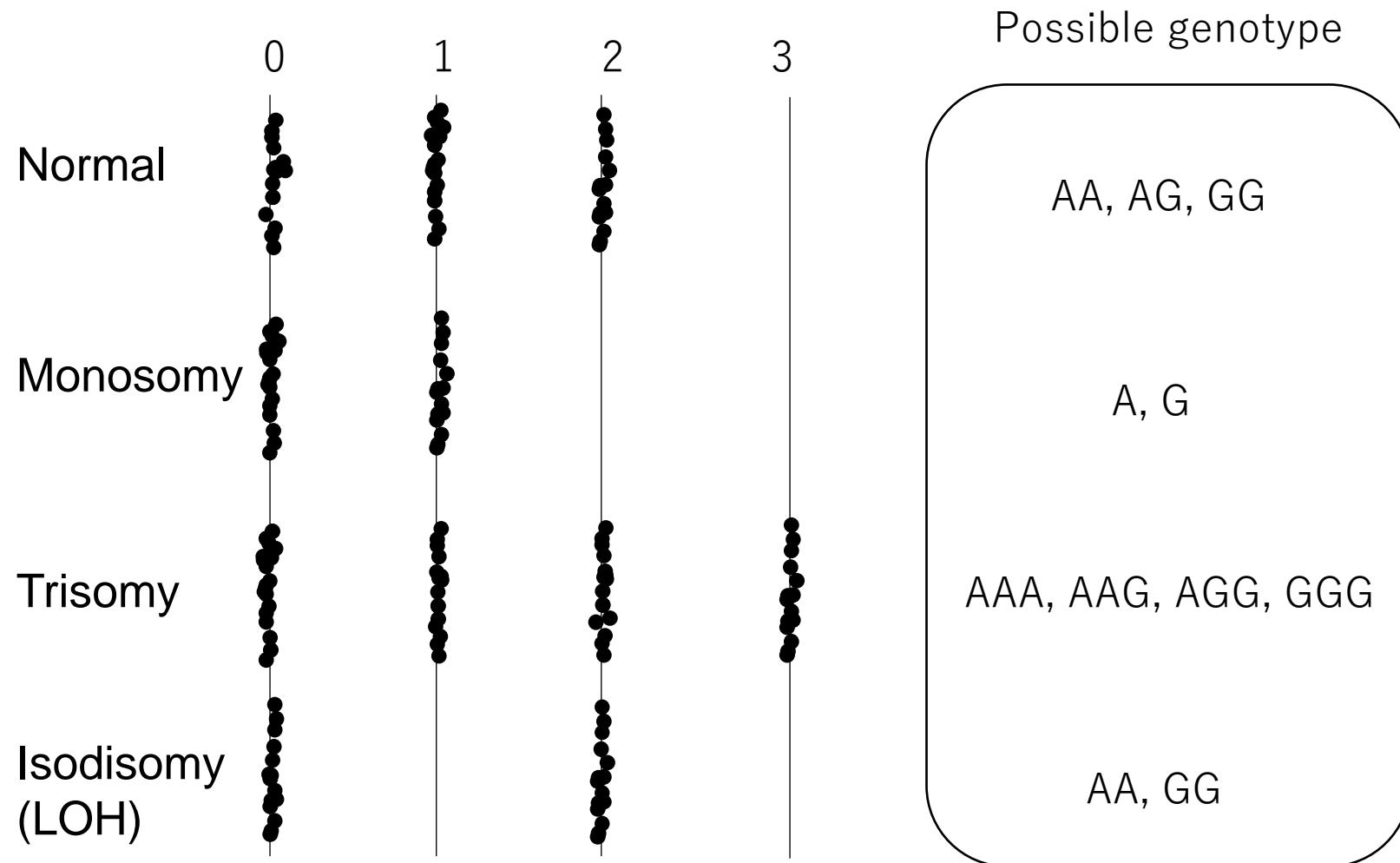
## Genome View (Amp/Del)



# CGH法の原理



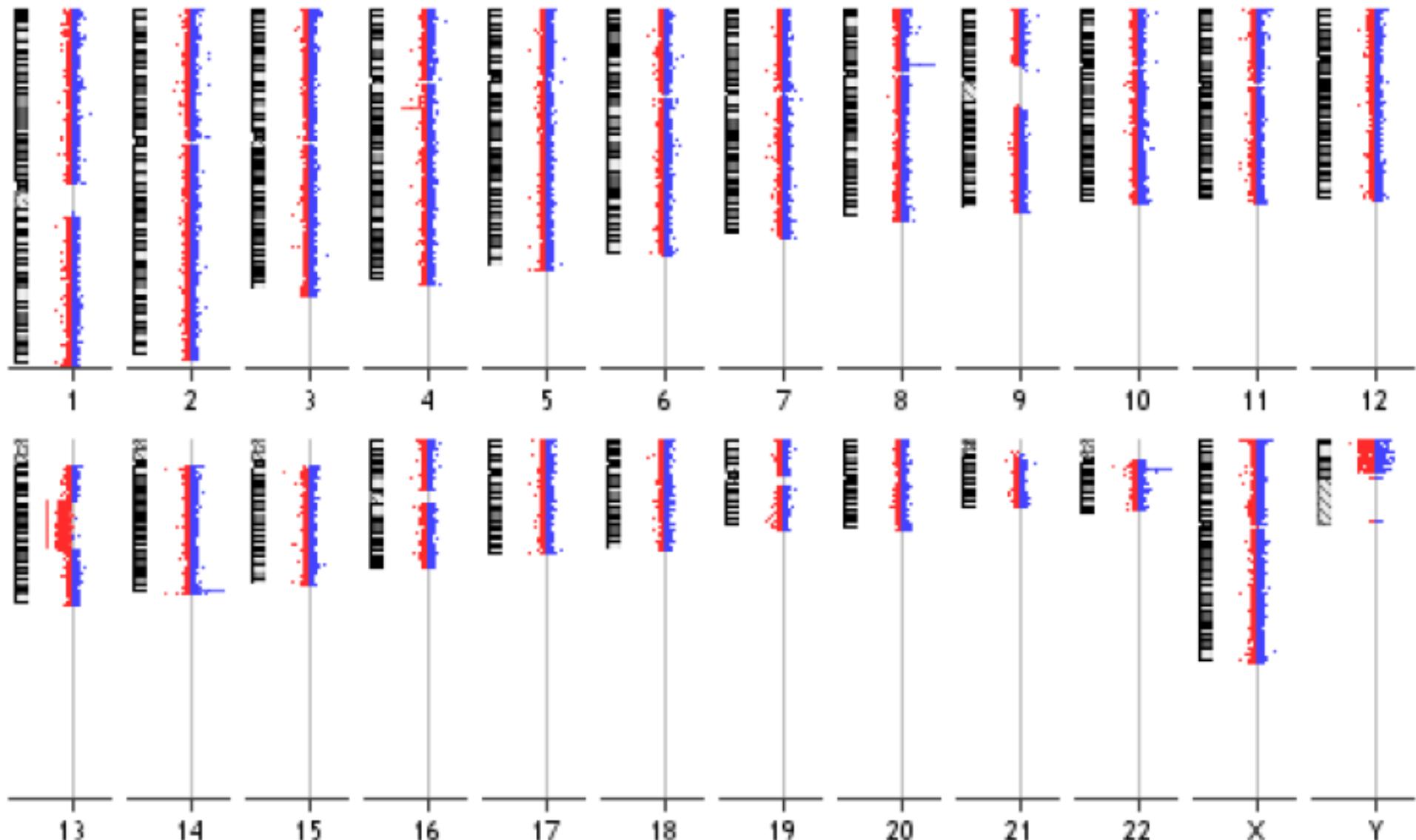
# Agilent社製SNPアレイの原理



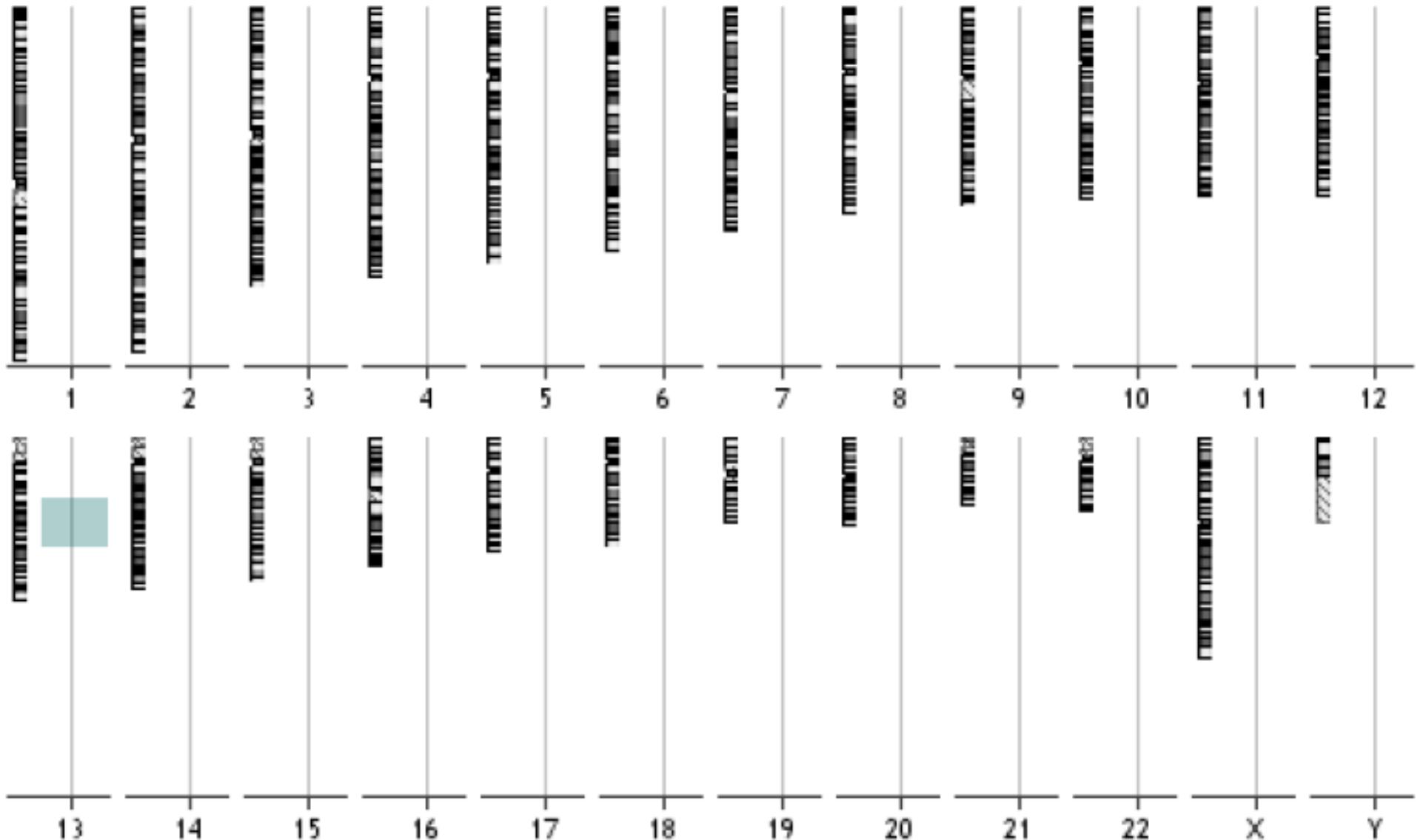
切断されないalleleの数が示される

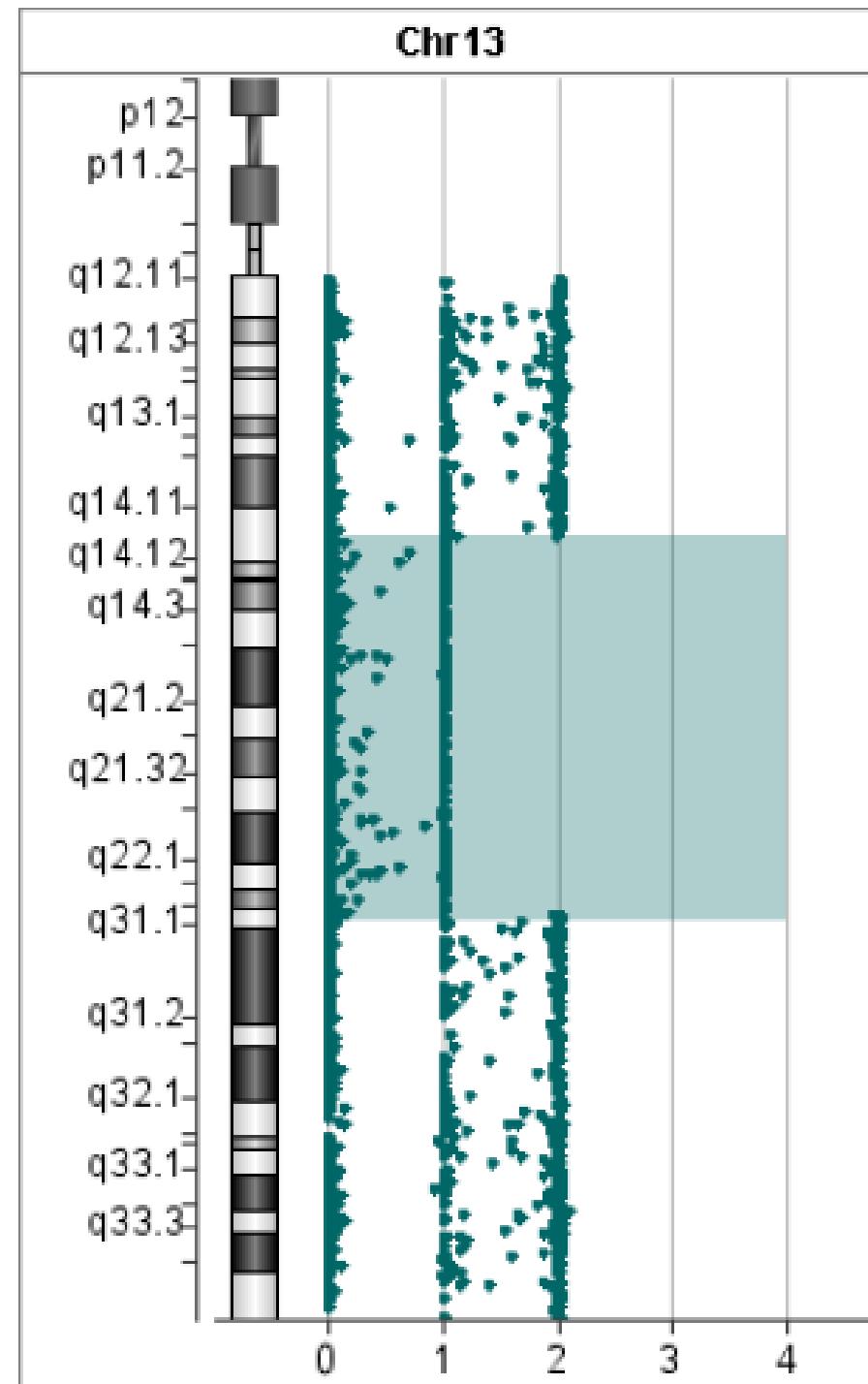
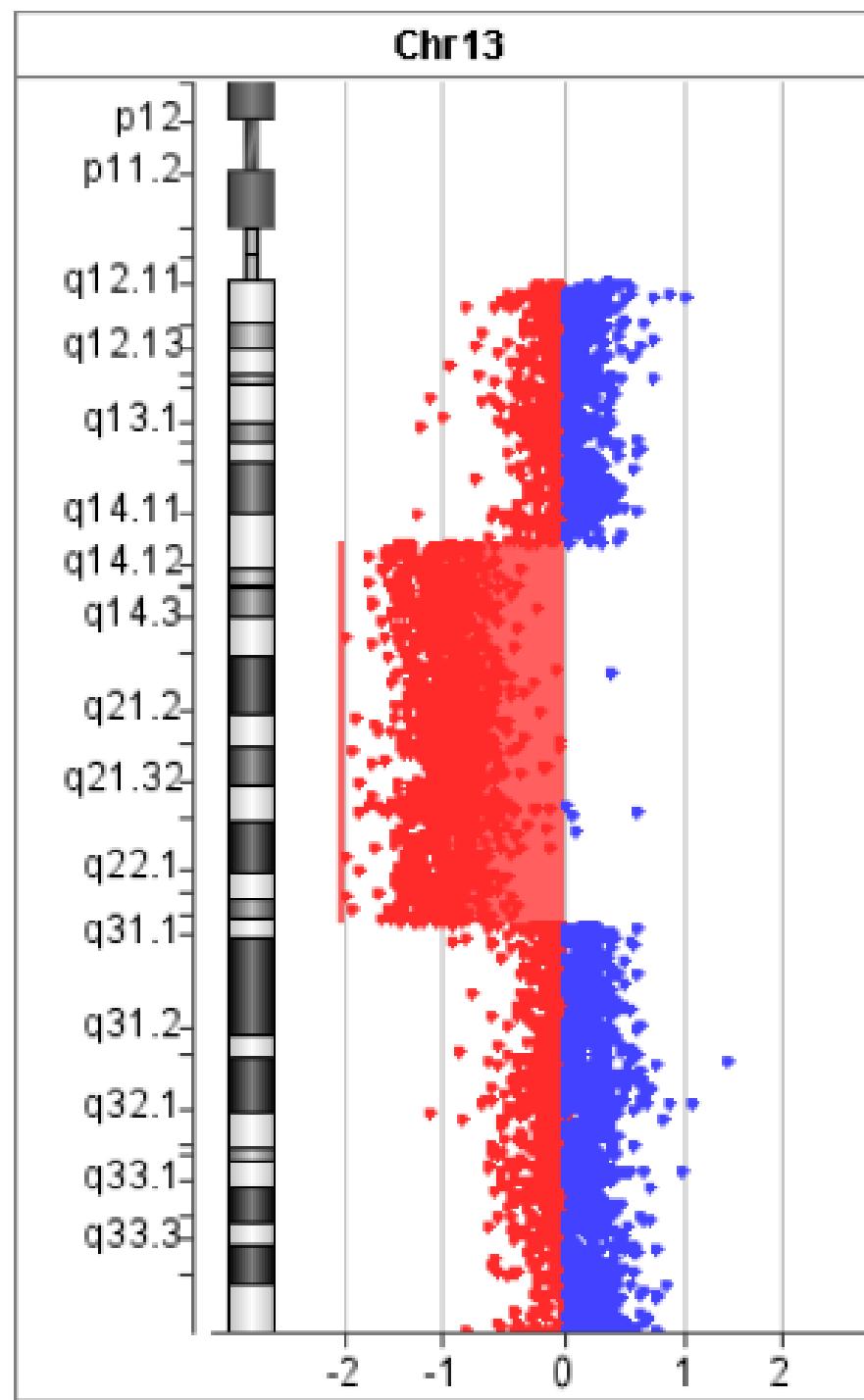
Agilent Technologies社のCGH-SNPアレイでは、使用するDNAについて事前にAluI/RsaI制限酵素で処理を行うため、切断サイトのSNP変化に伴い、切断の有無が異なることを利用

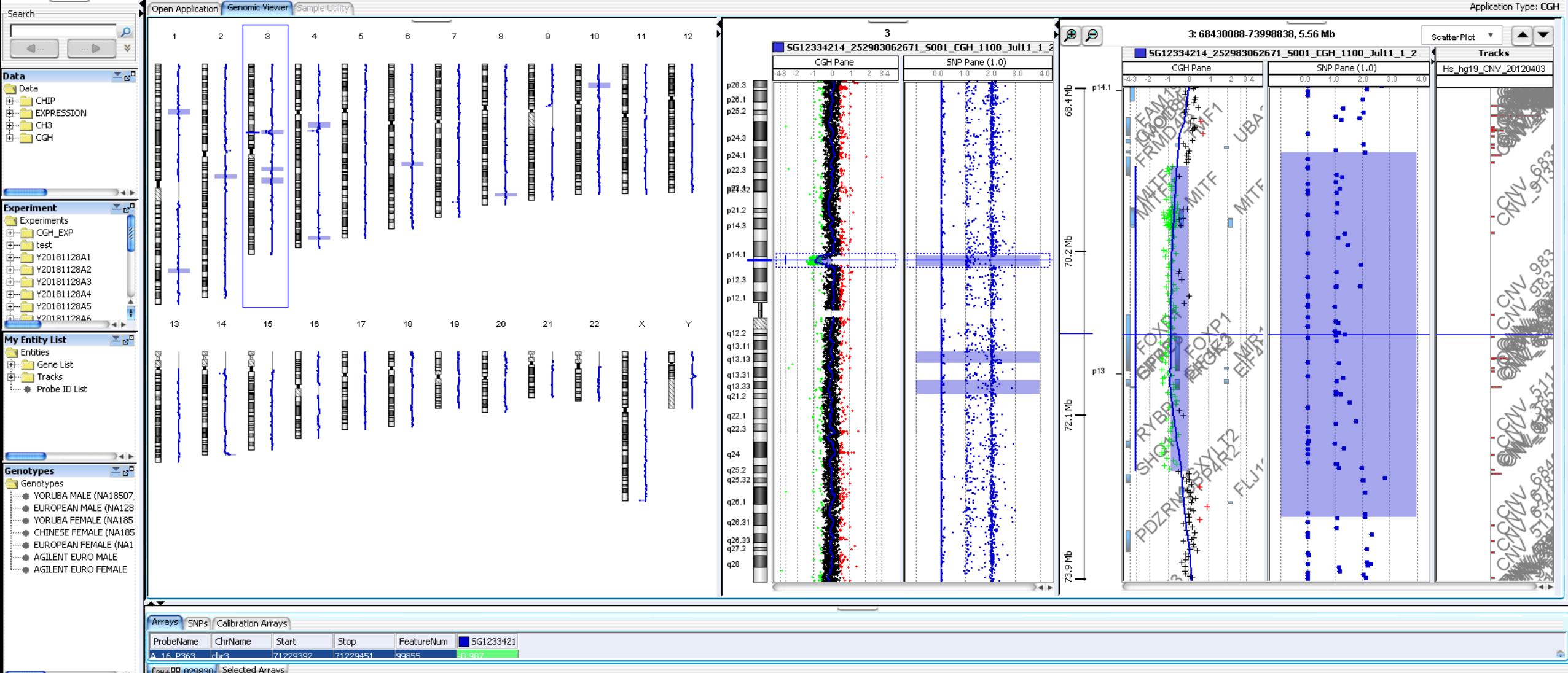
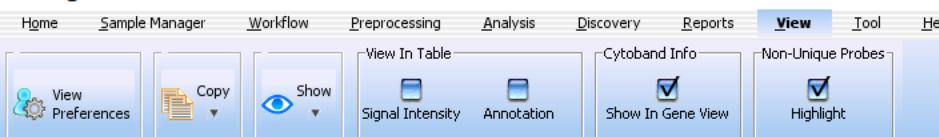
## Genome View (Amp/Del)



## Genome View (LOH)







Amp/Gain/Loss/Del Intervals Table

Chr	Start-Stop(bp)	Cytoband	Size(kb)	#Probes	Amp/Gain/ Loss/Del	P-value	Annotations
chr2	15615419-16002185	p24.3	386.767	30	0.300	3.264E-11	NBAS, DDX1, LINC01804...
chr2	88922723-89082329	p11.2	159.607	7	1.007	1.316E-23	
chr3	4045291-4109283	p26.2	63.993	3	1.170	3.893E-16	
chr4	69075171-69165872	q13.2	90.702	3	-5.113	3.063E-60	UGT2B17
chr8	15957300-16054667	p22	97.368	4	1.022	3.497E-14	MSR1
chr8	39378051-39500671	p11.23 - p11.22	122.621	5	5.816	1.27E-100	ADAM5, ADAM3A
chr11	1973251-1973735	p15.5	0.485	7	1.301	3.377E-42	HOTS, H19
chr12	62772-159968	p13.33	97.197	13	0.623	2.144E-19	IQSEC3, LOC574538
chr13	42157454-76906579	q14.11 - q22.3	34,749.126	1424	-0.960	4.9E-324	FAM216B, LINC01050, LINC00428...
chr14	18504575-19491517	q11.1 - q11.2	986.943	11	0.624	1.484E-16	POTEK, LOC101929572, POTEH-AS1...
chr14	21389103-22022119	q11.2	633.017	24	-0.473	1.707E-20	LOC105370401
chr14	105476748-105609525	q32.33	132.778	4	4.787	7.913E-74	ADAM6
chr14	105736164-106028995	q32.33	292.832	9	0.908	1.34E-27	LINC00226, LINC00221
chr14	106219784-106253703	q32.33	33.92	9	-0.751	1.838E-19	
chr15	18676258-20384607	q11.2	1,708.35	30	0.385	3.66E-11	CHEK2P2, HERC2P3, GOLGA6L6...
chr15	22884031-22884851	q11.2	0.821	10	-0.461	3.518E-12	SNHG14
chr15	41682925-41738012	q15.3	55.088	22	0.427	1.258E-15	STRC, CATSPER2, PPIP5K1P1- CATSPER2
chr22	19611791-19616962	q11.21	5.172	4	-0.757	8.979E-10	CRKL
chr22	21386562-21558483	q11.22	171.922	7	4.384	1.291E-129	MIR650, MIR5571
chrY	2714852-2716217	p11.31	1.366	13	-0.546	8.518E-10	SRY

Amp=Amplification Del=Deletion

Total Amp/Gain/Loss/Del Intervals: 20

# レポートされるCNVのほとんどはbenign

重複の場合log2は+0.5のはず  
中途半端な値は  
アーチファクトかbenign CNV

		Size(kb)	#Probes	Amp/Gain/ Loss/Del	P-value	Annotations	
c	c	741.664	24	0.290	5.57E-10	BRINP3	
c	c	54.582	3	1.040	7.745E-15	CFHR3, CFHR1	
chr2	15998433-16002185	p24.3	3.753	16	0.421	MYCNOS, MYCN	
chr2	24373765-25694872	p23.3	1,321.108	43	-0.261	ITSN2, NCOA1, PTRHD1...	
chr2	45023575-45024666	p21	1.092	11	0.472	SIX3	
chr2	88966417-89082329	p11.2	115.912	5	0.978	3.202E-21	
chr4	69075171-69165872	q13.2	1.741	3	-6.220	UGT2B17	
chr6	186875-238615	p25.3	11.741	13	-0.434	DUSP22	
chr7	38290450-38349092	p11.2	58.643	4	-0.814	TRG-AS1	
chr7	62110540-62145694	q13.2	35.155	45	0.298	5.896E-18	
chr		2.436	12	0.462	3.006E-12	PEG10	
chr		370.028	19	-0.394	8.488E-14	MTRNR2L6, PRSS1	
chr		890.43	7	-0.882	7.532E-24	ZNF705G, DEFB4B, DEFB103A...	
chr9	20200250-20500271	-11.22	-11.22	212.012	7	0.636	APAM5, APAM2A

欠失の場合log2は-1のはず  
中途半端な値は  
アーチファクトかbenign CNV

# アーチファクトも多い

Chr	Start-Stop(bp)	Cytoband	Size(kb)	#Probes	Amp/Gain/ Loss/Del	P-value	Annotations
chr1	187828838-188570391	q31.1	741.554	24	0.290	5.57E-10	BRINP3
chr1	195011344-195065925	q31.3	54.582	3	1.040	7.745E-15	CFHR3, CFHR1
chr2	15998433-16002185	p24.3	3.77	16	0.421	2.354E-13	MYCNOS, MYCN
chr2	24373765-25694872	p23.3	1.108	43	-0.261	9.552E-14	ITSN1, NCOA1, PTRHD1...
chr3	113000000-113000000	q31.1	1.000	11	0.472	8.825E-12	SIX3
chr3	113000000-113000000	q31.1	1.000	5	0.978	3.202E-21	
chr3	113000000-113000000	q31.1	1.000	3	-6.220	9.707E-65	UGT2B17
chr3	113000000-113000000	q31.1	1.000	13	-0.434	9.52E-12	DUSP22
chr7	38290450-38349092	p14.1	58.643	4	-0.814	1.391E-12	TRG-AS1
chr7	62110540-62145694	q11.21	35.155	45	0.298	5.896E-18	
chr7	94123650-94126085	q21.3	2.436	12	0.462	3.006E-12	PEG10
chr7	141770262-142140289	q34	370.028	19	-0.394	8.488E-14	MTRNR2L6, PRSS1
chr8	7226901-8117330	p23.1	890.43	7	-0.882	7.532E-24	ZNF705G, DEFB4B, DEFB103A...
chr9	202900650-20500071	q11.22-q11.22	212.012	7	-0.636	3.666E-15	ADAM5, ADAM24

含まれるProbe数が極端に少ないものは  
アーチファクトの可能性大



## Our tool

- **Genome Browser**  
interactively visualize genomic data
  - **COVID-19 Research**  
use the SARS-CoV-2 genome browser and explore coronavirus database
  - **BLAT**  
rapidly align sequences to the genome
  - **Table Browser**  
download data from the Genome Browser database
  - **Variant Annotation Integrator**  
get functional effect predictions for variant calls
  - **Data Integrator**  
combine data sources from the Genome Browser database
  - **Genome Browser in a Box (GBiB)**  
run the Genome Browser on your laptop or server
  - **In-Silico PCR**  
rapidly align PCR primer pairs to the genome
  - **LiftOver**  
convert genome coordinates between assemblies
  - **Track Hubs**  
import and view external data tracks
  - **REST API**  
returns data in JSON format

[More tools](#)







Scale

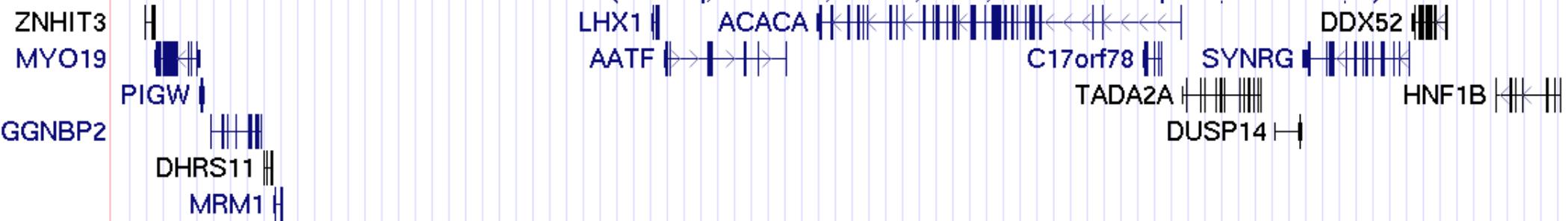
chr17: 35,000,000

500 kb

hg19

36,000,000

UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)



chr17\_gl383560\_fix

Reference Assembly Fix Patch Sequence Alignments

Alt Haplotypes

Reference Assembly Alternate Haplotype Sequence Alignments

UCSC RefSeq

RefSeq genes from NCBI

Sequences  
SNPs

Publications: Sequences in Scientific Articles



ここに入力して検索



15°C 晴れのちくもり へ ☁ 2/4 A 9:55 2021/10/23



Human hg19 chr17:34815184-36 x +

https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType...

Mapping and Sequencing

refresh

Base Position dense ▾	P13 Updated Fix Patches pack ▾	P13 Updated Alt Haplotypes dense ▾	Assembly hide ▾	BAC End Pairs hide ▾	BU ORCHID hide ▾
Chromosome Band hide ▾	18 deCODE Recomb hide ▾	ENCODE Pilot [No data-chr17]	Exome Probesets hide ▾	18 FISH Clones hide ▾	18 Fosmid End Pairs hide ▾
Gap hide ▾	GC Percent hide ▾	GRC Incident hide ▾	GRC Map Contigs hide ▾	Hg18 Diff hide ▾	Hg38 Diff hide ▾
■ Hg38 Mapping hide ▾	■ Hi Seq Depth hide ▾	■ INSDC hide ▾	■ LRG Regions hide ▾	■ Map Contigs hide ▾	■ Mappability hide ▾
■ Problematic Regions hide ▾	Recomb Rate hide ▾	RefSeq Acc hide ▾	Restr Enzymes hide ▾	Short Match hide ▾	STS Markers hide ▾

Genes and Gene Predictions

refresh

UCSC Genes pack ▾	■ NCBI RefSeq dense ▾	CCDS hide ▾	CRISPR Targets hide ▾	Updated Ensembl Genes hide ▾	17 EvoFold hide ▾
Exoniphy hide ▾	■ GENCODE hide ▾	■ H-Inv 7.0 hide ▾	IKMC Genes Mapped hide ▾	■ lncRNAs hide ▾	LRG Transcripts hide ▾
MGC Genes hide ▾	Old UCSC Genes hide ▾	ORFeome Clones hide ▾	Other RefSeq hide ▾	Pfam in UCSC Gene hide ▾	New ■ Prediction Archive hide ▾
Retroposed Genes sno/miRNA hide ▾	■ TransMap V5 hide ▾	tRNA Genes hide ▾	UCSC Alt Events hide ▾	■ UniProt hide ▾	
■ Vega Genes hide ▾	Yale Pseudo60 hide ▾				

Phenotype and Literature

refresh

■ Publications dense ▾	■ CADD hide ▾	■ ClinGen hide ▾	■ ClinGen CNVs hide ▾	■ ClinVar Variants hide ▾	Coriell CNVs hide ▾
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9:56 15°C 晴れのちくもり 2021/10/23

ここに入力して検索



Human hg19 chr17:34,815,184-36,241,526 x +

<https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType...>

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## UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly

move <<< << < > >> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

multi-region chr17:34,815,184-36,241,526 1,426,343 bp enter position, gene symbol, HGVS or search terms go

chr17 (q12) 13.3 13.2 p13.1 17p12 17p11.2 17q11.2 17q12 21.31 17q22 24.2 24.3 q25.1 17q25.3

Scale 500 kb hg19  
chr17: 35,000,000 35,500,000 36,000,000

Chromosome Bands Localized by FISH Mapping Clones 17q12

Chromosome Band

UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)

ZNHIT3  
MYO19  
PIGW  
GGNBP2  
DHRS11  
MRM1  
LHX1  
ACACA  
AATF  
C17orf78  
SYNRG  
TADA2A  
DDX52  
HNF1B  
DUSP14

move start < 2.0 > move end < 2.0 >

Click on a feature for details. Click+shift+drag to zoom in. Click side bars for track options. Drag side bars or labels up or down to reorder tracks. Drag tracks left or right to new position. Press "?" for keyboard shortcuts.

track search default tracks default order hide all manage custom tracks track hubs configure reverse resize refresh

collapse all expand all

Use drop-down controls below and press refresh to alter tracks displayed.  
Tracks with lots of items will automatically be displayed in more compact modes.

Custom Tracks refresh

Track1 hide

Mapping and Sequencing

9:58 15°C 晴れのちくもり 2021/10/23

ここに入力して検索

Human hg19 chr17:34815184-36 x +

https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType...

hide

### Mapping and Sequencing

refresh

- Base Position
- P13 Updated Fix Patches
- P13 Updated Alt Haplotypes
- Assembly
- BAC End Pairs
- BU ORCHID

- Chromosome Band
- 18 deCODE Recomb
- ENCODE Pilot [No data-chr17]
- Exome Probesets
- 18 FISH Clones
- Fosmid End Pairs

- Gap
- GC Percent
- GRC Incident
- GRC Map Contigs
- Hg18 Diff
- Hg38 Diff

- Hg38 Mapping
- Hi Seq Depth
- INSDC
- LRG Regions
- Map Contigs
- Mappability

- Problematic Regions
- Recomb Rate
- RefSeq Acc
- Restr Enzymes
- Short Match
- STS Markers

hide

### Genes and Gene Predictions

refresh

- UCSC Genes
- NCBI RefSeq
- CCDS
- CRISPR Targets
- Ensembl Genes
- EvoFold

- Exoniphy
- GENCODE
- H-Inv 7.0
- IKMC Genes Mapped
- lincRNAs
- LRG Transcripts

- MGC Genes
- Old UCSC Genes
- ORFeome Clones
- Other RefSeq
- Pfam in UCSC Gene
- Prediction Archive

- Retroposed Genes sno/miRNA
- TransMap V5
- Yale Pseudo60
- tRNA Genes
- UCSC Alt Events
- UniProt

- Vega Genes
- Yale Pseudo60

hide

### Phenotype and Literature

refresh

- Publications
- CADD
- ClinGen
- ClinVar Variants
- Coriell CNVs

- ClinGen

Deprecated

https://genome.ucsc.edu/cgi-bin/hgTrackUi?hgSID=1193175675\_j2XxagC2DaMvo5ivDYk5WN0HaEXH&db=hg19&c=chr17&g=knownGene

9:58 2021/10/23

ここに入力して検索

15°C 晴れのちくもり

18

UCSC Genes Track Settings

https://genome.ucsc.edu/cgi-bin/hgTrackUi?hgsid=1193175675\_j2XagC2DaMvo5ivDYk5WNoHaEXH&db=hg19&c=chr17...

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## UCSC Genes Track Settings

### UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics) (^All Genes and Gene Predictions tracks)

Display mode: pack  ②

Label:  gene symbol  UCSC Known Gene ID  UniProt Display ID  OMIM ID

Show:  non-coding genes  splice variants

Color track by codons: genomic codons  ①

Show codon numbering:

Display data as a density graph:  ①

[View table schema](#)

Data last updated at UCSC: 2013-06-14

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## Description

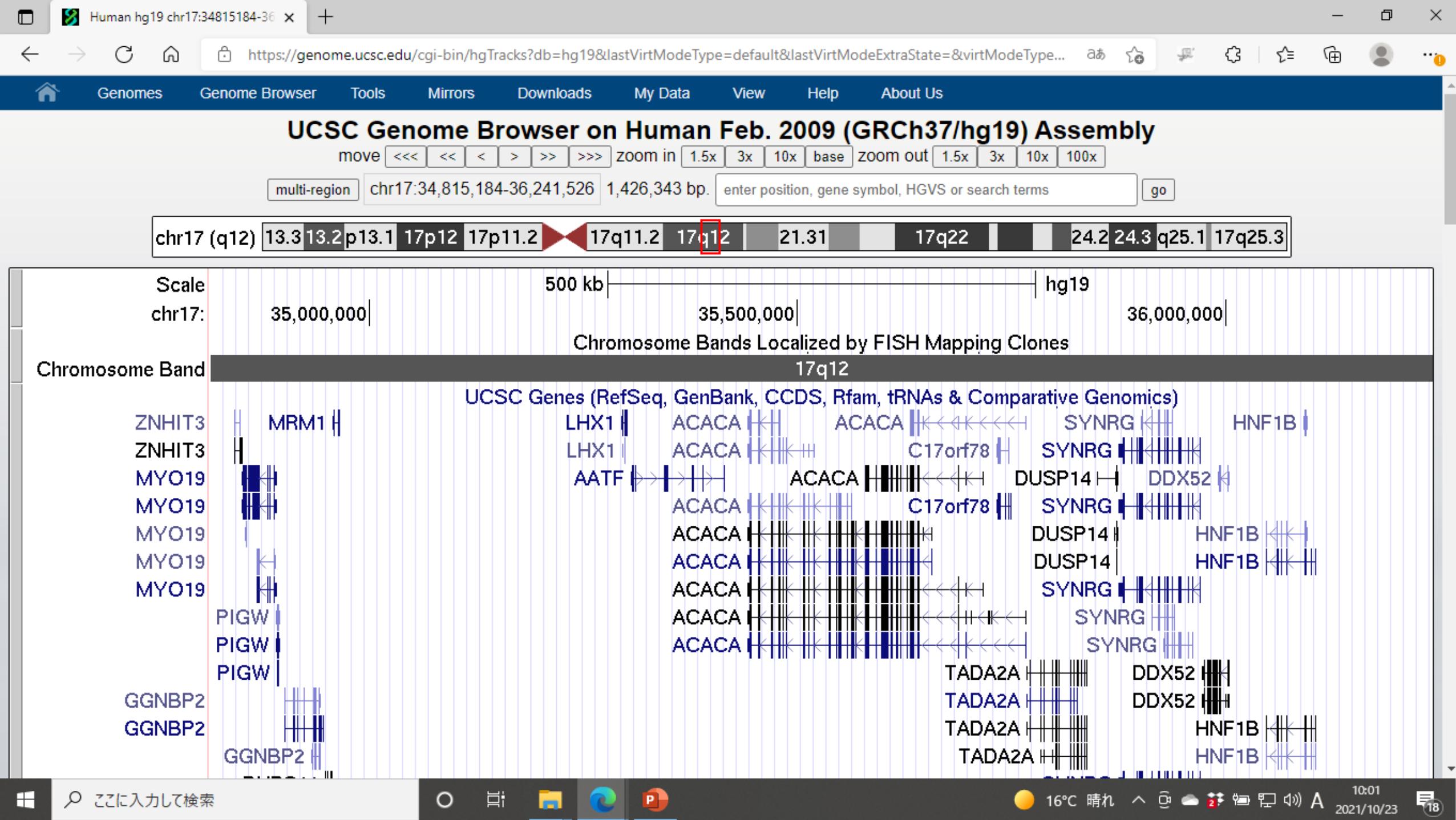
The UCSC Genes track is a set of gene predictions based on data from RefSeq, GenBank, CCDS, Rfam, and the [tRNA Genes](#) track. The track includes both protein-coding genes and non-coding RNA genes. Both types of genes can produce non-coding transcripts, but non-coding RNA genes do not produce protein-coding transcripts. This is a moderately conservative set of predictions. Transcripts of protein-coding genes require the support of one RefSeq RNA, or one GenBank RNA sequence plus at least one additional line of evidence. Transcripts of non-coding RNA genes require the support of one Rfam or tRNA prediction. Compared to RefSeq, this gene set has generally about 10% more protein-coding genes, approximately four times as many putative non-coding genes, and about twice as many splice variants.

For more information on the different gene tracks, see our [Genes FAQ](#).

## Display Conventions and Configuration

ここに入力して検索

16°C 晴れ 9:59 A 2021/10/23





Human hg19 chr17:34815184-36

https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType...

## Genes and Gene Predictions

refresh

UCSC Genes pack	NCBI RefSeq hide	CCDS hide	CRISPR Targets hide	Updated Ensembl Genes hide	17 EvoFold hide
Exoniphy hide	GENCODE hide	H-Inv 7.0 hide	IKMC Genes Mapped hide	lincRNAs hide	LRG Transcripts hide
MGC Genes hide	Old UCSC Genes hide	ORFeome Clones hide	Other RefSeq hide	Pfam in UCSC Gene hide	New Prediction Archive hide
Retroposed Genes sno/miRNA hide	TransMap V5 hide	Yale Pseudo60 hide	tRNA Genes hide	UCSC Alt Events hide	UniProt hide
Vega Genes hide					

## Phenotype and Literature

refresh

Publications hide	CADD hide	ClinGen hide	Deprecated ClinGen CNVs squish	ClinVar Variants hide	Coriell CNVs hide
COSMIC Regions hide	Decipher CNVs full	DECIPHER SNVs hide	Component Delay hide	GAD View hide	Gene Interactions hide
GeneReviews hide	GWAS Catalog hide	Haploinsufficiency hide	Genetics Variants dense	Lens Patents hide	LOVD Variants hide
18 MGI Mouse QTL hide	OMIM Alleles hide	OMIM Cyto Loci hide	Genomic Variants squish	REVEL Scores hide	18 RGD Human QTL hide
18 RGD Rat QTL hide	SNPedia hide	UniProt Variants hide	OMIM Genes pack	Web Sequences hide	

## COVID-19

refresh

COVID GWAS v4 hide	COVID GWAS v3 hide	Rare Harmful Vars hide			

mRNA and EST

refresh

16°C 晴れ 10:09 2021/10/23

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File icon

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Search icon

Power icon

Network icon

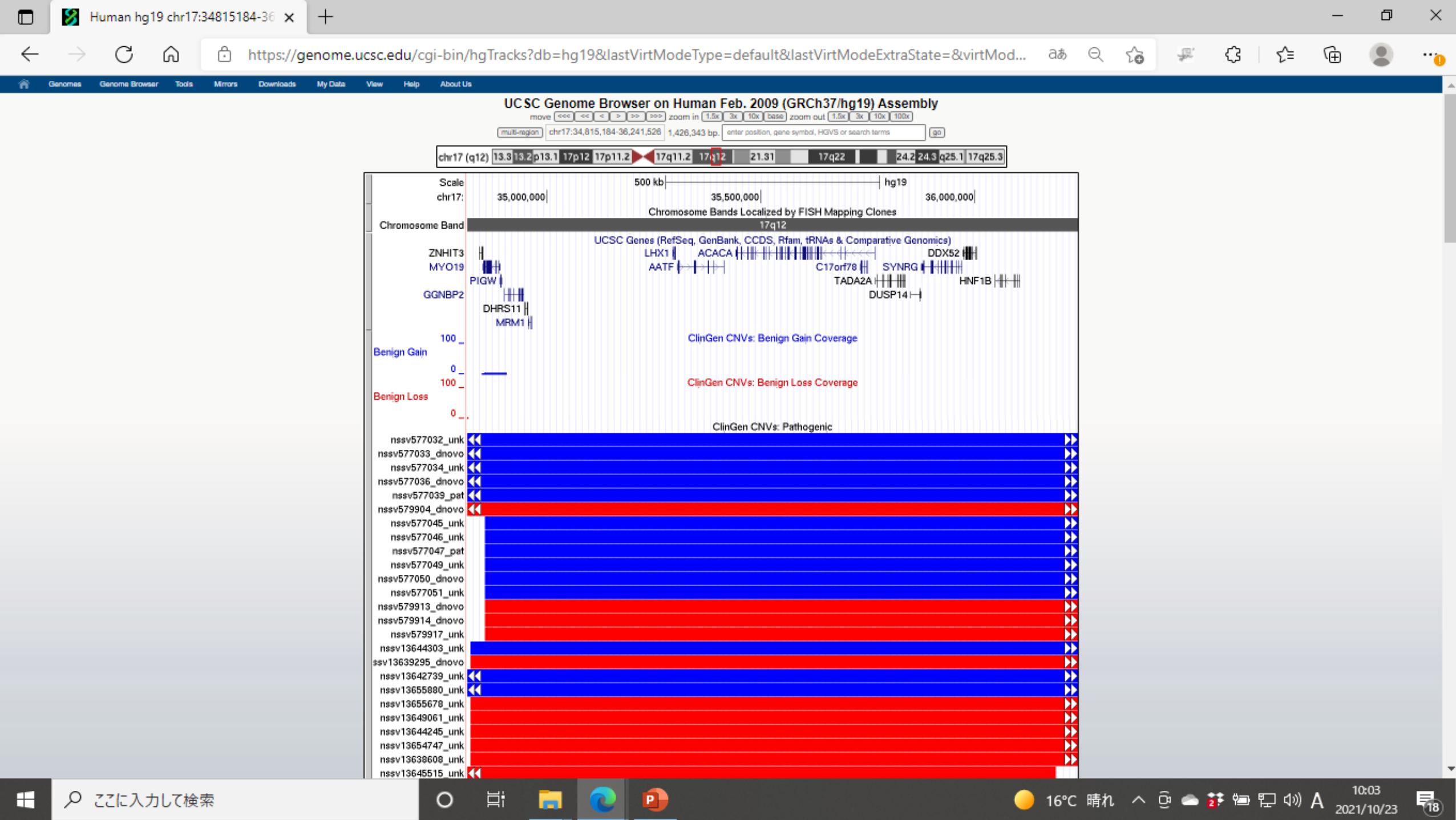
Cloud icon

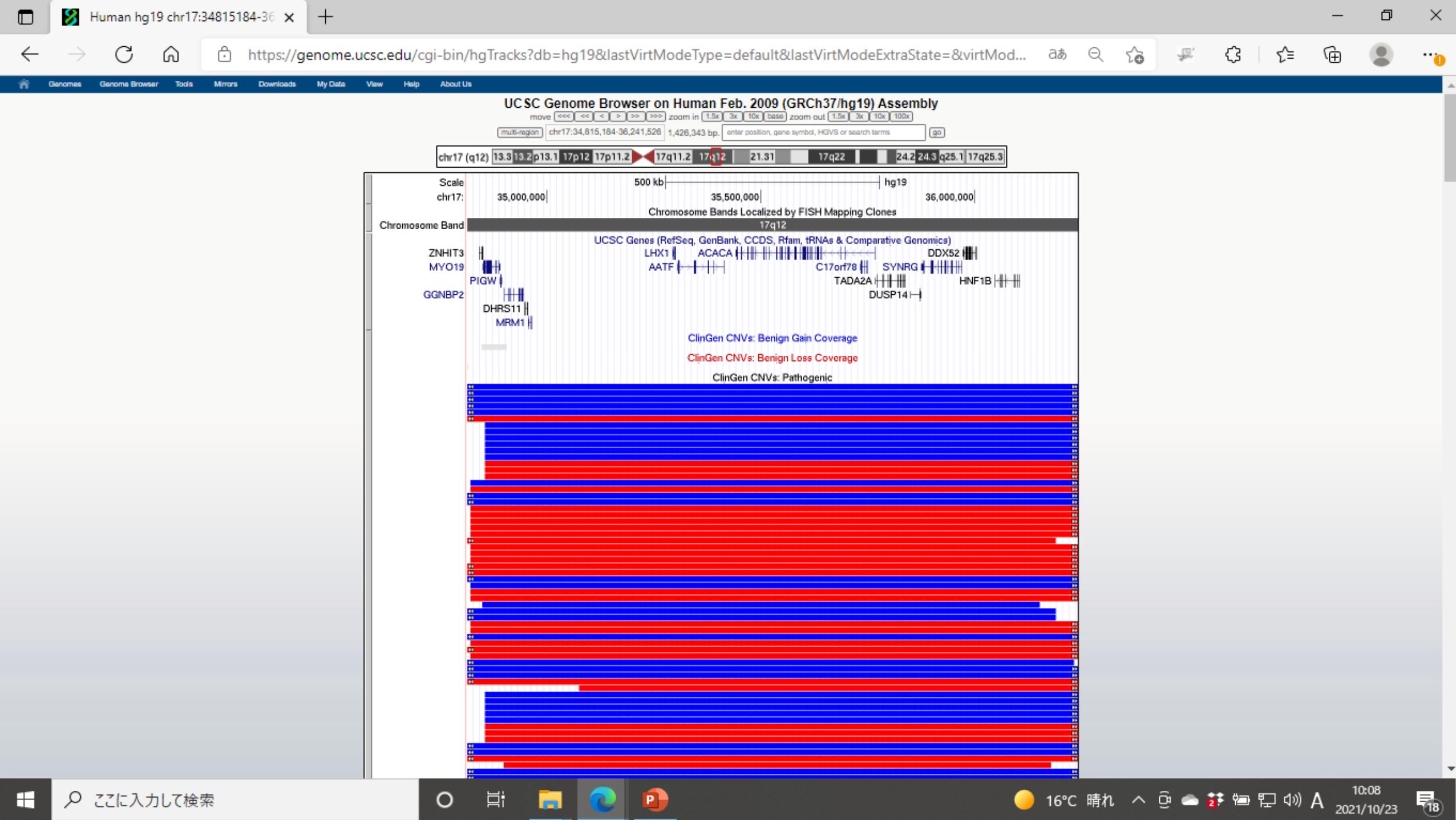
Print icon

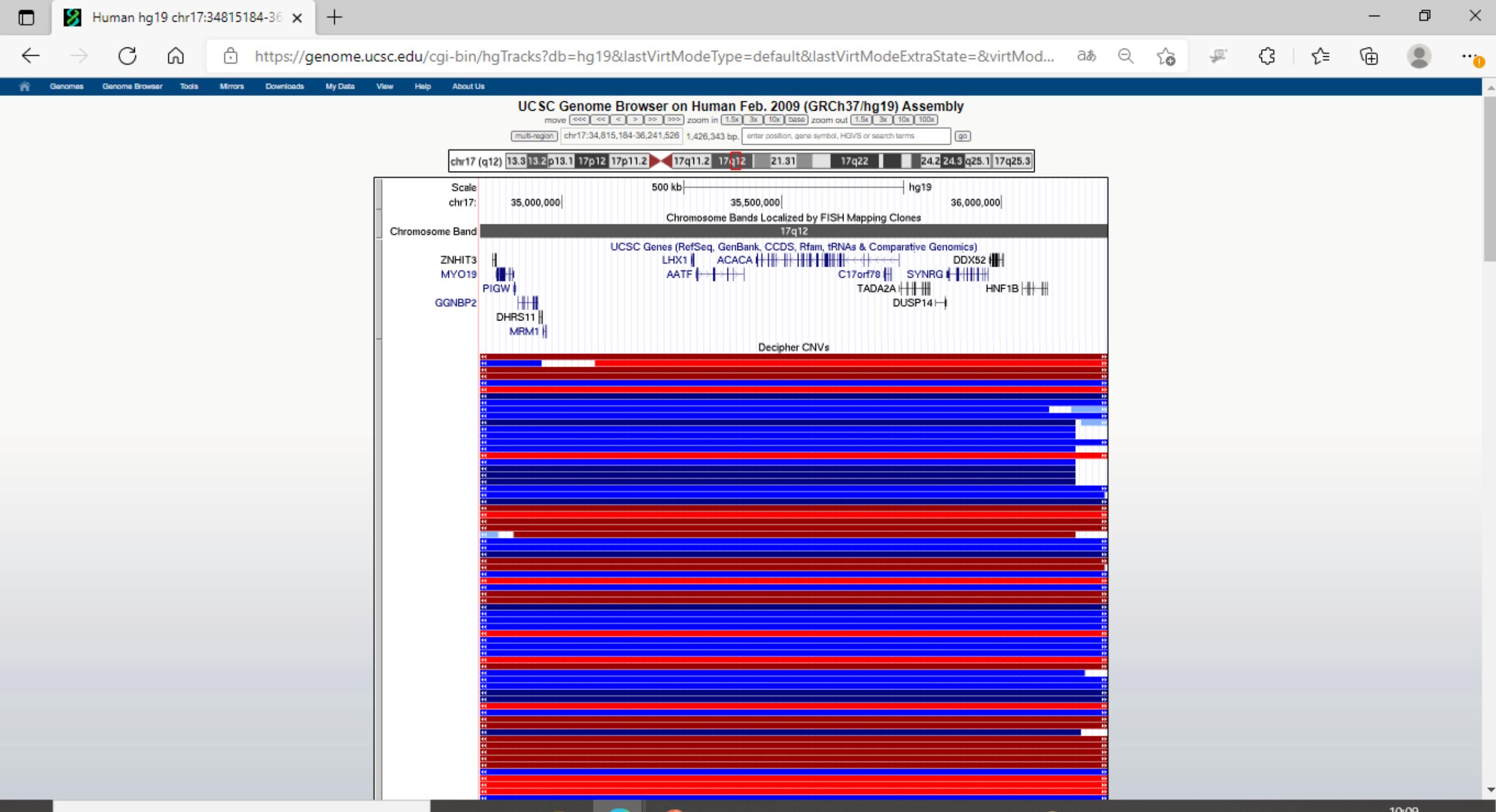
Speaker icon

User icon

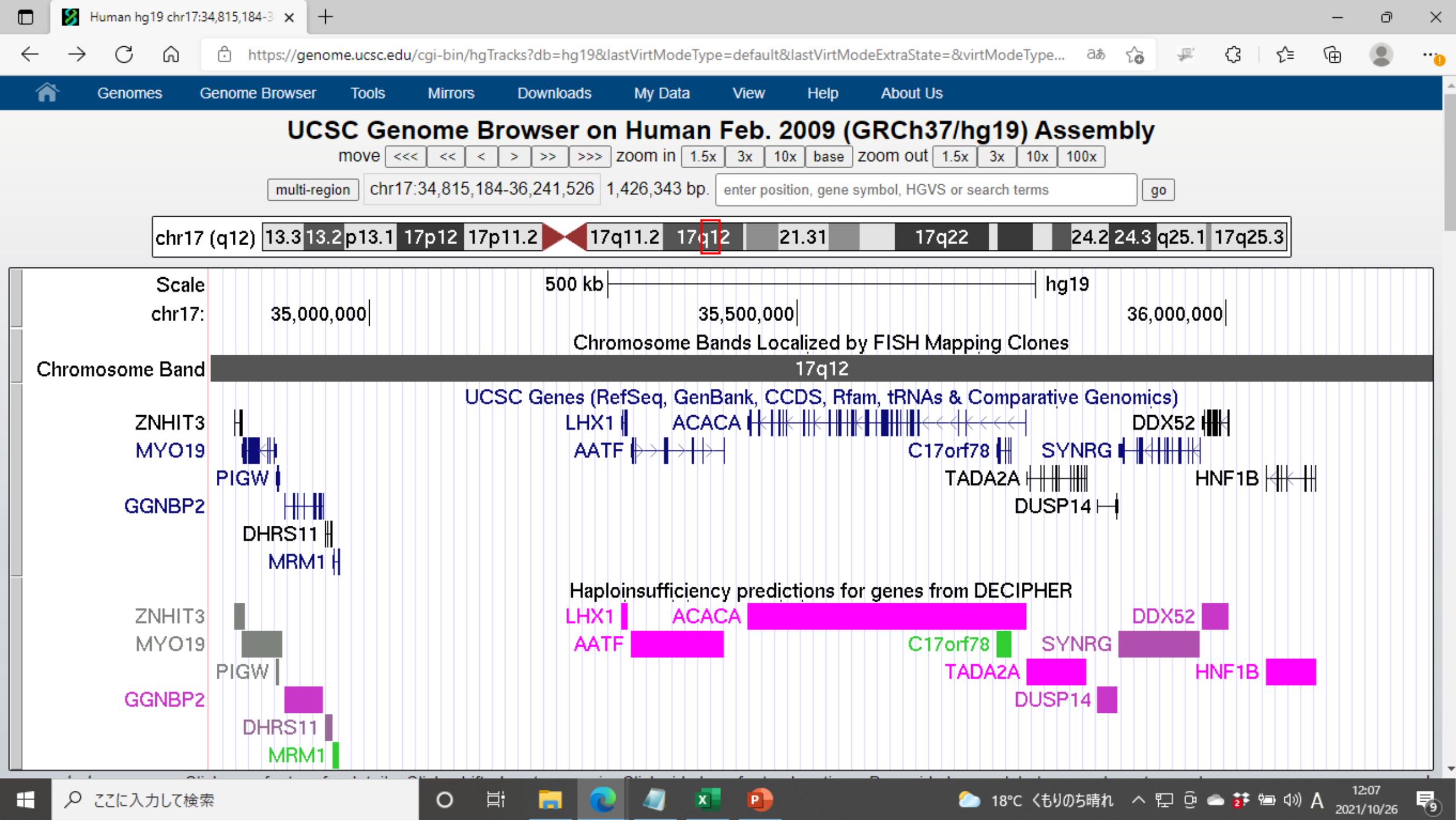
Help icon



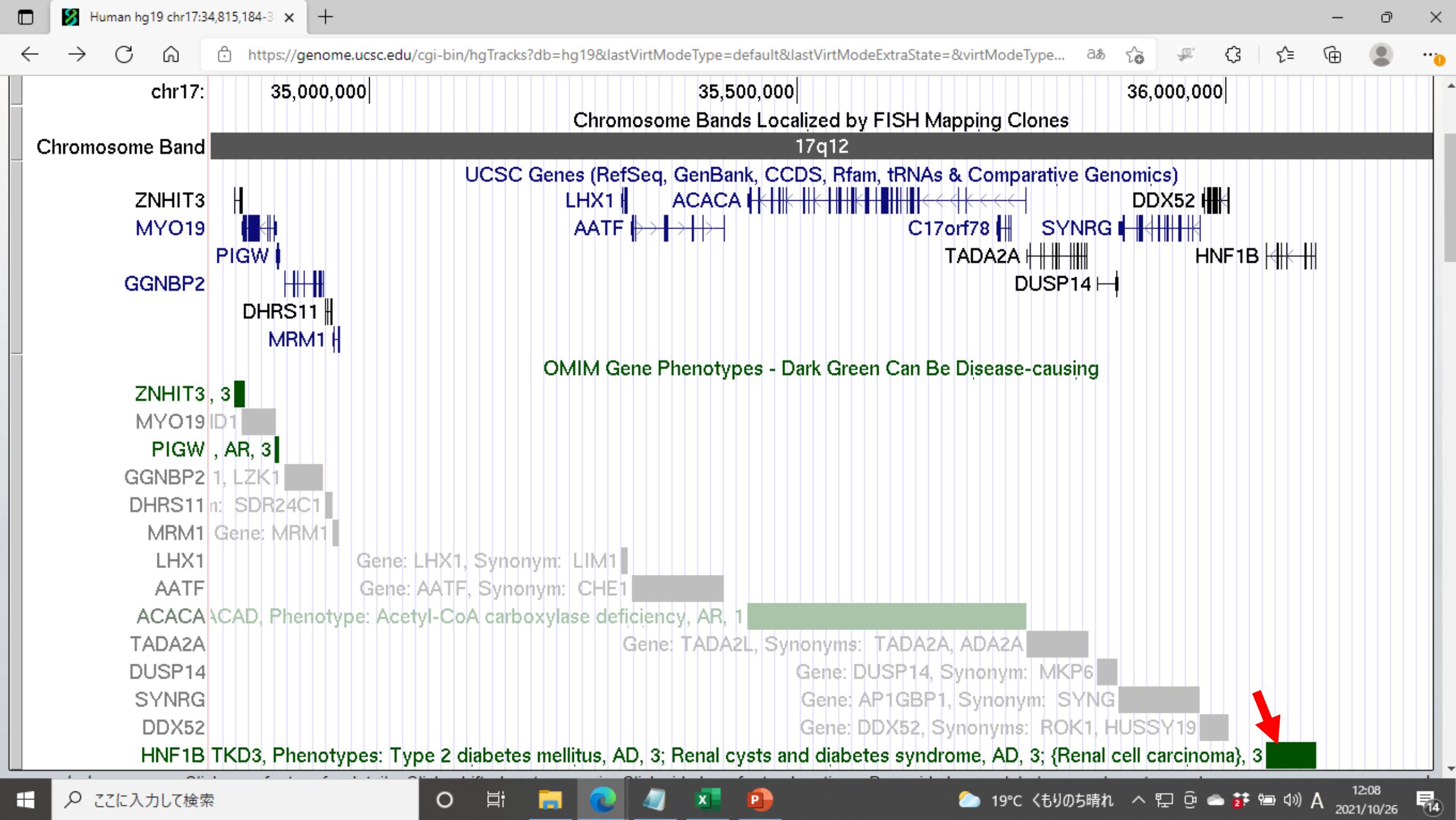












OMIM genes - 189907

MIM gene number: 189907

**HGNC-approved symbol:** HNF1B — HNF1 homeobox B (transcription factor 2)

**Position:** chr17:36046434-36105050

Band: 17q12

**Genomic Size:** 58617

**Alternative symbols:** TCF2, HNF2, RCAD, T2D, ADTKD3

**RefSeq Gene(s):** NM\_000458, NM\_001165923, NM\_001304280

**Related Transcripts:** uc010wdj.2, uc021twy.1, uc021tvu.1, uc002hok.

**Related GeneReviews disease(s):** [mody-ov](#) (Maturity-Onset Diabetes of the Young Overview), [mde17q12](#) (17q12 Recurrent Deletion Syndrome)

<b>Phenotype</b>	<b>Phenotype MIM Number</b>	<b>Inheritance</b>	<b>Phenotype Key</b>
Renal cysts and diabetes syndrome	<a href="#">137920</a>	Autosomal dominant	3 - molecular basis of the disease is known
Type 2 diabetes mellitus	<a href="#">125853</a>	Autosomal dominant	3 - molecular basis of the disease is known
{Renal cell carcinoma}	<a href="#">144700</a>		3 - molecular basis of the disease is known

[View table schema](#)

[Go to OMIM Genes track controls](#)

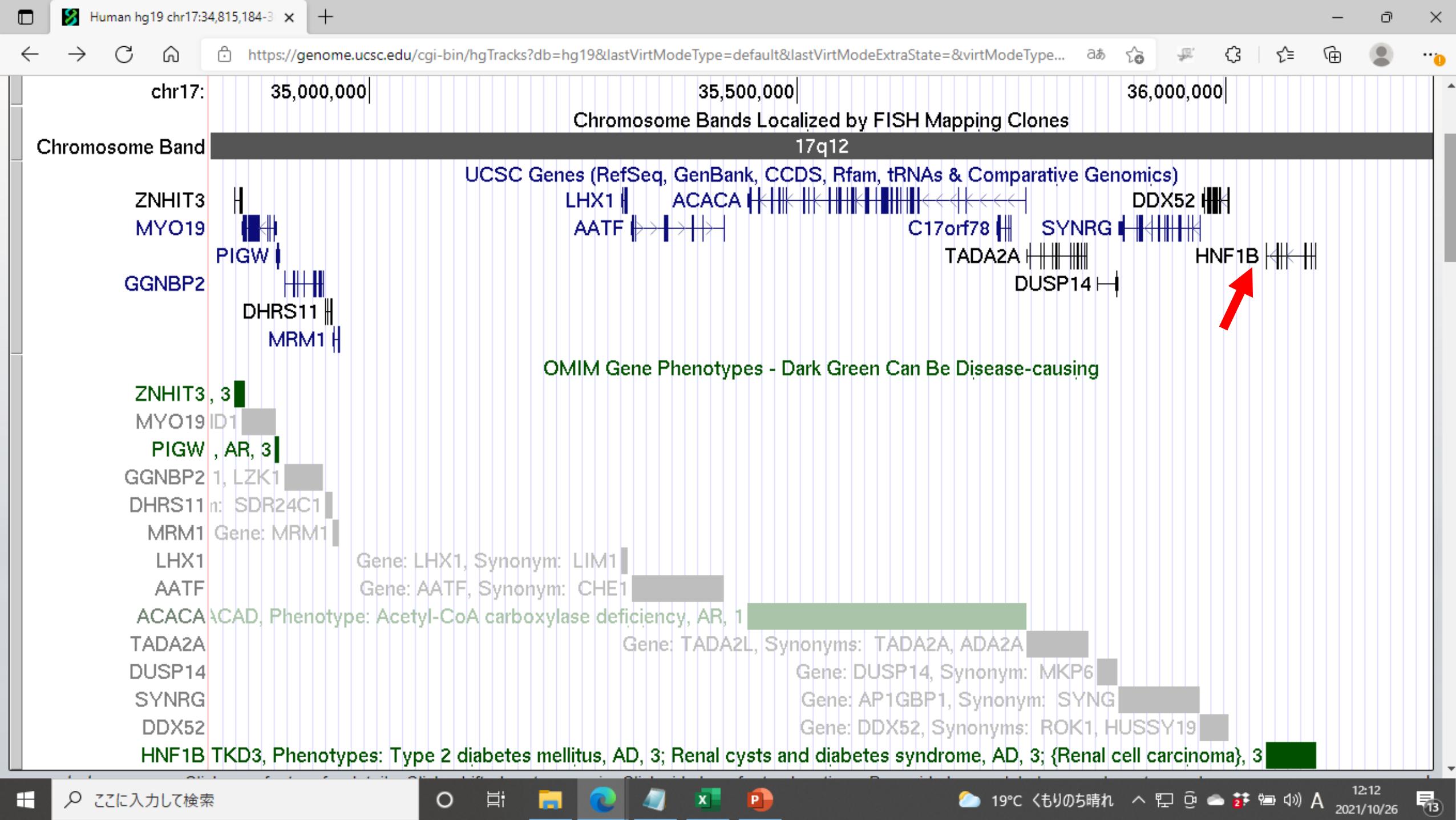
Data last updated at UCSC: 2021-10-20

## Description

**NOTE:**

OMIM is intended for use primarily by physicians and other professionals concerned with genetic disorders, by genetics researchers, and by advanced students in science and medicine. While the OMIM





Human Gene HNF1B (uc002hok.4)

**Description:** Homo sapiens HNF1 homeobox B (HNF1B), transcript variant 1, mRNA

**RefSeq Summary (NM\_000458):** This gene encodes a member of the homeodomain-containing superfamily of transcription factors. The protein binds to DNA as either a homodimer, or a heterodimer with the related protein hepatocyte nuclear factor 1-alpha. The gene has been shown to function in nephron development, and regulates development of the embryonic pancreas. Mutations in this gene result in renal cysts and diabetes syndrome and noninsulin-dependent diabetes mellitus, and expression of this gene is altered in some types of cancer. Multiple transcript variants encoding different isoforms have been found for this gene.[provided by RefSeq, Sep 2009].

## Multiple transcript variants on Transcript (Including UTRs)

**Position:** hg19 chr17:36,046,434-36,105,096 **Size:** 58,663 Total Exon Count: 9 Strand:

### Coding Region

**Position:** hg19 chr17:36 047 375-36 104 875 **Size:** 57 501 **Coding Exon Count:** 9

Page Index	Sequence and Links	UniProtKB Comments	Genetic Associations	MalaCards	CTD
Gene Alleles	Microarray Expression	RNA Structure	Protein Structure	Other Species	GO Annotations
mRNA Descriptions	Pathways	Other Names	GeneReviews	Model Information	Methods

Data last updated at UCSC: 2013-06-14

- Sequence and Links to Tools and Database

Genomic Sequence (chr17:36,046,434-36,105,096)			mRNA (may differ from genome)		Protein (557 aa)
Gene Sorter	Genome Browser	Other Species FASTA	VisiGene	Gene interactions	Table Schema
BioGPS	CGAP	Ensembl	Entrez Gene	ExonPrimer	GeneCards
GeneNetwork	H-INV	HGNC	HPRD	Lynx	MGI
neXtProt	OMIM	PubMed	Reactome	Treefam	UniProtKB
Wikipedia					

## - Comments and Description Text from UniProtKB

ID: HNF1B HUMAN

**DESCRIPTION:** RecName: Full=Human acute nuclear factor 1-beta; Short=LINE-1-beta; Short=LINE-1B; AltName: Full=Lymphocyte protein LEP2; AltName: Full=Transcription factor 2;



Search OMIM...



Options

\*189907

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Title

Gene-Phenotype

Relationships

Text

Description

Cloning and Expression

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Mapping

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Genotype/Phenotype

Correlations

Animal Model

Allelic Variants

Table View

See Also

References

Contributors

Creation Date

Edit History

\* 189907

ICD+

## HNF1 HOMEobox B; HNF1B

*Alternative titles; symbols*

TRANSCRIPTION FACTOR 2; TCF2

TRANSCRIPTION FACTOR, LIVER-SPECIFIC, 3

HEPATOCYTE NUCLEAR FACTOR-1-BETA

HEPATIC NUCLEAR FACTOR-1-BETA

HEPATOCYTE NUCLEAR FACTOR 2; HNF2

*HGNC Approved Gene Symbol: HNF1B*

*Cytogenetic location: 17q12   Genomic coordinates (GRCh38): 17:37,686,430-37,745,058 (from NCBI)*

### Gene-Phenotype Relationships

Location	Phenotype	Clinical Synopses	Phenotype MIM number	Inheritance	Phenotype mapping key
17q12	Renal cysts and diabetes syndrome		137920	AD	3
	Type 2 diabetes mellitus		125853	AD	3
	{Renal cell carcinoma}		144700		3

### External Links

▶ Genome

▶ DNA

▶ Protein

▶ Gene Info

▶ Clinical Resources

### Variation

1000 Genome

ClinVar

gnomAD

GWAS Catalog

GWAS Central

HGMD

NHLBI EVS

PharmgKB

▶ Animal Models

▶ Cellular Pathways



ここに入力して検索



19°C

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Human Gene HNF1B (uc002hok) OMIM Entry - # 137920 - RENAL +

https://omim.org/entry/137920

About Statistics Downloads Contact Us MIMmatch Donate Help ?

Search OMIM... Options

#137920 **# 137920** ICD+ **RENAL CYSTS AND DIABETES SYNDROME; RCAD**

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Title Phenotype-Gene Relationships Clinical Synopsis Phenotypic Series Text Description Clinical Features Molecular Genetics Cytogenetics Genotype/Phenotype Correlations History References Contributors Creation Date Edit History

Alternative titles; symbols

MATURITY-ONSET DIABETES OF THE YOUNG, TYPE 5; MODY5  
HYPERURICEMIC NEPHROPATHY, FAMILIAL JUVENILE, ATYPICAL  
FJHN, ATYPICAL  
TUBULOINTERSTITIAL KIDNEY DISEASE, AUTOSOMAL DOMINANT, 3; ADTKD3  
GLOMERULOCYSTIC KIDNEY DISEASE, HYPOPLASTIC TYPE  
GLOMERULOCYSTIC KIDNEY, FAMILIAL HYPOPLASTIC  
CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT WITH DIABETES  
CAKUT WITH DIABETES

External Links

Protein Clinical Resources Clinical Trials DECIPHER EuroGentest Gene Reviews Genetic Alliance GTR GARD OrphaNet POSSUM Animal Models

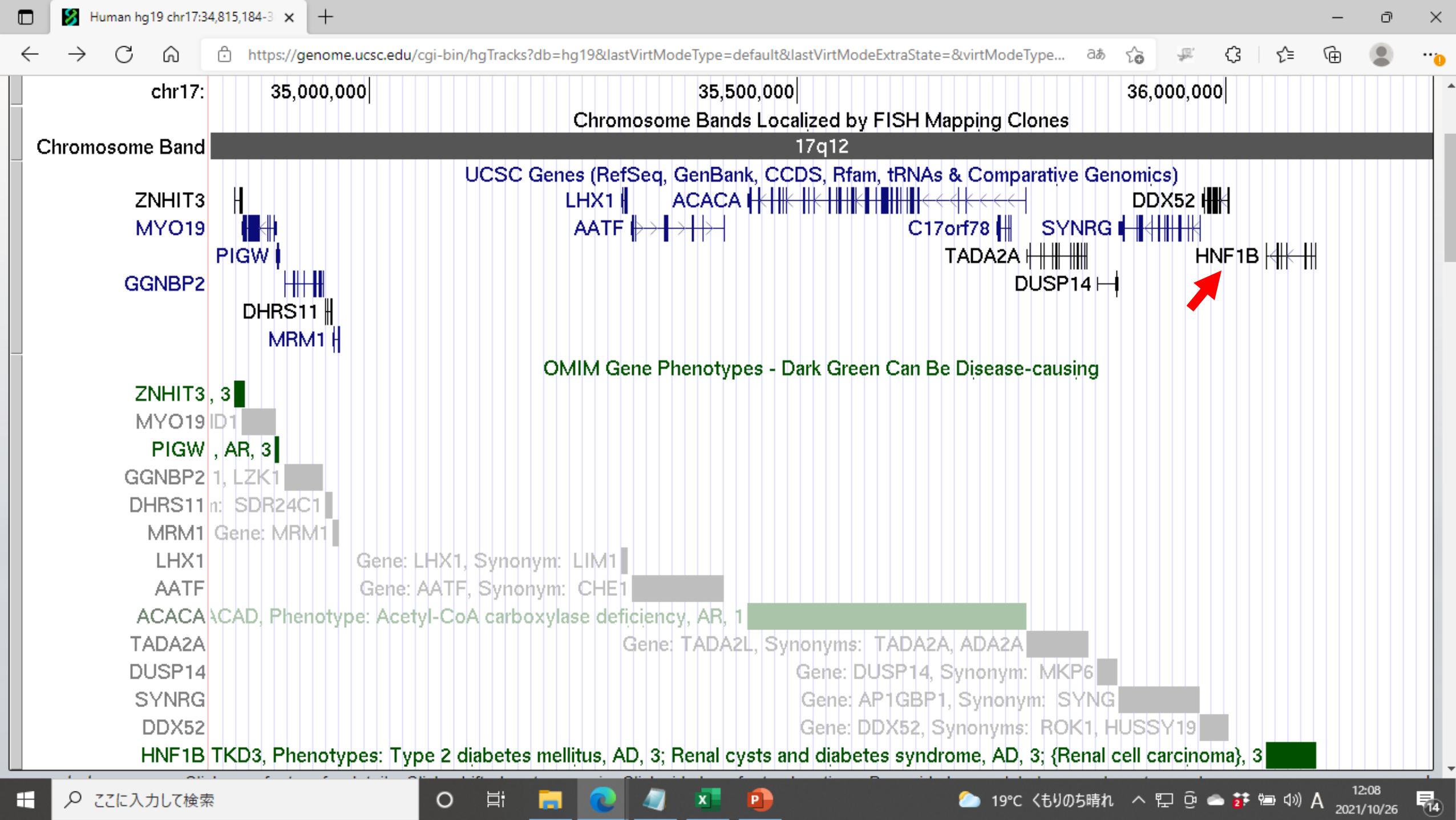
Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
17q12	Renal cysts and diabetes syndrome	137920	AD	3	HNF1B	189907

Clinical Synopsis Phenotypic Series PheneGene Graphics ?

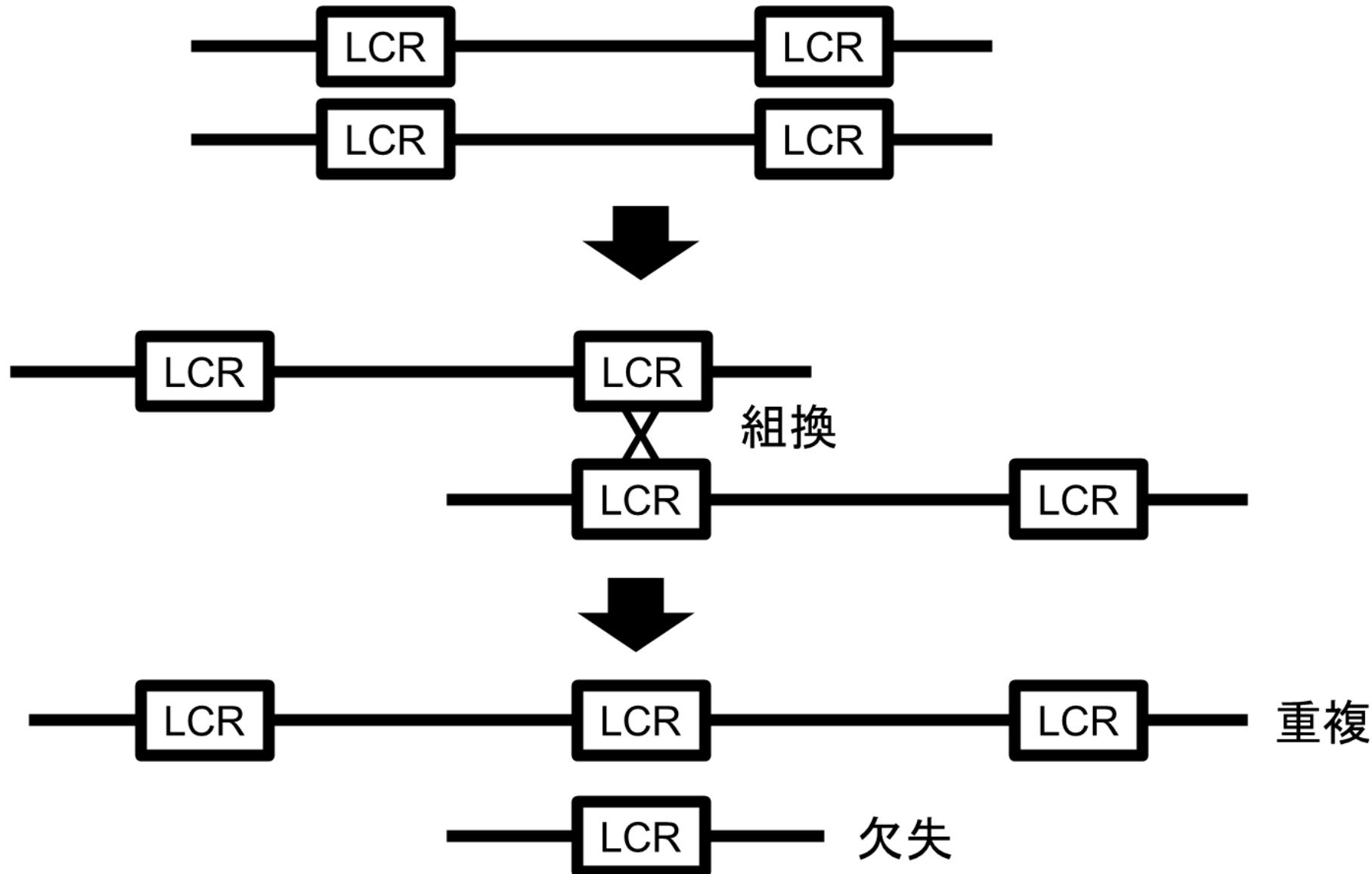
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19°C くもりのち晴れ 12:15 2021/10/26

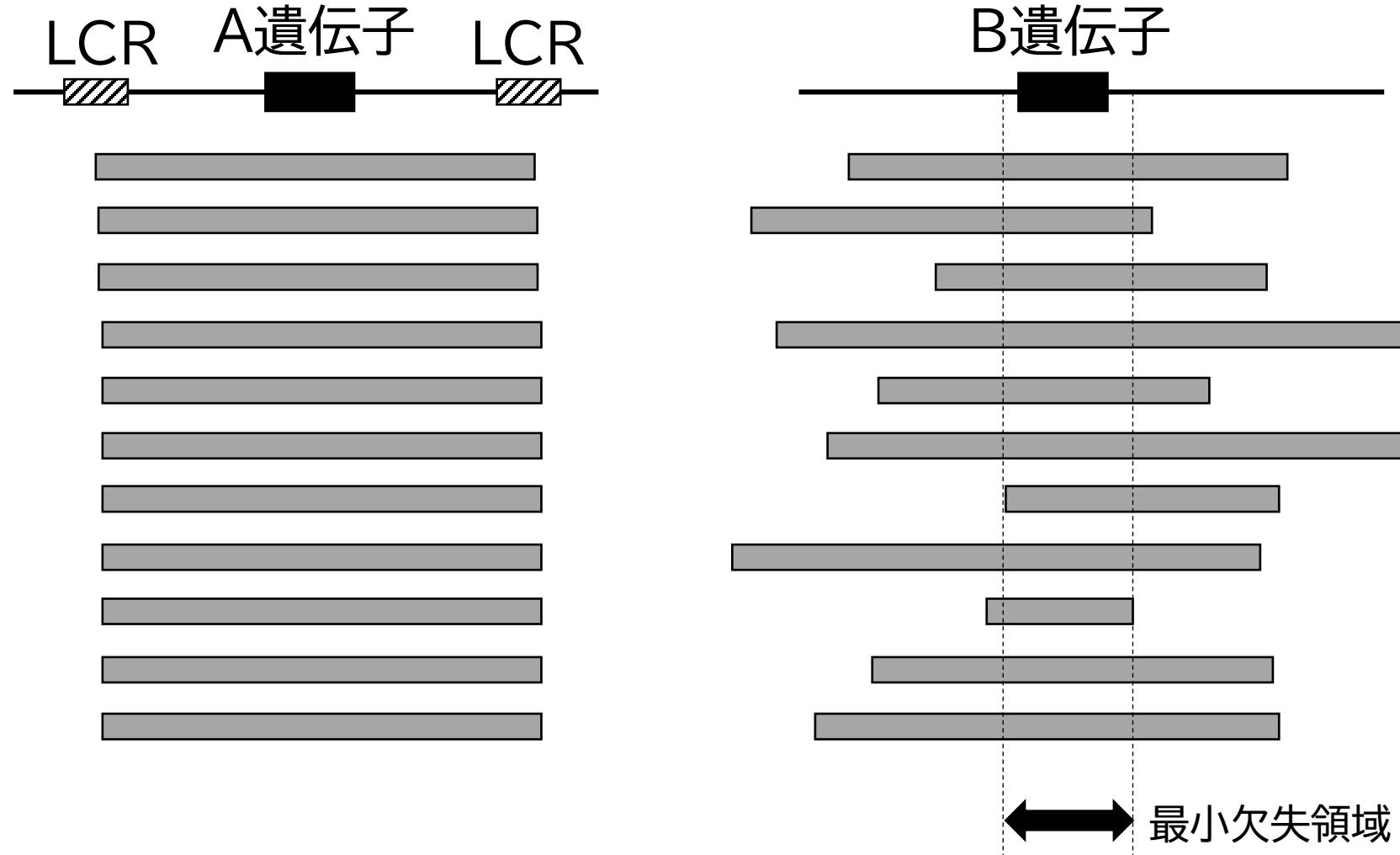




# LCRが染色体組換に介在する



# 染色体中間部の構造異常



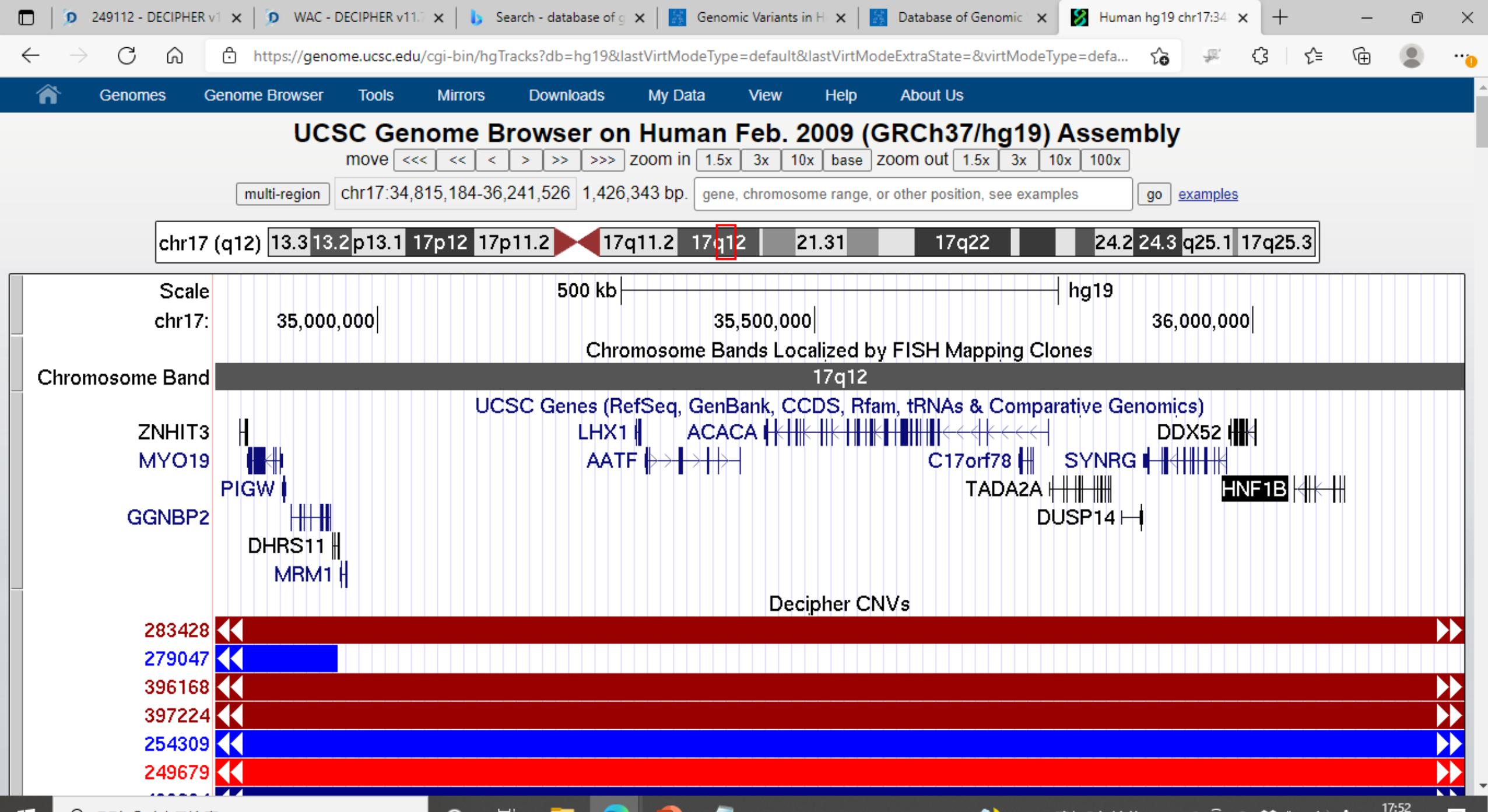
# 古典的染色体微細欠失領域の重複

欠失症候群名	染色体位置	重複の場合	症状
22q11.2欠失症候群	22q11.2	22q11.2重複症候群	発達障害
Williams症候群	7q11.23	7q11.23重複症候群	発達障害
Prader-Willis症候群 /Angelman症候群	15q11.2	15q11.2重複症候群	発達障害
Smith-Magenis症候群	17p11.2	Potocki-Lupski症候群	発達障害
Sotos症候群	5q35	Hunter-McAlpine症候群	発達障害

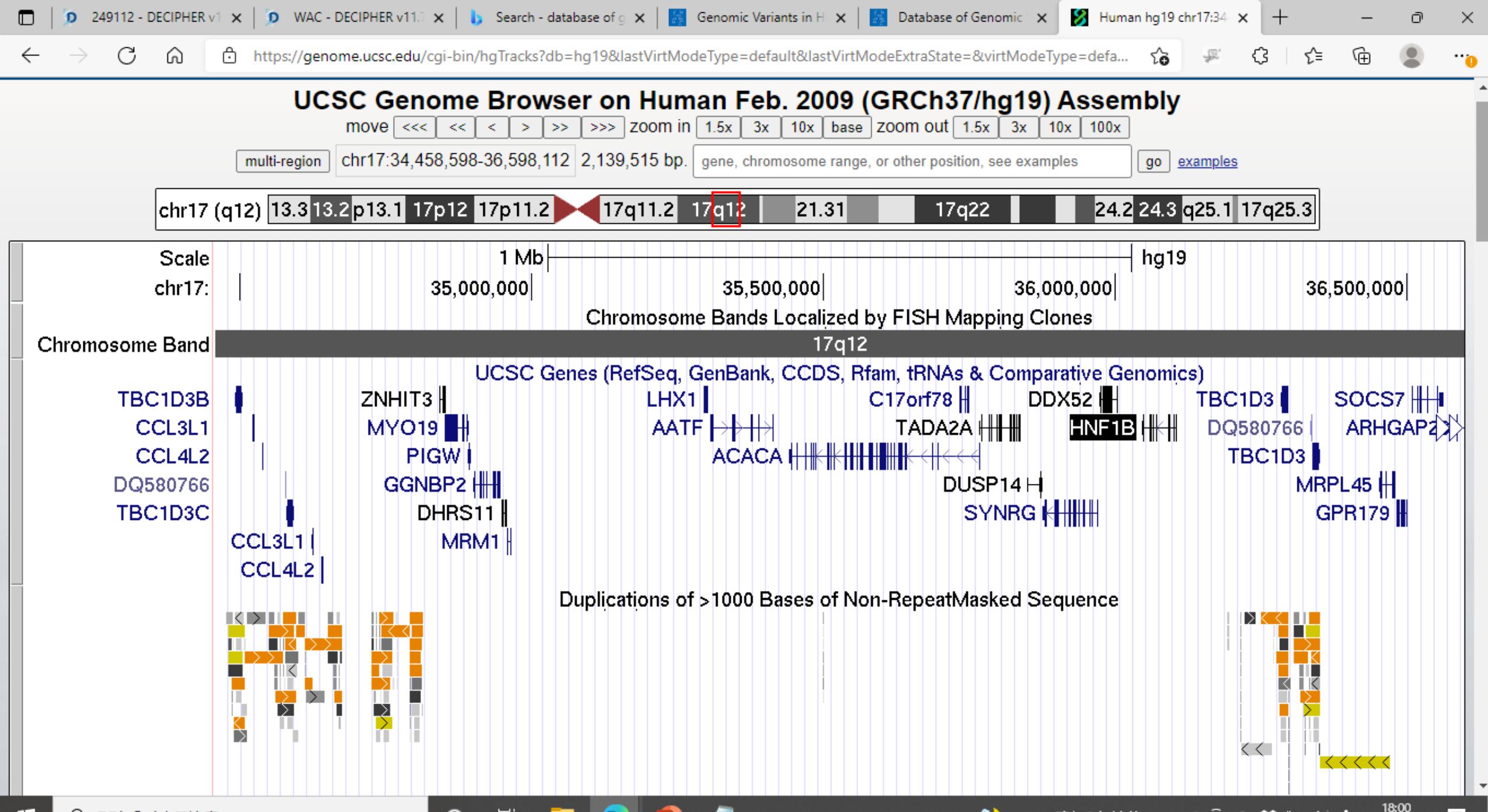
染色体の微細欠失だけではなく、微細な重複も存在しており、よく知られた染色体微細欠失症候群の領域がそのまま重複している場合もしばしば認められる。これらは欠失を来たした場合の症状とはまったく異なる症状を示すことが多く、多くの場合ADHDや自閉など、発達障害の原因となっており、臨床症状だけでは診断に辿り着くことは困難である。

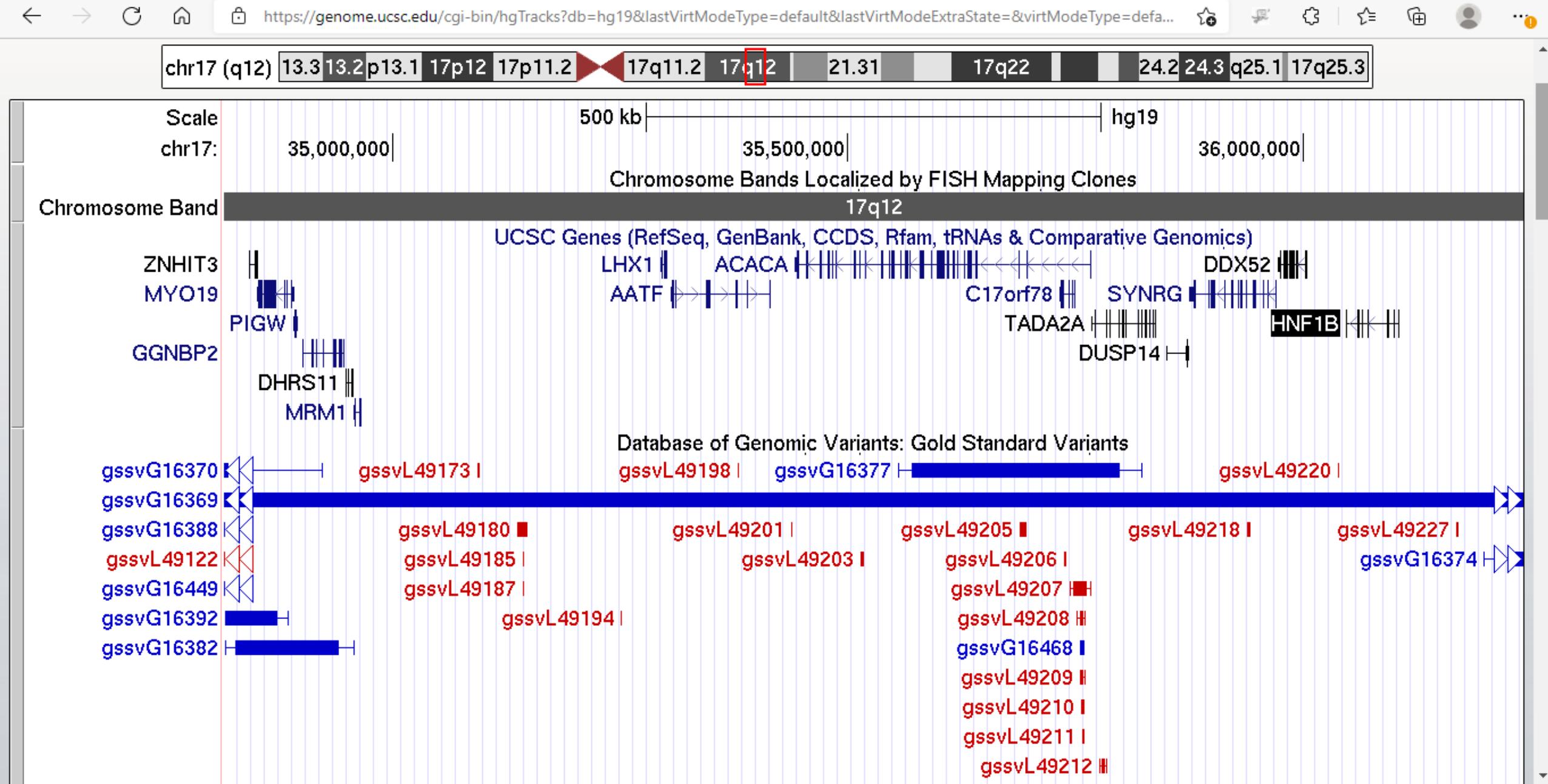
# 新たに確立した染色体中間部の構造異常

	責任(候補)遺伝子	主な症状
A:リピート構造によるもの		
1q21.1欠失/重複症候群		発達遅滞、特徴的顔貌、先天奇形
3q29欠失症候群	<i>DLG1, PAK2</i>	発達遅滞、精神疾患との関連(?)
15q13.3欠失症候群	<i>CHRNA7</i>	精神遅滞、てんかん
16p11.2欠失/重複		自閉症、発達遅滞
17q12欠失/重複	<i>HNF1B</i>	若年性糖尿病
17q21.31欠失/重複症候群	<i>CRHR1, MAPT</i>	筋緊張低下、発達遅滞、特徴的顔貌
B:リピート構造によらないもの		
proximal 1p36欠失		
1q32欠失	<i>IRF6</i>	Van der Woude症候群
1q41q42欠失	<i>DISP1</i>	発達遅滞、特徴的顔貌、てんかん、など
2p15-p16.1欠失		自閉症関連症状
2q23.1欠失	<i>MBD5</i>	重度精神発達遅滞、てんかん、小頭症など
5q14欠失	<i>MEF2C</i>	重度精神発達遅滞、てんかん、脳形成障害など
5q31.3欠失	<i>PURA, NRG2</i>	重度精神発達遅滞、てんかん、など
8q24欠失症候群	<i>EXT1, TRPS1</i>	Langer-Giedion症候群
9q22.3欠失症候群	<i>PTCH1</i>	Gorlin症候群
10q23欠失	<i>PTEN</i>	若年性ポリポーラス
11p13欠失	<i>WT1, PAX6</i>	WAGR症候群
16q24.3欠失	<i>ANKRD11, ZNF778</i>	自閉症関連症状
17p13.1欠失	<i>DLG4, GABARAP</i>	精神遅滞、てんかん
Xp22.3欠失	<i>KAL1</i>	Kallmann症候群
Xp21-22欠失	<i>CDKL5, ARX</i>	てんかん脳症
Xp11.4欠失	<i>CASK</i>	精神発達遅滞、小頭症
Xq11.1欠失	<i>ARHGEF9</i>	精神発達遅滞、てんかん









Scale

1 Mb

hg19

chr17:

35,000,000

35,500,000

36,000,000

36,500,000

## Chromosome Bands Localized by FISH Mapping Clones

Chromosome Band

17q12

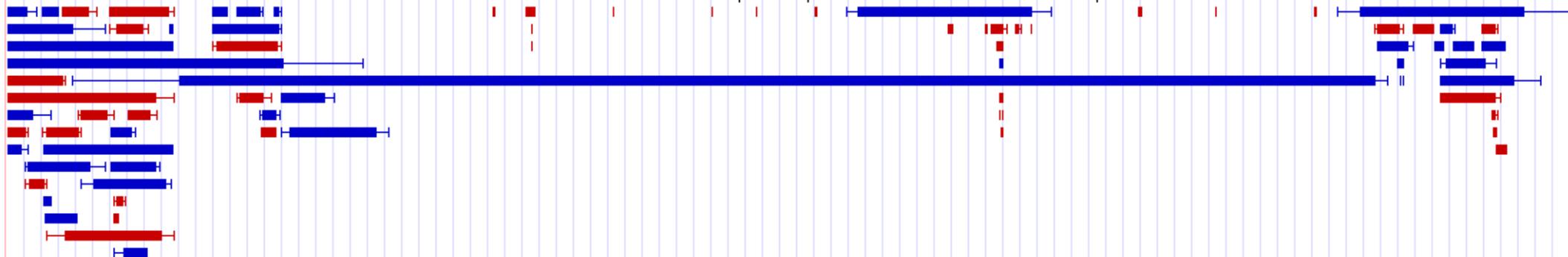
## UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs &amp; Comparative Genomics)



## Duplications of &gt;1000 Bases of Non-RepeatMasked Sequence



## Database of Genomic Variants: Gold Standard Variants



# Database of Genomic Variants

A curated catalogue of human genomic structural variation

About the Project   Downloads   Links   Statistics   FAQ  
Genome Browser   Query Tool   Submissions   Contact Us   Training Resources

Keyword, Landmark or Region Search:   GRCh37/hg19 ▾

Examples: RP11-34P13; CFTR, 7q11.21; chr7:71890181-72690180

## Find DGV Variants

[by Study](#) [by Sample](#)  
[by Method](#) [by Variant](#)  
[by Platform](#) [by Chromosome](#)

## Summary Statistics

Stat      Merged-level      Sample-level

CNVs: 983845 7021692

Inversions: 4083 32044

[Number of Studies:](#) 75

[News: February 2020 Update and Newsletter has been issued](#)

# Database of Genomic Variants

A curated catalogue of human genomic structural variation

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Examples: RP11-34P13; CFTR, 7q11.21; chr7:71890181-72690180

## Find DGV Variants

[by Study](#)   [by Sample](#)  
[by Method](#)   [by Variant](#)  
[by Platform](#)   [by Chromosome](#)

## Summary Statistics

### Stat   Merged-level   Sample-level

CNVs: 983845 7021692

Inversions: 4083 32044

[Number of Studies:](#) 75

[News: February 2020 Update and Newsletter has been issued](#)

*D*atabase of *G*enomic *V*ariants

## *A curated catalogue of human genomic structural variation*

About the Project	Downloads	Links	Statistics	FAQ
Genome Browser	Query Tool	Submissions	Contact Us	Training Resources

**Keyword, Landmark or Region Search:** chr17:34815184-36241526  GRCh37/hg19

**Examples:** RP11-34P13; CFTR, 7q11.21; chr7:71890181-72690180

## Find DGV Variants

[by Study](#)    [by Samp](#)

[by Method](#) [by Variant](#)

### by Platform by Chromosome

## Summary Statistics

Stat	Merged-level	Sample-level
CNVs:	983845	7021692
Inversions:	4083	32044

[News: February 2020 Update and Newsletter has been issued](#)

# Database of Genomic Variants

*A curated catalogue of human genomic structural variation*

File ヘルプ

Genomic Variants in Human Genome (Build GRCh37: Feb. 2009, hg19): 1.426 Mbp の範囲を chr17 から表示、塩基番号 34,815,184 から 36,241,526

[Browser](#) [Select Tracks](#) [Custom Tracks](#) [Preferences](#)

- 檢索

## ランドマークまたは領域:

chr17:34,815,184-36,241,526

检索

例: chr7:71890181..72690180, CFTR, AC108171.3, nsy529033

データソース

Genomic Variants in Human Genome (Build GRCh37; Feb. 2009, hg19) ✓

スクロール/ズーム: << < = 表示 1.426 Mbp + > >> 反転

## Filter variants

study

[Filter](#) [Reset](#)

chr17

0M 10M 20M 30M 40M 50M 60M 70M 80M

chromosome

chr17: 1.426 Mbp

500 kbp

35M 36M

RefSeq Genes

LHX1|NM\_005568

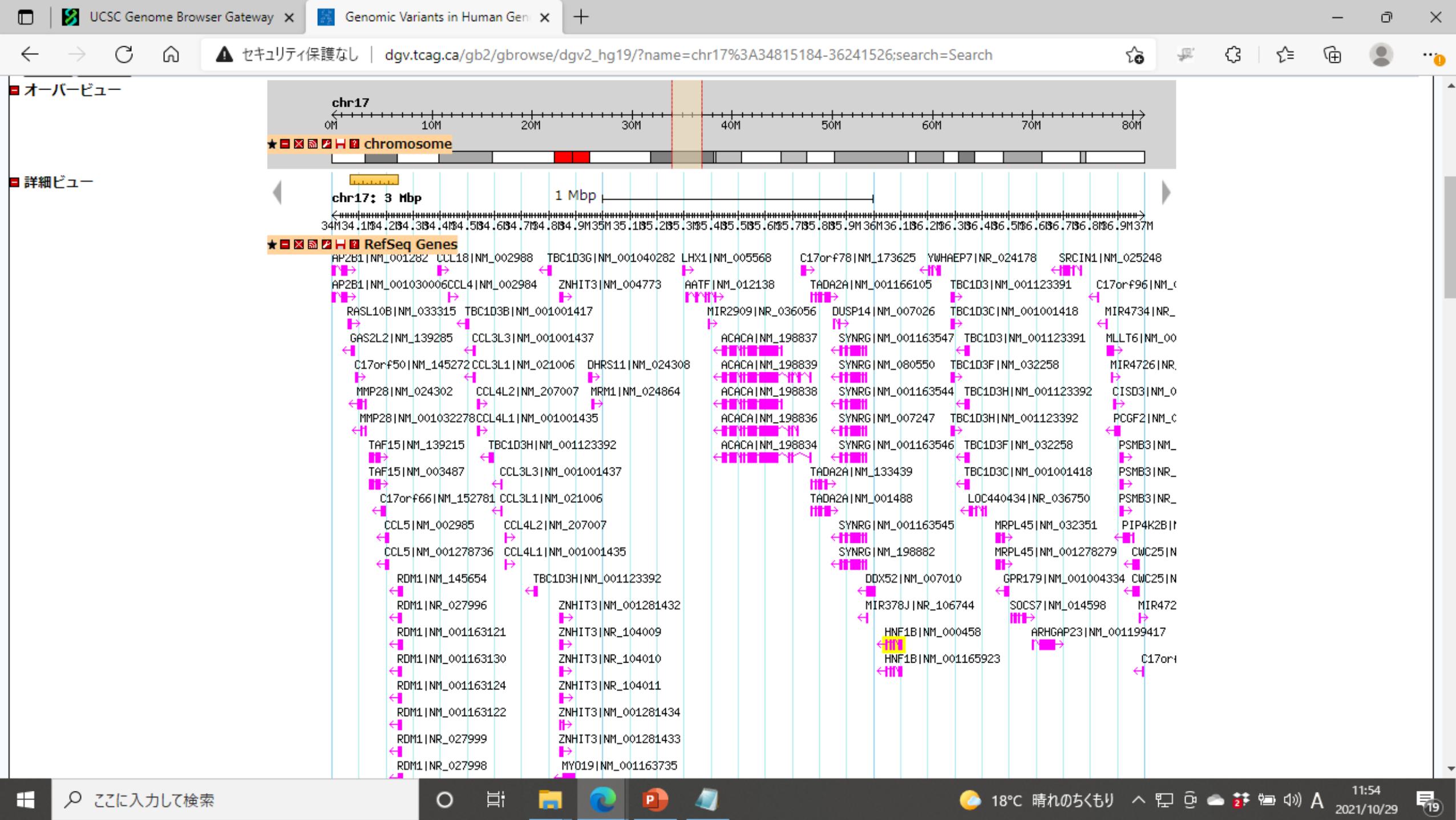
AATF|NM\_012138

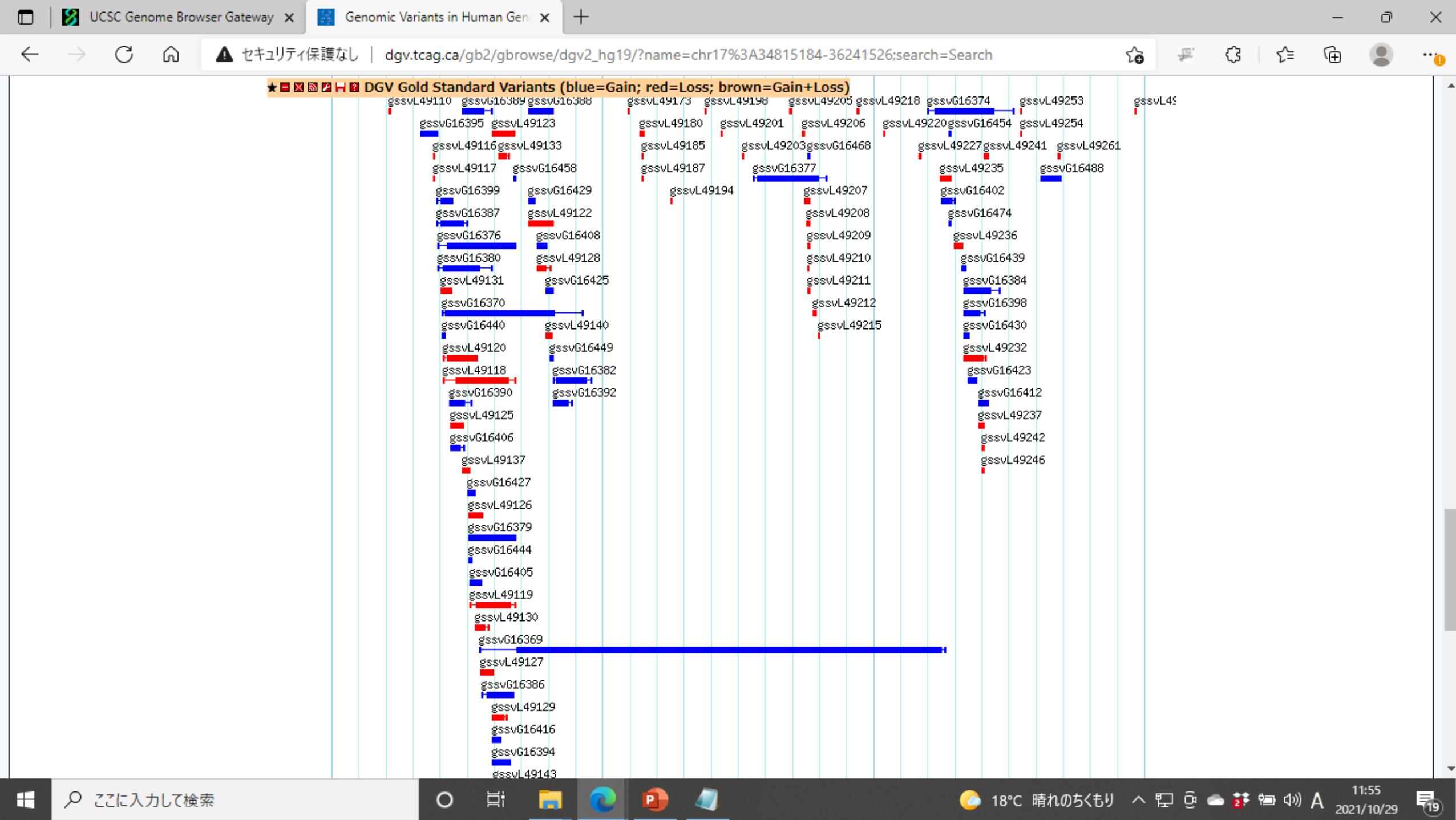
TADA2A|NM\_001166105

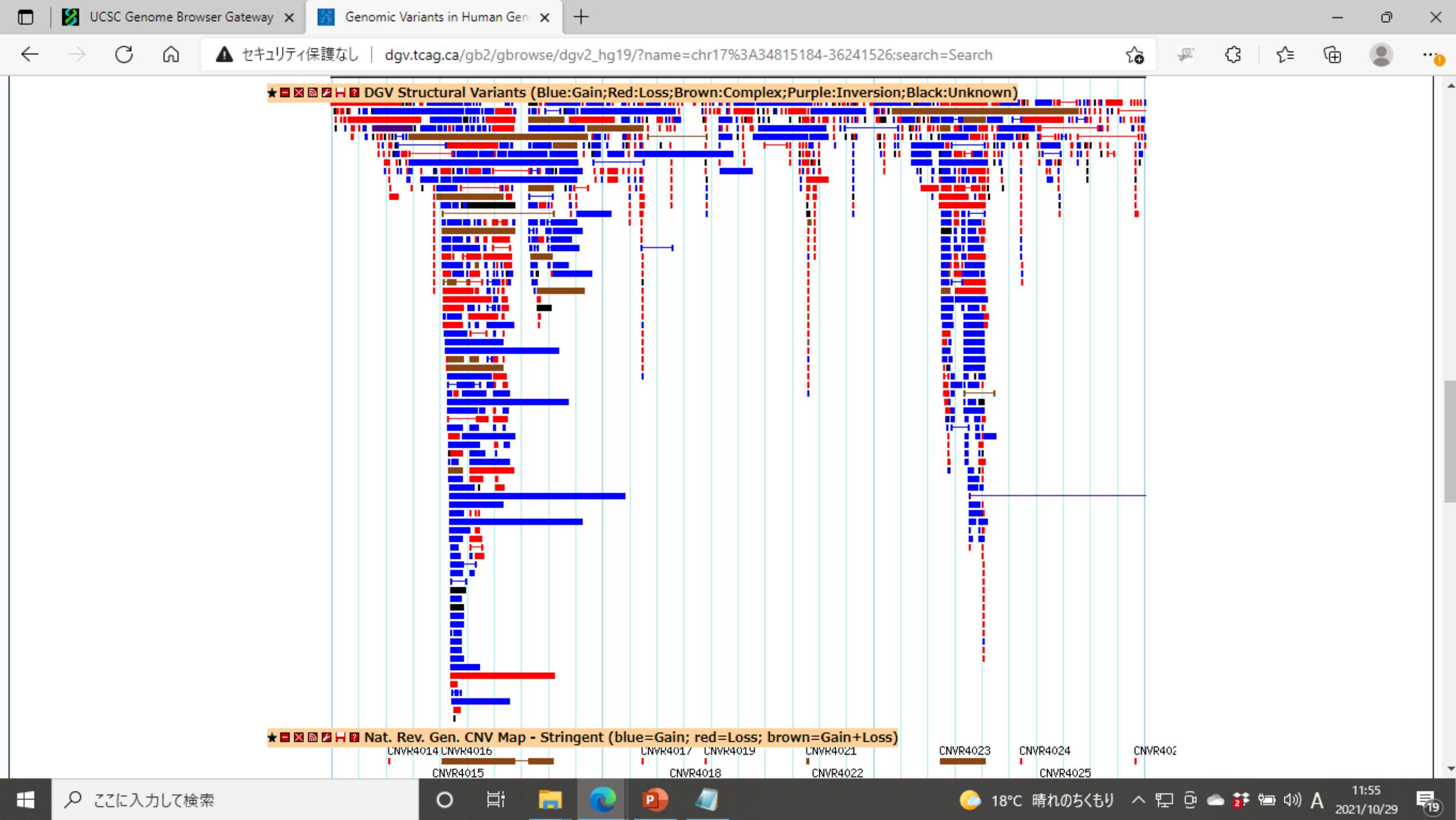
HNF1B|NM\_000458

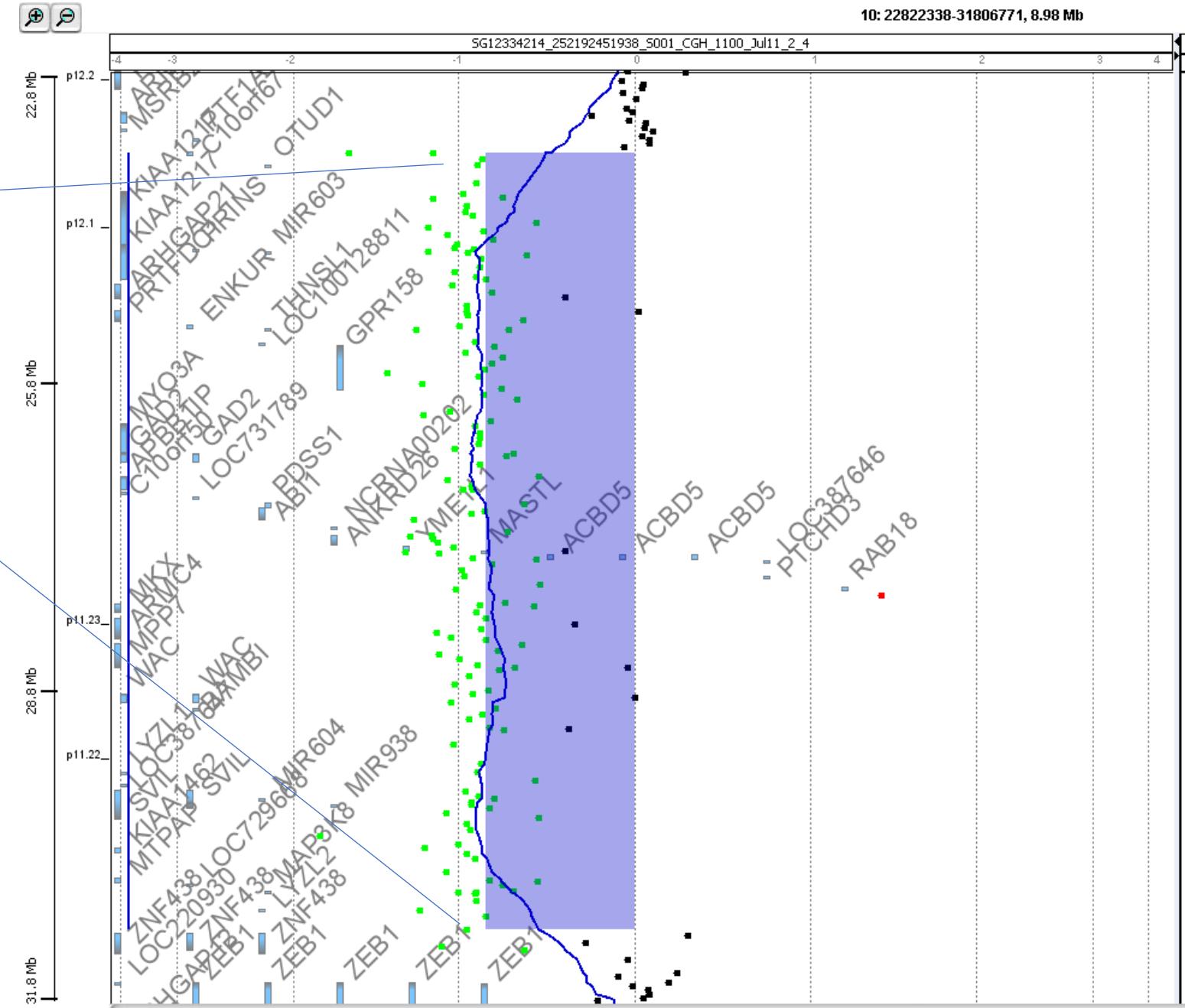
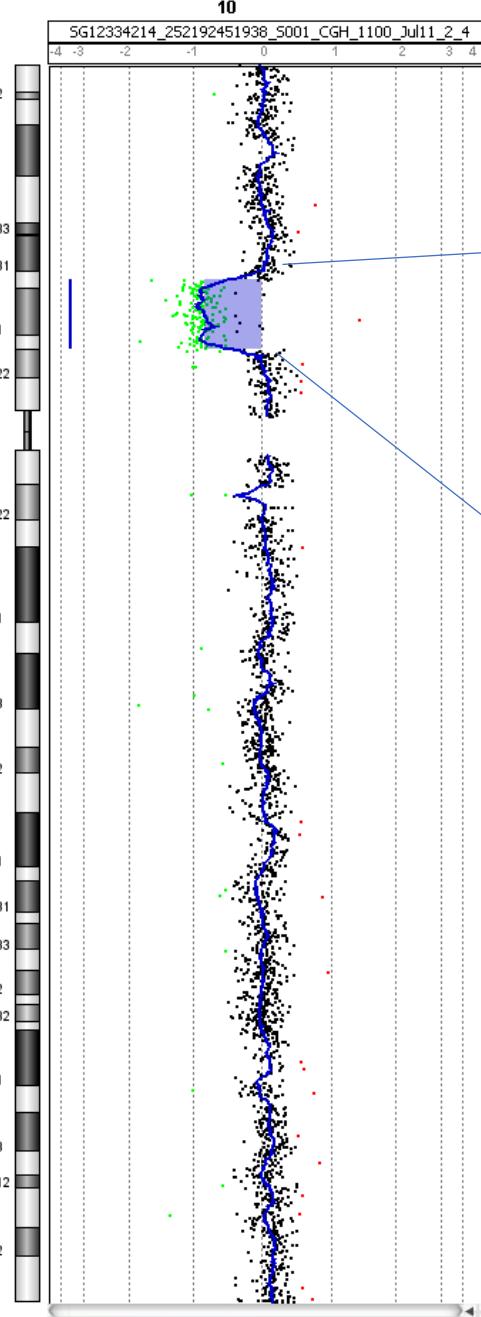
ZNHIT3|NM\_004733

ZNHIT3|NM\_001281432









arr[hg19] 10p12.2p11.23(23609705\_31093021)X1

Scale

2 Mb

hg19

chr10:

25,000,000

26,000,000

27,000,000

28,000,000

29,000,000

30,000,000

31,000,000

## Chromosome Bands Localized by FISH Mapping Clones

Chromosome Band

10p12.2

10p12.1

10p11.23

C10orf67

KIAA1217

ARHGAP21

PRTFDC1

ENKUR

THNSL1

GPR158-AS1

GPR158

## UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs &amp; Comparative Genomics)

MYO3A

ABI1

RAB18

WAC

LYZL1

MTPAP

MAP3K8

LYZL2

AK302694

GAD2

YME1L1

MKX

BAMBI

AX747507

PTCHD3P1

SVIL

APBB1IP

ACBD5

MPP7

ARMC4

PDSS1

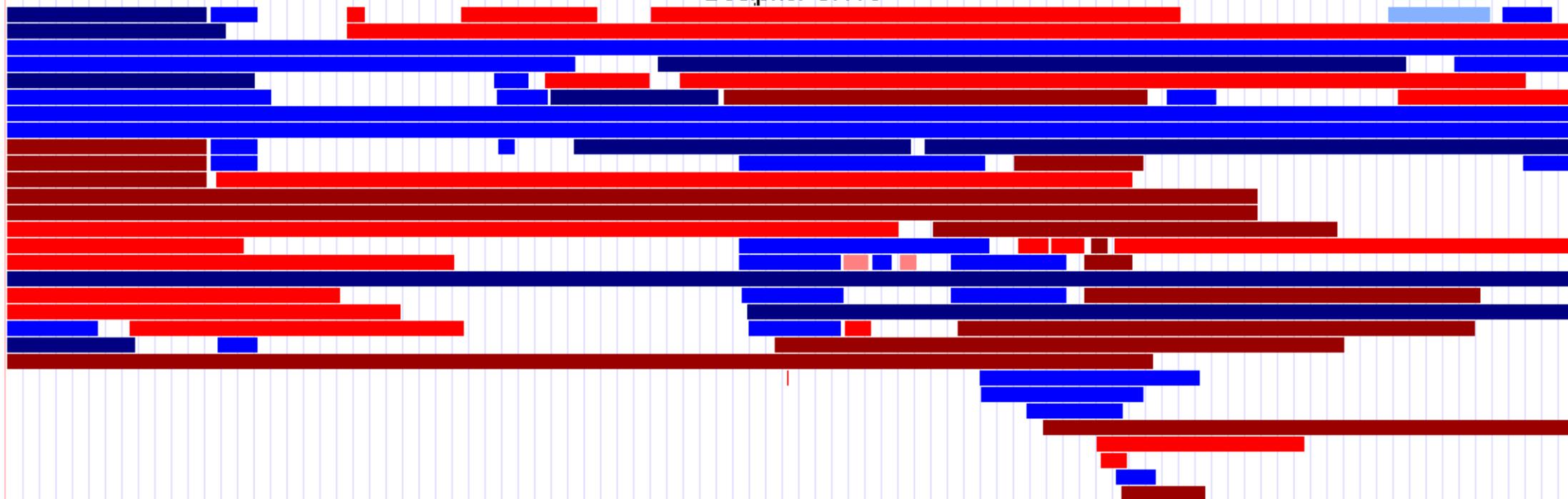
ANKRD26

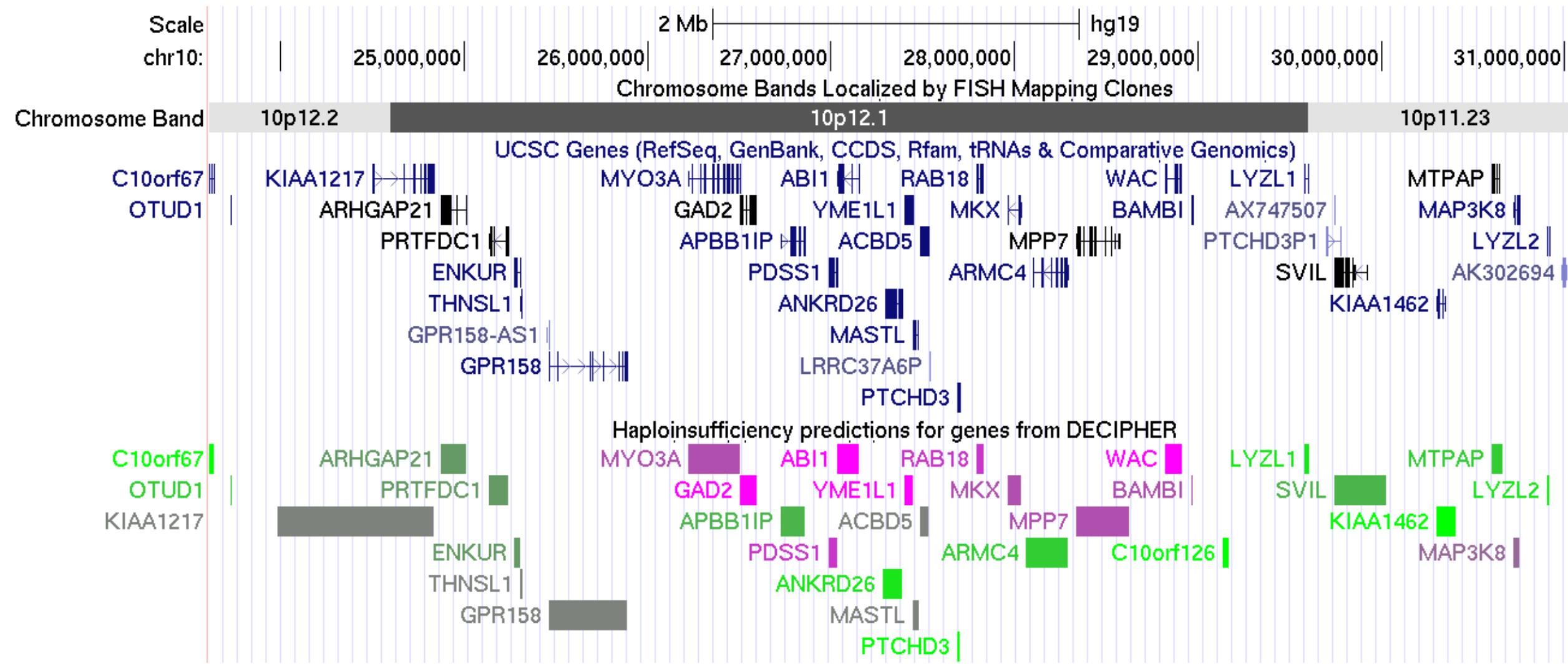
MASTL

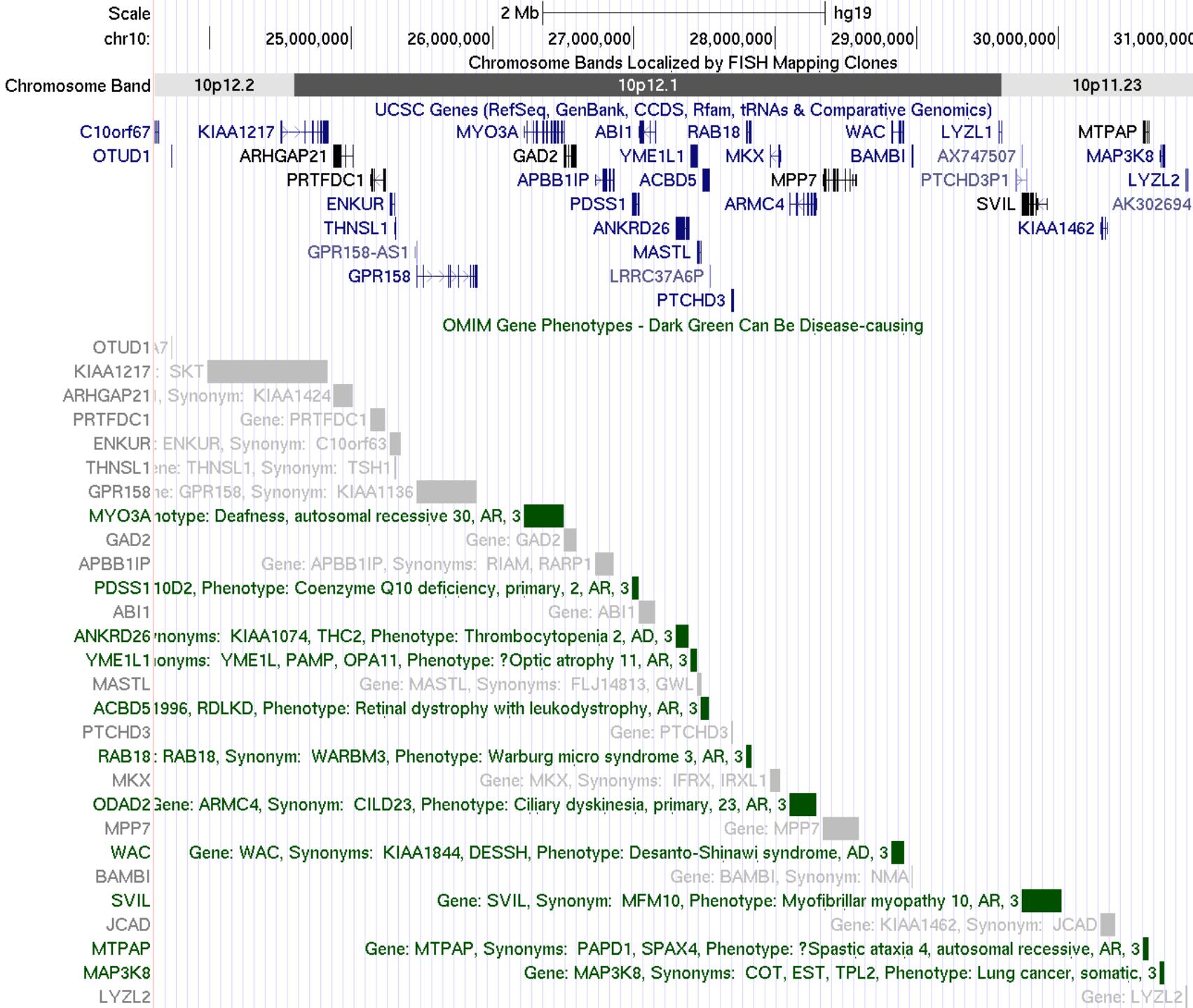
LRRC37A6P

PTCHD3

## Decipher CNVs









OMIM Entry - # 616708 - DESAN

https://www.omim.org/entry/616708

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Search OMIM... Options Display:  Change Bars

#616708  
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Title  
Phenotype-Gene Relationships  
Clinical Synopsis  
Text  
Description  
Clinical Features  
Cytogenetics  
Molecular Genetics  
References  
Creation Date  
Edit History

# 616708  
**DESANTO-SHINAWI SYNDROME; DESSH**

*Alternative titles; symbols*  
DEVELOPMENTAL DELAY, BEHAVIORAL ABNORMALITIES, FACIAL DYSMORPHISM, AND OCULAR ABNORMALITIES

Other entities represented in this entry:  
**CHROMOSOME 10p12-p11 DELETION SYNDROME, INCLUDED**

**Phenotype-Gene Relationships**

Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
10p12.1	Desanto-Shinawi syndrome	616708	AD	3	WAC	615049

Clinical Synopsis PheneGene Graphics ?

▼ TEXT

ここに入力して検索

19°C 晴れのちくもり 14:12 2021/10/26

[move start](#)

< 2.0 >

move end

Click on a feature for details. Click+shift+drag to zoom in. Click side bars for track options. Drag side bars or labels up or down to reorder tracks. Drag tracks left or right to new position. Press "?" for keyboard shortcuts.

< 2.0 >

track search default tracks default order hide all manage custom tracks track hubs configure reverse resize refresh

[collapse all](#)

[expand all](#)

Use drop-down controls below and press refresh to alter tracks displayed.

Tracks with lots of items will automatically be displayed in more compact modes.

[https://genome.ucsc.edu/cgi-bin/hgc?hgSID=1195924131\\_0SA8s1uFENSzIVZgPnZaXMZXwwJP&db=hg19&c=chr10&l=28766406&r=28968054&o=28817838&t=28936752&g=decipher&i=249112](https://genome.ucsc.edu/cgi-bin/hgc?hgSID=1195924131_0SA8s1uFENSzIVZgPnZaXMZXwwJP&db=hg19&c=chr10&l=28766406&r=28968054&o=28817838&t=28936752&g=decipher&i=249112)

refresh

chr10: 28,800,000

28,850,000

28,900,000

28,950,000

## Chromosome Bands Localized by FISH Mapping Clones

10p12.

UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)

WAC

BAME

## Decipher CNVs

The image displays a horizontal bar chart with 100 categories. The bars are composed of three colors: red, blue, and white. The total length of all bars combined is roughly 85% of the chart's width. The bars are arranged in a sequence from left to right, with varying lengths and colors.

Click on a feature for details. Click+shift+drag to zoom in. Click on tracks. Drag tracks left or right to new position. Press "?" for help. End

Position: chr10:28817839-28936752, Size: 118914, Type: Deletion, Significance: Unknown, Phenotypes: Abnormality of the gingiva, Abnormality of the upper respiratory tract, others - click to see full list. Affected genes: MIR5586, WAC, others - click see full list.

track search default tracks default order hide all manage custom tracks track hubs configure reverse resize refresh

[collapse all](#)

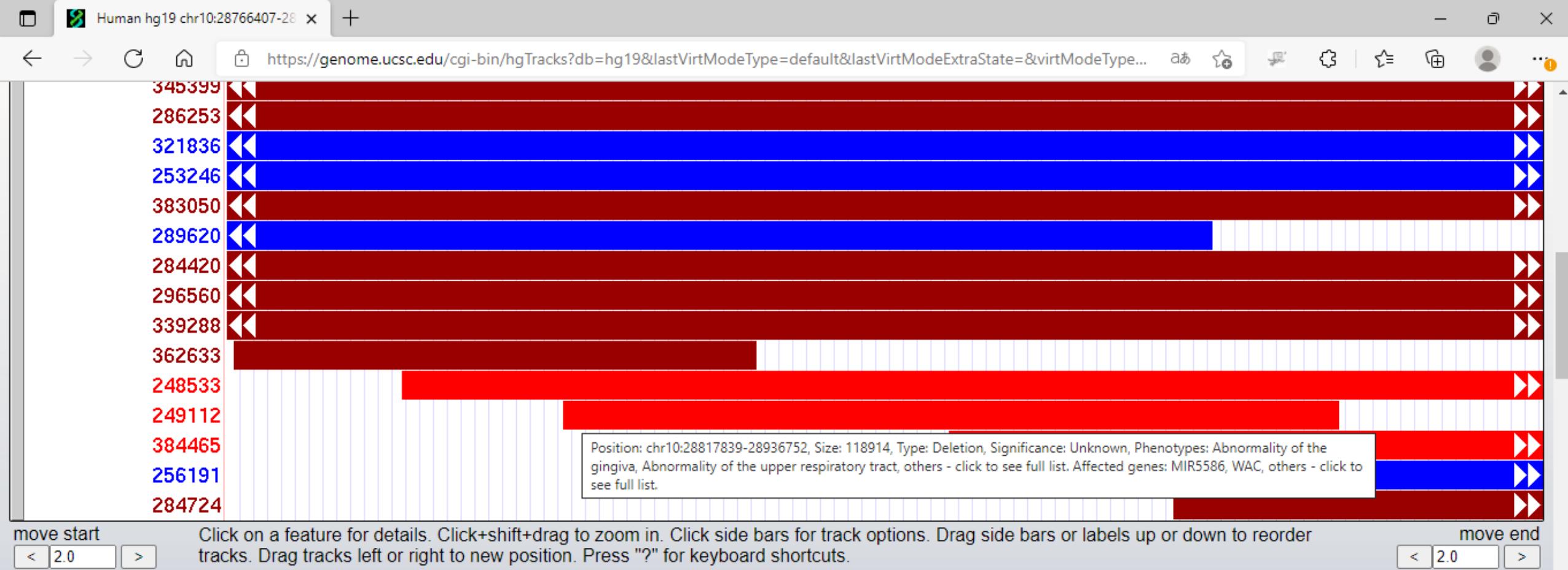
band all

Use drop-down controls below and press refresh to alter tracks displayed.

Tracks with lots of items will automatically be displayed in more compact modes.

[https://genome.ucsc.edu/cgi-bin/hgc?hgSID=1195924131\\_0SA8s1uFENSzIVZgPnZaXMZXwwJP&db=hg19&c=chr10&l=28766406&r=28968054&o=28817838&t=28936752&g=decipher&i=249112](https://genome.ucsc.edu/cgi-bin/hgc?hgSID=1195924131_0SA8s1uFENSzIVZgPnZaXMZXwwJP&db=hg19&c=chr10&l=28766406&r=28968054&o=28817838&t=28936752&g=decipher&i=249112)

refresh



move start < 2.0 > move end < 2.0 >

Click on a feature for details. Click+shift+drag to zoom in. Click side bars for track options. Drag side bars or labels up or down to reorder tracks. Drag tracks left or right to new position. Press "?" for keyboard shortcuts.

track search default tracks default order hide all manage custom tracks track hubs configure reverse resize refresh

collapse all

Use drop-down controls below and press refresh to alter tracks displayed.

Tracks with lots of items will automatically be displayed in more compact modes.

expand all

### Custom Tracks

refresh

Track1

hide ▾

-

### Mapping and Sequencing

refresh

Base Position

P13 Updated Fix

Patches

P13 Updated Alt Haplotypes

hide

Assembly

hide

BAC End Pairs

BU ORCHID

hide

mid End

## Decipher CNVs (249112)

### Decipher Patient View: [249112](#)

Item: 249112

**Score: 0**

**Position:** [chr10:28817839-28936752](#)

Band: 10p12.1

**Genomic Size:** 118914

[View DNA for this feature \(hg19/Human\)](#)

Size of variant	118914
Mean Ratio	-1.00
Genotype	Heterozygous
Variant Class	Deletion
Inheritance	Unknown
Pathogenicity	Unknown
Contribution	Unknown
Phenotypes	Abnormality of the gingiva, Abnormality of the upper respiratory tract, Bifid tongue, Broad foot, Broad hallux, Depressed nasal ridge, Frontal bossing, Hoarse voice, Hypertelorism, Intellectual disability, Long palpebral fissure, Low posterior hairline, Pes cavus, Short foot, Short nose, Synophrys, Thick eyebrow, Wide mouth
Genes in this region	MIR5586, WAC, WAC-AS1

[Go to Decipher CNVs track controls](#)

Data last updated at UCSC: 2020-12-06 04:14:04



About Browse DDD (UK)

Search DECIPHER



Help Join Log in

Patient: 249112

Overview

Genotype 1

Phenotypes 18

Assessments 0

Karyotype

Citations 0

Contact

Age at last clinical assessment

17 years

Chromosomal sex

46XY

Is open-access?

Yes

Feedback

## Information

- [About DECIPHER](#)
- [Advisory Board](#)
- [Affiliations](#)
- [Project Proposal](#)

## Downloads

- [Ethical Framework](#)
- [Data Flowchart](#)
- [Data Files](#)

## Forms

- [Consent](#)
- [Assent](#)
- [Family Pack](#)

## Policies

- [Legal](#)
- [Cookies Policy](#)
- [Data Sharing](#)
- [Citing](#)

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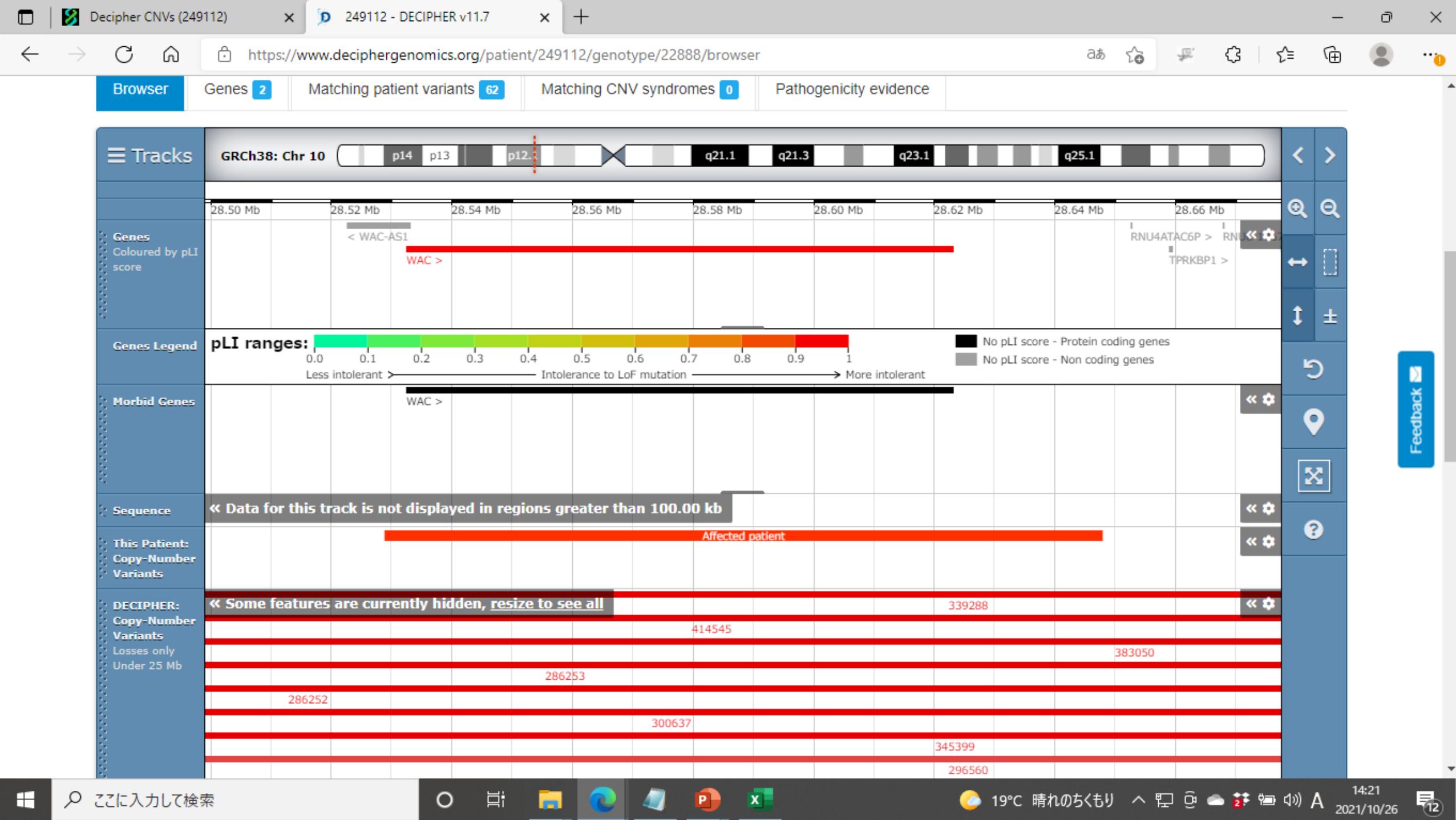
Report a bug or feed back

[contact@deciphergenomics.org](mailto:contact@deciphergenomics.org)



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## GRCh38/hg38 10p12.1-11.23(chr10:27046685-30228891)x1 AND See cases

Clinical significance: Pathogenic (Last evaluated: Aug 12, 2011)  
Review status: ★ ★ ★ ★

[Help](#)[Turn Off](#) [Clear](#)

Based on: 1 submission [\[Details\]](#)  
Record status: current  
Accession: RCV000052503.4

### Allele description [\[Variation Report for GRCh38/hg38 10p12.1-11.23\(chr10:27046685-30228891\)x1\]](#)

GRCh38/hg38 10p12.1-11.23(chr10:27046685-30228891)x1

Genes:

- BAMBI:BMP and activin membrane bound inhibitor [\[Gene\]](#) [\[OMIM\]](#) [\[HGNC\]](#)
- MKX-AS1:MKX antisense RNA 1 [\[Gene\]](#) [\[HGNC\]](#)
- RAB18:RAB18, member RAS oncogene family [\[Gene\]](#) [\[OMIM\]](#) [\[HGNC\]](#)
- SVIL-AS1:SVIL antisense RNA 1 [\[Gene\]](#) [\[HGNC\]](#)
- WAC-AS1:WAC antisense RNA 1 (head to head) [\[Gene\]](#) [\[HGNC\]](#)
- WAC:WW domain containing adaptor with coiled-coil [\[Gene\]](#) [\[OMIM\]](#) [\[HGNC\]](#)
- YME1L1:YME1 like 1 ATPase [\[Gene\]](#) [\[OMIM\]](#) [\[HGNC\]](#)

[...more](#)

Variant type: copy number loss

Cytogenetic location: 10p12.1-11.23

Genomic location:  
[Chr10: 27046685 - 30228891 \(on Assembly GRCh38\)](#)  
[Chr10: 27335614 - 30517820 \(on Assembly GRCh37\)](#)  
[Chr10: 27375620 - 30557826 \(on Assembly NCBI36\)](#)

### Recent activity

73314[AlleleID] (1)

ClinVar

hnf1b[gene] (536)

ClinVar

HNF1B HNF1 homeobox B [Homo sapiens]

Gene

chr17 : 34815184-36241526 (1)

ClinVar

424616[AlleleID] (1)

ClinVar

[See more...](#)

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12:51

2021/10/29

19





About Browse DDD (UK)

Search DECIPHER



Help Join Log in

Patient: 249112

Overview

Genotype 1

Phenotypes 18

Assessments 0

Karyotype

Citations 0

Contact

Please click the 'Initiate contact' button below and fill in the form to request contact with the clinician for this patient. Your request will be validated by the DECIPHER team and forwarded to the clinician on your behalf. For this reason, it is important that you provide as much information as possible for reasons for contacting the clinician (collaboration, request for more information, etc.). You can also provide other DECIPHER identifiers in your request if you wish to contact more than one clinician.

Initiate contact via DECIPHER

Feedback

## Information

- [About DECIPHER](#)
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20°C 晴れのちくもり 14:23  
2021/10/26



# DECIPHER

Databas**E** of **C**hromosome **I**mbalance and **P**henotype  
in **H**umans using **E**nsembl **R**esources

The New Shorter Oxford English Dictionary (OUP 1993)  
defines **decipher** as “to give the key to discover the  
meaning of (something obscure and perplexing)”

# DECIPHERデータベースは何を開発したか？

- 微細な染色体の変化はゲノムのどこでも発生する可能性があるが、特定の変化は非常に稀である。臨床医や科学者が情報を共有できるように情報をまとめることで、稀な状態や遺伝子機能の理解に向けた進歩が加速する。

# DECIPHERデータベースは何をするのか？

- DECIPHERは、ヒトゲノムプロジェクトの配列データを使用して、高解像度の分子技術、特にマイクロアレイ染色体検査によってもたらされる結果を把握し、超顕微鏡的な染色体の不均衡に関する知識を増大させる。
- DECIPHERは、マイクロアレイ染色体検査で特定された病的コピー数変化と良性コピー数変化を区別することを可能にする。
- 正確なゲノム位置を表現型と関連付けることにより、DECIPHERは、未知の機能の遺伝子、特に人間の発達に影響を与える遺伝子の機能を見つけるための強力なツールである。

# DECIPHERは誰のためのものであるか？

- DECIPHERは、臨床遺伝学、細胞遺伝学、分子生物学を専門とする者のためのツールである。DECIPHERに保持されている同意の上で完全に匿名化されたデータは、公開されたホームページを介して利用可能となる。

# 臨床遺伝専門医にとってのDECIPHERの利点は何か？

- DECIPHERは、同様の染色体の不均衡が以前に報告されているかどうかを検証し、それがどのような表現型に関係しているかを示す。これは、マイクロアレイ染色体検査で特定されたコピー数変化の潜在的な臨床的重要性を判断する上で非常に価値がある。
- DECIPHERは、OMIM遺伝子を含む、変化のあった領域に関するすべての既知および候補遺伝子を示す。確立された臨床的意義のある遺伝子は、接尾辞「M」で強調されている。インプリンティング遺伝子は、接尾辞「I」で強調表示される。
- DECIPHERは、同じ、あるいは類似の微細欠失/重複を持つ患者の存在を示すだけでなく、データを提供した施設の責任者との接触を促進し、それによって新しい症候群を提唱・確立させる研究を加速させる。
- DECIPHER Syndromesは、既知の微細欠失/重複症候群に関する情報を、関連する文献やサポートグループへのリンクとともに提供する。

# 細胞遺伝学を専門とする者にとってのDECIPHERの利点は？

- CNVトラックと一緒にマイクロアレイ染色体検査によって特定された欠失/重複の染色体位置を即座に確認する機能。
- FISHによる検証のためのクローンの選択を容易にするために、タイリングパスクローンセットと一緒にEnsemblゲノムブラウザーで微細欠失/重複を表示する機能。
- 臨床医や患者とのコミュニケーションを促進するために、核型表意文字を使用してマイクロアレイデータまたはFISHデータから書面によるレポートを生成する機能。

# 研究者にとってのDECIPHERの利点は何か？

- DECIPHERは、ゲノムコピー数多型に関連する表現型の遺伝的基礎を理解するまでの進歩を可能にし、遺伝子同定およびdysmorphologyの進歩に寄与する。

# DECIPHERに保持されているデータの公開に関するポリシー

- DECIPHERデータベースに含まれるデータを参照する論文は、Decipher Consortiumに対して謝辞を記載する必要がある。
- DECIPHERデータベースに含まれる患者データを論文に含めたい場合、その患者データを掲載した施設の責任者に連絡し、当該センターの少なくとも1人を共著者とすべきである。

## Background

Many patients suffering from Rare Disease harbour genomic variants (sequence variants or copy number variants) that by disrupting normal gene expression lead to disease. However, many variants are novel or extremely rare, making clinical interpretation problematic and genotype-phenotype correlations uncertain. Identification of patients sharing variants in a given gene and having phenotypic features in common leads to greater certainty in the pathogenic nature of the gene and enables the role of novel genes in development and disease to be defined. Furthermore, analysis of the type of genomic variant and of its consequence (eg. Loss of function or gain of function) enables insight into the mechanism of disease and potential therapeutic targets.

DECIPHER Project Proposal 

## DECIPHER

DECIPHER (DatabasE of genomic variation and Phenotype in Humans using Ensembl Resources) is an interactive web-based database which incorporates a suite of tools designed to aid the interpretation of genomic variants.

DECIPHER enhances clinical diagnosis by retrieving information from a variety of bioinformatics resources relevant to the variant found in the patient. The patient's variant is displayed in the context of both normal variation and pathogenic variation reported at that locus thereby facilitating interpretation.

## The DECIPHER Community

Contributing to the DECIPHER database is an international community of academic departments of clinical genetics and rare disease genomics now numbering more than 270 centres and having uploaded more than 36,000 cases. Each contributing centre has a nominated rare disease clinician or clinical geneticist who is responsible for overseeing data entry and membership for their centre. DECIPHER enables a flexible approach to data-sharing. Each centre maintains control of its own patient data (which are password protected within the centre's own DECIPHER project) until consent is given to share the data with chosen parties in a collaborative group or to allow anonymous genomic and phenotypic data to become freely viewable within Ensembl and other genome browsers (see below). Once data are shared, consortium members are able to gain access to the patient report and contact each other to discuss patients of mutual interest.

DECRYPTER v11.7: Mapping the cl... +

https://www.deciphergenomics.org/user/dashboard

DECIPHER GRCh38 About Browse My Patients DDD (UK) Search DECIPHER Help Toshiyuki Yamamoto

Dashboard Projects My Notifications 0 My Profile

Find patient by reference

Project: TWM Reference: -select- Go to patient

Recently-edited patients

Patient ID	Reference	Date
No data available in table		

Create new patient

Project: TWM Add Patient

DECIPHER News

## DECIPHER v11.7 Released

We released DECIPHER v11.7 on the 22th September 2021.

Improvements include:

- Detailed information about [ClinGen expert panel](#) specifications for ACMG/AMP variant interpretation are now displayed in the sequence variant pathogenicity interface. If gene recommendations are available for a criterion, this is indicated under the criterion and popups provide details of the expert panel recommendations. This assists users in accessing the relevant expert panel specifications.

Available evidence types

Selected evidence

Feedback

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2021/10/26

## Legend

## Copy-Number Variants

L

A genomic map of Chromosome 1. The chromosome is represented by a horizontal bar divided into bands of different shades of gray and black. Gene locations are indicated by vertical arrows pointing to specific bands. The genes shown are p31.3, p31.1, q12, q32.1, q41, and q43. A red rectangular box highlights a segment on the right side of the chromosome, spanning from approximately band 41 to band 43. This indicates a region of interest or a copy-number variant.

— 1 —

A genomic map of Chromosome 2. The chromosome is represented by a horizontal line with vertical bands of different shades of gray. A scale at the bottom indicates bands from p21 to q35. A blue horizontal bar is positioned in the q34 band, representing a copy-number variant.

Genomic map of Chromosome 4 showing bands p15.1, p14, q12, q24, q25, q26, and q28.3. A red box highlights a region on band q24.

A genomic map of Chromosome 5. The chromosome is represented by a series of vertical bars of different shades of gray and black, indicating banding patterns. A large white arrowhead points to the right, spanning bands q11.2 through q34. Above the chromosome, labels indicate the bands: q11.2, q14.3, q15, q32, and q34. Below the chromosome, the text "Copy-Number Variants" is followed by a red horizontal bar, which corresponds to the position of the arrowhead.

Chromosome 7

Copy-Number Variants

Copy-Number Variants

This figure shows a genomic track for copy-number variants. A single red horizontal bar is positioned on a black and white checkered background, indicating a region of altered DNA copy number.

#### **Copy-Number Variants**

Chromosome 14

Copy-Number Variants

[View Details](#)

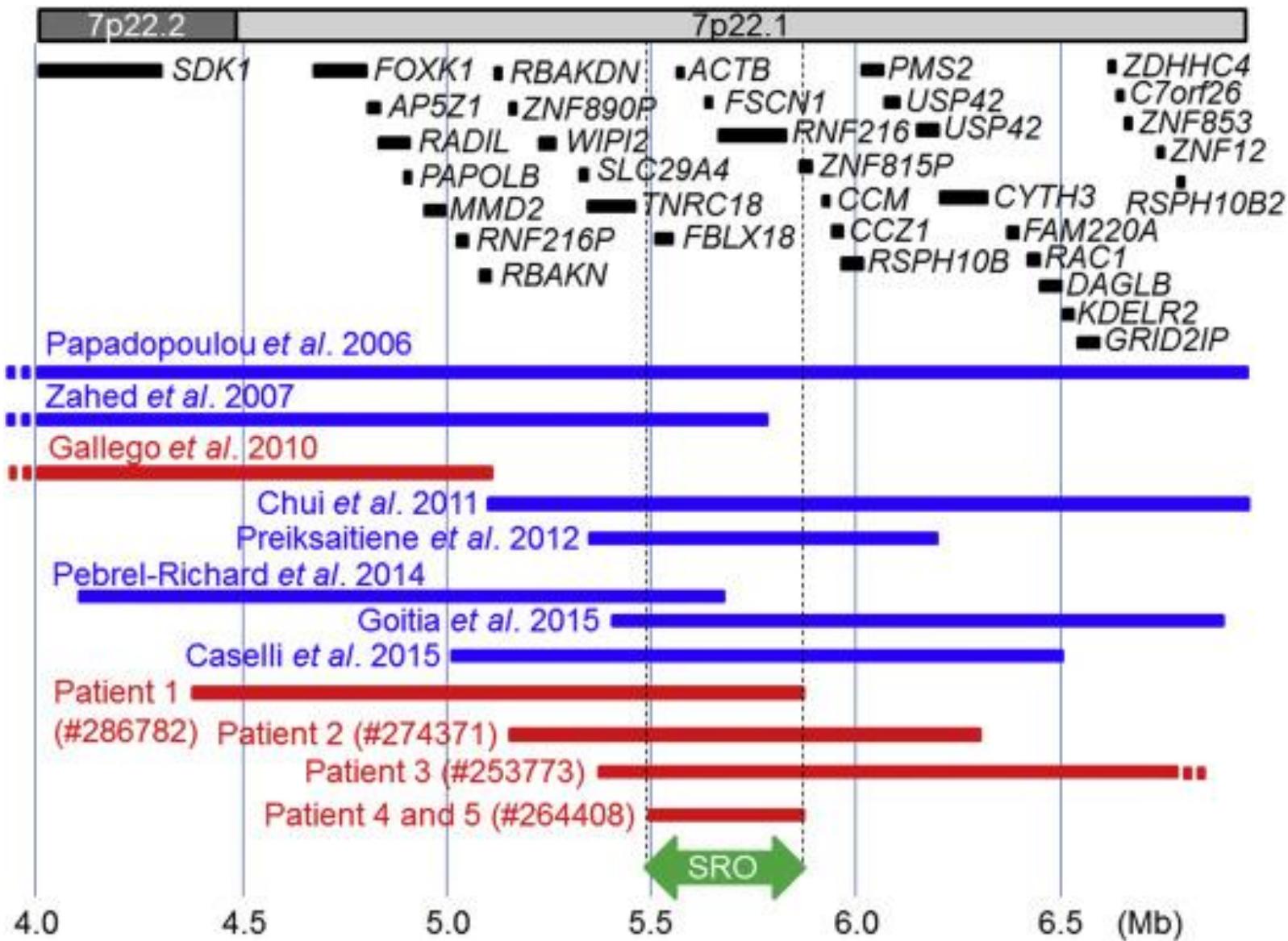
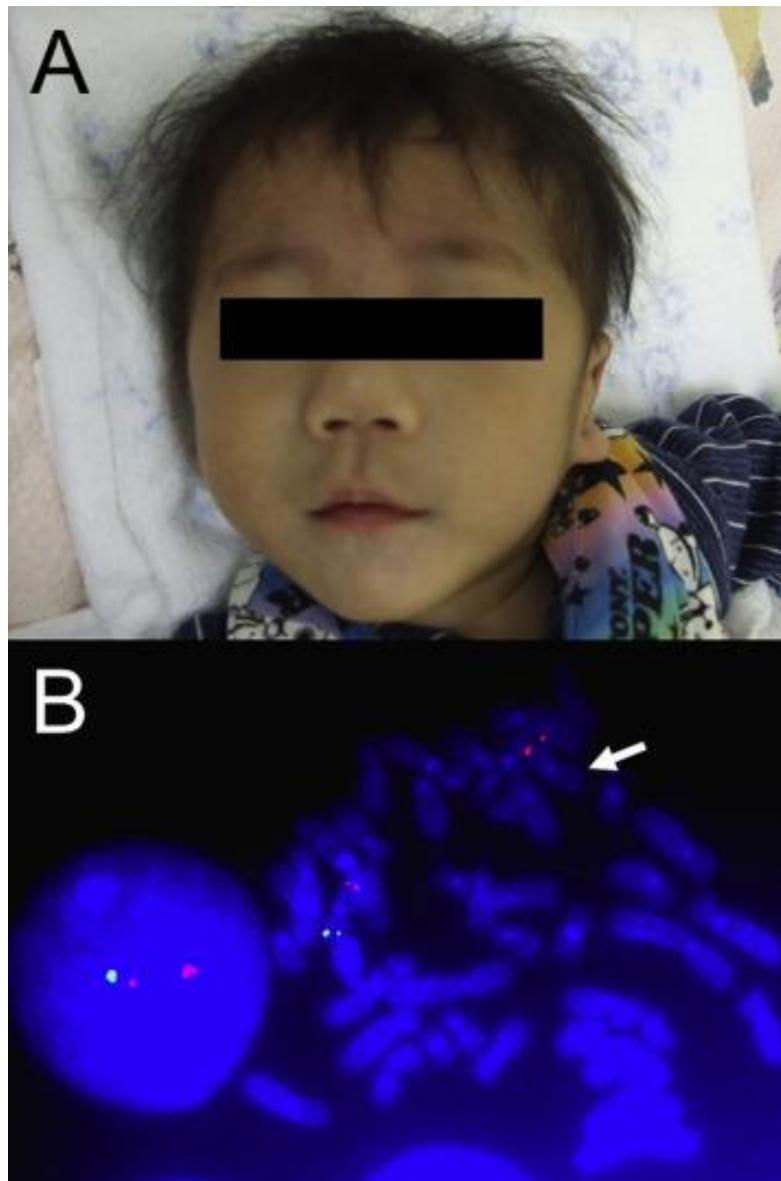


# DECIPHERメンバーシップ基準

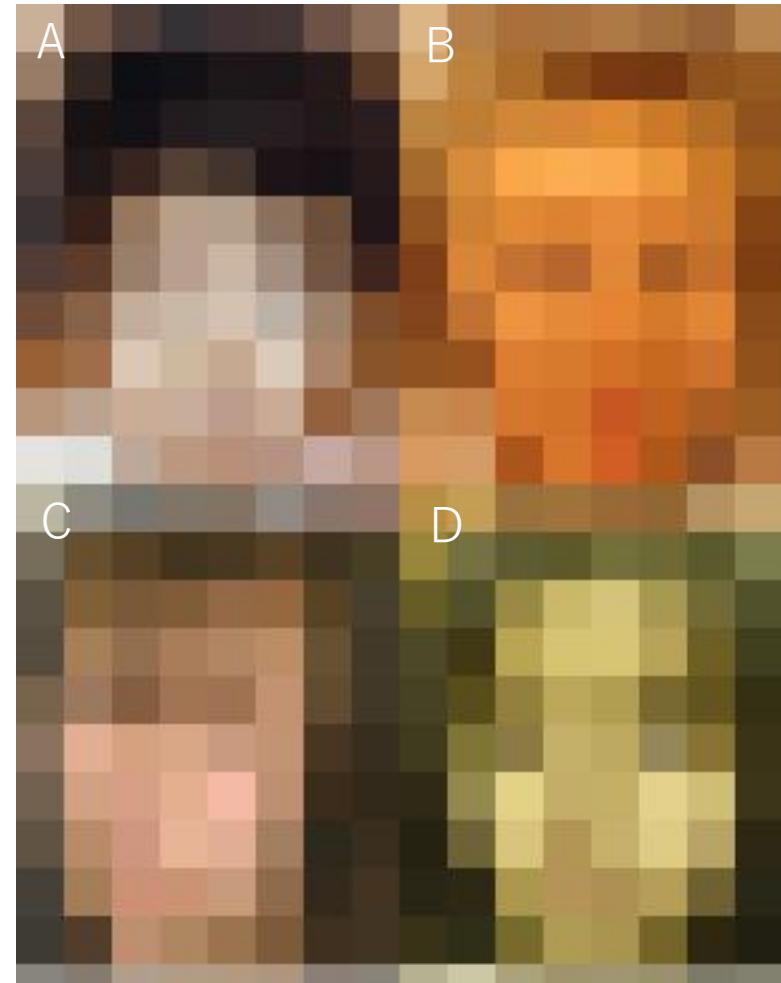
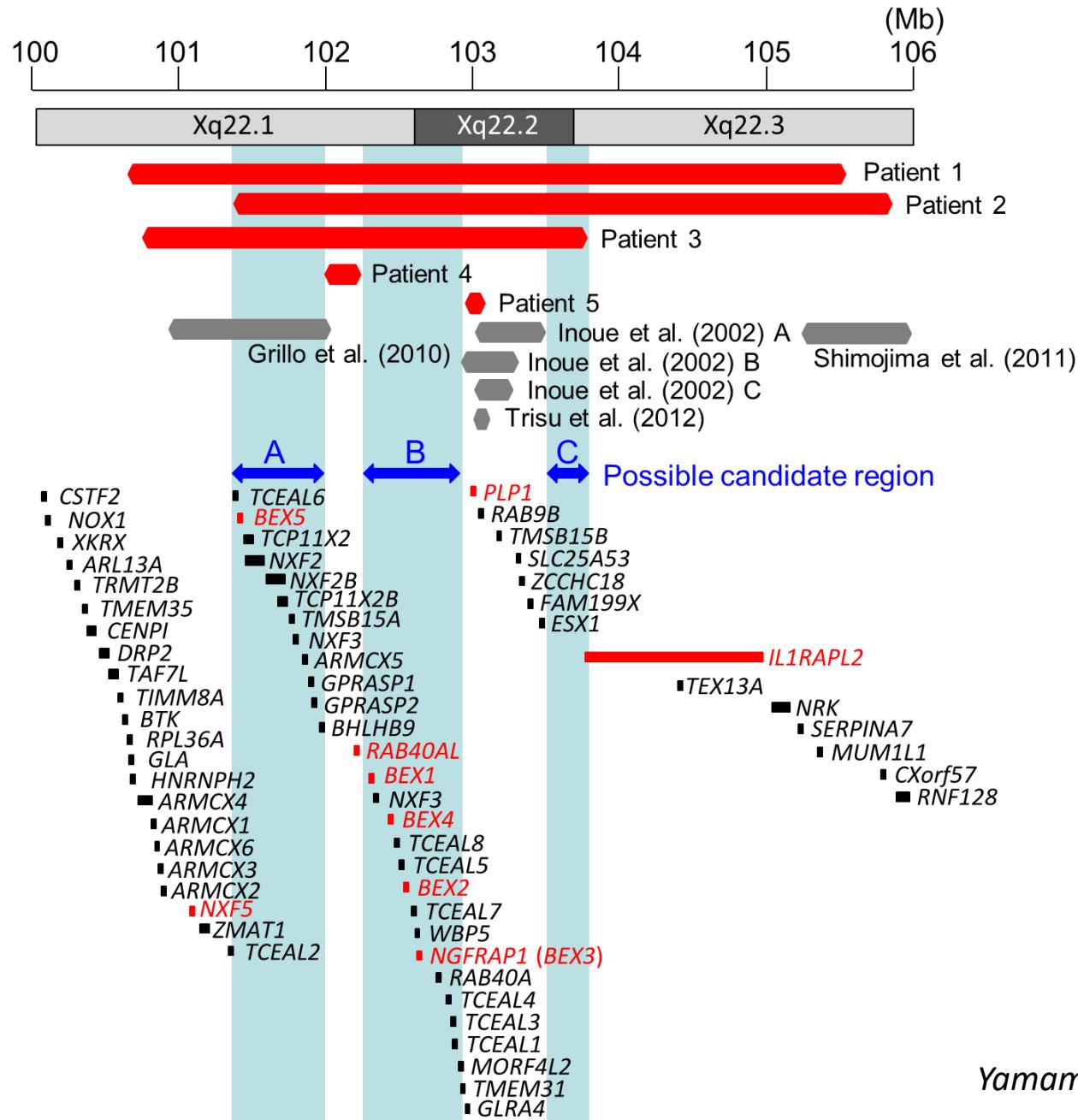
1. このプロジェクトは、遺伝性疾患の診療を行う病院を所管する組織が行う。
2. このプロジェクトは、大学等のアカデミアにおける人類遺伝学・臨床遺伝学においても行われる。
3. このプロジェクトは、遺伝性疾患患者の診療を行う指導的立場の医師の指導の元で行われる。
4. このプロジェクトは、研究室における基礎研究者と診療部門における臨床医は、同じメンバーとしてチームを構成して行われる。
5. このプロジェクトは、同意を得て共有が許された患者データ(表現型にリンクされたバリエントデータ)をDECIPHERに提出することによって、他施設とデータ共有を行い、共同研究を促進させることを目的としている。

メンバーになるためには申請を行い、認められる必要がある  
ゲノムコピー数変化に関する先行業績が必要

# ACTNBを含む7p22.1微細欠失

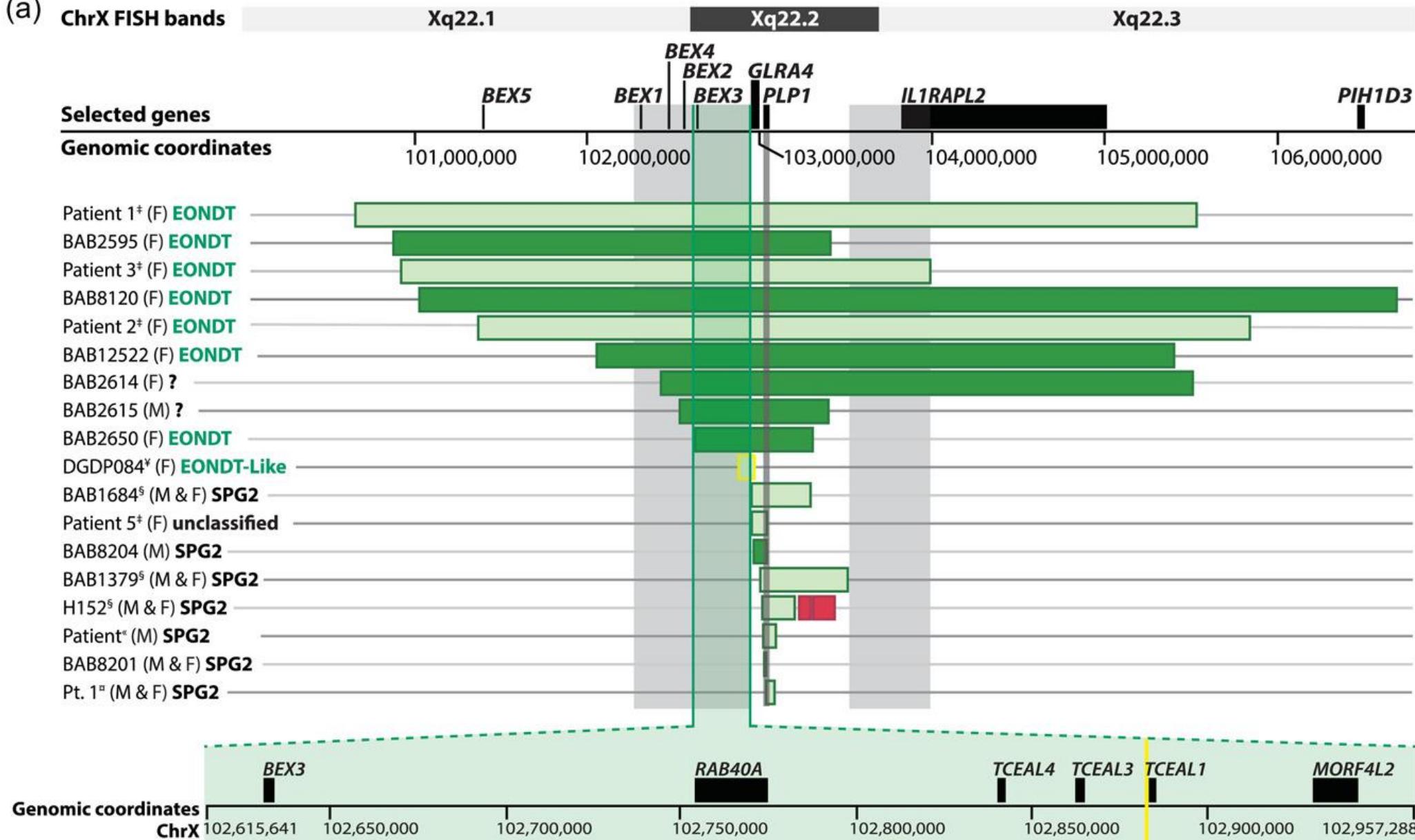


# 重度の神経発達障害を示すXq22欠失女性

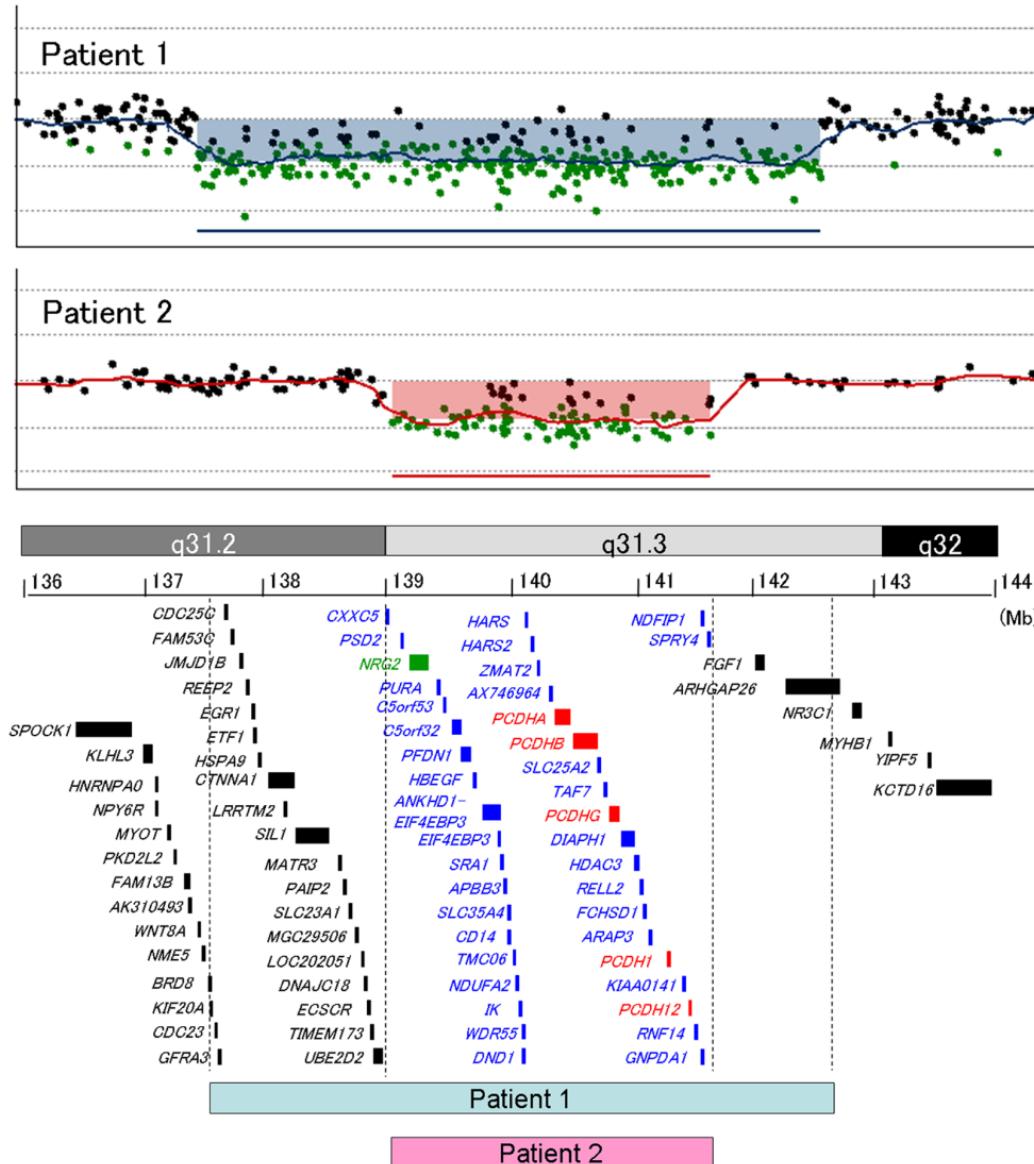
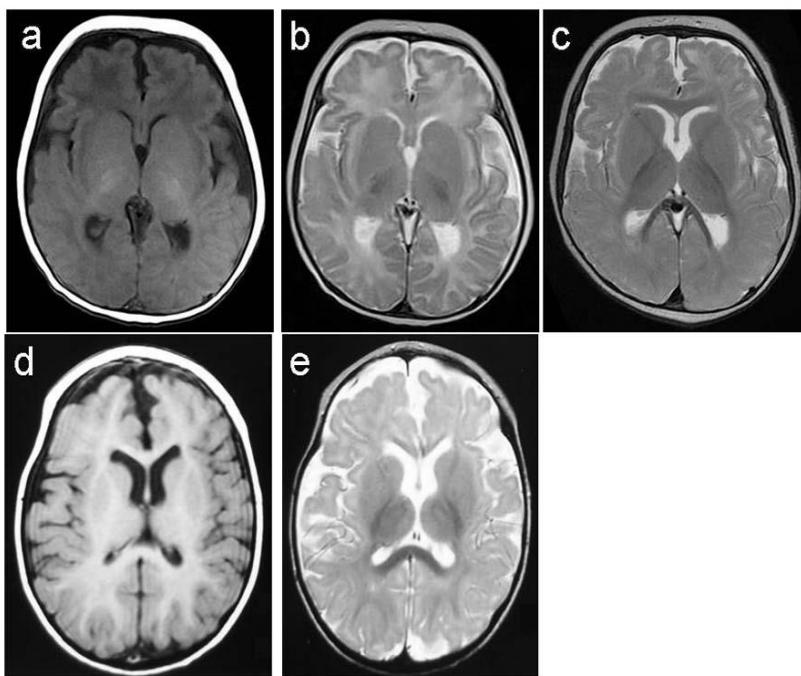
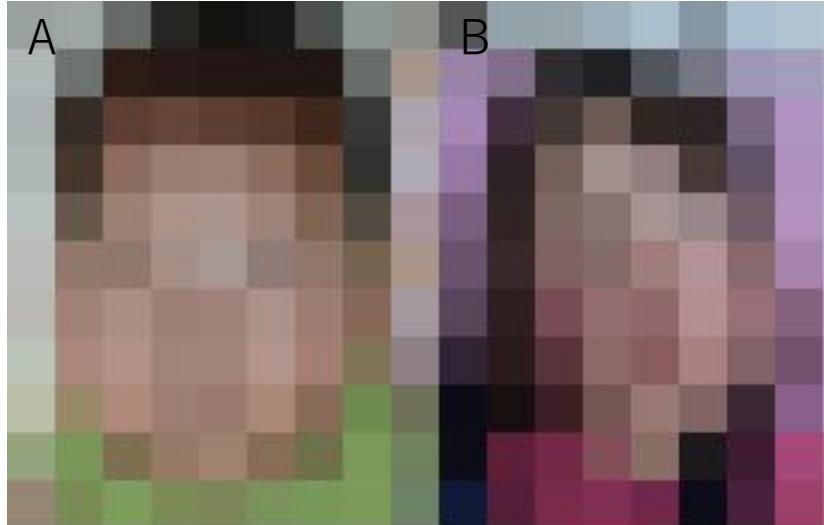


# Xq22 deletion 疾患概念の確立

(a) ChrX FISH bands

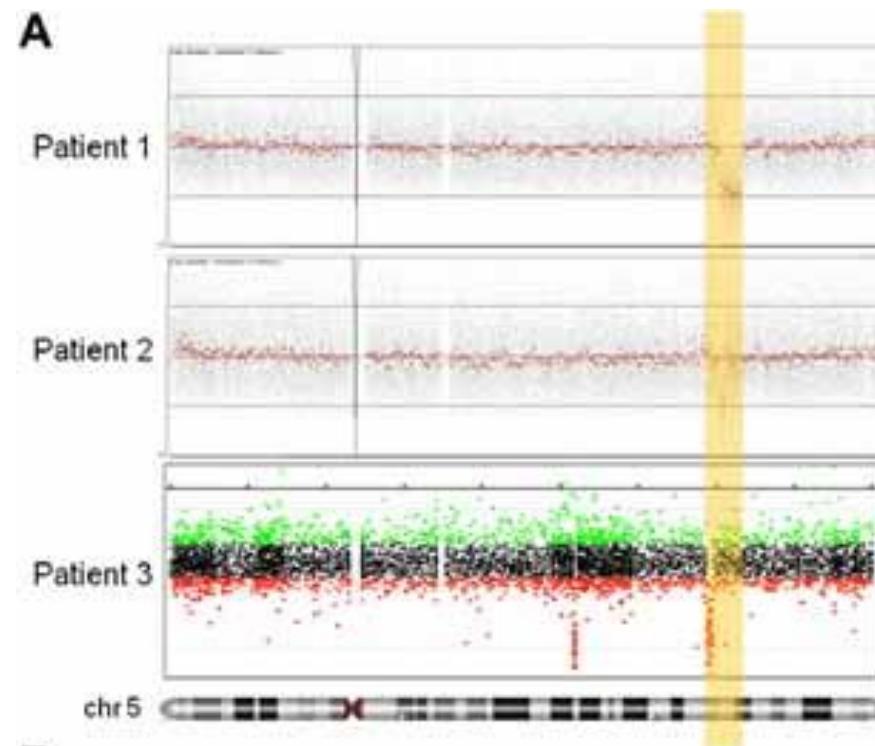
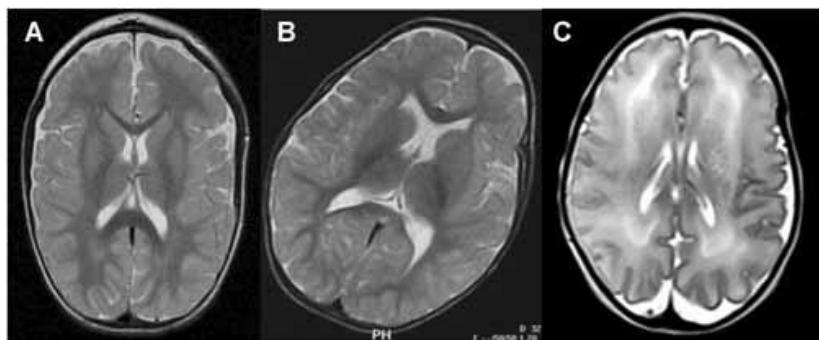
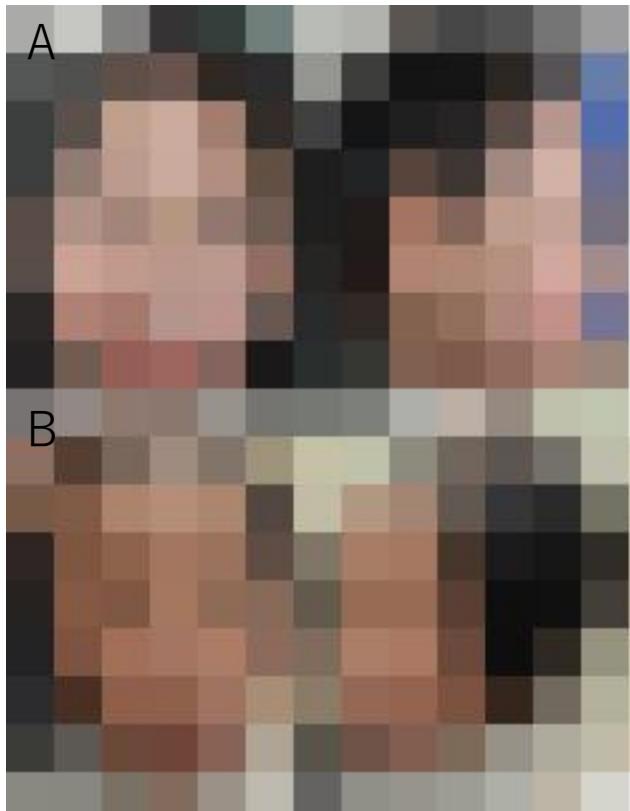


# 新規5q31染色体微細欠失症候群

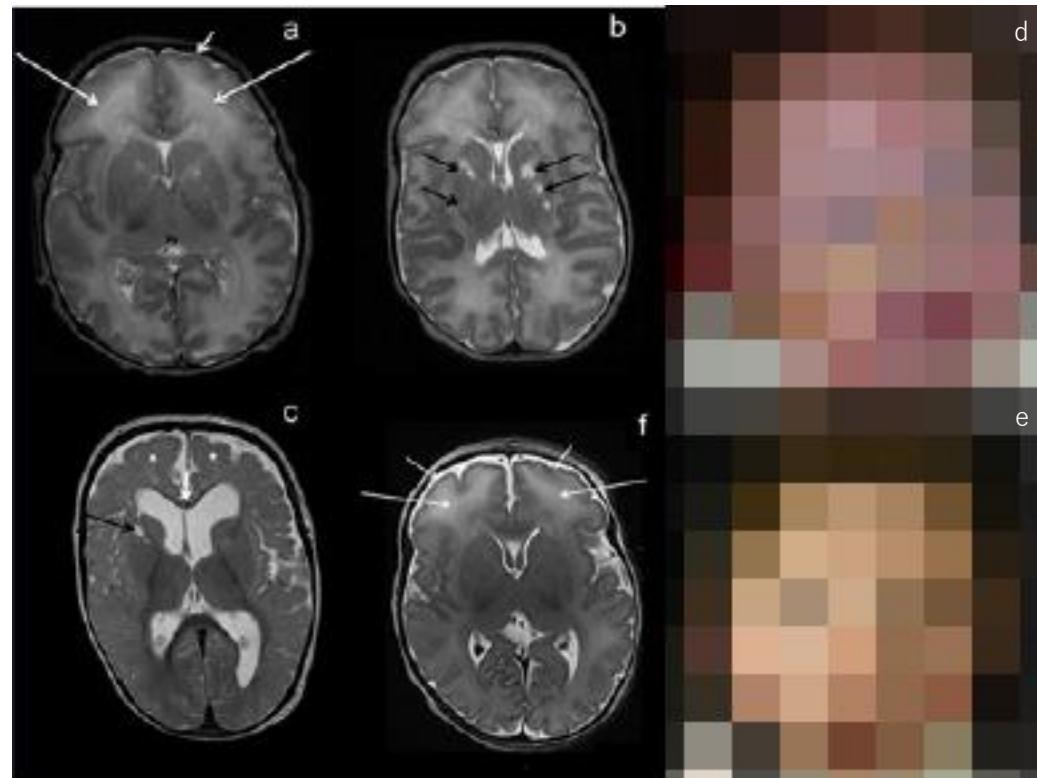


Shimojima et al. Am J Med Genet 2011

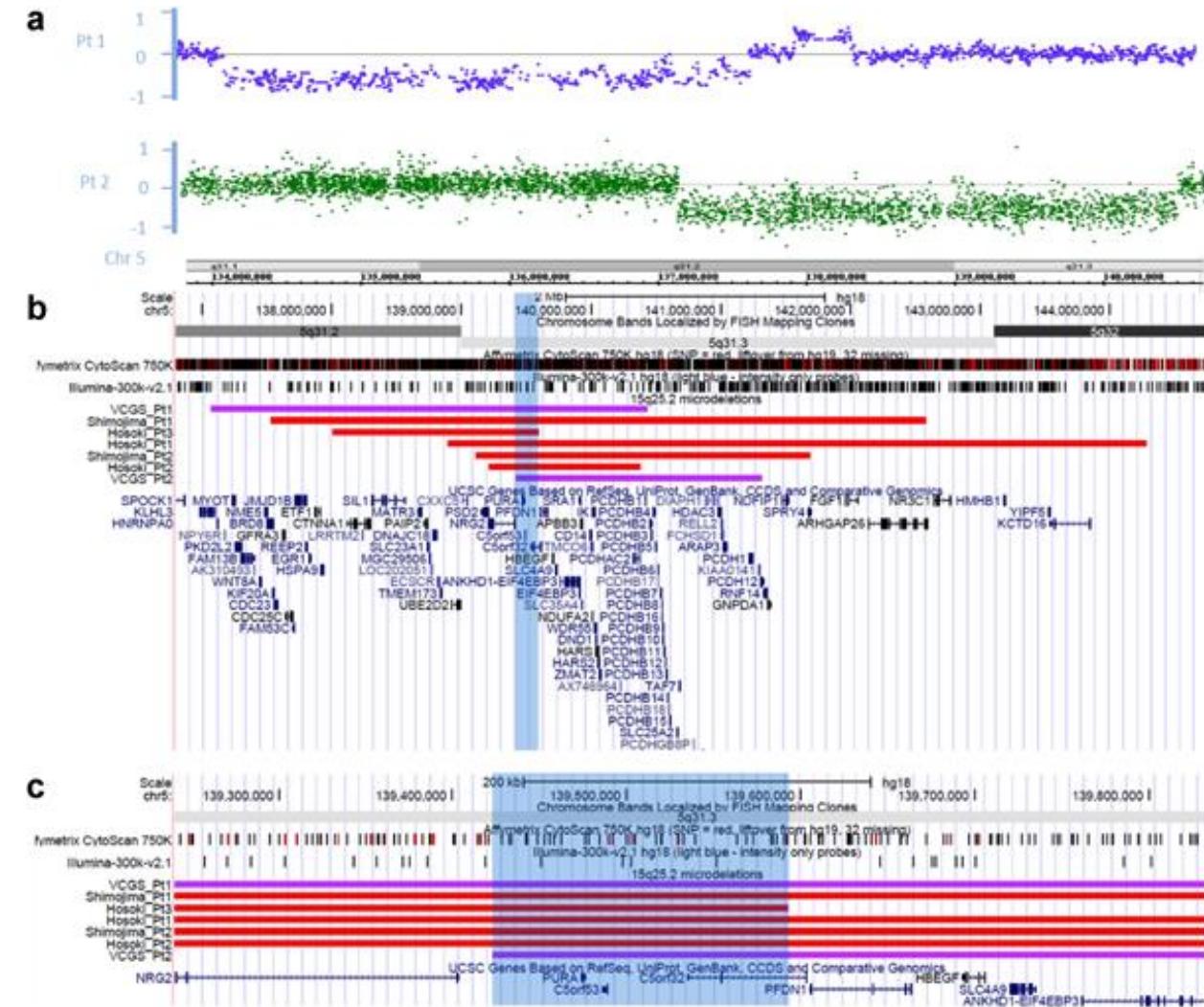
# 新規5q31染色体微細欠失症候群



# 新規5q31染色体微細欠失症候群



from Australia



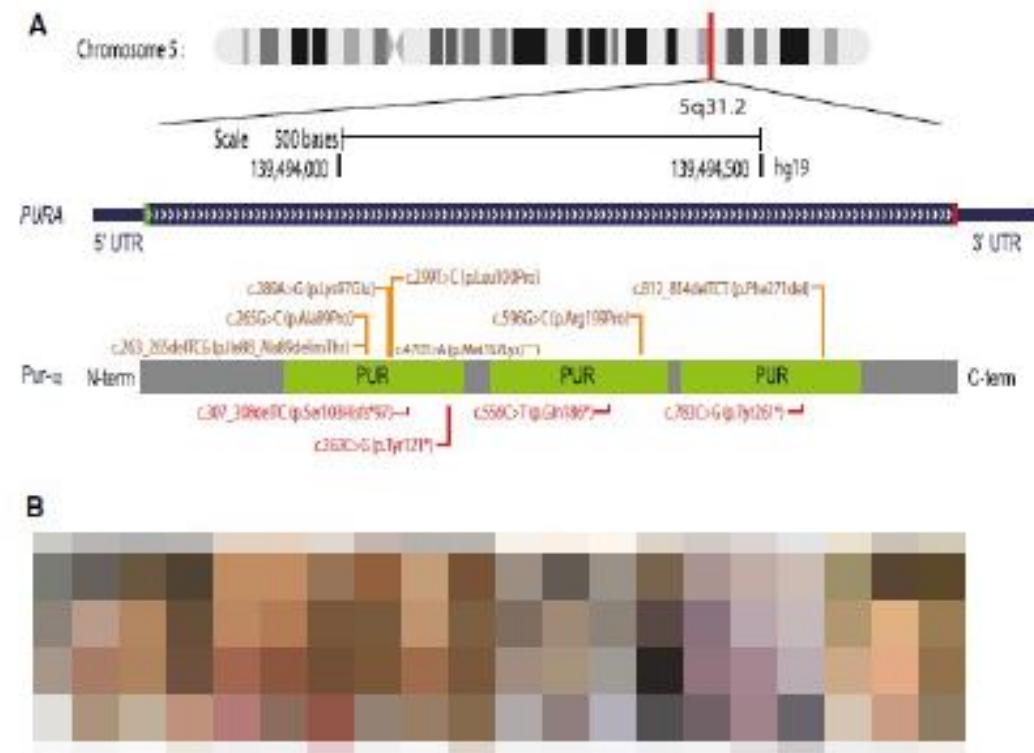
# 新規5q31染色体微細欠失症候群

## REPORT

### Mutations in *PURA* Cause Profound Neonatal Hypotonia, Seizures, and Encephalopathy in 5q31.3 Microdeletion Syndrome

Seema R. Lalani,<sup>1,17,\*</sup> Jing Zhang,<sup>1,17</sup> Christian P. Schaaf,<sup>1,3,17</sup> Chester W. Brown,<sup>1,11,17</sup> Pilar Magoulas,<sup>1</sup> Anne Chun-Hui Tsai,<sup>4</sup> Areeg El-Gharbawy,<sup>5</sup> Klaas J. Wierenga,<sup>6</sup> Dennis Bartholomew,<sup>7</sup> Chin-To Fong,<sup>8</sup> Tina Barbaro-Dieber,<sup>9</sup> Mary K. Kukolich,<sup>9</sup> Lindsay C. Burrage,<sup>1</sup> Elise Austin,<sup>1</sup> Kory Keller,<sup>4</sup> Matthew Pastore,<sup>7</sup> Fabio Fernandez,<sup>10,11</sup> Timothy Lotze,<sup>10,11</sup> Angus Wilfong,<sup>10,11</sup> Gabriela Purcarin,<sup>13</sup> Wenmiao Zhu,<sup>1</sup> William J. Craigen,<sup>1</sup> Marianne McGuire,<sup>1</sup> Mahim Jain,<sup>1</sup> Erin Cooney,<sup>1</sup> Mahshid Azamian,<sup>1</sup> Matthew N. Bainbridge,<sup>2</sup> Donna M. Muzny,<sup>2,14</sup> Eric Boerwinkle,<sup>2,15</sup> Richard E. Person,<sup>1,14</sup> Zhiyv Niu,<sup>1,14</sup> Christine M. Eng,<sup>1,14</sup> James R. Lupski,<sup>1,2,11,12</sup> Richard A. Gibbs,<sup>1,2</sup> Arthur L. Beaudet,<sup>1</sup> Yaping Yang,<sup>1,14</sup> Meng C. Wang,<sup>1,16</sup> and Fan Xia<sup>1,14,\*</sup>

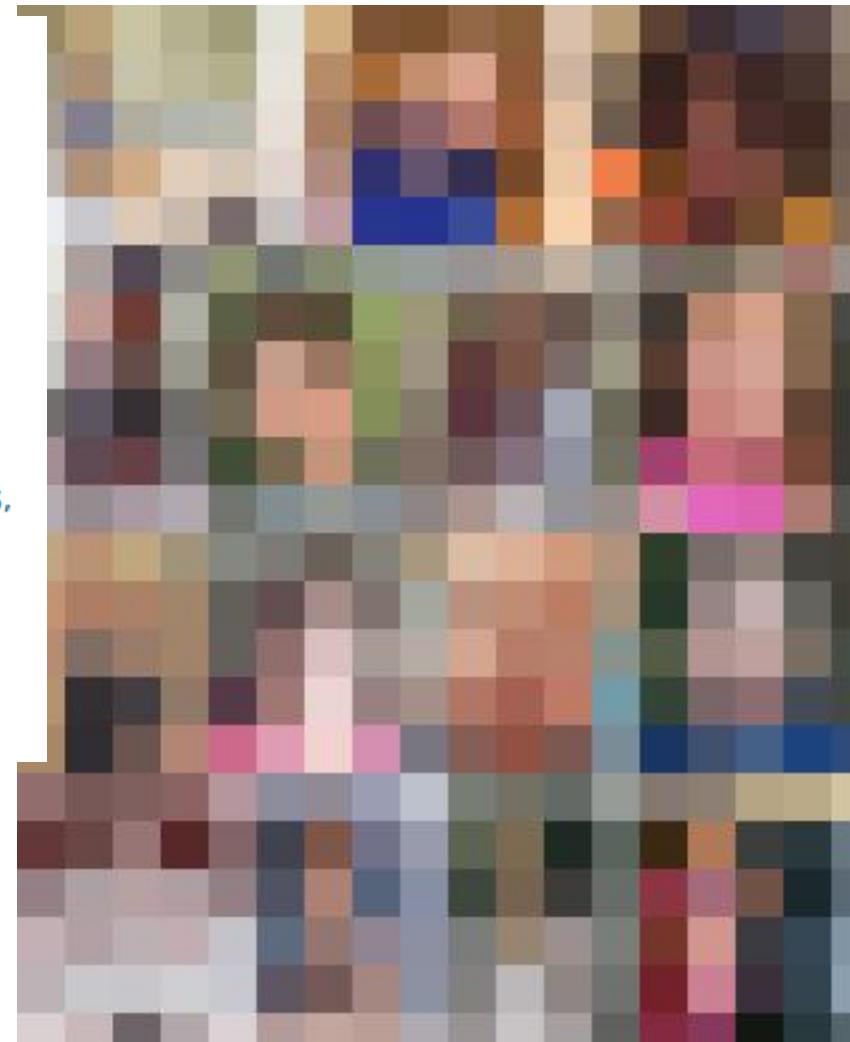
5q31.3 microdeletion syndrome is characterized by neonatal hypotonia, encephalopathy with or without epilepsy, and severe developmental delay, and the minimal critical deletion interval harbors three genes. We describe 11 individuals with clinical features of 5q31.3 microdeletion syndrome and de novo mutations in *PURA*, encoding transcriptional activator protein Pur- $\alpha$ , within the critical region. These data implicate causative *PURA* mutations responsible for the severe neurological phenotypes observed in this syndrome.



## Expanding the neurodevelopmental phenotype of *PURA* syndrome

Bo Hoon Lee, Margot R. F. Reijnders, Oluwatobi Abubakare, Emily Tuttle, Brynn Lape, Kelly Q. Minks, Christopher Stodgell, Loisa Bennetto, Jennifer Kwon, Chin-To Fong, Karen W. Gripp, Eric D. Marsh, Wendy E. Smith, Ahm M. Huq, Stephanie A. Coury, Wen-Hann Tan, Orestes Solis, Rupal I. Mehta, Richard J. Leventer, Diana Baralle, David Hunt, Alex R. Paciorkowski 

First published: 17 November 2017 | <https://doi.org/10.1002/ajmg.a.38521>

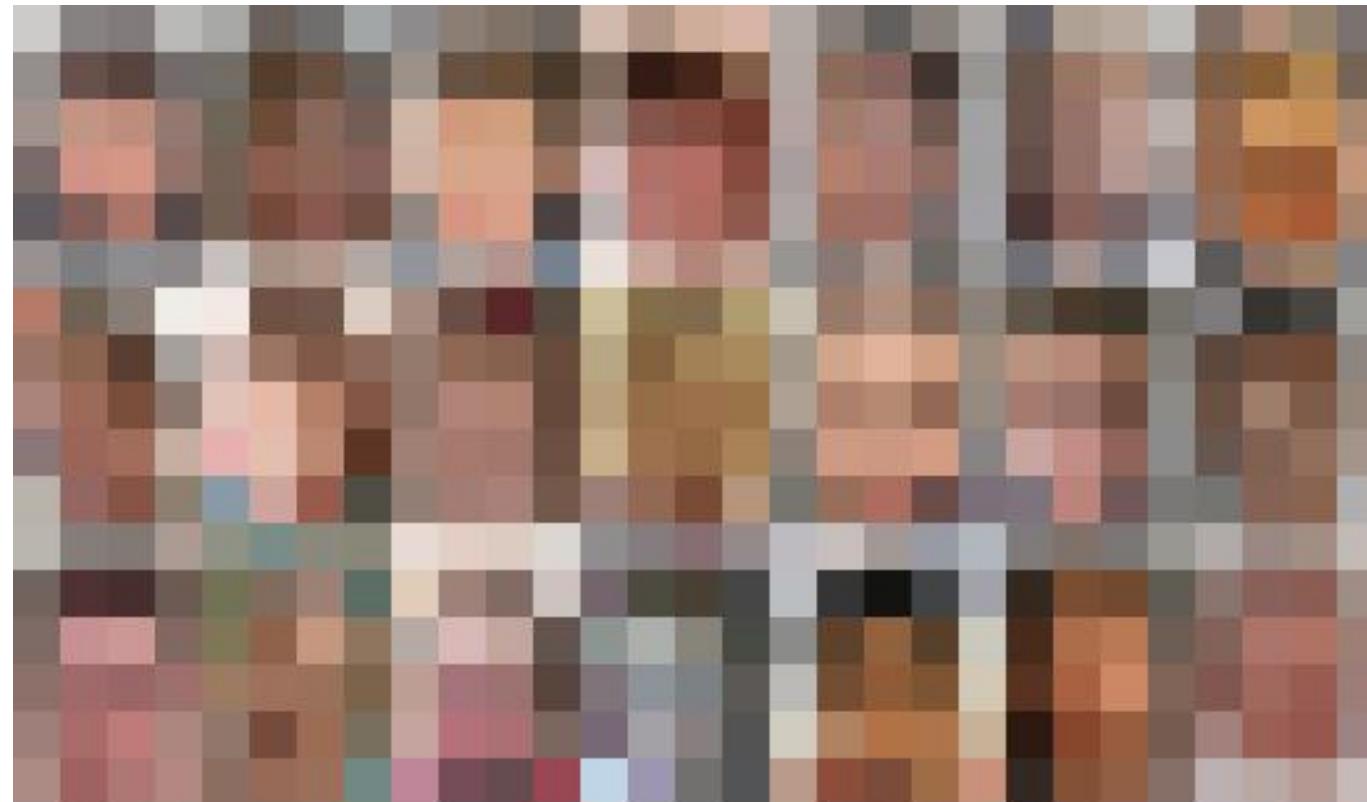




# PURA syndrome: clinical delineation and genotype-phenotype study in 32 individuals with review of published literature

Margot R F Reijnders,<sup>1</sup> Robert Janowski,<sup>2</sup> Mohsan Alvi,<sup>3</sup> Jay E Self,<sup>4,5</sup> Ton J van Essen,<sup>6</sup> Maaike Vreeburg,<sup>7</sup> Rob P W Rouhl,<sup>8,9,10</sup> Servi J C Stevens,<sup>7</sup> Alexander P A Stegmann,<sup>7</sup> Jolanda Schieving,<sup>11</sup> Ralph Pfundt,<sup>1</sup> Katinka van Dijk,<sup>12</sup> Eric Smeets,<sup>7</sup> Connie T R M Stumpel,<sup>7</sup> Levinus A Bok,<sup>13</sup> Jan Maarten Cobben,<sup>14</sup> Marc Engelen,<sup>15</sup> Sahar Mansour,<sup>16</sup> Margo Whiteford,<sup>17</sup> Kate E Chandler,<sup>18</sup> Sofia Douzgou,<sup>19</sup> Nicola S Cooper,<sup>19</sup> Ene-Choo Tan,<sup>20</sup> Roger Foo,<sup>21,22</sup> Angeline H M Lai,<sup>23</sup> Julia Rankin,<sup>24</sup> Andrew Green,<sup>25</sup> Tuula Lönnqvist,<sup>26</sup> Pirjo Isohanni,<sup>26,27</sup> Shelley Williams,<sup>28</sup> Ilene Ruhoy,<sup>29</sup> Karen S Carvalho,<sup>30</sup> James J Dowling,<sup>31</sup> Dorit L Lev,<sup>32</sup> Katalin Sterbova,<sup>33</sup> Petra Lassuthova,<sup>33</sup> Jana Neupauerová,<sup>33</sup> Jeff L Waugh,<sup>34</sup> Sotirios Keros,<sup>35</sup> Jill Clayton-Smith,<sup>36</sup> Sarah F Smithson,<sup>37</sup> Han G Brunner,<sup>1,7</sup> Ceciel van Hoeckel,<sup>38</sup> Mel Anderson,<sup>38</sup> Virginia E Clowes,<sup>39</sup> Victoria Mok Siu,<sup>40</sup> The DDD study,<sup>41</sup> Paulo Selber,<sup>42</sup> Richard J Leventer,<sup>43</sup> Christoffer Nellaker,<sup>44,45,46</sup> Dierk Niessing,<sup>2,47</sup> David Hunt,<sup>48,49</sup> Diana Baralle<sup>48,49</sup>

JMG 2018

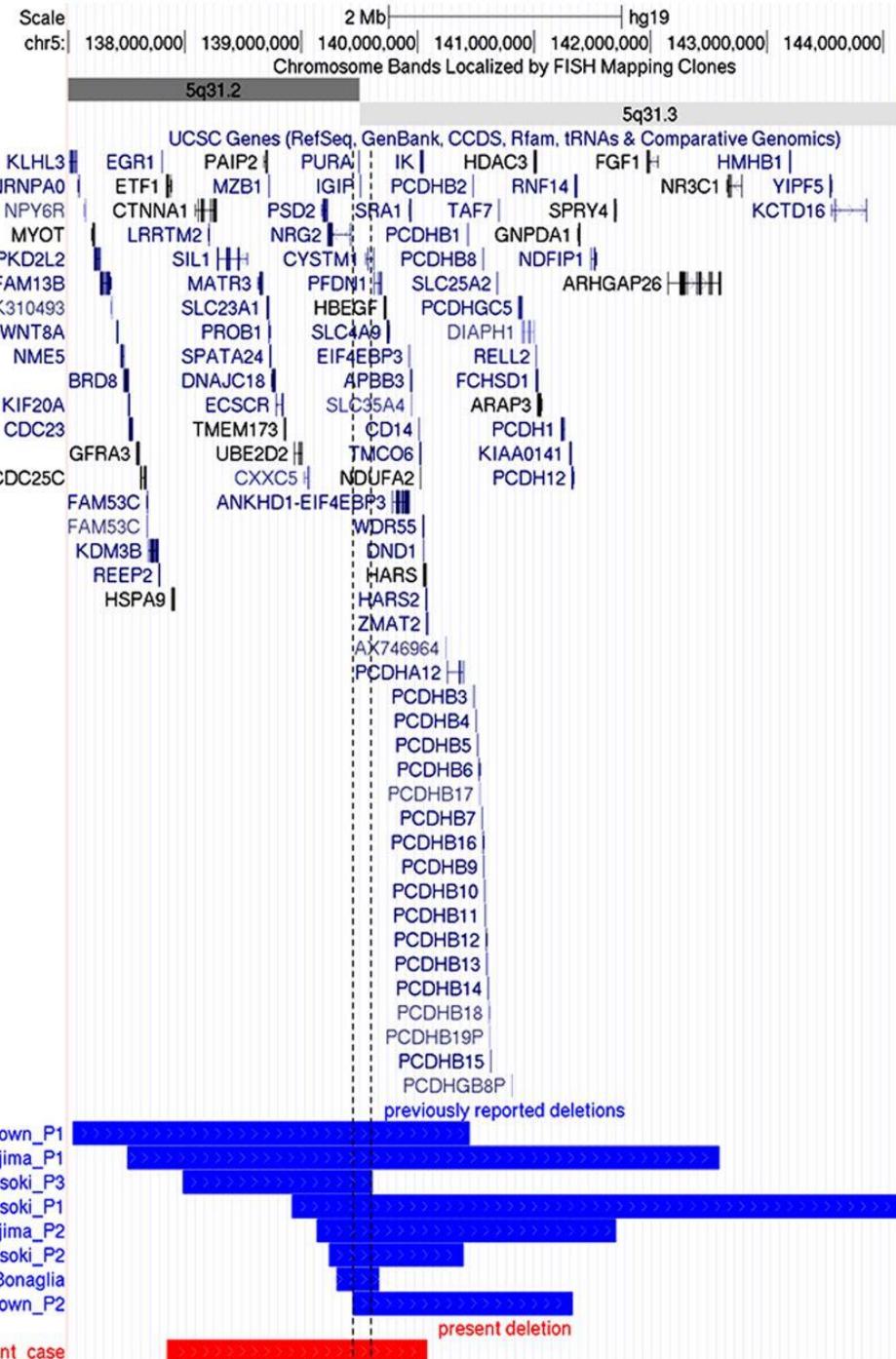
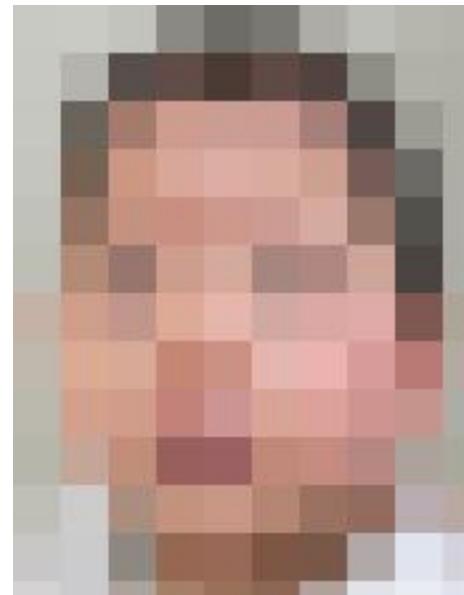


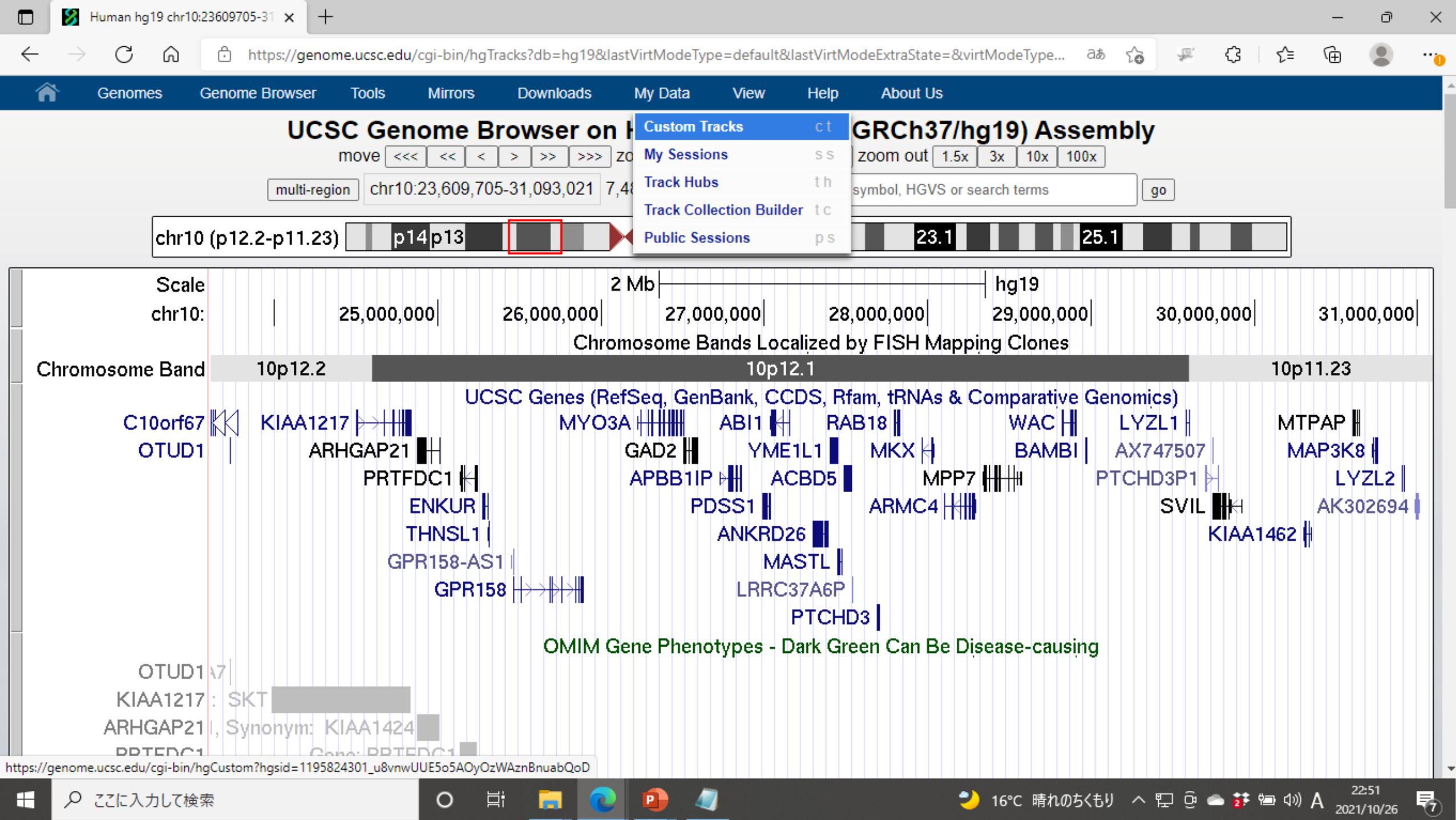
## DATA REPORT

Infantile spasms related to a 5q31.2-q31.3 microdeletion including *PURA*Keiko Shimojima<sup>1,2</sup>, Nobuhiko Okamoto<sup>3</sup>, Kayo Ohmura<sup>4</sup>, Hiroaki Nagase<sup>5</sup> and Toshiyuki Yamamoto<sup>1,2</sup>

Recently, haploinsufficiency of *PURA* has been identified as an essential cause of 5q31.3 microdeletion syndrome, which is characterized by severe psychomotor developmental delay, epilepsy, distinctive features, and delayed myelination. A new 5q31.2-q31.3 microdeletion that included *PURA* was identified in a patient with infantile spasms. Approximately 50% of patients with *PURA*-related neurodevelopmental disorders exhibited epilepsy regardless of whether they harbor a 5q31.3 deletion or *PURA* mutation. Patients with the 5q31.3 deletion or a *PURA* mutation should be carefully monitored for epileptic seizures.

Human Genome Variation (2018) 5, 18007; doi:10.1038/hgv.2018.7; published online 29 March 2018





## Managing Custom Tracks

This section provides a brief description of the columns in custom track management table. For more details about managing custom tracks, see the [Genome Browser User's Guide](#).

- **Name** - a hyperlink to the update page where you can edit your track data.
  - **Description** - the value of the "description" attribute from the track line, if present. If no description is included in the input file, this field contains the track name.
  - **Type** - the track type, determined by the Browser based on the format of the data.
  - **Doc** - displays "Y" (Yes) if a description page has been uploaded for the track; otherwise the field is blank.
  - **Items** - the number of data items in the custom track file. An item count is not displayed for tracks lacking individual items (e.g. wiggle format data).
  - **Pos** - the default chromosomal position defined by the track file in either the browser line "position" attribute or the first data line. Clicking this link opens the Genome Browser or Table Browser at the specified position (note: only the chromosome name is shown in this column). The Pos column remains blank if the track lacks individual items (e.g. wiggle format data) and the browser line "position" attribute hasn't been set.

## Add Custom Tracks

clade Mammal genome Human assembly Feb. 2009 (GRCh37/hg19)

Display your own data as custom annotation tracks in the browser. Data must be formatted in [bigBed](#), [bigBarChart](#), [bigChain](#), [bigGenePred](#), [bigInteract](#), [bigLolly](#), [bigMaf](#), [bigPsl](#), [bigWig](#), [BAM](#), [barChart](#), [VCF](#), [BED](#), [BED detail](#), [bedGraph](#), [broadPeak](#), [CRAM](#), [GFF](#), [GTF](#), [hic](#), [interact](#), [MAF](#), [narrowPeak](#), [Personal Genome SNP](#), [PSL](#), or [WIG](#) formats.

- You can paste just the URL to the file, without a "track" line, for bigBed, bigWig, bigGenePred, BAM and VCF.
  - To configure the display, set [track](#) and [browser](#) line attributes as described in the [User's Guide](#).

Examples are [here](#). If you do not have web-accessible data storage available, please see the [Hosting](#) section of the Track Hub Help documentation.

Please note a much more efficient way to load data is to use Track Hubs, which are loaded from the Track Hubs Portal found in the menu under My Data.

Paste URLs or data: Or upload:  ファイルの選択  ファイルが選択されていません

**Clear**

Optional track documentation: Or upload:  ファイルが選択されていません

**Clear**

Click [here](#) for an HTML document template that may be used for Genome Browser track descriptions.



## Managing Custom Tracks

This section provides a brief description of the columns in custom track management table. For more details about managing custom tracks, see the [Genome Browser User's Guide](#).

- **Name** - a hyperlink to the update page where you can edit your track data.
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UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

multi-region chr10:23,609,705-31,093,021 7,483,317 bp. enter position, gene symbol, HGVS or search term

go

Genomic map of chromosome 10 (p12.2-p11.23) showing bands p14, p13, q21.1, 21.3, 23.1, and 25.1.

Scale 2 Mb hg19

chr10: 25,000,000 26,000,000 27,000,000 28,000,000 29,000,000 30,000,000 31,000,000

Chromosome Band 10p12.2 10p12.1 10p11.23

identified deletion

UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)

OMIM Gene Phenotypes - Dark Green Can Be Disease-causing

OTUD1A7 | KIAA1217 : SKT

## Displaying Your Own Annotations in the Genome Browser

The Genome Browser provides dozens of aligned annotation tracks that have been computed at UCSC or have been provided by outside collaborators. In addition to these standard tracks, it is also possible for users to upload their own annotation data for temporary display in the browser. These custom annotation tracks are viewable only on the machine from which they were uploaded and are automatically discarded 48 hours after the last time they are accessed, unless they are saved in a [Session](#). Optionally, users can make custom annotations viewable by others as well. For a more stable option for custom annotations, we suggest using [track hubs](#). A third, more technical, option is to operate a mirror. Custom tracks work well for quickly displaying data, while track hubs are more configurable and permanent.

Custom tracks are a wonderful tool for research scientists using the Genome Browser. Because space is limited in the Genome Browser track window, many excellent genome-wide tracks cannot be included in the standard set of tracks packaged with the browser. Other tracks of interest may be excluded from distribution because the annotation track data is too specific to be of general interest or can't be shared until journal publication. In the past, many individuals and labs contributed custom tracks to the Genome Browser website for use by others. To view a list of these custom annotation tracks, click [here](#).

Track hubs are now the preferred approach for viewing and sharing data on the Browser. Labs, consortia, and institutions submit their hubs to be listed as a [Public Hub](#). Track hubs require remotely hosted data. They use binary index files which allow the browser to quickly access only what is relevant for the current region being viewed in the browser. See the [track hub help page](#) for more information.

Genome Browser annotation tracks are based on files in line-oriented format. Each line in the file defines a display characteristic for the track or defines a data item within the track. Annotation files contain three types of lines: browser lines, track lines, and data lines. Empty lines and those starting with "#" are ignored.

To construct an annotation file and display it in the Genome Browser, follow these steps:

#### **Step 1.** Format the data set:

Format your data as a tab-separated file using one of the formats supported by the Genome Browser. Annotation data can be in standard **GFF** format or in a format designed specifically for the Human Genome Project or UCSC Genome Browser, including **bedGraph**, **GTF**, **PSL**, **BED**, **bigBed**, **WIG**, **bigGenePred**, **bigNarrowPeak**, **bigMaf**, **bigChain**, **bigPsl**, **barChart**, **bigBarChart**, **interact**, **bigInteract**, **bigWig**, **BAM**, **CRAM**, **VCF**, **MAF**, **BED detail**, **Personal Genome SNP**, **broadPeak**, **narrowPeak**, and **microarray** (BED15). GFF and GTF files *must* be tab-delimited rather than space-delimited to display correctly. Chromosome references must be of the form *chrN* (the parsing of chromosome names *is* case-sensitive). You may include more than one data set in your annotation file; these need not be in the same format.

## **Step 2.** Define the Genome Browser display characteristics

Add one or more optional **browser lines** to the beginning of your formatted data file to configure the overall display of the Genome Browser when it initially shows your annotation data. Browser lines allow you to configure such things as the genome position that the Genome Browser will initially open to, the width of the display, and the configuration of the other annotation tracks that are shown (or hidden) in the initial display. NOTE: If the browser position is not explicitly set in the annotation file, the initial display will default to the position setting most recently used by the user.



About Browse DDD (UK)

Search DECIPHER



Help Join Log in

# WAC 10:28532493-28623112

Forward strand gene: WW domain containing adaptor with coiled-coil

Also known as: **MGC10753, BM-016, PRO1741, FLJ31290, Wwp4, ENSG00000095787**

**Function:** "Acts as a linker between gene transcription and histone H2B monoubiquitination at 'Lys-120' (H2BK120ub1) (PubMed:21329877). Interacts with the RNA polymerase II transcriptional machinery via its WW domain and with RNF20-RNF40 via its coiled coil region, thereby linking and ..." [Show more >](#) Source: [UniProt](#)

DECIPHER holds 29 sequence variants in this gene, in 29 open-access patients

Overview Matching patient variants 63 Matching DDD research variants 0 Phenotypes Phenotype browser Transcripts 27 Browser

Clinical Protein / Genomic

Feedback

## Gene/disease association

OMIM  
615049

Morbid  
• Desanto-Shinawi syndrome (Autosomal dominant)

GeneReviews  
• WAC-Related Intellectual Disability

Gene2Phenotype ?  
• Monoallelic Loss of function: Desanto-Shinawi Syndrome (DD, Confirmed)

ClinGen gene/disease ?

## Predictive scores

pLI	1.00	
%HI	9.63	
LOEUF	0.08	
sHet	0.303	

## Search databases

- [PubMed](#)
- [Gene Tests](#)
- [Genomics England PanelApp ?](#)
- [LSDB](#)
- [Entries in DECIPHER for this gene](#)



ここに入力して検索

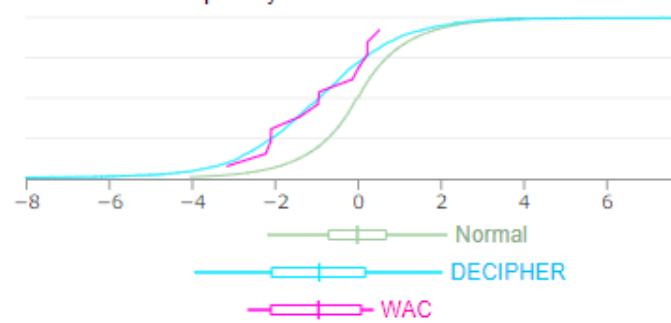


17°C にわか雨 A 11:32 2021/10/27

16

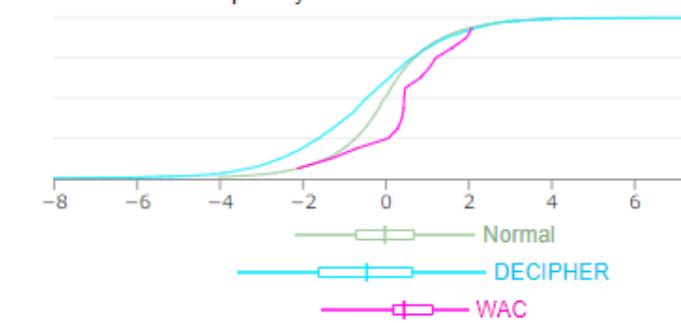
Height (SD) n = 12

Cumulative frequency



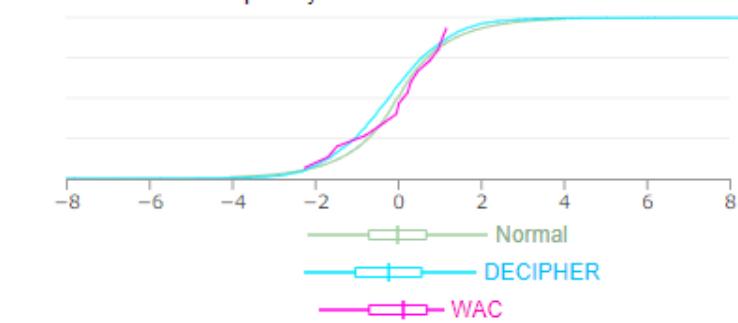
Weight (SD) n = 15

Cumulative frequency



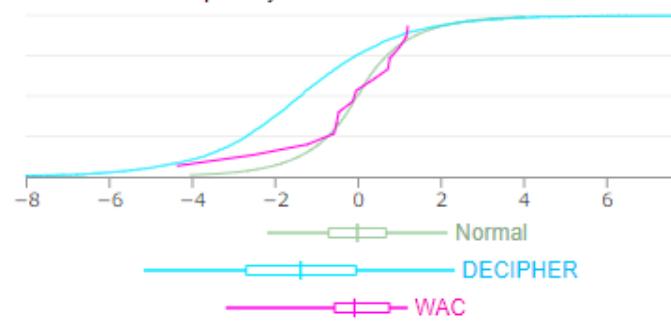
Birth Weight (SD) n = 14

Cumulative frequency



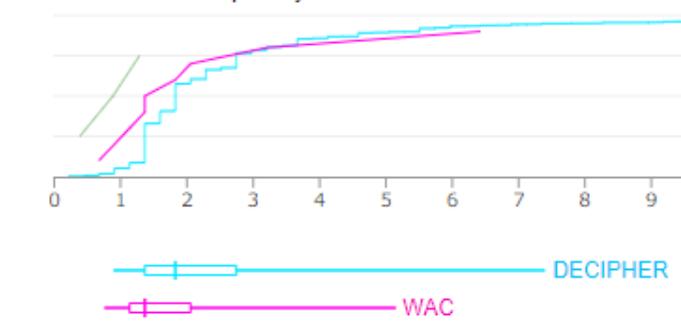
Occipital Frontal Circumference (SD) n = 14

Cumulative frequency



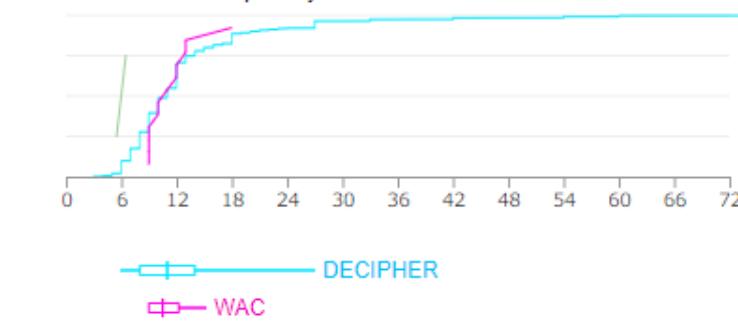
Social Smile (months) n = 9

Cumulative frequency



Sat unaided (months) n = 12

Cumulative frequency



Walked Unaided (months) n = 14

Cumulative frequency



First Words (months) n = 12

Cumulative frequency



Sex ratio n = 23

DECIPHER

Female: 2490 (46%)

Male: 2885 (54%)

WAC

Female: 11 (48%)

Male: 12 (52%)

Feedback



Patient	Sex	Transcript / Location (GRCh38)	Consequence	Pathogenicity / Contribution	Inheritance / Genotype	Phenotypes
259380	46XX	WAC ENST00000354911.9 c.498-2A>G 10:28590718	splice_acceptor_variant	Pathogenic Full <b>PM2</b> <b>PVS1</b> <b>PS2</b>	De novo Heterozygous	Anisocoria; Drooling; Global developmental delay; Hypermetropia; Neonatal hypotonia; Recurrent respiratory infections; Thoracic scoliosis; Ventricular septal defect
261751	46XX	WAC ENST00000354911.9 c.1852C>T 10:28617762	stop_gained p.Gln618Ter (618 Q/*)	Likely pathogenic Full	De novo Heterozygous	Ankle flexion contracture; Autism; Intellectual disability; Low posterior hairline
266225	46XY	WAC ENST00000354911.9 c.1838G>C 10:28617748	missense_variant p.Arg613Pro (613 R/P)	Likely pathogenic Full	De novo Heterozygous	Constipation; Deeply set eye; Everted lower lip vermilion; Global developmental delay; Wide mouth
266820	46XY	WAC ENST00000354911.9 c.1757T>G 10:28617667	stop_gained p.Leu586Ter (586 L/*)	Pathogenic Full	De novo Heterozygous	Asymmetry of the ears; Intellectual disability, moderate; Plagiocephaly
266962	46XY	WAC ENST00000354911.9 c.1664_1665insTG 10:28616280	frameshift_variant p.Leu555PhefsTer6 (555 L/FX)	Pathogenic Full	De novo Heterozygous	Abnormality of the palmar creases; Broad forehead; Chronic constipation; Delayed closure of the anterior fontanelle; Delayed gross motor development; Delayed speech and language development; Depressed nasal bridge; Hypoplastic areola; Pineal cyst
272788	46XY	WAC ENST00000424454.5 c.80_81insG 10:28534235	frameshift_variant p.Thr28AspfsTer24 (27 V/VX)	Uncertain None	Unknown Heterozygous	Abnormality of neuronal migration; Agenesis of corpus callosum; Capillary hemangioma; Cerebellar dysplasia; Large cafe-au-lait macules with irregular margins;

Feedback



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20°C 晴れのちくもり 16:57  
2021/10/28

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WAC - DECIPHER v11.7 https://www.deciphergenomics.org/gene/WAC/patient-overlap/cnvs

# WAC 10:28532493-28623112

Forward strand gene: WW domain containing adaptor with coiled-coil

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**Function:** "Acts as a linker between gene transcription and histone H2B monoubiquitination at 'Lys-120' (H2BK120ub1) (PubMed:21329877). Interacts with the RNA polymerase II transcriptional machinery via its WW domain and with RNF20-RNF40 via its coiled coil region, thereby linking and ..." [Show more >](#) Source: [UniProt](#)

DECIPHER holds 29 sequence variants in this gene, in 29 open-access patients

Overview Matching patient variants **63** Matching DDD research variants **0** Phenotypes Phenotype browser Transcripts **27** Browser

Sequence variants **29** Copy-number variants **32** Other variants **2**

Feedback

Patients with copy-number variants matching this gene

**Filters:** Sex ▾ Size ▾ Pathogenicity ▾ Contribution ▾ Gain/Loss ▾ Genotype ▾ Inheritance ▾ Phenotypes ▾ Enter text...

**Gain/Loss**

- Gain: 34%
- Loss: 66%

**Inheritance**

- De novo: 56%
- Inherited from normal parent: 3%
- Unknown: 41%

**Size**

- 0.01-0.1 Mb: 3%
- 0.1-1 Mb: 25%
- 1-10 Mb: 47%
- 10-100 Mb: 25%

**Phenotypes present in multiple matching patients**

- 9 Intellectual disability
- 6 Delayed speech and language development

17°C にわか雨 11:33 2021/10/27

Patient	Sex	Size	Type	Pathogenicity / Contribution	Inheritance / Genotype	Phenotypes
2475	46XX	4.02 Mb	Deletion	De novo Heterozygous	Blepharophimosis; Delayed speech and language development; Hypotonia; Intellectual disability; Patent ductus arteriosus; Short stature; Strabismus	<a href="#">✉</a>
3807	46XY	36.64 Mb	Duplication	De novo Heterozygous	Flexion contracture; Lower limb peromelia; Micrognathia	<a href="#">✉</a>
248533	46XX	990.50 kb	Deletion	De novo Heterozygous	Abnormal dermatoglyphics; Abnormality of the helix; Aplasia/Hypoplasia involving the metacarpal bones; Autism; Coarse hair; Flat occiput; Intellectual disability; Microtia; Patent ductus arteriosus; Scoliosis; Spasticity; Strabismus	<a href="#">✉</a>
249112	46XY	118.91 kb	Deletion	Unknown Heterozygous	Abnormality of the gingiva; Abnormality of the upper respiratory tract; Bifid tongue; Broad foot; Broad hallux; Depressed nasal ridge; Frontal bossing; Hoarse voice; Hypertelorism; Intellectual disability; Long palpebral fissure; Low posterior hairline; Pes cavus; Short foot; Short nose; Synophrys; Thick eyebrow; Wide mouth	<a href="#">✉</a>
249200	46XX	2.52 Mb	Deletion	De novo Heterozygous	Downslanted palpebral fissures; Intellectual disability; Short neck; Short nose	<a href="#">✉</a>
249958	46XY	6.59 Mb	Deletion	De novo Heterozygous		<a href="#">✉</a>
253246	46XY	769.54 kb	Duplication	Inherited from normal parent		<a href="#">✉</a>

Feedback ▾



About Browse DDD (UK)

Search DECIPHER



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[Overview](#)[Matching patient variants 63](#)[Matching DDD research variants 0](#)[Phenotypes](#)[Phenotype browser](#)[Transcripts 27](#)[Browser](#)[Clinical](#)[Protein / Genomic](#)[Feedback](#)

## Gene/disease association

[OMIM](#)[615049](#)[Morbid](#)

- [Desanto-Shinawi syndrome](#) (Autosomal dominant)

[GeneReviews](#)

- [WAC-Related Intellectual Disability](#)

[Gene2Phenotype](#) 

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[ClinGen gene/disease](#) 

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- [LSDB](#)
- [Entries in DECIPHER for this gene](#)



ここに入力して検索

17°C にわか雨 A 11:32  
2021/10/27

16

# pLIスコアについて

probability of loss-of-function intolerance (pLI) (機能喪失非許容スコア)

Genome Aggregation Database (gnomAD)において、一般集団において予測されるバリエントの自然発生割合に対して、実際に観察されるLoFバリエントの割合が隔たっている場合、LoF不耐症というバイアスが考えられる。

より大きな値(1に近い)を持つ遺伝子は、突然変異に対してより不寛容

pLIスコアが高い遺伝子( $pLI \geq 0.9$ ) $\rightarrow$ LoF不耐性 $\rightarrow$ 片アリルの機能喪失で表現型に影響

pLIスコアが低い遺伝子( $pLI \leq 0.1$ ) $\rightarrow$ LoF耐性 $\rightarrow$ 片アリルの機能喪失は表現型に影響しない

# その他のスコアについて

## pHI(または%HI):

高いランク(例えば0~10%) → LoF不耐性

低いランク(例えば90~100%) → LoF耐性

## LOEUF:

より小さい値(ゼロに近い)の遺伝子は、突然変異に対してより不寛容

## sHet:

より大きな値(1に近い)を持つ遺伝子は、突然変異に対してより不寛容

gnomAD

gnomAD browser

gnomAD v2.1.1

Search

About News Downloads Terms Publications Feedback Changelog Help

# gnomAD



Genome Aggregation Database

gnomAD v2.1.1

Search by gene, region, or variant

Or

- Find co-occurrence of two variants
- Download gnomAD data
- Read gnomAD publications

Please note that gnomAD v2.1.1 and v3.1.2 have substantially different but overlapping sample compositions and are on different genome builds. For more information, see "Should I switch to the latest version of gnomAD?"

Examples

ここに入力して検索

21°C 晴れのちくもり 12:08  
2021/10/28

**WAC** WW domain containing adaptor with coiled-coil

Dataset gnomAD v2.1.1 ▾ gnomAD SVs v2.1 ▾

Genome build GRCh37 / hg19

**Ensembl gene ID** ENSG00000095787.17

**Ensembl canonical transcript** ? ENST00000354911.4

**Other transcripts** ENST00000345541.6, ENST00000442148.1, and 17 more

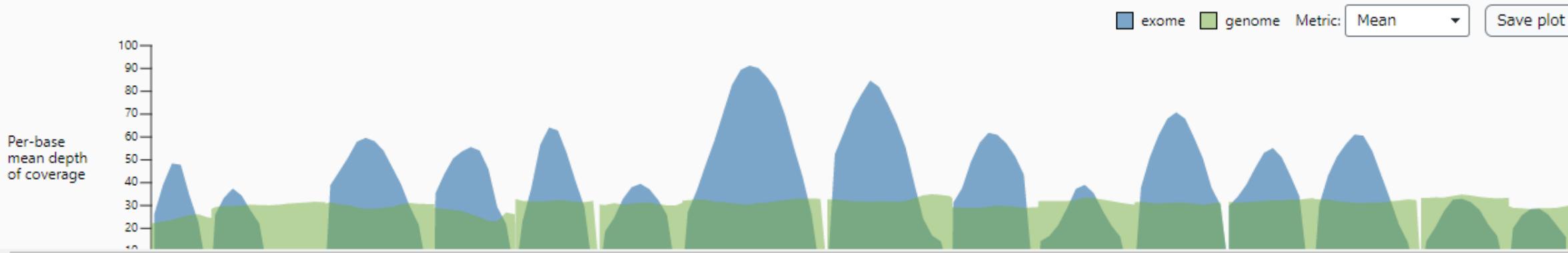
Region 10:28821422-28912041

**External resources** Ensembl, UCSC Browser, and more

## Constraint ?

Category	Expected SNVs	Observed SNVs	Constraint metrics
Synonymous	127	133	Z = -0.42 o/e = 1.05 (0.91 - 1.21) 0  1
Missense	340.5	262	Z = 1.51 o/e = 0.77 (0.69 - 0.85) 0  1
pLoF	35.6	0	pLI = 1 o/e = 0 (0 - 0.08) 0  1

Constraint metrics based on Ensembl canonical transcript ([ENST00000354911.4](#)).



### ClinVar variants

Pathogenic / likely pathogenic only  Uncertain significance / conflicting only  Benign / likely benign only  Other only

pLoF only    Missense / Inframe indel only    Synonymous only    Other only

[Expand to all variants](#)

Only show ClinVar variants that are in gnomAD



Data displayed here is from ClinVar's 2021年10月2日 release.

## gnomAD variants

gnomAD v2.1.1  
variants (7)

### [Viewing in table](#)

28,822,434      28,823,161      28,872,258      28,878,790      28,884,710      28,897,157      28,899,725      28,900,675      28,903,620      28,906,553      28,908,601

pLoF  only    Missense / Inframe indel  only    Synonymous  only    Other  only    Exomes  Genomes  SNVs  Indels    Filtered variants

## Search variant table

[Export variants to CSV](#)

## Configure table

**Note** Only variants located in or within 75 base pairs of a coding exon are shown here. To see variants in UTRs or introns, use the [region view](#).

The table below shows the HGVS consequence and VEP annotation for each variant's most severe consequence across all transcripts in this gene. Cases where the most severe consequence occurs in a non-canonical transcript are denoted with †. To see consequences in a specific transcript, use the [transcript view](#).

Overview Matching patient variants 63 Matching DDD research variants 0 Phenotypes Phenotype browser Transcripts 27 Browser

Clinical Protein / Genomic

## Gene/disease association

### OMIM

615049

### Morbid

- Desanto-Shinawi syndrome (Autosomal dominant)

### GeneReviews

- WAC-Related Intellectual Disability

### Gene2Phenotype

- Monoallelic Loss of function: Desanto-Shinawi Syndrome (DD, Confirmed)

### ClinGen gene/disease

#### ClinGen DS

- Haploinsufficiency: Sufficient evidence for dosage pathogenicity (3)
- Triplosensitivity: No evidence for dosage pathogenicity (0)

### GenCC

Definitive:

1

Strong:

2

(Assessed by Invitae, Illumina, TGMII|G2P, with respect to Autosomal dominant inheritance)

## Quantitative data

This data is taken from open-access sequence variants in DECIPHER that have been assessed by the depositing centre as being pathogenic or likely pathogenic. Data from the WAC

## Predictive scores

pLI	1.00	?
%HI	9.63	?
LOEUF	0.08	?
sHet	0.303	?

## Search databases

- PubMed
- Gene Tests
- Genomics England PanelApp
- LSDB
- Entries in DECIPHER for this gene



ClinGen Dosage Sensitivity Curation Page

WAC

### Curation Status: Complete

id: ISCA-547

Date last evaluated: 2018-02-28

Issue Type: ClinGen Gene Curation

Gene type: protein-coding

ClinGen: Search for information about WAC at [clinicalgenome.org](http://clinicalgenome.org)

Entrez Gene: <https://www.ncbi.nlm.nih.gov/gene/5132>

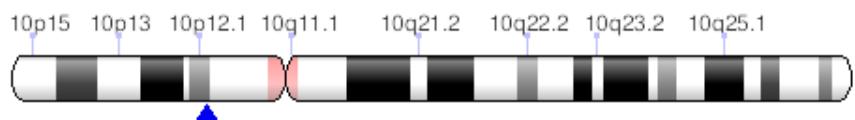
OMIM: <https://www.omim.org/entry/615049?search=WAC&highlight=wac>

Gene Reviews: <https://www.ncbi.nlm.nih.gov/books/NBK465012>

ClinGen Haploinsufficiency Score: 3

ClinGen Triplosensitivity Score: 0

ExAC pl | score: 1.0



## Location Information

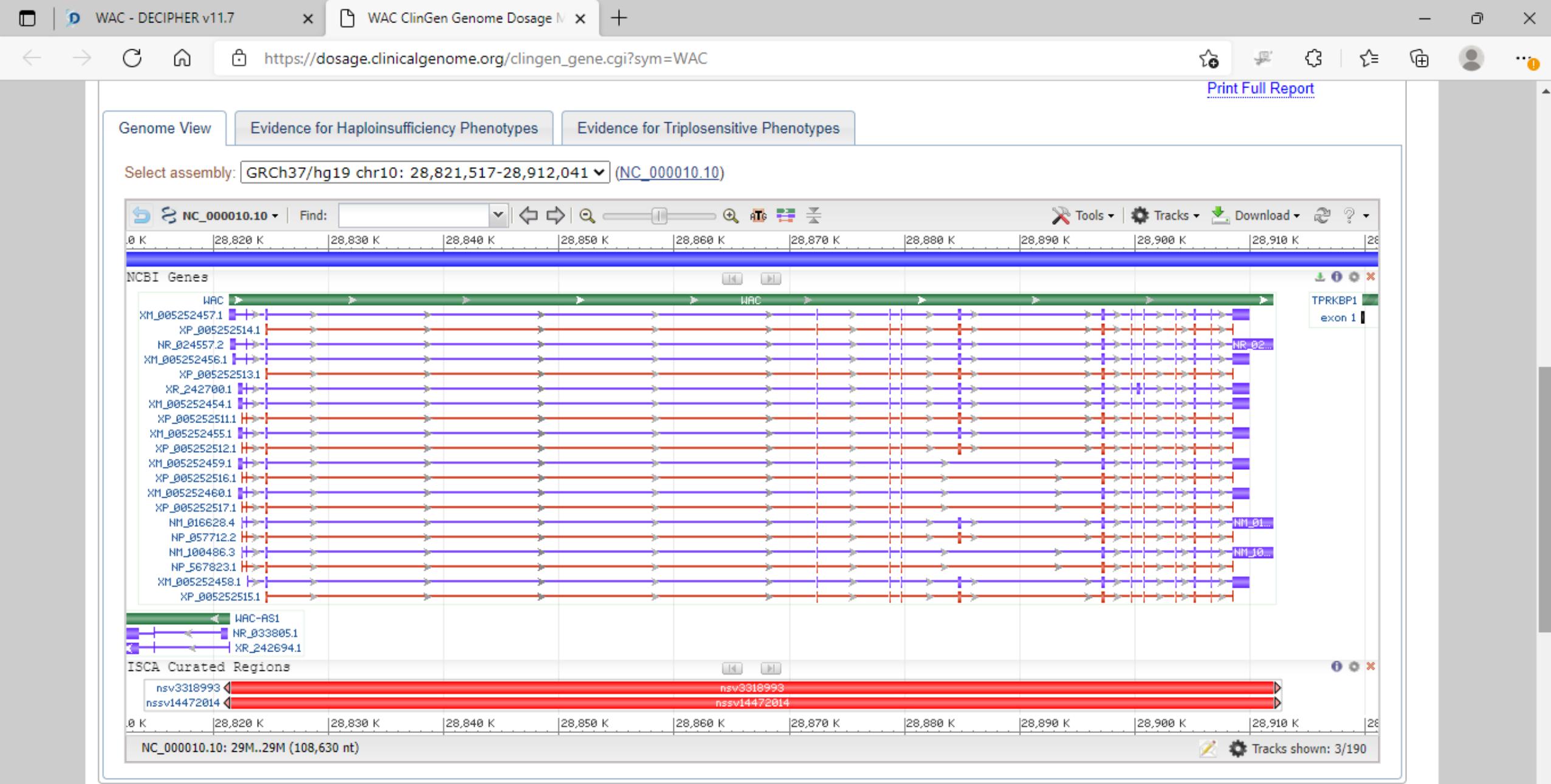
10p12.1|10p12.1-p11.2

GRCh37/hg19 chr10: 28,821,517-28,912,041

View: NCBI | Ensembl | UCSC

GRCh38/hg38 chr10: 28,532,772-28,623,112

View: NCBI | Ensembl | UCSC



ここに入力して検索



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2021/10/28

WAC - DECIPHER v11.7 WAC ClinGen Genome Dosage M +

https://dosage.clinicalgenome.org/clingen\_gene.cgi?sym=WAC

Print Full Report

Genome View Evidence for Haploinsufficiency Phenotypes Evidence for Triplosensitive Phenotypes

Haploinsufficiency score: 3

Strength of Evidence (Disclaimer): Sufficient evidence for dosage pathogenicity

Haploinsufficiency Phenotype: [DESGANTO-SHINAWI SYNDROME](#); [DESSH](#)

Evidence for haploinsufficiency phenotype

PubMed ID	Description
<a href="#">26757981</a>	Lugtenberg et al. (2017) identified 10 individuals with de novo loss of function variants in WAC (4 nonsense, 1 exon del, 5 frameshift) in a cohort of 2300 individuals with unexplained intellectual disability (ID) using whole exome sequencing (WES) and subsequent targeted testing. All but one individual had mild-to-severe ID accompanied by language and motor delay. In addition, individuals showed a variety of neurological problems including hypotonia (6/9), with remarkable manifestation in the oral region resulting in dysarthria, and behavioral problems (10/10). The latter recurrently included autism (4/9), anxiety (3/10), concentration disorder (4/10) and/or sleep disturbance (6/10). Other overlapping features consisted of unexplained reduced vision (3/9) and respiratory problems (7/9) with recurrent respiratory infections reported most often (5/7). Notably, all individuals had overlapping facial dysmorphisms consisting of a square shape of the face, deep set eyes, long palpebral fissures, broad mouth and broad chin. NOTE: One individual (previously reported by De Ligt 2012) also carried a de novo mutation in the MIB1 gene (autosomal dominant for Left ventricular noncompaction 7, OMIM:615092), and it has been reported twice in ExAC. Moreover, one missense and one nonsense mutation in MIB1 were identified previously and segregated each in two large dominant families with cardiomyopathy, but without ID. Therefore, its contribution as a potential modifier of the more severe phenotype is unlikely.
<a href="#">26264232</a>	DeSanto et al. (2015) used WES and identified 6 patients with idiopathic ID and de novo WAC loss of function mutations (3 nonsense, 2 frameshift). Clinical findings included developmental delay (6/6), hypotonia (6/6), behavioral problems (5/6), eye abnormalities (5/6), constipation (5/6), feeding difficulties (4/6), seizures (2/6) and sleep problems (2/6). All patients exhibited common dysmorphic features, including broad/prominent forehead, synophrys and/or bushy eyebrows, depressed nasal bridge, and bulbous nasal tip. Posteriorly rotated ears, hirsutism, deep-set eyes, thin upper lip, inverted nipples, hearing loss and branchial cleft anomalies were also noted. Germline mosaicism has been suggested in genotypically normal parents of affected siblings carrying nonsense variants (patient 1 & 2). NOTE: Patient 4 also has a de novo missense variant in the MED12 gene (X-linked recessive) that is conserved in vertebrates but is predicted to be benign by SIFT and PolyPhen.
<a href="#">28263302</a>	Yuen et al (2017) used whole genome sequencing (WGS) on 5,205 samples from families with ASD and identified 18 new candidate ASD-risk genes including WAC. 1 individual had a de novo frameshift mutation and a phenotype including speech language impairment, hyperactivity, sleep issues, shallow mid facial area, fairly prominent eyelids, hypertelorism, slightly prominent forehead, mildly broad great toe, other toes look short relative to the feet, mild low to mid frequency hearing loss, and EEG - Focal epileptiform discharge in left temporal region.
<a href="#">26795593</a>	Helbig et al. (2016) used WES and subsequent targeted sequencing of 1131 patients with or without epilepsy, identifying a de novo nonsense mutation in a patient with infan-

https://dosage.clinicalgenome.org/clingen\_gene.cgi?sym=WAC#loss\_evidence

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2021/10/28



## ClinGen Dosage Sensitivity Map

The Clinical Genome Resource (ClinGen) consortium is curating genes and regions of the genome to assess whether there is evidence to support that these genes/regions are dosage sensitive and should be targeted on a cytogenomic array.

All data are shown in GRCh37 and GRCh38 coordinates.

New! The ClinGen Dosage Sensitivity curations and downloads that are available at this site are now also available at [www.clinicalgenome.org](http://www.clinicalgenome.org). Click on the button to access Dosage Sensitivity in the context of ClinGen's other curated information, including Gene-Disease Validity and Clinical Actionability.

[See New Dosage Map](#)

**NOTICE: On or about January 1st, 2022, all Dosage Sensitivity Map requests will be redirected to the equivalent pages at [www.clinicalgenome.org](http://www.clinicalgenome.org) as described above.**

### Search By Gene Name

Symbol:

Or click on the following examples: [ZEB2](#), [PTEN](#), [MAPT](#)

### Search By Location (GRCh37, GRCh38)

GRCh37:  GRCh38:

Location:

Examples: [chr2:44,000,000-45,500,000](#), [2p21-2p16.2](#)

### Links

[ClinGen Home Page](#)

[Help with this site](#)

[FAQ](#)

[Contact Us](#)

[Curation of Recurrent CNVs](#)

[Curation of the ACMG 59 Genes](#)

[FTP](#)



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15

WAC - DECIPHER v11.7 https://www.deciphergenomics.org/gene/WAC/overview/clinical-info

Overview Matching patient variants 63 Matching DDD research variants 0 Phenotypes Phenotype browser Transcripts 27 Browser

Clinical Protein / Genomic

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(Assessed by Invitae, Illumina, TGMI|G2P, with respect to Autosomal dominant inheritance)

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Feedback



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2021/10/28





 DECIPHER  
GRCh38

About Browse ▾ My Patients DDD (UK)

Search DECRYPTER



Help  0 Toshiyuki Yamamoto ▾

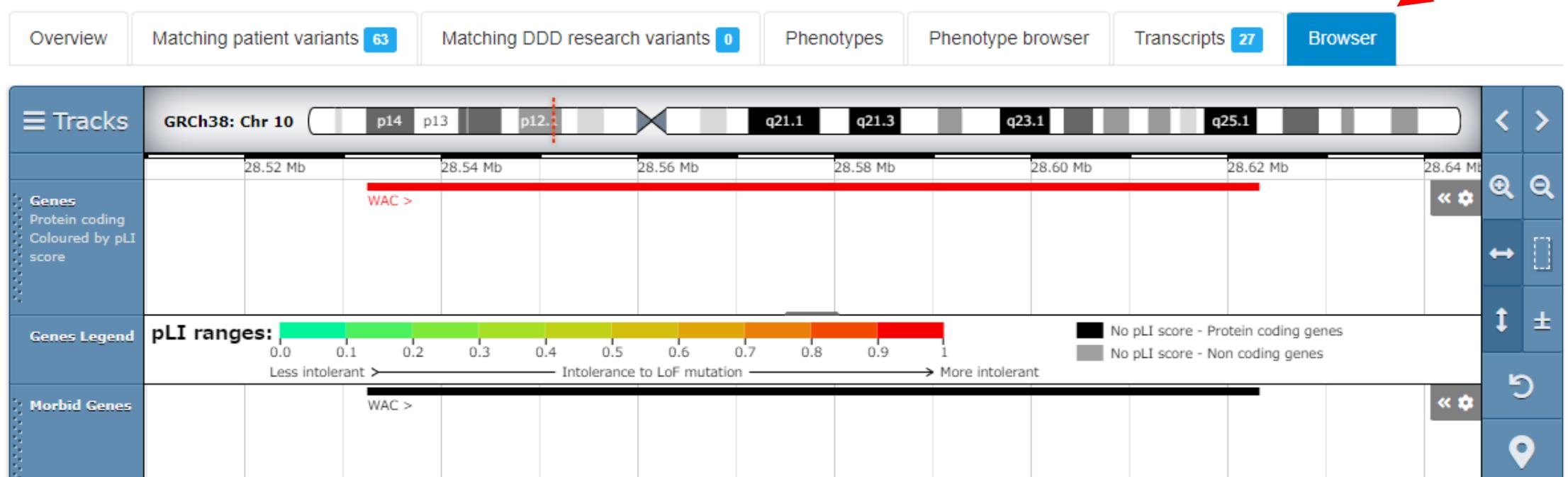
WAC 10:28532493-28623112

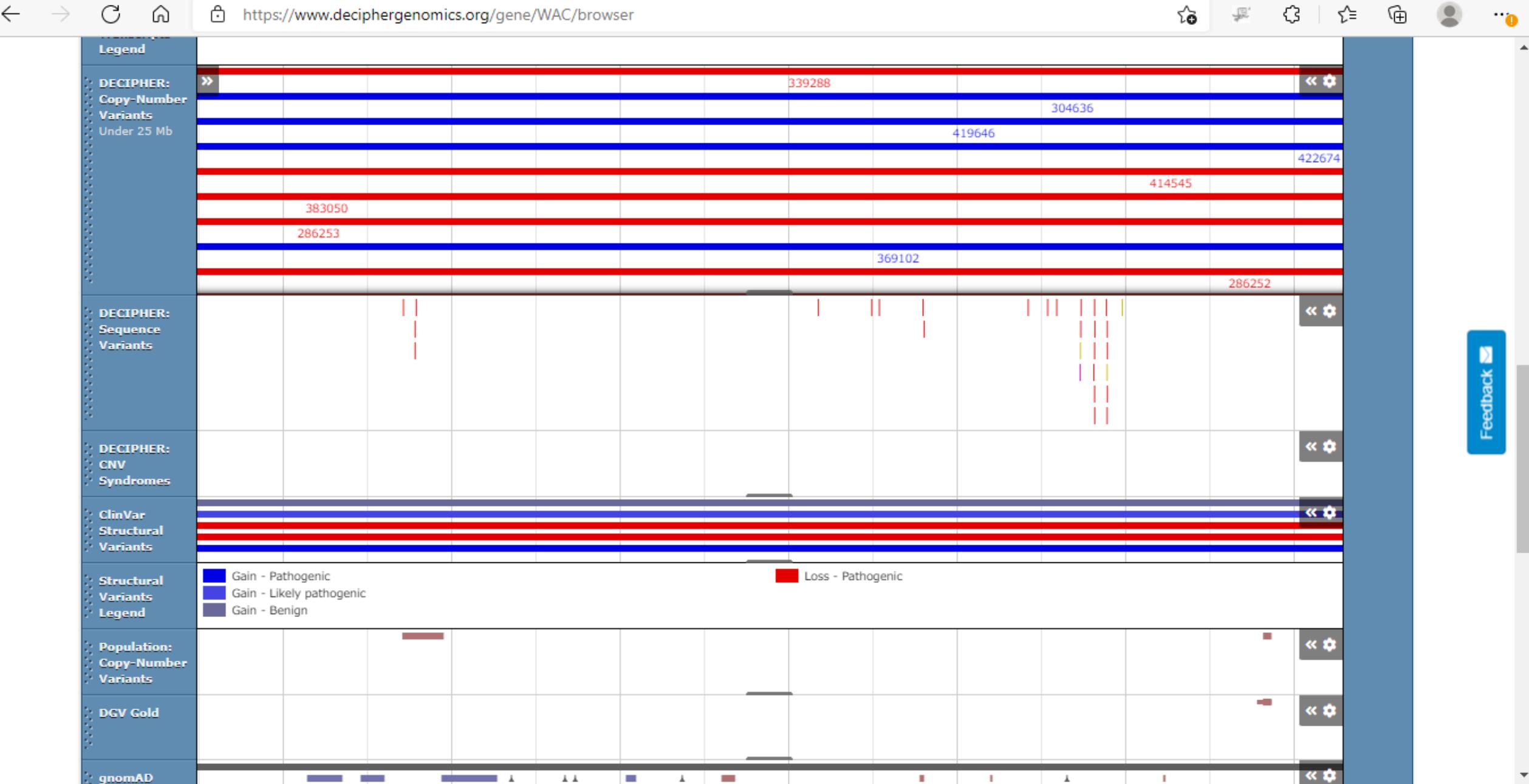
Forward strand gene: WW domain containing adaptor with coiled-coil

Also known as: MGC10753, BM-016, PRO1741, FLJ31290, Wwp4, ENSG00000095787

**Function:** "Acts as a linker between gene transcription and histone H2B monoubiquitination at 'Lys-120' (H2BK120ub1) (PubMed:21329877). Interacts with the RNA polymerase II transcriptional machinery via its WW domain and with RNF20-RNF40 via its coiled coil region, thereby linking and ..." [Show more >>](#) Source: [UniProt](#)

DECIPHER holds 29 sequence variants in this gene, in 29 open-access patients







https://www.deciphergenomics.org/patient/28678/genotype/60758/browser

Add a variant

Variant class \* -select-

Cancel Reset Save

Deletion 7:4334387-5825220

Browser Genes 27 Variant plot Matching patient variants 173 Matching CNV syndromes 0 Pathogenicity evidence

Tracks GRCh38: Chr 7 p21.3 p14.3 p14.1 q21.11 q22.1 q31.1 q33 q34 q35

Genes Protein coding Coloured by pLI score

Some features are currently hidden, resize to see all

AP5Z1 > RBAK-RBAKDN > WIPI2 > TNRC18 < ACTB < RNF216 OCM > PMS2 CCZ1 > AIMP2 > RSPH10B EIF2AK1

pLI ranges: 0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 Less intolerant Intolerance to LoF mutation More intolerant

No pLI score - Protein coding genes No pLI score - Non coding genes

Morbid Genes AP5Z1 > WIPI2 > < ACTB < RNF216 < PMS2 AIMP2 > EIF2AK1

Feedback

https://www.deciphergenomics.org/patient/286782/genotype/60758/browser

# DECIPHER

GRCh38

Projects / TWM / Patient 286782

Overview Images 0 Genotype 1

Variants: 1 to 1 of 1

Location	Type	Gene
7 4334387 - 5825220	Deletion	27
GRCh38	Mean ratio: -1	
	Deposited 2014-07-02	

Deletion 7:4334387-5825220

Browser Genes 27 Variant plot

Tracks GRCh38: Chr 7 p21.3

Variant class \* Sequence Variant

Assembly \* -select-

HGVS code

Verify

Chromosome \* -select-

Genomic start \*

Ref sequence \*

Alt sequence \*

Gene/Transcript -select-

Check this box if your variant is upstream/downstream/intergenic

Genotype \* -select-

Inheritance \* Unknown

Pathogenicity -select-

Help Toshiyuki Yamamoto

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Show more

Add a variant

# DECIPHER

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Help

Toshiyuki Yamamoto

## Sequence Variant deposition help

### Depositing in GRCh37/hg19

If providing coordinates in GRCh37/hg19, please press the "Liftover to GRCh38 button". DECIPHER will attempt to remap the variant from GRCh37/hg19 to GRCh38 using an algorithm based on the [UCSC LiftOver tool](#), with at least 80% of bases being remapped.

### Depositing by HGVS code (GRCh38 only)

DECIPHER will try to automatically interpret the following types of HGVS codes:

#### Transcript-based

[NM\\_001032221.3:c.175G>A](#)

[NM\\_005921.1:c.2072\\_2075del](#)

[ENST00000541395:c.197dupA](#)

#### Gene-based

[ARID1B:c.123\\_124del](#)

#### Chromosome-based

[chr2:g.240961655T>C](#)

[NC\\_000011.9:g.111959693T>G](#)

If you have an HGVS code similar to the above examples, when you enter it and

### Constraints

To deposit a sequence variant to DECIPHER, reference and alternate sequences must not be longer than 100 bp

### Depositing by genomic coordinates

#### Examples:

Mutation of C>G at position 103969467  
in chromosome 7

Chromosome: [7](#)  
Genomic start: [103969467](#)  
Ref sequence: [C](#)  
Alt sequence: [G](#)

Deletion of TTT from position  
110324657 (TTT>.)

Genomic start: [110324657](#)  
Ref sequence: [TTT](#)  
Alt sequence: [.](#)

Insertion of GG after C from position  
110324657

Genomic start: [110324657](#)  
Ref sequence: [C](#)  
Alt sequence: [CGG](#)

## [Decipher-announce] DECIPHER November 2021 Update

1件のメッセージ

Julia Foreman <jf11@sanger.ac.uk>

2021年11月5日 23:29

To: "decipher-announce@sanger.ac.uk" <decipher-announce@sanger.ac.uk>

Dear All,

Greetings from sunny, chilly, autumnal East Anglia.

In this update:

- Wellcome funding and move to EBI
- DECIPHER v11.8 Released
  - New sequence variant and protein pages
  - Clinvar annotation tab
  - Deposition of mosaicism by tissue, for mosaic UPD variants
- Optional DECIPHER ClinVar submission

## Wellcome funding and move to EBI

=====

We are pleased to announce that DECIPHER has been awarded a new Wellcome grant to continue its work through to 2025.

Key goals include better support for variants in the non-coding genome, helping users find relevant functional evidence, and building models to link genes and disorders with phenotypes. The grant will allow us to keep DECIPHER up to date with best practice and emerging opportunities in clinical interpretation as the landscape evolves.

The grant also provides for a transition of DECIPHER's hosting and development from the Wellcome Sanger Institute (where DECIPHER began and has been based for the last 17 years) to the European Bioinformatics Institute (EMBL-EBI; <https://www.ebi.ac.uk>), which runs Ensembl and its Variant Effect Predictor (VEP), Gene2Phenotype and many other resources which are critical to DECIPHER's work. It is intended that the team will move in April 2022. Co-PI Helen Firth will remain the clinical lead; Matt Hurles will step back as co-PI but will remain involved as a collaborator and Fiona Cunningham, who leads EBI's Genome Interpretation Team, will join as co-PI. Both institutes are committed to a smooth transition and the migration will not involve any changes to the address (URL), the appearance, or the functionality of DECIPHER.

The Deciphering Developmental Disorders (DDD) project (<https://www.ddduk.org>), which has recruited nearly 14,000 families in the UK and Ireland, will still deliver results through DECIPHER, while the research work will remain at Sanger. We expect to provide further information on the arrangements to DECIPHER depositors closer to the time of the move.

## DECIPHER v11.8 Released

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You can also view this on the web at: <https://www.deciphergenomics.org/about/news>

It is now possible to search for information about single sequence and protein variants. DNA sequence variant search supports searching by GRCh38 location, by SPDI, HGVSc or Ensembl stable IDs, in addition to HGVSc plus HGNC gene symbol or Refseq transcript. Protein variant search supports searching by HGVSp (single letter or trigraph) plus HGNC gene symbol of Refseq transcript. Searching for sequence variants now takes you to a dedicated sequence variant page, which displays information relevant to that variant. The following page provides information on a missense variant in SPOP: <https://www.deciphergenomics.org/sequence-variant/17-49619031-C-T/patient-overlap/identical>. Searching for protein variants takes you to a dedicated protein variant page, which displays information relevant to that protein change. The following page provides information on a Arginine to Tryptophan change in PACS1: <https://www.deciphergenomics.org/protein-variant/ENSG00000175115-203-R-W/protein>

A new Clinvar annotation tab is available on patient variant, sequence variant and protein variant pages. This tab contains information about ClinVar assertions. In this example, the variant has 0, 1 and 2 star ClinVar assertions: <https://www.deciphergenomics.org/protein-variant/ENSG00000175115-203-R-W/annotation/clinvar>

It is now possible for depositors to record mosaicism by tissue, for mosaic UPD variants.

## Optional DECIPHER ClinVar submission

---

DECIPHER now supports the deposition of variant data to ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar>) to enable the greater sharing and aggregation of variant data globally. Submission is optional and the coordinator(s) of a DECIPHER project must approve ClinVar deposition before DECIPHER will deposit data to ClinVar on their behalf.

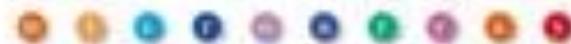
DECIPHER will only deposit variant data from openly shared patient records, for which explicit patient consent for open sharing has been recorded in DECIPHER. Only openly shared data will be included in the submission. DECIPHER will deposit variant information and high level phenotype information, in addition to a link to the relevant DECIPHER patient record.

If you are interested in DECIPHER submitting the openly consented data in your project to ClinVar, please speak with the coordinator(s) of the project at your centre and/or contact us at [contact@deciphergenomics.org](mailto:contact@deciphergenomics.org)

# まとめ

1. 解析によって明らかになったゲノムコピー数多型(CNV)が表現型に関連しているかどうか検索する具体的な方法について解説した。
2. UCSCゲノムブラウザでCNVの領域を表示させ、①その領域内に位置する遺伝子を検索する方法、②UCSCゲノムブラウザでDECIPHERに登録されているCNVを閲覧し、③表現型との関連を調べ、④連携されている他のデータベースをも閲覧する方法、そして⑤DECIPHERにCNVを登録する方法などについて解説した。
3. CNVの解釈に留まらず、論文発表や多施設共同研究に発展させる方法についても解説した。

臨床遺伝に関わる人のための  
**マイクロアレイ  
染色体検査**



●山本俊至

東京女子医科大学 医生基幹学部 教授



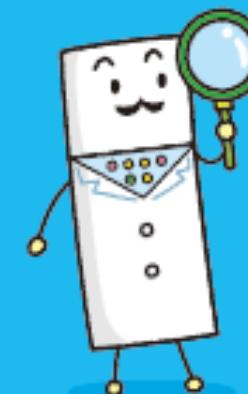
Chromosomal  
Microarray  
Testing for  
Medical Geneticists

診断と治療社

Prof. 山本の  
**マイクロアレイ  
染色体検査入門**

山本 俊至 [著]

東京女子医科大学ゲノム診療科



診断と治療社

