

Using ClinVar and CIViC Web Interfaces

Querying variants against the ClinVar interface

1. Go the ClinVar web interface at <https://www.ncbi.nlm.nih.gov/clinvar/> and query the following variant in the search bar at the top: “BRAF V600E”

2. Click on the second variant listed under “Search Results”. The selected entry should look like:

The screenshot shows the ClinVar web interface. At the top, there is a search bar with the text "Search by gene symbols, location, HGVS expressions, c-dot, p-dot, conditions, i" and a "Search ClinVar" button. Below the search bar, there are navigation links: "About", "Access", "Submit", "Stats", "FTP", and "Help". The main content area displays the variant "NM_004333.6(BRAF):c.1798_1799delinsAA" with options to "Cite", "Follow", "Print", and "Download". There are two sections for classification: "Germline" and "Somatic". The "Germline" section has a toggle switch set to "Off" and the text "No data submitted for germline classification". The "Somatic" section has a toggle switch set to "On" and the text "No data submitted for somatic clinical impact". To the right of the "Somatic" section, there is an "Oncogenicity" section with a star rating of 1 and the text "Oncogenic criteria provided, single submitter". On the right side of the page, there is a "On this page" sidebar with links: "Classification Sun", "Variant Details", "Genes", "Germline", "Submissions", "Citations", "Somatic", "Conditions", "Submissions", "Citations", and "Text mined Citatic". Below the variant details, there is a "Variant Details" section with a link icon. The "Variant Details" section contains the following information: "This haplotype includes the following variants" with a list of two variants: "NM_004333.6(BRAF):c.1799T>A (p.Val600Glu) - Variation ID 13961" and "NM_004333.6(BRAF):c.1798G>A (p.Val600Met) - Variation ID 44815". Below this, there is a section for "NM_004333.6(BRAF):c.1798_1799delinsAA" with fields for "Other names:", "Functional consequence:", and "Links:", all of which are currently empty.

3. Examine the different categories on the page. Do you think this is a trustworthy oncogenicity assessment? Why or why not?

Querying variants against the CIViC interface

1. Go to the CIViC web interface at <https://civicdb.org/> and again query the following variant in the search bar at the top: “BRAF V600E”. Click on the second item that appears in the search bar

The screenshot shows the CIViC web interface. At the top, there is a search bar with the text "BRAF V600E". Below the search bar, there are navigation links: "Home", "About CIViC", "Help", and "Documentation". The search results are displayed in a list. The first result is "BRAF - V600E — Feature: BRAF". The second result is "BRAF V600E", which is highlighted with a red box. The third result is "BRAF - V600E+V600K — Feature: BRAF".

2. Examine the molecular profile entry. What different categories do you see on the page?

3. Go to the “Evidence” box and click on one of the evidence IDs. What evidence item did you choose? What rating was associated with that evidence item and why?

Evidence 35 of 187 displayed

EID	Disease	Therapies
EID10785	Anaplastic Thyroid...	Dabrafenib/Trametini...
EID11244	Melanoma	Dabrafenib
EID12161	Solid Tumors, Advanced	Dabrafenib Trametinib
EID12162	Low Grade Glioma	Trametinib Dabrafenib
EID11312	Pleomorphic...	Dabrafenib Trametinib
EID11313	Pilocytic Astrocytoma	Dabrafenib Trametinib
EID2120	Colorectal Cancer	Bevacizumab

4. Go to the “BRAF V600E Assertions” box and click on one of the assertion IDs. What assertion item did you choose? What was the variant origin and AMP/ASCO/CAP category associated with the assertion?

BRAF V600E Assertions 4 of 4 displayed

AID	Molecular Profile	Disease
AID20	BRAF V600E	Colorectal Cancer
AID7	BRAF V600E	Melanoma
AID10	BRAF V600E	Melanoma
AID23	BRAF V600E	Colorectal Cancer