

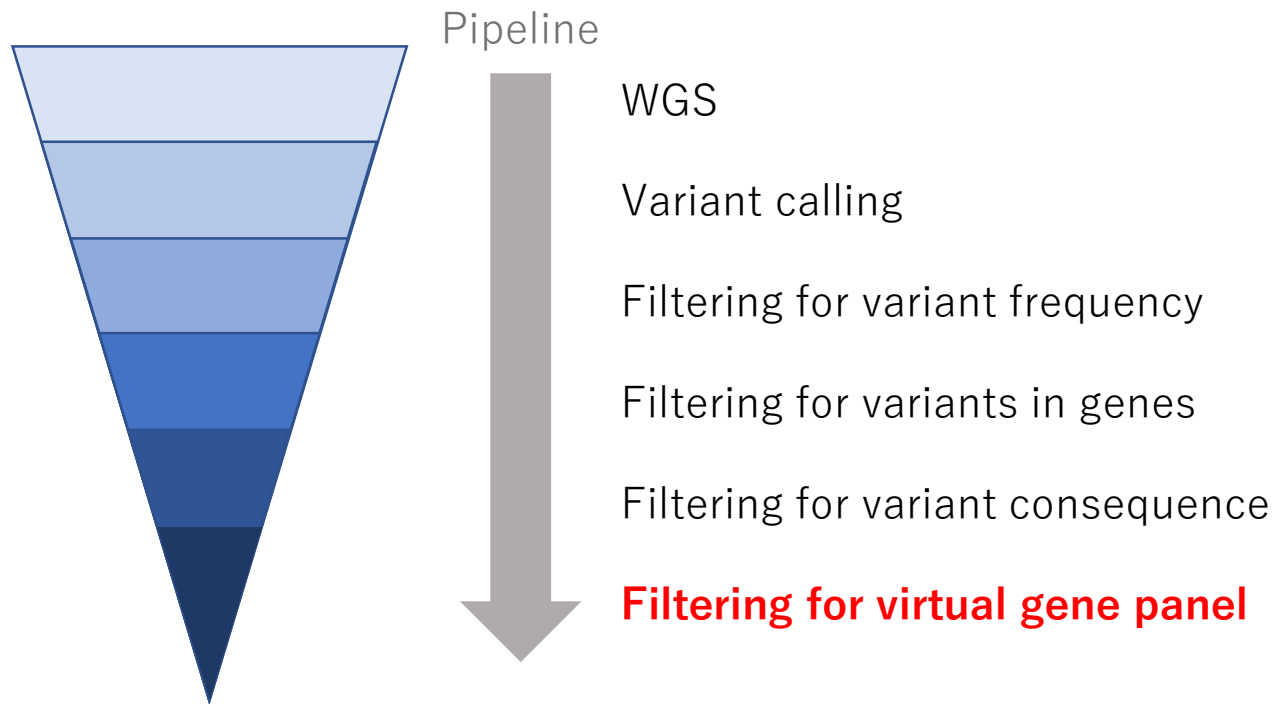
## PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けた Virtual Gene Panel構築機能の提案

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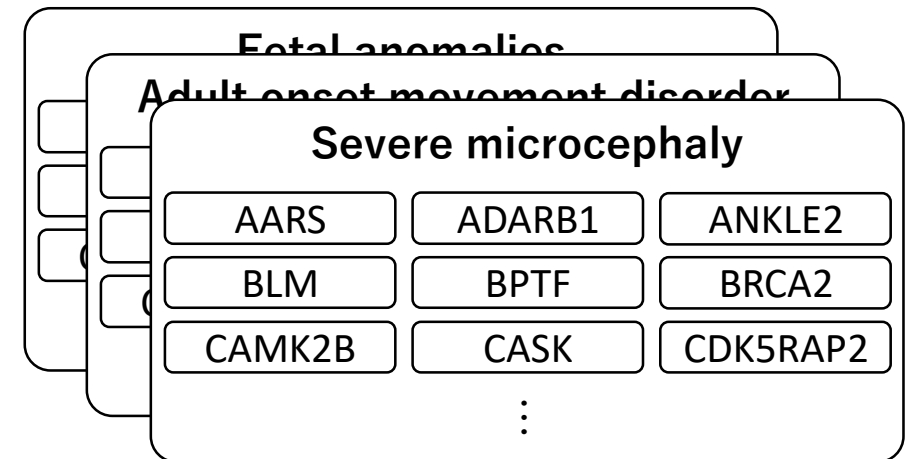
# PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けた Virtual Gene Panel 構築機能の提案

- 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 を用いてバリエーションをフィルタリング

# 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ーションを取りこぼす (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

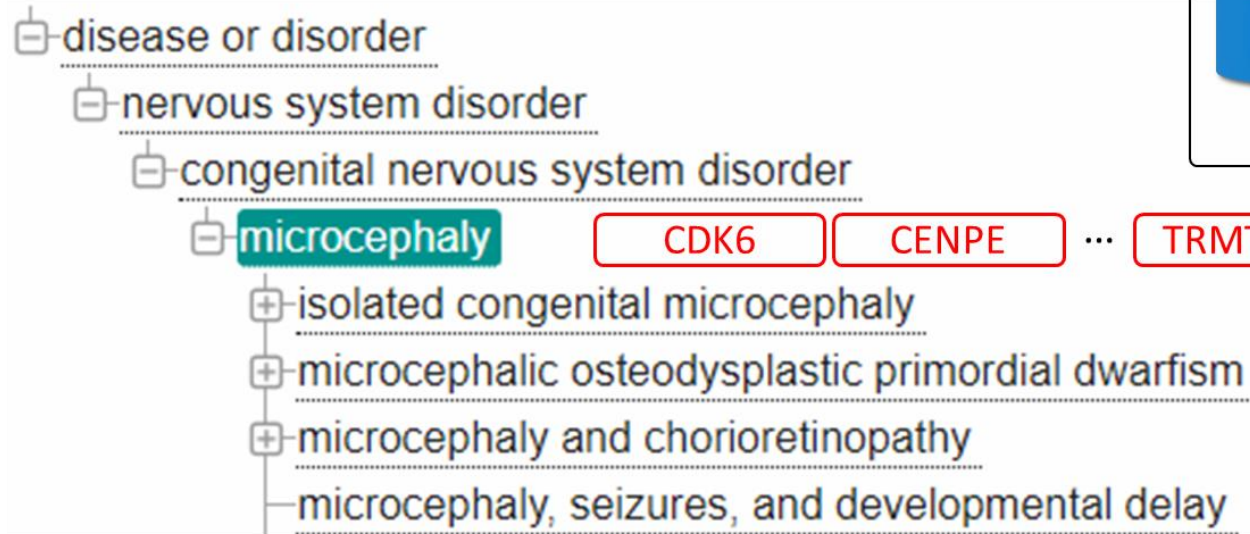
Disease name (Mondo)	Causative gene (NCBI Gene)	PanelApp	PanelApp Australia
22,051	4,025	322	273

The screenshot shows the PubCaseFinder web application. At the top, there are search filters for diseases: HP:0000253 Progressive microcephaly, HP:0001263 Global developmental delay, and HP:0008499 High hypermetropia. Below these, a 'Filter' dropdown is set to 'Virtual Gene Panel(5)'. A red box highlights the 'Set up a virtual gene panel' section, which includes examples like 'microcephaly (dise...)', 'Severe microcephaly', and 'Microcephaly', along with genes 'CTNNB1' and 'PYCR2' connected by 'OR' operators. The interface also shows '240 results' and options for 'Matched Phenotype', 'Disease Name', and 'Mode of Inheritance'.

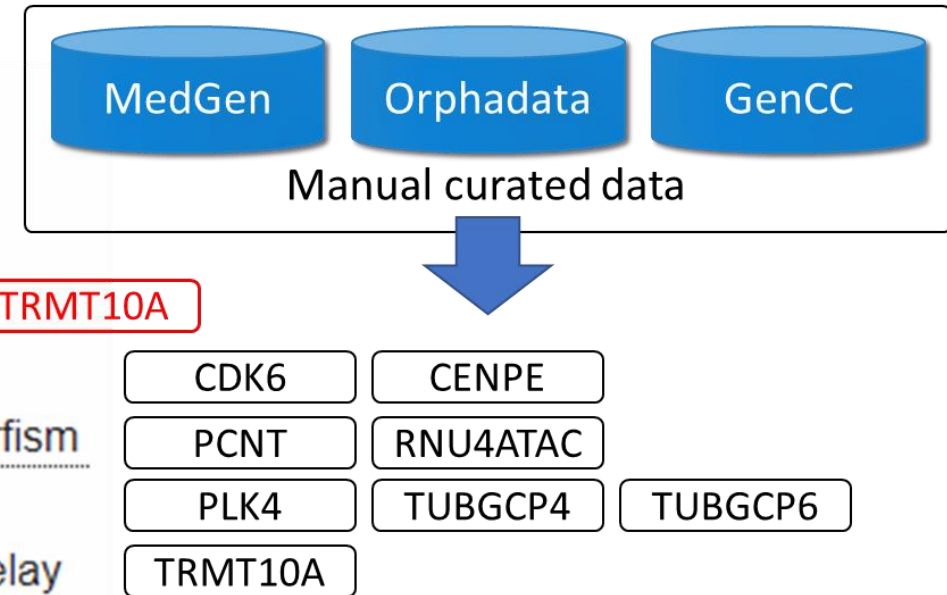
# PubCaseFinder 2022 update: 全ゲノム解析の社会実装に向けた Virtual Gene Panel 構築機能の提案

- 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 with the following components:

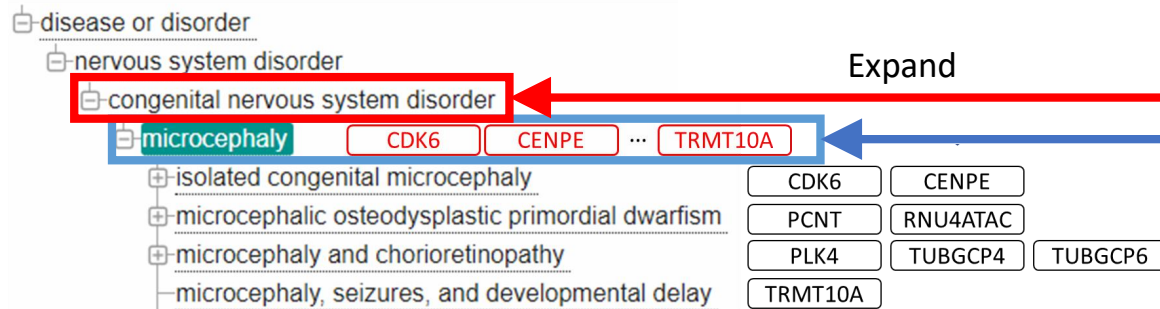
- Search Filters (Red box):** HP:000253 Progressive microcephaly, HP:0001263 Global developmental delay, HP:0008499 High hypermetropia.
- Filter to narrow your search results (Yellow box):** GENEID:84808 PERM1, GENEID:79258 MMEL1, GENEID:400735 PRAMEF4, GENEID:51032 CELA2B, GENEID:126917 IFFO2, GENEID:1889 ECE1, GENEID:2048 EPHB2, GENEID:2268 FGR.
- Set up a virtual gene panel (Blue box):** MONDO:0001149 microcephaly (dise...).
- Search Results (Green box):** 2 results. PYCR2 - pyrroline-5-carboxylate reductase 2. Also known as: HLD10, P5CR2. (73.9%) Matched Phenotype: Progressive microcephaly, Global developmental delay, Nystagmus. Copy: hypomyelinating leukodystrophy 10, autosomal recessive primary microcephaly.

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## 74 clinical cases

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## Mondo disease ontology



PubCaseFinder

Filter(351) Virtual Gene Panel(1)

Filter to narrow your search results | Examples: Example1 Example2 Example3

Query box

Set up a virtual gene panel | Examples: Example1 Example2 Example3

Expand

Genetic Disease Rare Disease Gene Case

2 results

1 PYCR2 - pyrroline-5-carboxylate aminotransferase 1  
Also known as: HLD10, P50A  
(73.9%)  
Progressive microcephaly  
Copy  hypomyelinating leukodystrophy

Expand

22 results

1 CTNNB1 - catenin beta 1  
Also known as: CTNNB, EVR7, MRD19, N  
(81.6%)  
Microcephaly Global developmental delay  
Copy  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