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

マイクロアレイ染色体検査解釈 ハンズオンウェビナー

初級編　解説資料 症例１

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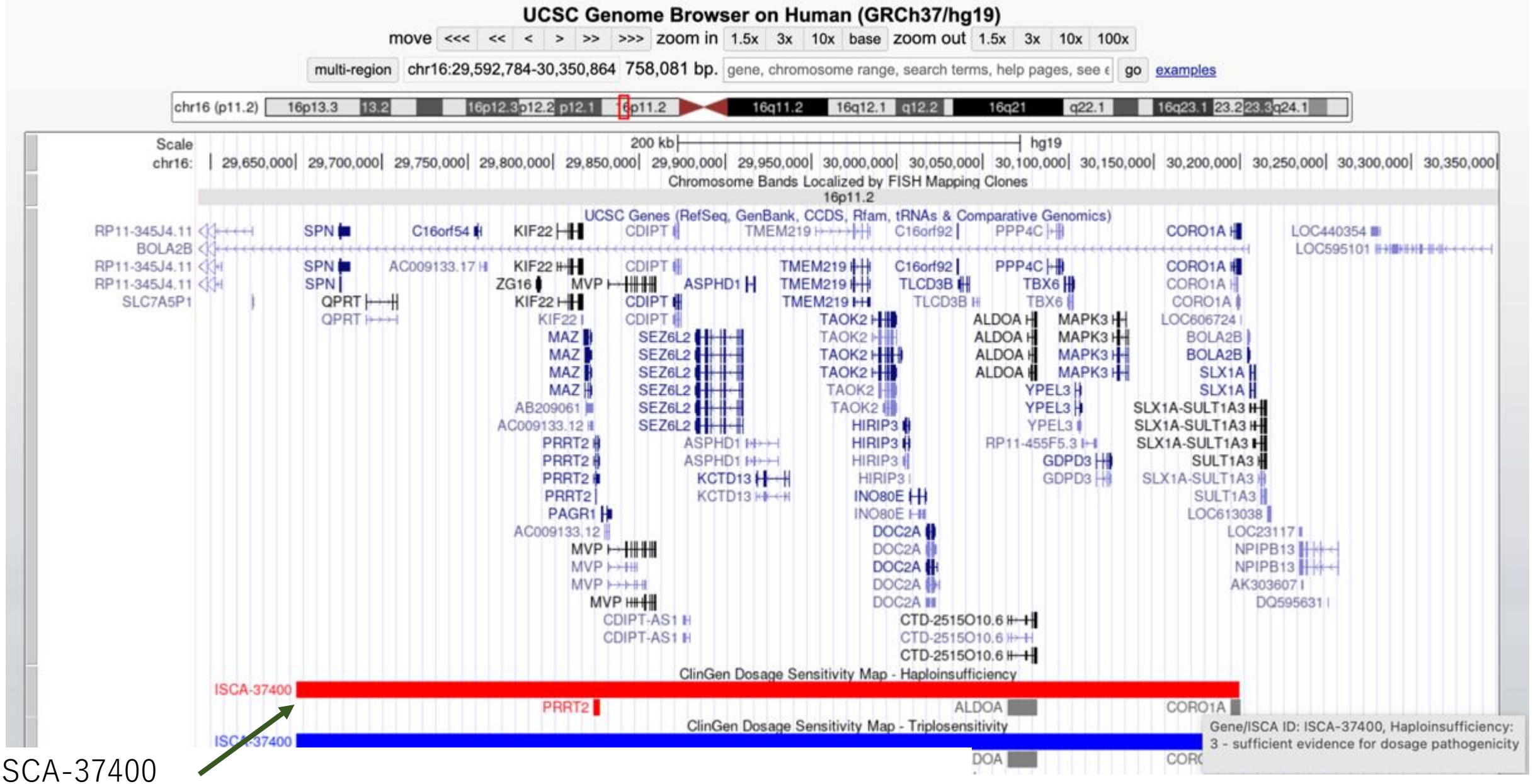
症例1解説

- 12歳男児、知的障害
- 【CNV】chr16:29,592,784-30,350,864 16p11.2
- 758kb deletion, log2ratio=-0.89 [Loss]
- *追加質問：両親の表現型はない。推測される遺伝性について述べよ



ISCA-37400
16p11.2 recurrent region (proximal, BP4-BP5) (includes TBX6)
Haploinsufficiency score 3
Sufficient evidence for dosage pathogenicity

ClinGen Dosage Sensitivity Map - Haploinsufficiency (ISCA-37400)

Item: ISCA-37400
Score: 0
Position: chr16:29649997-30199852
Band: 16p11.2
Genomic Size: 549856
View DNA for this feature (hg19/Human)

ClinGen URL	https://search.clinicalgenome.org/kb/gene-dosage/region/ISCA-37400
Gene Symbol or ISCA Region Name	ISCA-37400
Gene ID or ISCA ID	16p11.2 recurrent region (proximal, BP4-BP5) (includes TBX6)
Cytoband	16p11.2
Last evaluation date	2017-02-09
Haploinsufficiency score	3
Haploinsufficiency phenotype description	Sufficient evidence for dosage pathogenicity
Associated PubMed ID 1	20301775
Associated PubMed ID 2	18184952
Associated PubMed ID 3	21841781
Associated PubMed ID 4	
Associated PubMed ID 5	
Associated PubMed ID 6	
Mondo disease ontology ID	MONDO:0012756

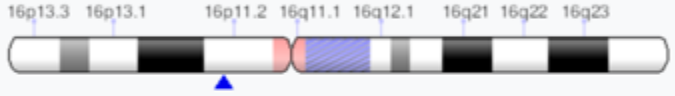
16p11.2 recurrent region (proximal, BP4-BP5) (includes TBX6)

3 Haplo Score
3 Triplo Score

Region Facts

Dosage Sensitivity Summary (Region)

Dosage ID: **ISCA-37400**



Curation Status: **Complete**

Issue Type: **Dosage Curation - Region**

Description: **The 16p11.2 region contains a cluster of low copy repeats that mediate recurrent copy number changes through non-allelic homologous recombination. This review refers to CNVs involving recurrent breakpoint (BP) regions BP4 and BP5.**

Note that genes used as landmarks are not necessarily causative of the complete phenotype(s) associated with the region.

Haploinsufficiency: **Sufficient Evidence for Haploinsufficiency (3)**

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HI score 3の
エビデンス
（論文から）

HI Disease: proximal 16p11.2 microdeletion syndrome Monarch

HI Evidence:

PUBMED: 20301775

GeneReviews article (https://www.ncbi.nlm.nih.gov/books/NBK11167/)

PUBMED: 18184952

Weiss et al. (2008) reported de novo deletions of this region at 16p11.2 in 10 patients with autism, developmental delay, and/or intellectual disability from three different large patient samples. Two deletions were inherited from

HI Evidence Comments:

Clinical features associated with 16p11.2 (TBX6) proximal region deletion may include: developmental delay; cognitive impairment; language delay; autism spectrum disorder; delayed language development (with more receptive than expressive language abilities); minor dysmorphic facial features that do not represent a consistent, recognizable pattern; neurologic issues including seizures or electroencephalogram abnormalities; obesity; psychiatric diseases; and cardiac malformations. Incomplete penetrance has been observed.

For additional references regarding the phenotype of 16p11.2 haploinsufficiency:
Hanson E, et al., 2016: PMID 25064419
Steinman KJ, et al., 2016: PMID 27410714
Zufferey F, et al., 2012: PMID 23054248

Bijlsma et al. (2009) PMID 19306953 reported deletions of this region at 16p11.2 in 14 of 4284 patients tested due to intellectual disability or congenital anomalies (0.3%). Six were de novo, six were inherited from parents with a mild or normal phenotype, and inheritance was unknown for two. Common clinical features included dysmorphic facial features, developmental delay of variable severity, and obesity. Only one patient had a formal autism diagnosis.

Proximal 16p11.2 microdeletion syndrome

- 知的障害、自閉症、発達遅滞を呈する。
- てんかん、肥満、先天性心疾患を認める例もある。
- 一般人口で0.01%、知的障害、発達遅滞例では1-1.5%と優位に多く認める。
- **不完全浸透**であり、両親由来の可能性がある。

- 不完全浸透：CNVを持っていても症状がないこともある

回答	症例1
CNV病原性(5段階評価)	Pathogenic
遺伝学的診断	Proximal 16p11.2 microdeletion syndrome
判断根拠 -使用したデータベースの結果や文献情報等より病原性や遺伝学的診断の判断　根拠を明確に（自由記載）	ClinGen Haploinsufficiency score 3 Sufficient Evidence for Haploinsufficiency (3) 知的障害の表現型からも合致している
追加質問 ＊両親の表現型はない。推測される遺伝性について述べよ	不完全浸透のCNVであり、症状には幅がある。 無症状の両親由来の可能性があり、次子再発率に注意が必要である。