

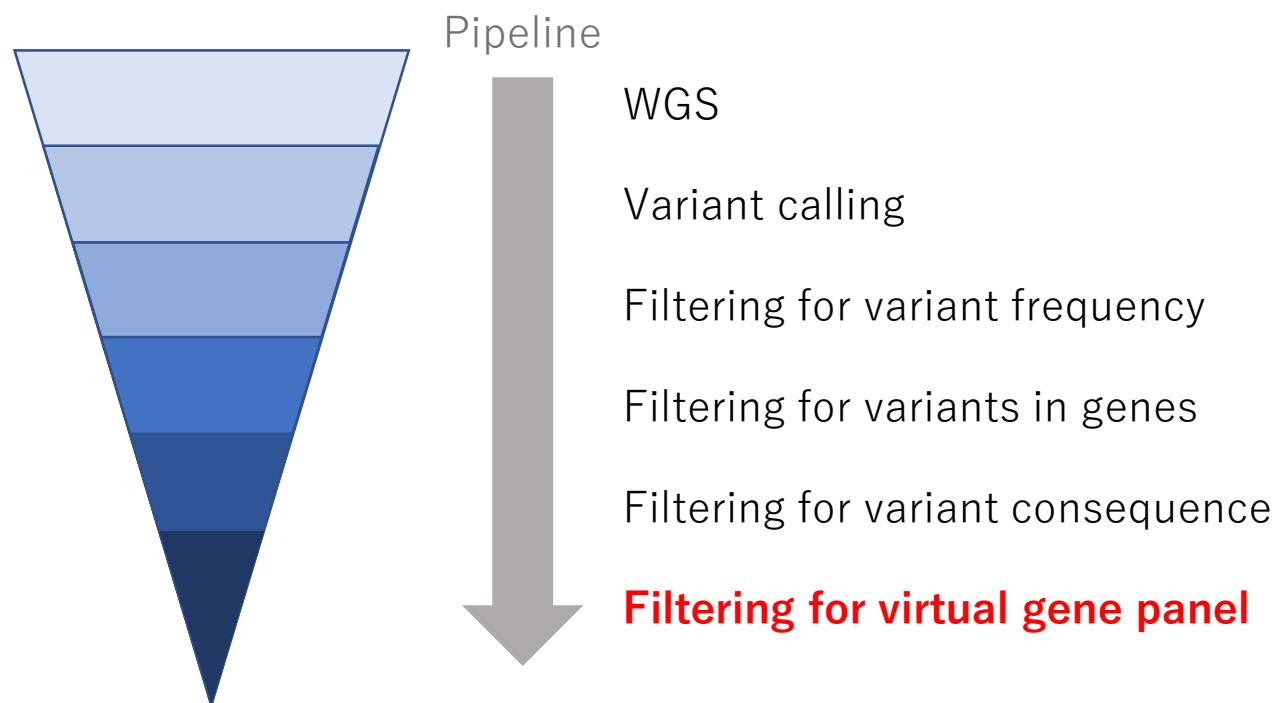
PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けた Virtual Gene Panel構築機能の提案

申 在紋¹、山口 敦子²、武藤 勇³、張 昊³、才津 浩智⁴、藤原 豊史¹

1. 情報・システム研究機構 ライフサイエンス統合データベースセンター (DBCLS)、
- 2.東京都市大学、3.ビツツ株式会社、4.浜松医科大学

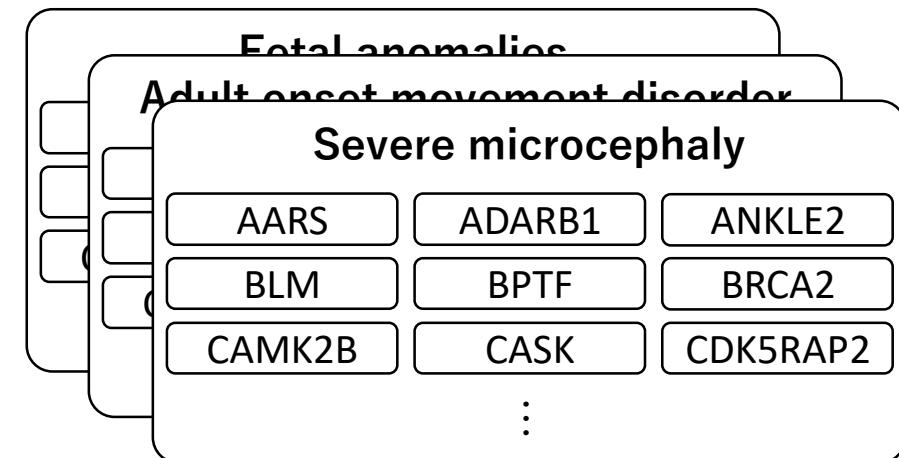
PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けたVirtual Gene Panel 構築機能の提案

- 全ゲノム解析 (WGS) および全エクソーム解析 (WES) の結果解釈に Virtual Gene Panel (VGP) が活用され始めている



【Genomics England 10万人ゲノムプロジェクト】

PanelApp VGP(332種類)



VGP を用いてバリアントをフィルタリング

PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けたVirtual Gene Panel 構築機能の提案

- PanelApp VGP の問題点
 - VGP のバリエーションが少ない (332種類, 2022年7月現在)
 - 臨床診断に対応する適切な VGP が存在しない場合がある
 - 取りこぼしが多い
 - 46% の Proband で正解となるバリエントを取りこぼす (Genomics England 10万人ゲノムプロジェクトの結果)
- 希少・遺伝性疾患検索システム PubCaseFinder 上に VGP を用いたフィルタリング機能を実装

Disease name (Mondo)	Causative gene (NCBI Gene)	PanelApp	PanelApp Australia
22,051	4,025	322	273

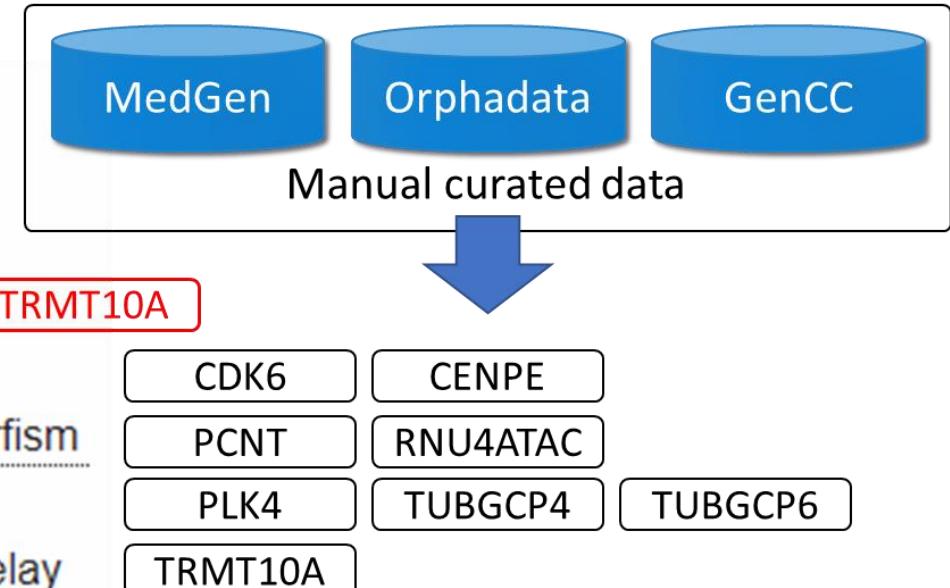
PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けたVirtual Gene Panel 構築機能の提案

- Mondo Disease Ontology (Mondo) と Disease-Gene Association data を用いて VGP を実現

Mondo disease ontology



Disease-Gene Association data



PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けたVirtual Gene Panel 構築機能の提案

- 実際のゲノム解析

74 clinical cases

Case ID	Definitive diagnosis	Clinical diagnosis	No. of phenotypes	No. of candidate genes
p00001	CTNNB1	microcephaly	3	353
p00002	COL4A1	Schizencephaly	3	452
p00003	MTOR	Megalencephaly	2	386
		:		

MEDIAN : 384

The screenshot shows the PubCaseFinder interface. At the top, there are three search terms: "HP-0000253 Progressive microcephaly", "HP-0001263 Global developmental delay", and "HP-0008499 High hypermetropia". Below the search bar are filter buttons for "Filter(351)" and "Virtual Gene Panel(1)". The main search area displays a grid of gene filters, each with a gene ID and name: PERM1, MMEL1, PRAMEF4, CELA2B, IFFO2, ECE1, EPHB2, and FGR. Below this is a section for "Set up a virtual gene panel" with a selected item: "MONDO:0001149 microcephaly (dise...)".

The results table at the bottom shows 2 results for "PYCR2 - pyrroline-5-carboxylate reductase 2". The results are listed as follows:

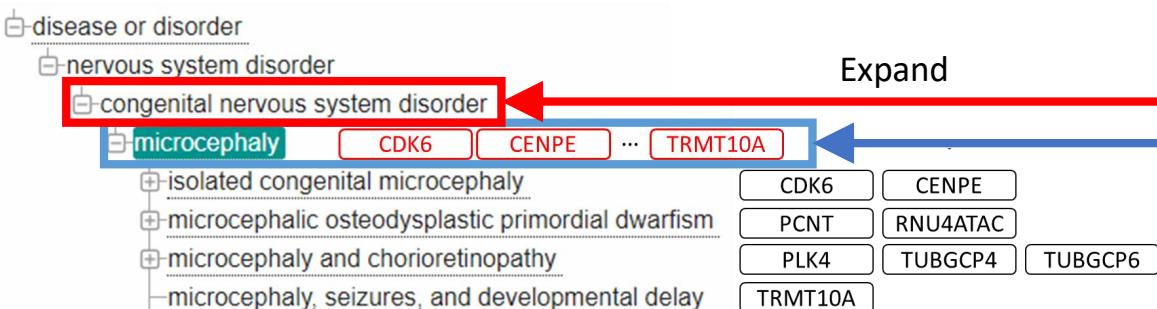
- 1 (73.9%) PYCR2 - pyrroline-5-carboxylate reductase 2
Also known as: HLD10, P5CR2
Progressive microcephaly | Global developmental delay | Nystagmus
hypomyelinating leukodystrophy 10 | autosomal recessive primary microcephaly

PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けたVirtual Gene Panel 構築機能の提案

74 clinical cases

Case ID	Definitive diagnosis	Clinical diagnosis	No. of phenotypes	No. of candidate genes
p00001	CTNNB1	microcephaly	3	353
p00002	COL4A1	Schizencephaly	3	452
p00003	MTOR	Megalencephaly	2	386

Mondo disease ontology



PubCaseFinder English

HP-0000253 Progressive microcephaly HP-0001263 Global developmental delay HP-0008499 High hypermetropia

Filter(351) Virtual Gene Panel(1) Display options

Filter to narrow your search results Examples: Example1 Example2 Example3

GENEID:84808 PERM1 GENEID:79258 MMEL1 GENEID:400735 PRAMEF4 GENEID:51032 CELA2B

GENEID:126917 IFFO2 GENEID:1889 ECE1 GENEID:2048 EPHB2 GENEID:2268 FGR

+ Query box

Set up a virtual gene panel Examples: Example1 Example2 Example3

MONDO:0001149 microcephaly (dise... Expand MONDO:0002320 congenital nervous ...

Expand

Genetic Disease Rare Disease Gene Case

2 results PYCR2 - pyrroline-5-ca... Expand 22 results CTNNB1 - catenin beta 1 ... Expand

1 (73.9%) Also known as: HLD10, P50 ... Copy

1 (81.6%) Also known as: CTNNB, EVR7, MRD19, N ... Copy

Progressive microcephaly hypomyelinating leukodystro... Microcephaly Global developmental delay pilomatricoma desmoid tumor severe int...

VGP を用いたフィルタリング機能の精度を評価

Expand function	Media no. of candidate genes	Sensitivity
Non-applied	1	48.6
Applied	15	93.2