UCSC Genome Browser: Latest resources for variant interpretation

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Introduction

The UCSC Genome Browser[1] is a free resource that contains much of the information required for variant analysis and interpretation. Below is a summary of the latest resources and features available:

- **Data annotations**: Brief list of most relevant datasets recently release/updated
- **Recommended Track Sets**: This feature simplifies the selection process by loading a preconfigured set of annotations
- **ClinGen ENIGMA Hub**: An example of a user-created dataset, aimed at optimizing interpretation using new BRCA guidelines
- **Features**: Some of the latest features that facilitate variant analysis

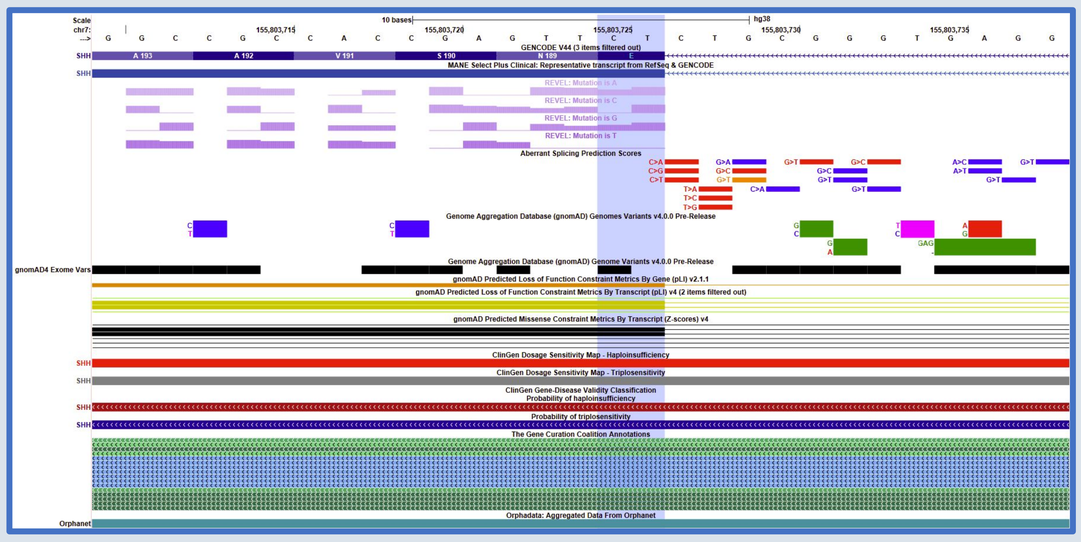
Annotations

We strive to keep our annotations up to date with the latest interpretation guidelines. Some of the most relevant datasets available in the Browser are as follows:

- **AbSplice**: Aberrant Splicing Prediction Scores
- **BayesDel**: Deleteriousness Metascore
- **REVEL** Pathogenicity Scores
- **gnomAD v4** data including **constraint mentrics**
- **Dosage Sensitivity**: pHaplo and pTriplo dosage sensitivity map
- 🔄 **DECIPHER** variants
- 🔄 **Orphadata**: Aggregated Data From Orphanet
- 🔄 **ClinGen** Curation (Dosage Sensitivity and Gene-Disease Validity)
- 🔄 **OMIM** Genes and Phenotypes
- 🔄 **Gene Curation Coalition** (GenCC) annotations
- 🔄 **NCBI RefSeq** gene annotations
- 🔄 **MANE** Select Plus Clinical gene annotations

Whenever possible, the latest annotations are shown. Many automatically update when the original source provides a new release. Designated by icon: 🔄

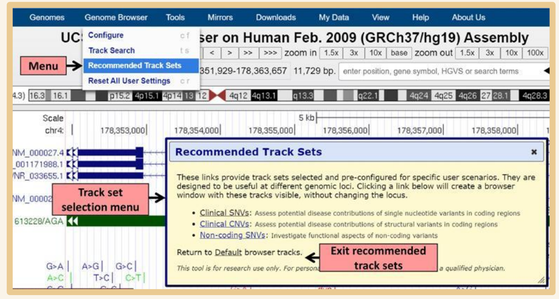
Are we missing any data you would like to see? **Email us and let us know!**

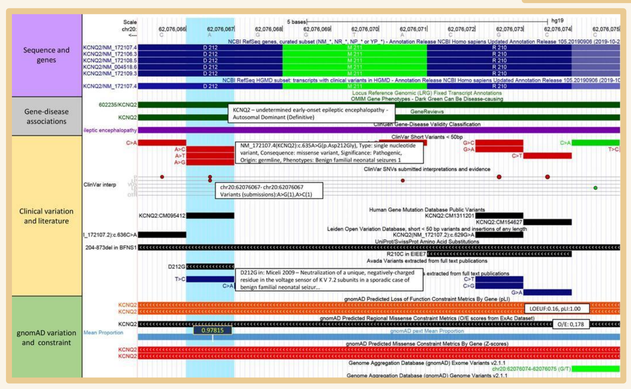


Example above shows some of the latest annotations on the start of the 3rd exon of SHH.

Recommended Track Sets

Recommended track sets are **curated track groupings** designed with specific themes. They can facilitate clinical variant interpretation by displaying the most relevant tracks in a single selection. They can be accessed via the **Genome Browser** blue bar menu (right).





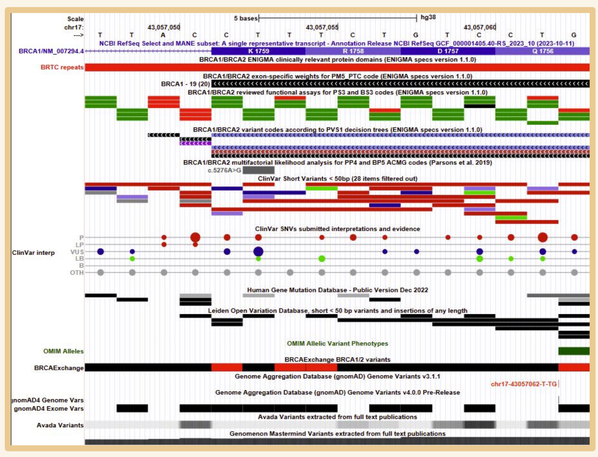
Recommended track sets are available on both **hg19** and **hg38**. The current track sets available are:

- Clinical SNVs (shown left)
- Clinical CNVs
- Non-coding SNVs
- Problematic Regions

See reference 2 to learn more.

ClinGen ENIGMA VCEP Hub for BRCA1/BRCA2

Hubs provide a way for anyone to display **custom annotations** with all the configuration options available to native Browser tracks. In this example, we collaborated to create a hub for the recent **ClinGen ENIGMA BRCA Expert Panel Specs to the ACMG/AMP Variant Interpretation Guidelines Version 1.1.0**. This hub presents all relevant data and considerably speeds up the process of biocuration and enhances the accuracy of genomic variant interpretation. Hubs like these can be **created by anyone**.



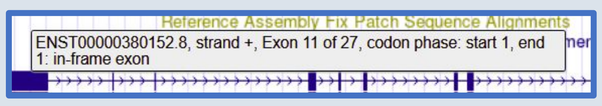
See left for an image of the hub on hg38/BRCA1. Please note that these data do not automatically update, ensure the hub name version matches latest specs.

Link/scan to load the hub:
https://bit.ly/GBenigmaV110

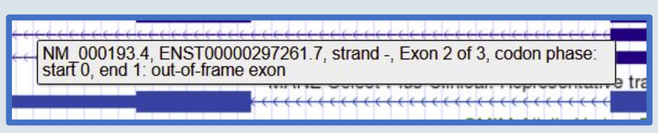
New Features for Variant Interpretation

Exon-frame now shown

All default gene tracks (or any custom data using genePred format), now display **exon-frame (phase)** information in the mouseover. This helps to understand if the skipping of an exon will produce a truncated transcript or not.



Above - Example of GENCODE track BRCA2 exon 11/27



Above - Example of MANE track SHH exon 2/3

Search historical RefSeq NMs

Searching for historical RefSeq (NM_) transcripts is now available on hg38. This issue was most notable when searching variants in papers or workflow examples. This search can be used to look up **entire NM accessions** as well as when using **HGVS terms**.

Example 1:
NM accession search: NM_198056.2

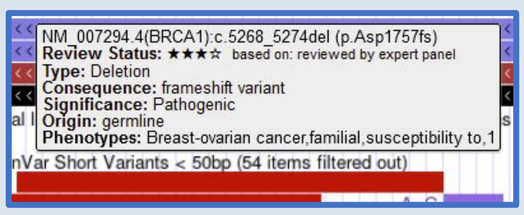
Now matches the entire length of transcript (.4 is latest)

Example 2:
HGVS term: NM_198576.2(AGRN):c.1057C>T

Now matches proper C>T position in historical transcript

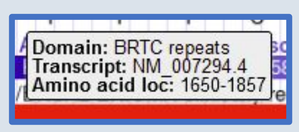
Improved mouseovers

Improved mouseovers now allow for full HTML elements to be embedded and are available for both native tracks and custom data. This allows for better depiction and structure of item information.



Left - New mouseover for ClinVar native track

Right - Example of mouseover on BRCA Exchange hub (custom data)



More Information

View this poster:

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For any questions or comments, email us at genome@soe.ucsc.edu or scan the QR code.

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References

The UCSC Genome Browser database: 2024 update. Raney BJ, Barber GP, Benet-Pagès A, Casper J, Clawson H, Cline MS, Diekhans M, Fischer C, Navarro Gonzalez J, Hickey G *et al*. *Nucleic Acids Res*. 2024 Jan 5;52(D1):D1082-D1088. PMID: 37953330.

Variant interpretation: UCSC Genome Browser Recommended Track Sets. Benet-Pagès A, Rosenbloom KR, Nassar LR, Lee CM, Raney BJ, Clawson H, Schmelter D, Casper J, Gonzalez JN, Perez G, Lee BT, Zweig AS, Kent WJ, Haeussler M, Kuhn RM.Hum Mutat. 2022 Jan 28;. PMID: 35088925