Giới thiệu về
GIẢI TRÌNH TỰ GEN THẾ HỆ MỚI

Ngày 22 tháng 02 năm 2025

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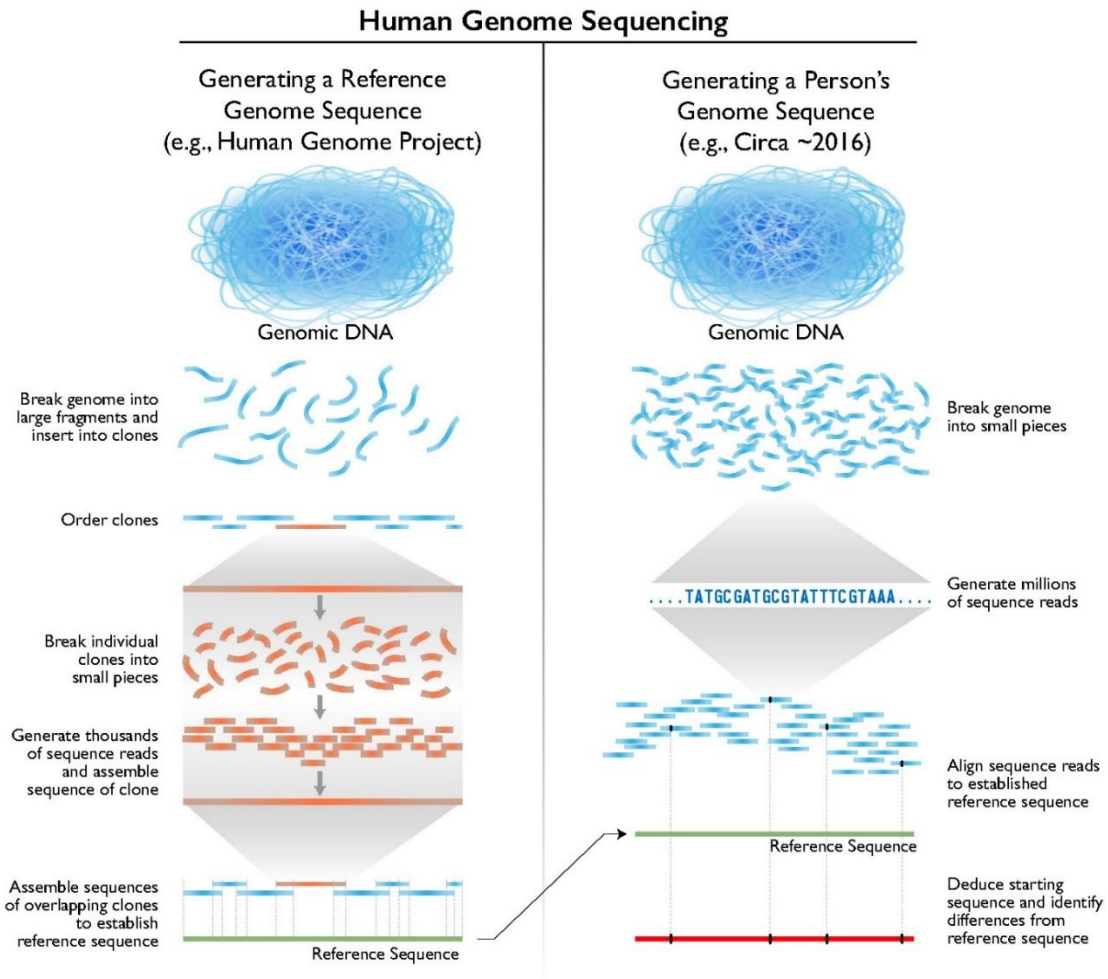
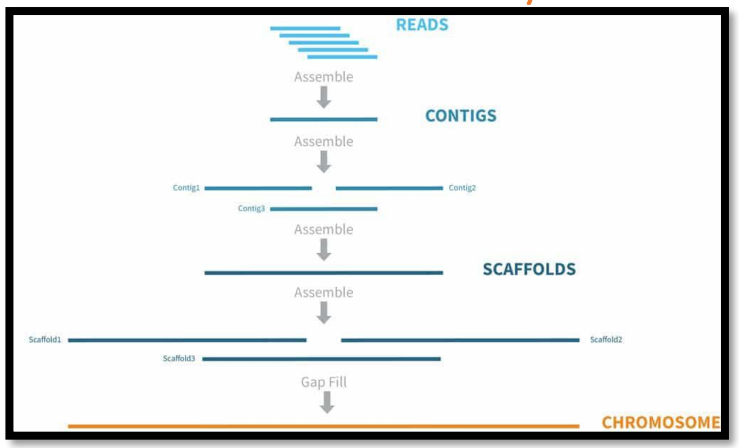
Giải trình tự gen thế hệ mới (NGS)

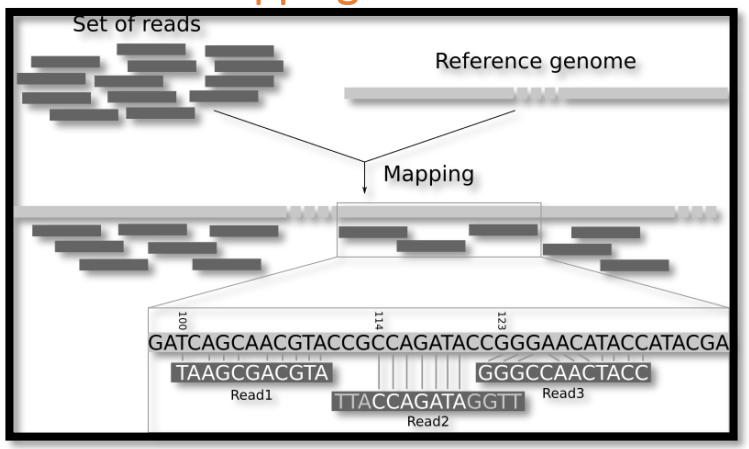


https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost

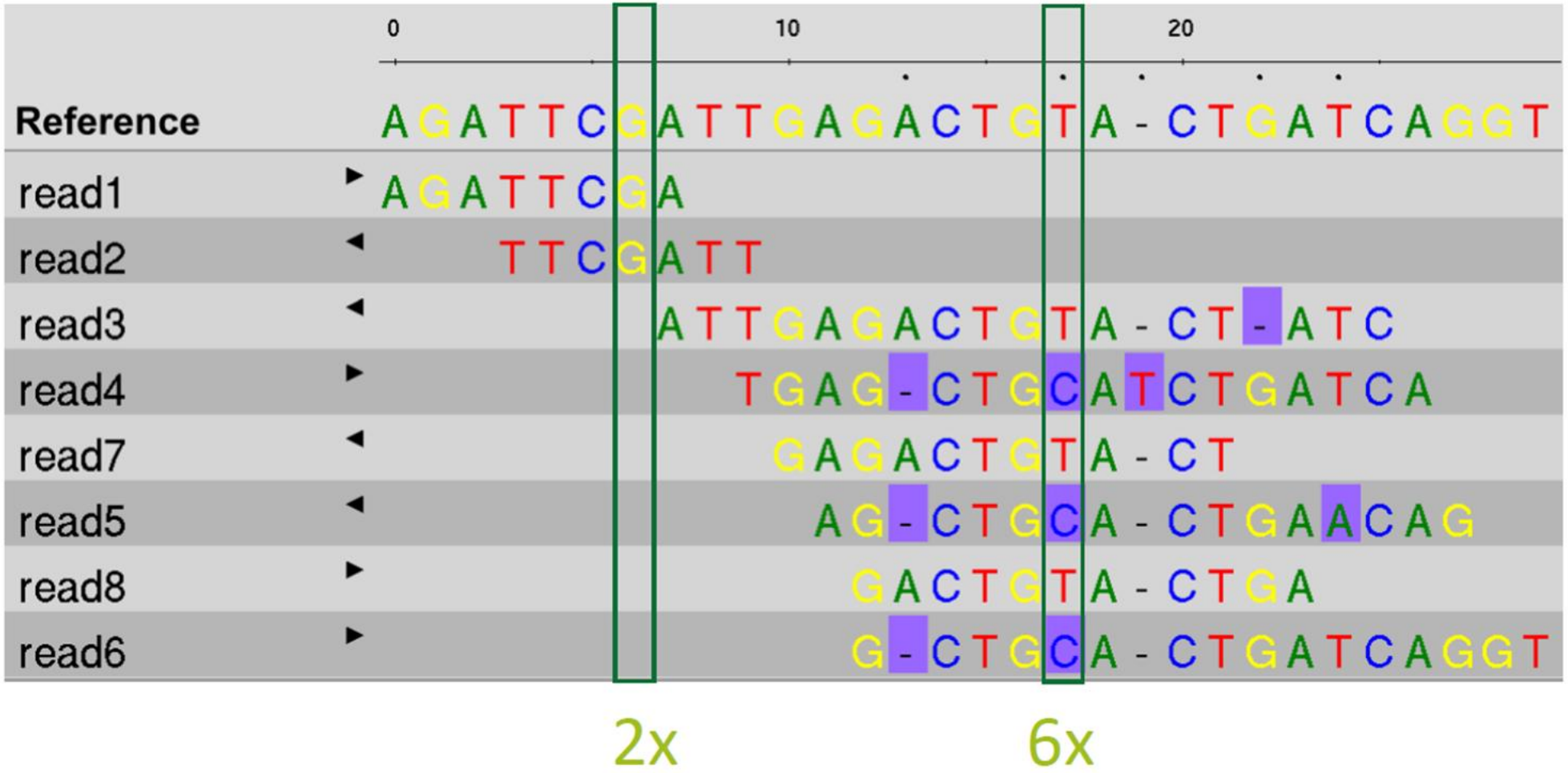
De novo assembly



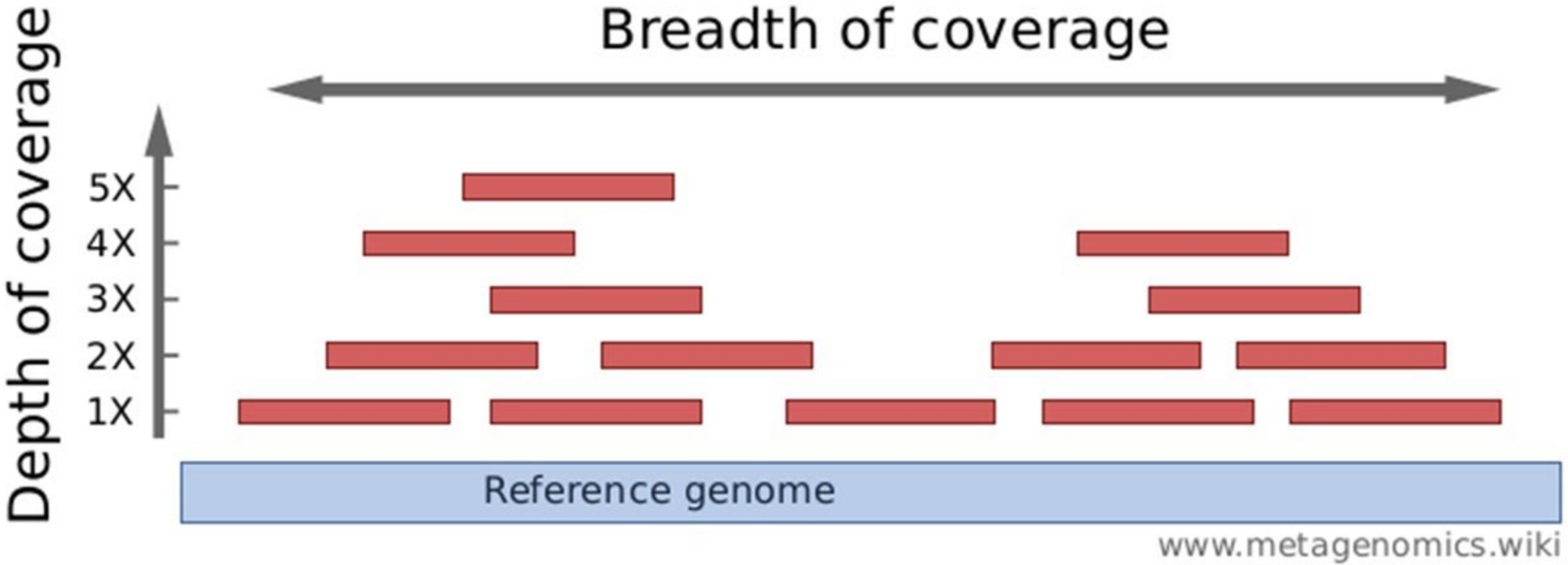
Mapping to reference



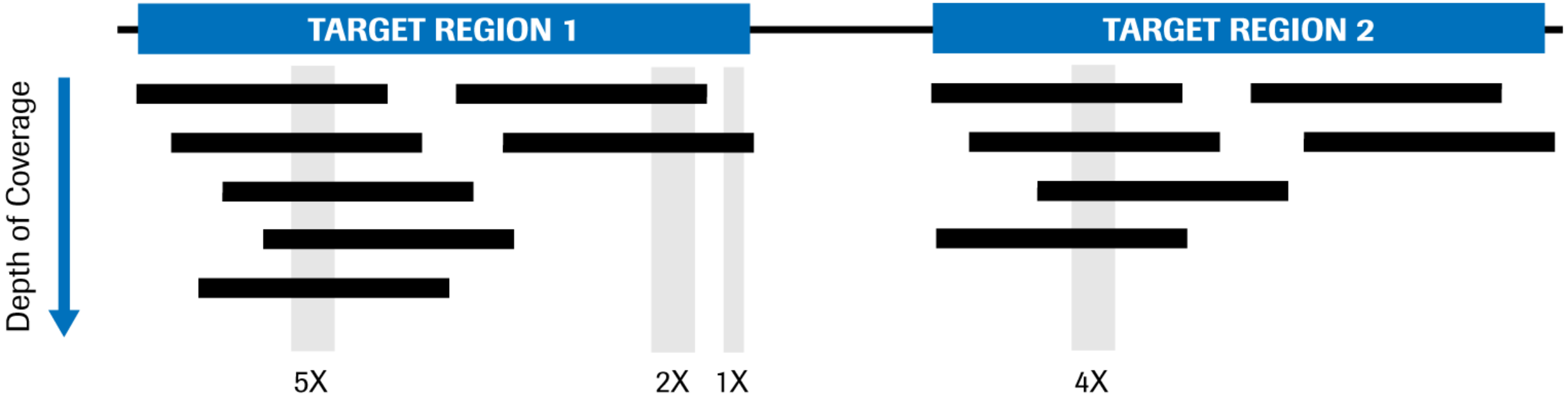
Kết quả của mapping



Depth vs Breadth of Coverage



Depth of Coverage



https://sequencing.roche.com/us/en/article-listing/metrics-for-target-enriched-ngs.html

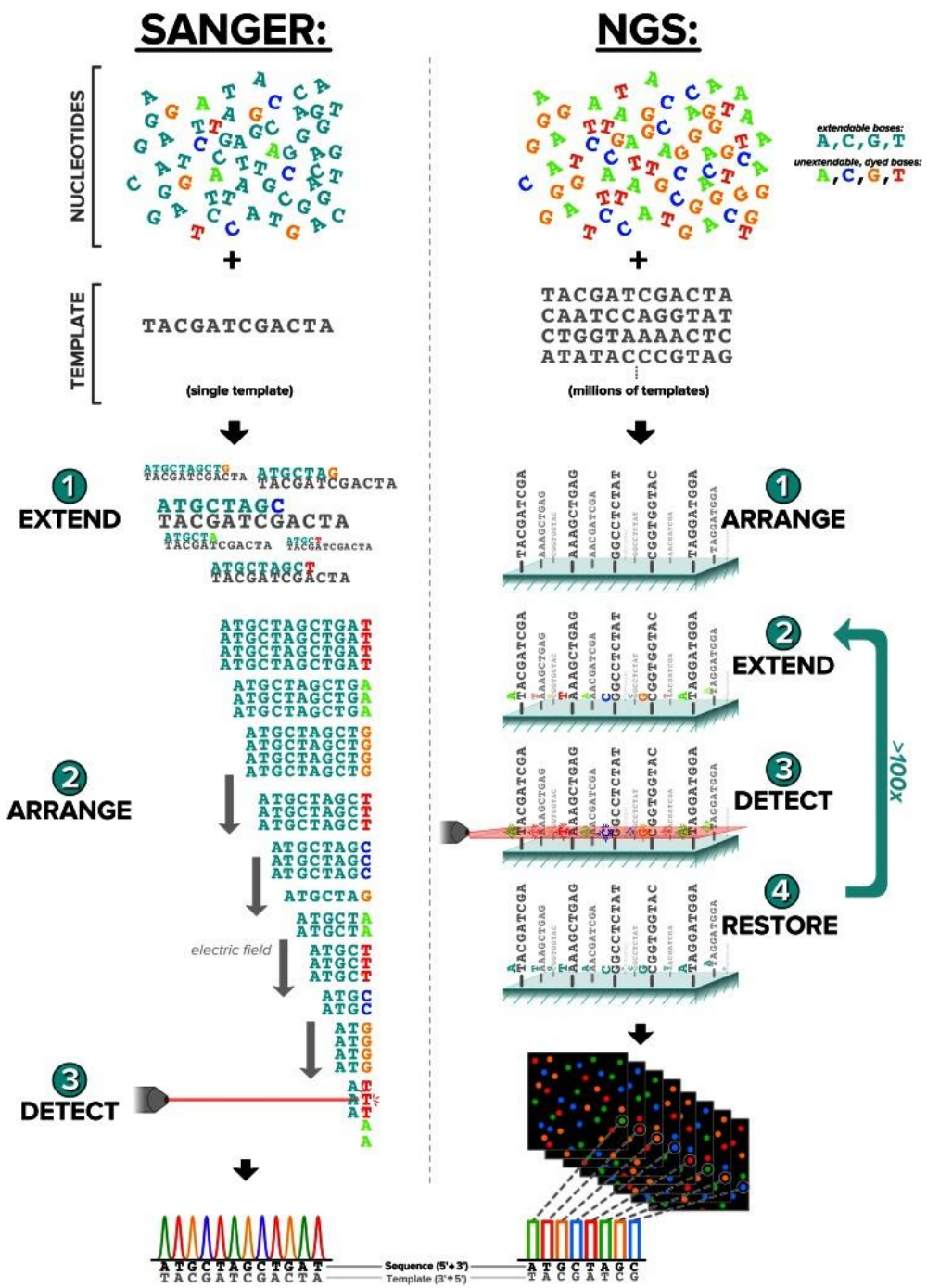
Giải trình tự gen thế hệ mới (NGS): Có hệ gen tham chiếu

De novo assembly

Mapping to reference

Giải trình tự gen thế hệ mới (NGS): giải trình tự song song

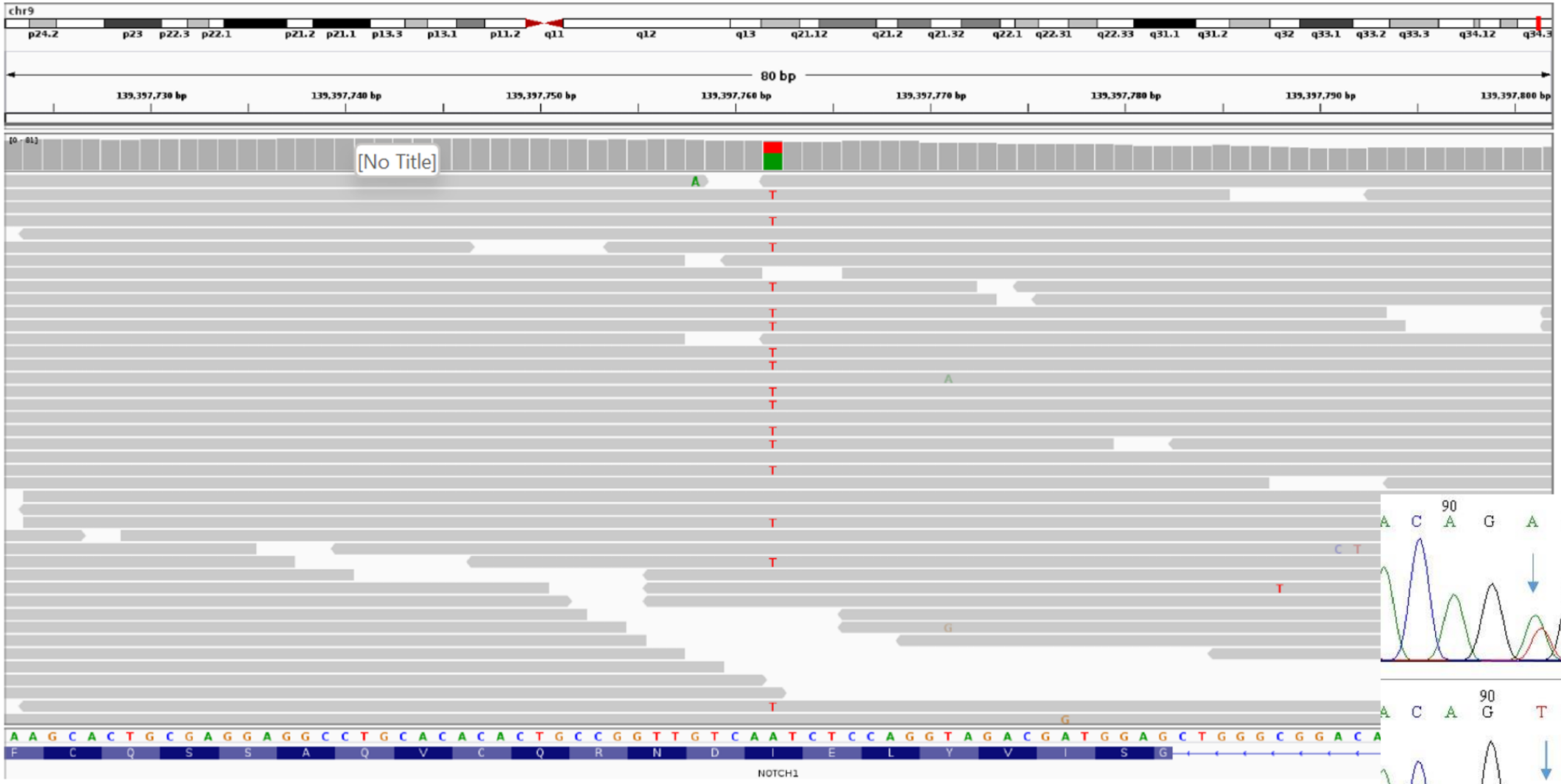
Read1:CTCGAATACG

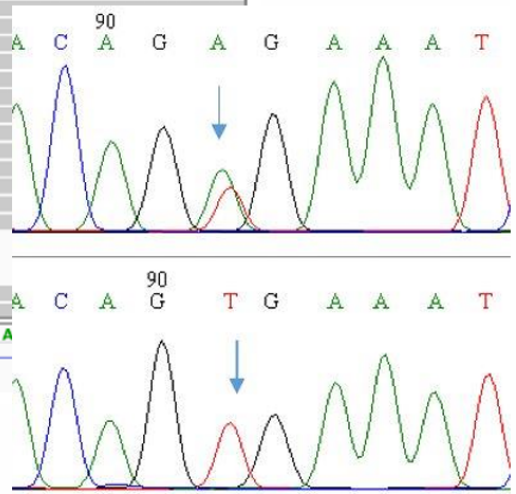


Read1:CTCGAATACG
Read2:CTCGAATACG
Read3:CTCGAATACG
Read4:CTCGAATACG
Read5:CGCGAATACG
Read6:CGCGAATACG
Read7:CGCGACTACG
Read8:CGCGAATACG

10.1007/s40142-015-0076-8

NGS vs Sanger

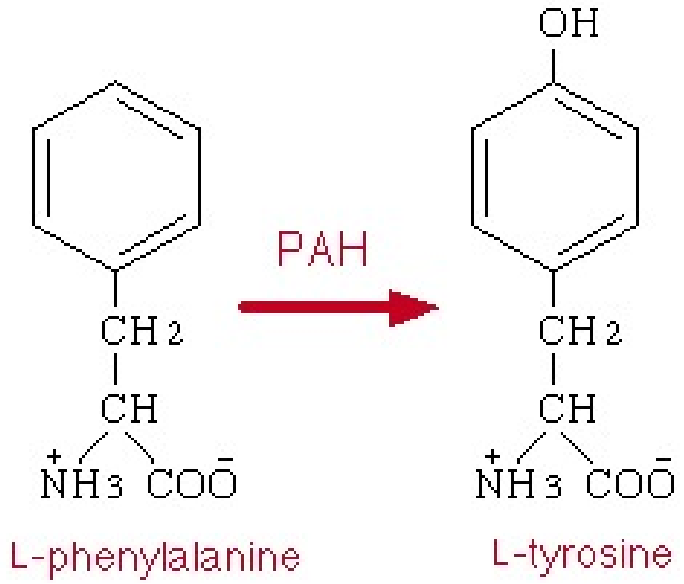




Ví dụ mối quan hệ của BIẾN THỂ GEN và BỆNH DI TRUYỀN

Phenylketonuria (PKU): Rối loạn chuyển hóa di truyền

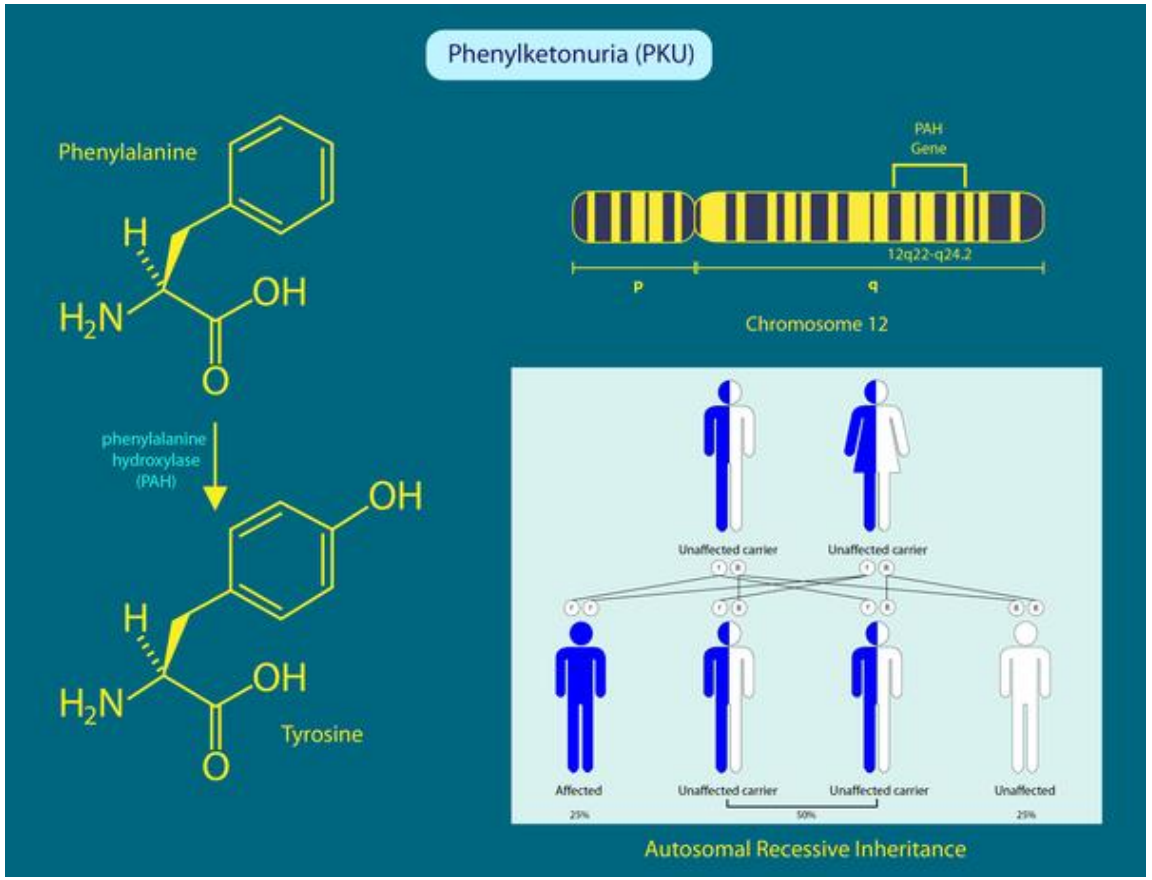
- Nguyên nhân do thiếu hụt enzyme phenylalanine hydroxylase.
- Sự mất enzyme này dẫn đến suy giảm trí tuệ, tổn thương cơ quan, tư thế bất thường.
- Tần suất xảy ra PKU khác nhau giữa các nhóm dân tộc và các vùng địa lý trên toàn thế giới. Ở Hoa Kỳ, PKU xảy ra ở 1 trong 25.000 trẻ sơ sinh.
- Hầu hết các trường hợp PKU được phát hiện ngay sau sinh bằng sàng lọc sơ sinh và điều trị được bắt đầu ngay lập tức.



The enzyme phenylalanine hydroxylase converts the amino acid phenylalanine to tyrosine.

https://www.ncbi.nlm.nih.gov/books/NBK22253/

Phenylketonuria (PKU): Rối loạn chuyển hóa di truyền



https://medlineplus.gov/genetics/condition/phenylketonuria/

Tên khác của PKU

- Folling disease
- Folling's disease
- PAH deficiency
- Phenylalanine hydroxylase deficiency
- Phenylalanine hydroxylase deficiency disease

Trình tự gen PAH ở người - Homo sapiens (5053)

Gene (Nucleotide)

NT seq — 1359 nt [NT seq]

```
atgtccactgcggtcctggaaaacccaggcttgggcaggaaactctctgactttggacag
gaaacaagctatattgaagacaactgcaatcaaaatggtgccatatcactgatcttctca
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aacctgacccacattgaatctagaccttctcgtttaaagaaagatgagtatgaatttttc
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attggaatcctttgcagtgccctccagaaaataaagtaa
```

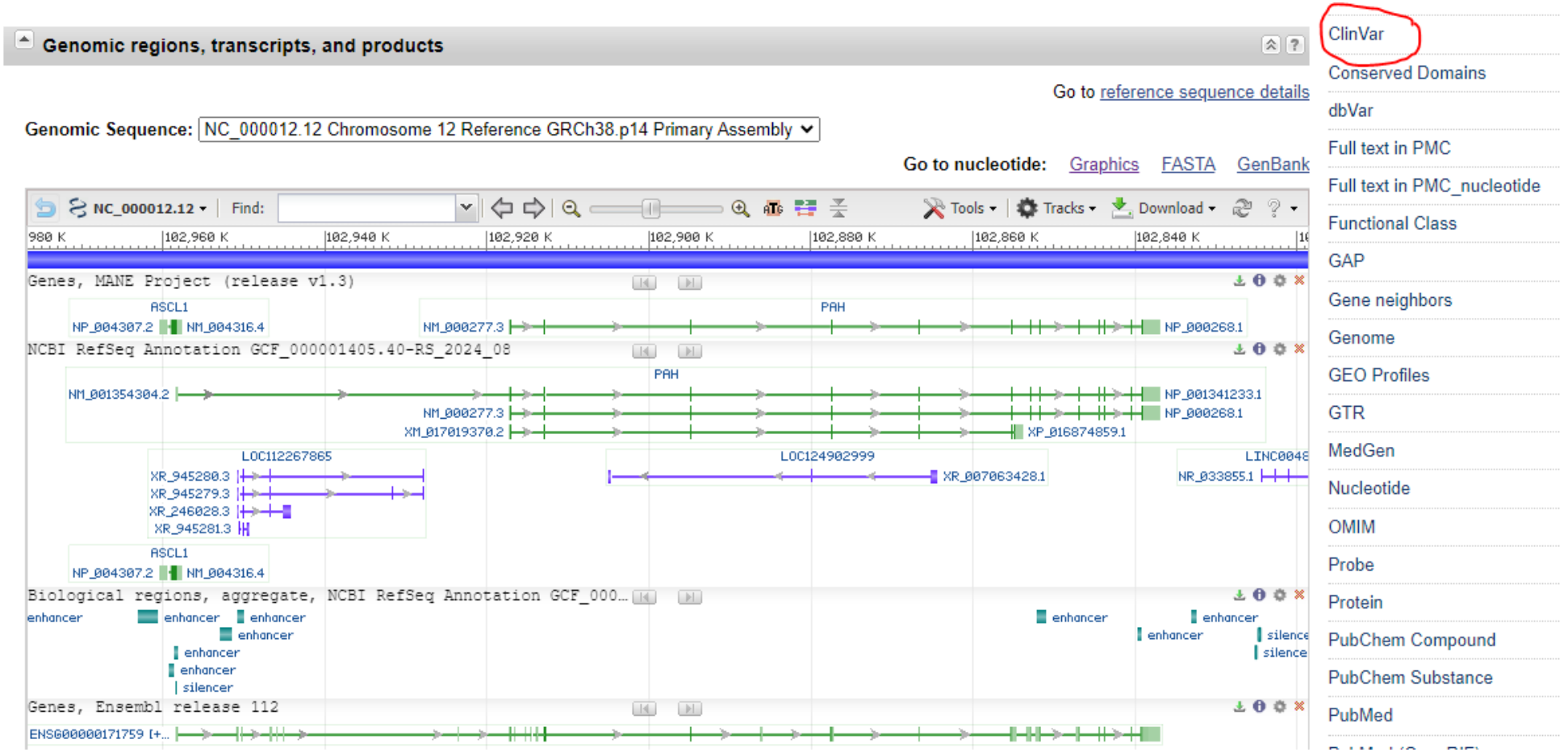
Protein (Amino Acid)

AA seq — 452 aa [AA seq] [DB search]

```
MSTAVLENPGLGRKLSDFGQETSYIEDNCNQNGAISLIFSLKEEVGALAKVLRLFEENDV
NLTHIESRPSRLKKDEYEFFTHLDKRSLPALTNIIKILRHDIGATVHELSRDKKKDTVPW
FPRTIQELDRFANQILSYGAELDADHPGFKDPVYRARRKQFADIAYNYRHGQPIPRVEYM
EEEKKTWGTVFKTLKSLYKTHACYEYNHIFPLLEKYCGFHEDNIPQLEDVSQFLQTCTGF
RLRPVAGLLSSRDFLGGLAFRVFHCTQYIRHGSKPMYTPEPDICHELLGHVPLFSDRSFA
QFSQEIGLASLGAPDEYIEKLATIYWFTVEFGLCKQGDSIKAYGAGLLSSFGELQYCLSE
KPKLLPLELEKTAIQNYTVTEFQPLYYVAESFNDAKEKVRNFAATIPRPFSVRYDPYTQR
IEVLDNTQQLKILADSINSEIGILCSALQKIK
```

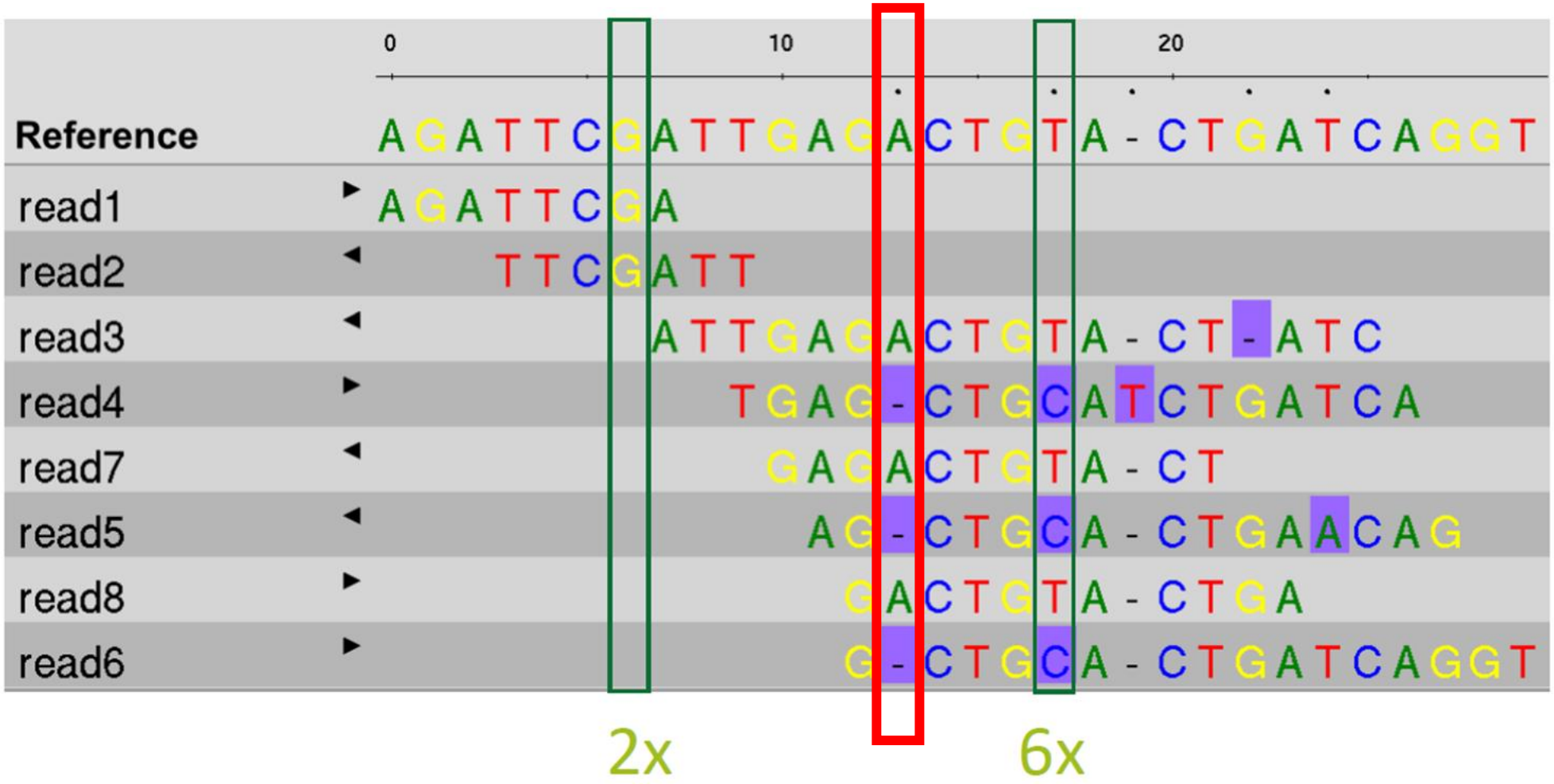
https://www.genome.jp/entry/T01001:5053

Gen PAH

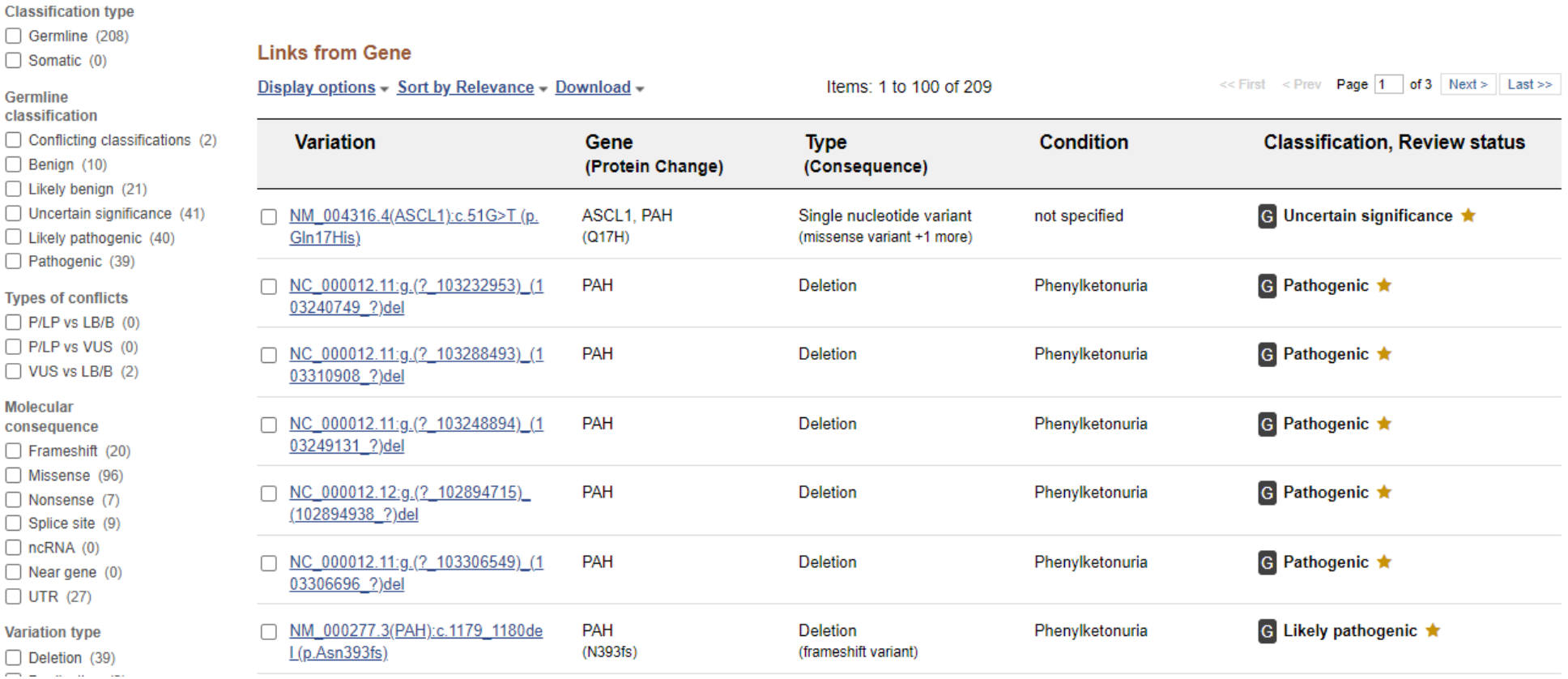


https://www.ncbi.nlm.nih.gov/gene/5053

Variants in PAH



Cơ sở dữ liệu ClinVar cho gen PAH



Classification type
- Germline (208)
- Somatic (0)

Germline classification
- Conflicting classifications (2)
- Benign (10)
- Likely benign (21)
- Uncertain significance (41)
- Likely pathogenic (40)
- Pathogenic (39)

Types of conflicts
- P/LP vs LB/B (0)
- P/LP vs VUS (0)
- VUS vs LB/B (2)

Molecular consequence
- Frameshift (20)
- Missense (96)
- Nonsense (7)
- Splice site (9)
- ncRNA (0)
- Near gene (0)
- UTR (27)

Variation type
- Deletion (39)

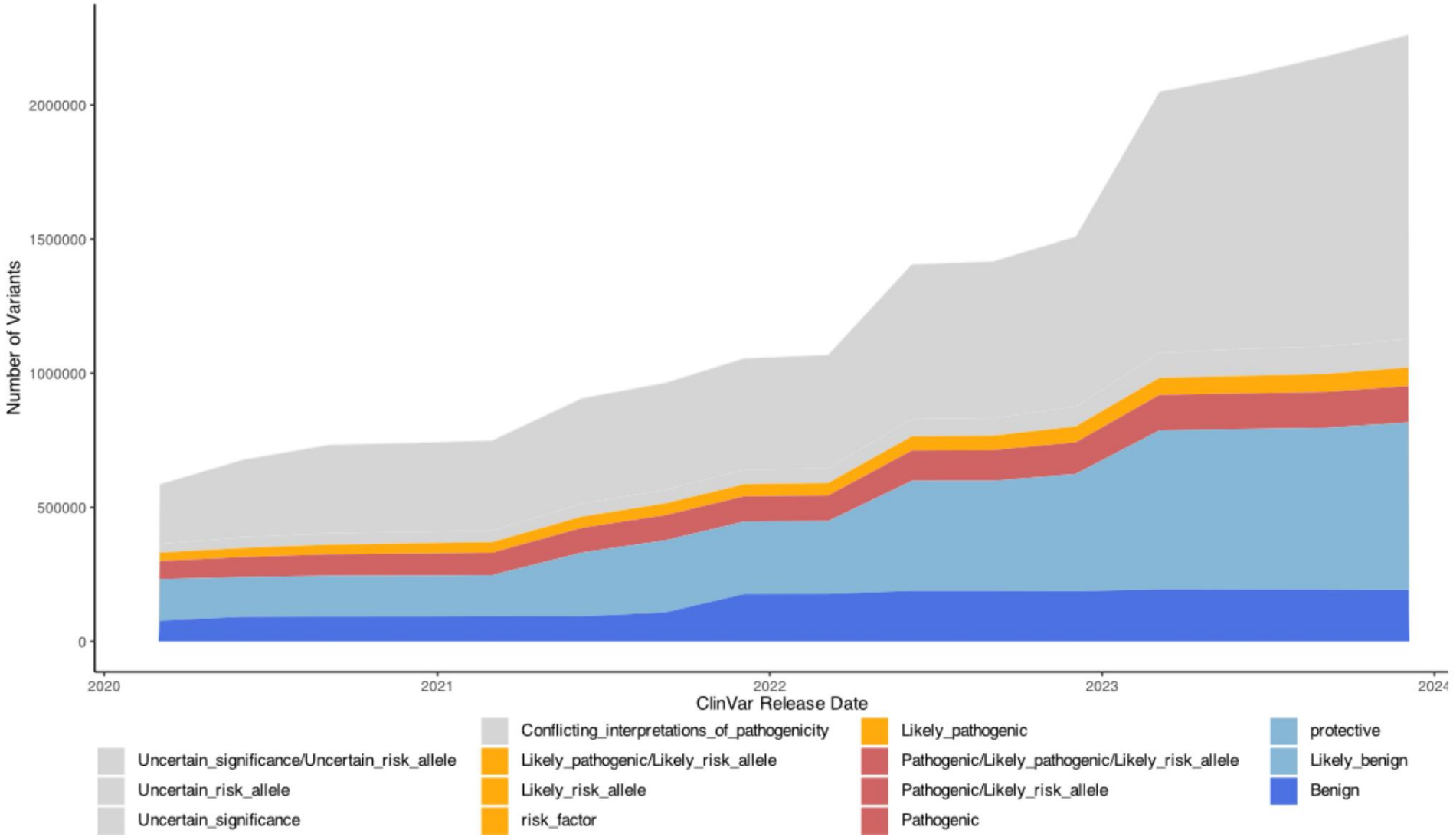
Links from Gene

Display options ▾ Sort by Relevance ▾ Download ▾ Items: 1 to 100 of 209 << First < Prev Page 1 of 3 Next > Last >>

Variation	Gene (Protein Change)	Type (Consequence)	Condition	Classification, Review status
NM_004316.4(ASCL1):c.51G>T (p.Gln17His)	ASCL1, PAH (Q17H)	Single nucleotide variant (missense variant +1 more)	not specified	Uncertain significance ★
NC_000012.11:g.(?_103232953)_(103240749_?)del	PAH	Deletion	Phenylketonuria	Pathogenic ★
NC_000012.11:g.(?_103288493)_(103310908_?)del	PAH	Deletion	Phenylketonuria	Pathogenic ★
NC_000012.11:g.(?_103248894)_(103249131_?)del	PAH	Deletion	Phenylketonuria	Pathogenic ★
NC_000012.12:g.(?_102894715)_(102894938_?)del	PAH	Deletion	Phenylketonuria	Pathogenic ★
NC_000012.11:g.(?_103306549)_(103306696_?)del	PAH	Deletion	Phenylketonuria	Pathogenic ★
NM_000277.3(PAH):c.1179_1180del (p.Asn393fs)	PAH (N393fs)	Deletion (frameshift variant)	Phenylketonuria	Likely pathogenic ★

https://www.ncbi.nlm.nih.gov/clinvar?LinkName=gene_clinvar&from_uid=5053

Overview of ClinVar release trends over time

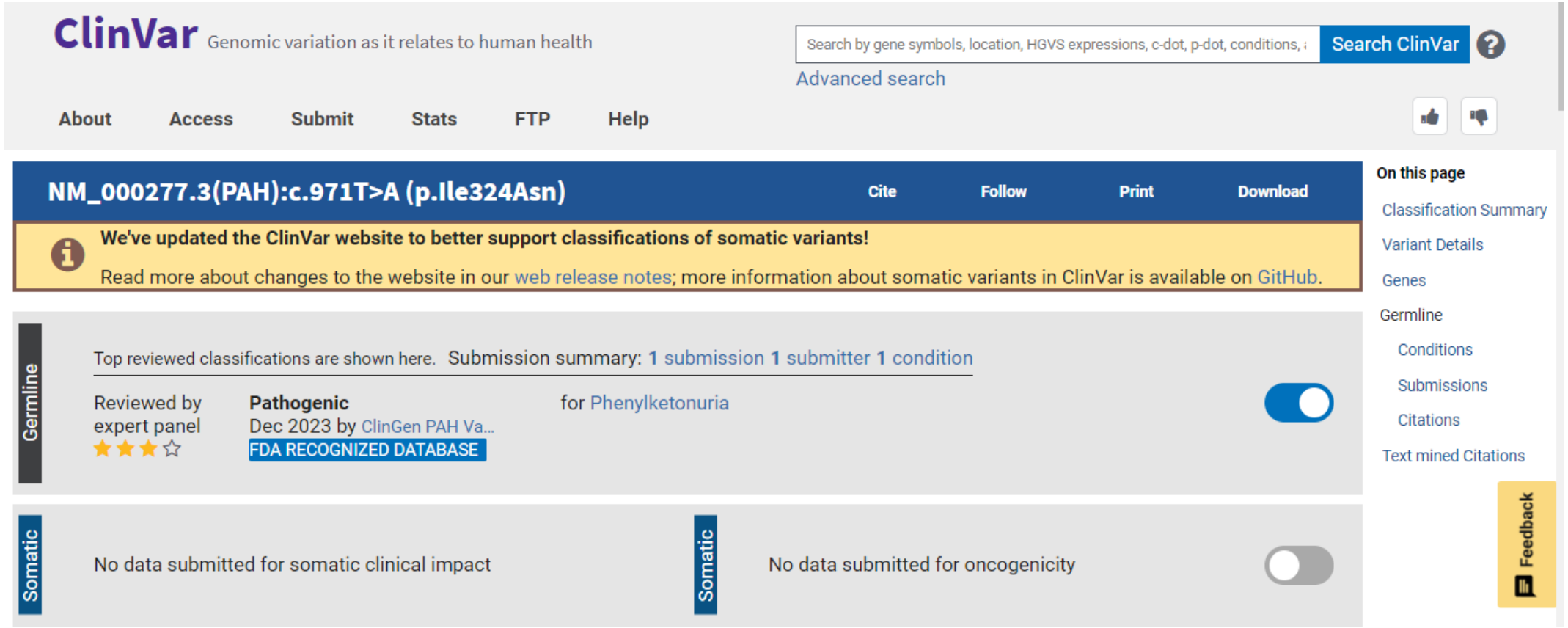


The classes have been divided into five colors to represent the degree of pathogenicity, from blue (benign) to red (pathogenic) with gray representing variants that are of uncertain clinical significance or have no clinical significance.

10.1186/s12967-024-05508-w

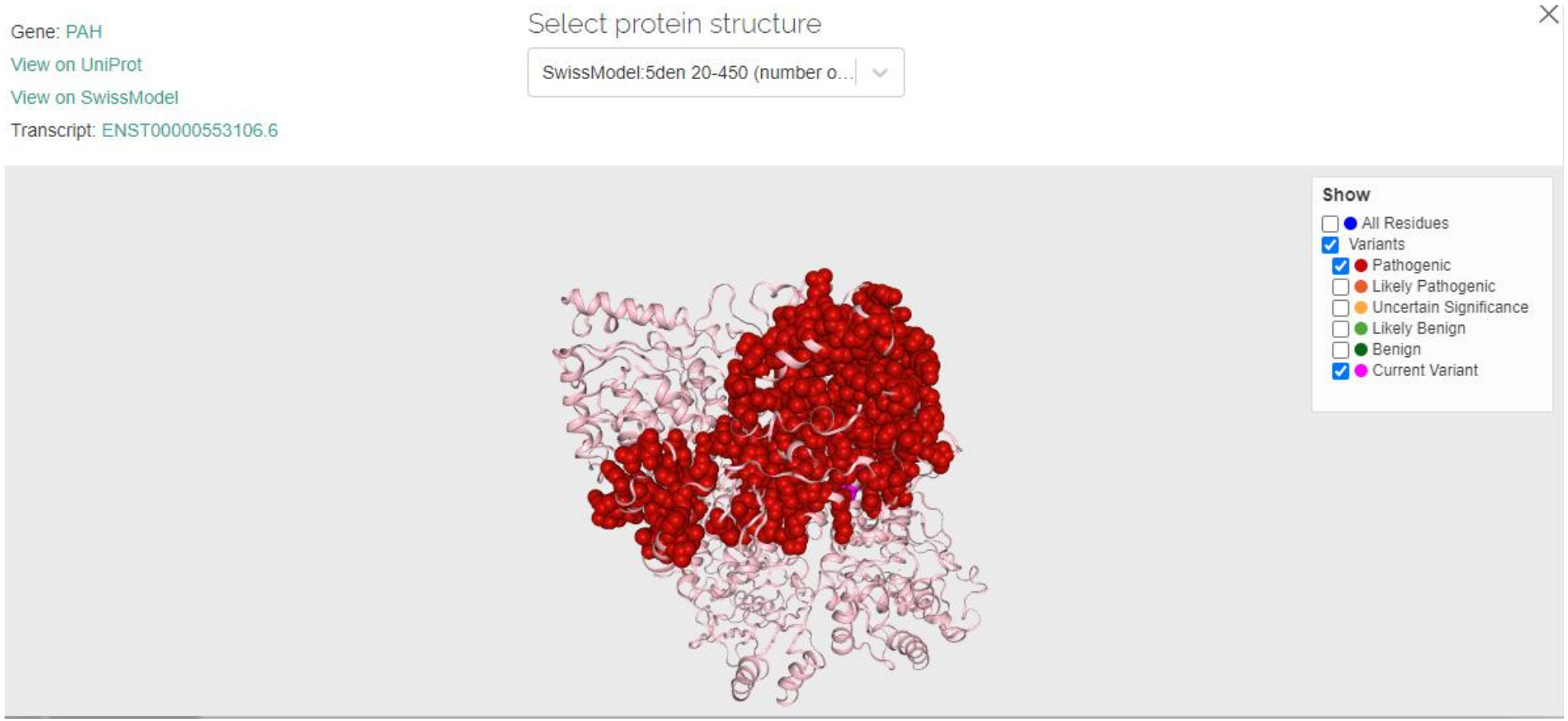
Biến thể gây bệnh - Pathogenic variant in PAH

NM_000277.3(PAH):c.971T>A (p.Ile324Asn)



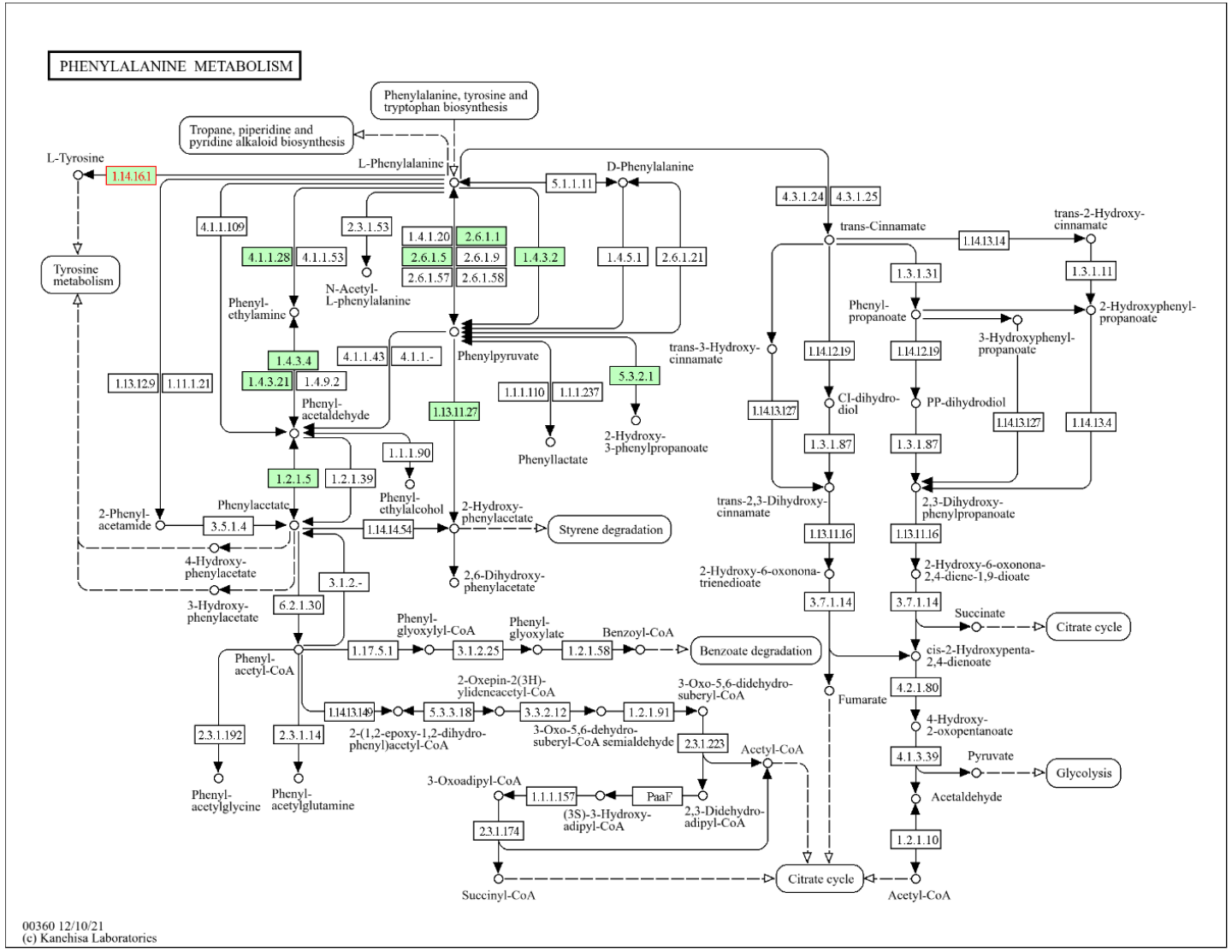
https://www.ncbi.nlm.nih.gov/clinvar/variation/2682170/

Các biến thể gây bệnh trên gen PAH



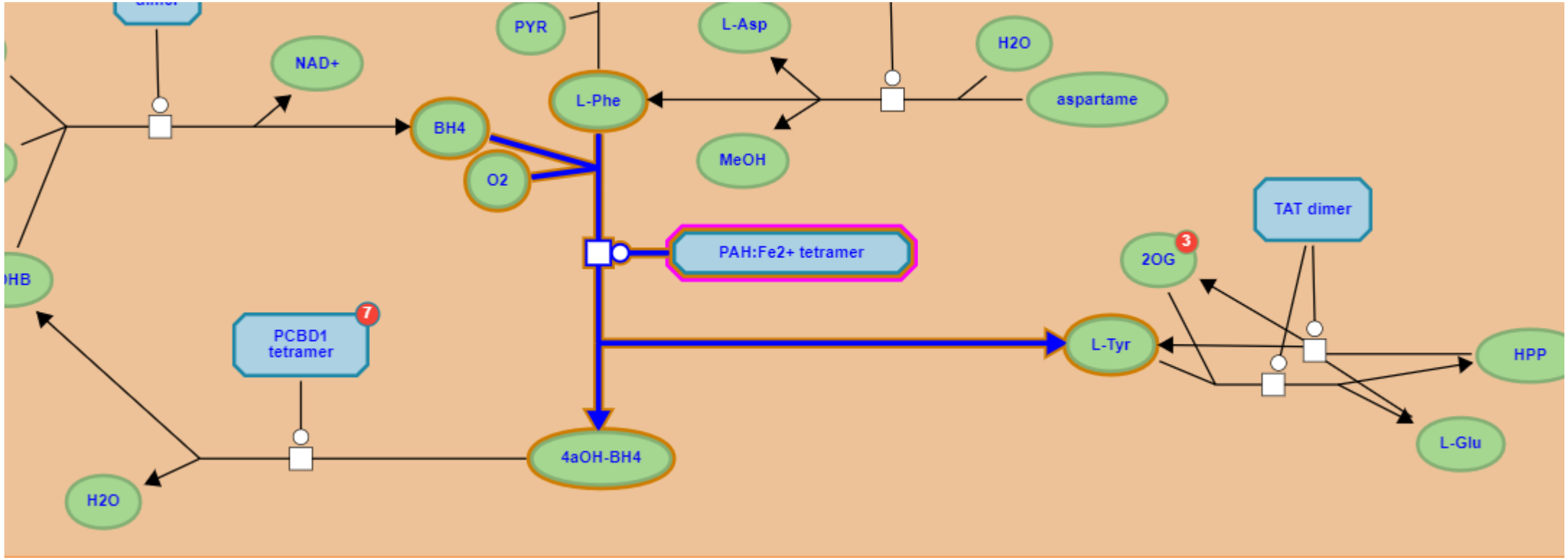
https://varsome.com/variant/hg38/chr12%3A102844430%3AA%3AT?

PAH: chuyển hóa Phenylalanine thành Tyrosine



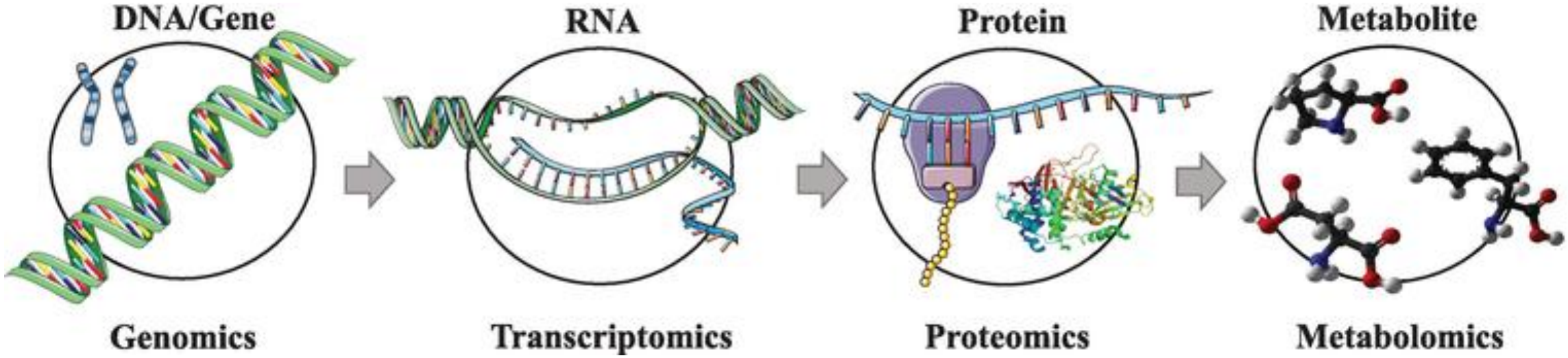
https://www.genome.jp/pathway/hsa00360+5053

PAH: chuyển hóa Phenylalanine thành Tyrosine



https://reactome.org/PathwayBrowser/#/R-HSA-8963691&SEL=R-HSA-71118&PATH=R-HSA-1430728,R-HSA-71291&FLG=UniProt:P00439

Mối liên kết: Biến thể gen và bệnh di truyền



PAH gene

Ref …ATCGAT…

P1 …AACGAT…

NM_000277.3(PAH):c.971T>A

PAH mRNA

Ref …AUCGAU…

P1 …AACGAU…

NM_000277.3(PAH):c.971T>A

PAH protein

Ref …Ile-Asp…

P1 …Asn-Asp…

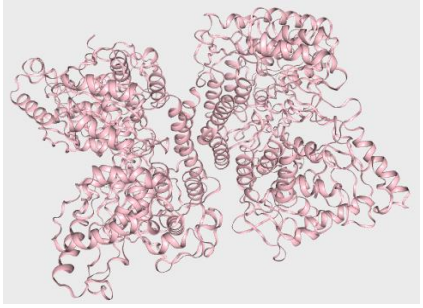
NM_000277.3(PAH):p.Ile324Asn

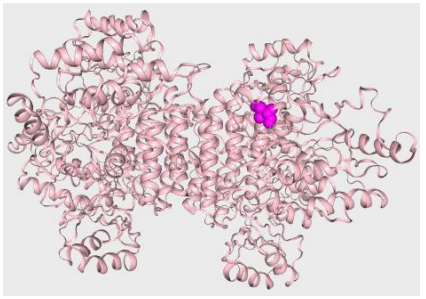
PAH

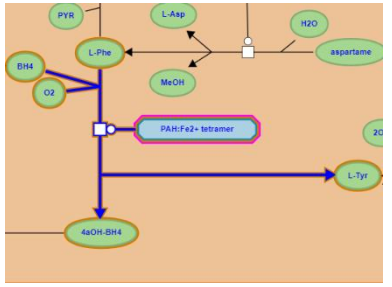
Ref Phe → Tyr

PAH

P1 Phe ~~→~~ Tyr

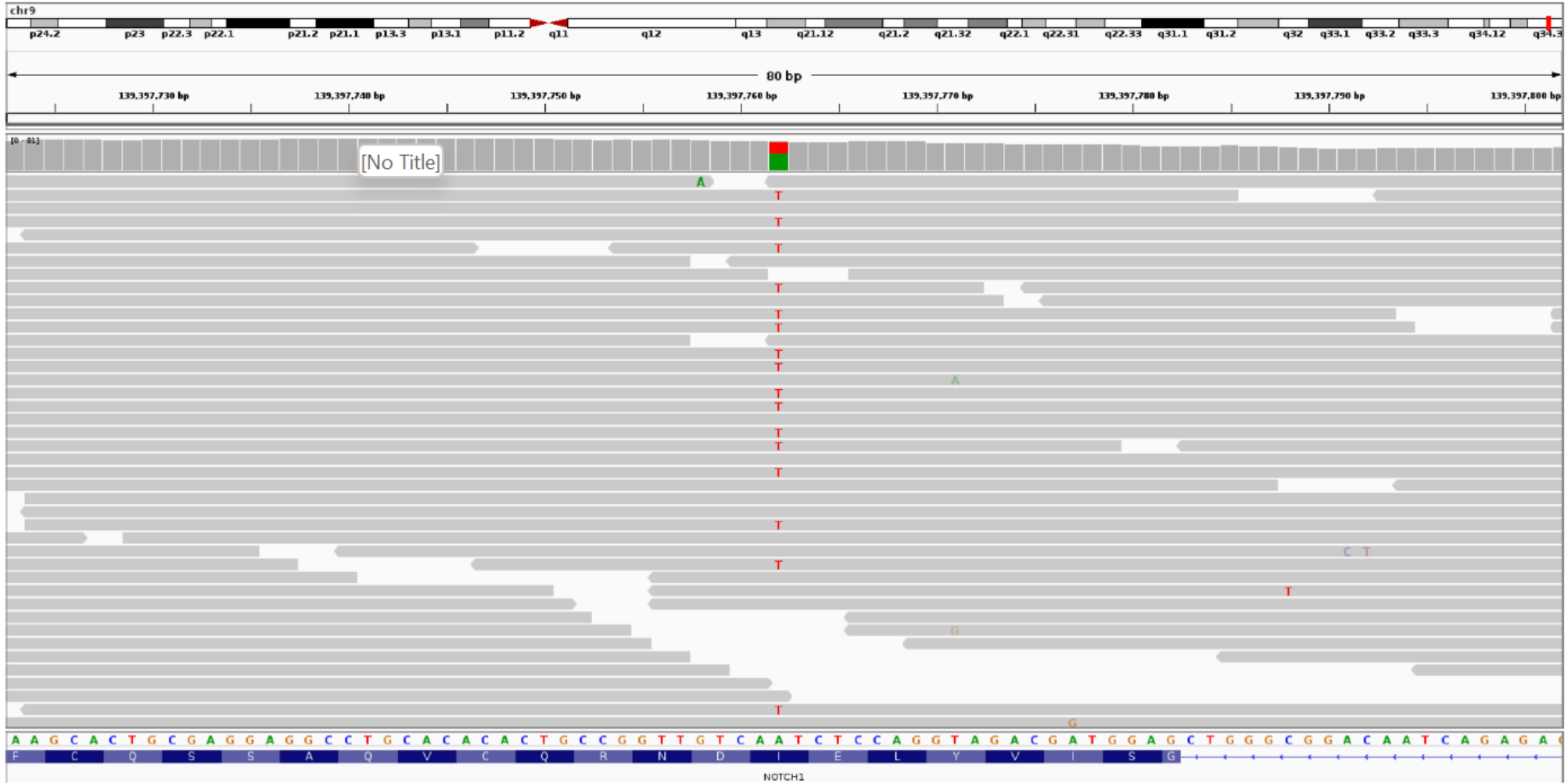






10.5772/intechopen.71769

Alignment and variant viewers



Xin chân thành cảm ơn!

Luu Phuc Loi, PhD

Email: luu.p.loi@googlemail.com

Zalo: 0901802182