User Guide: How utilize dsRNAscan results for your genes of interest using IGV and shiny

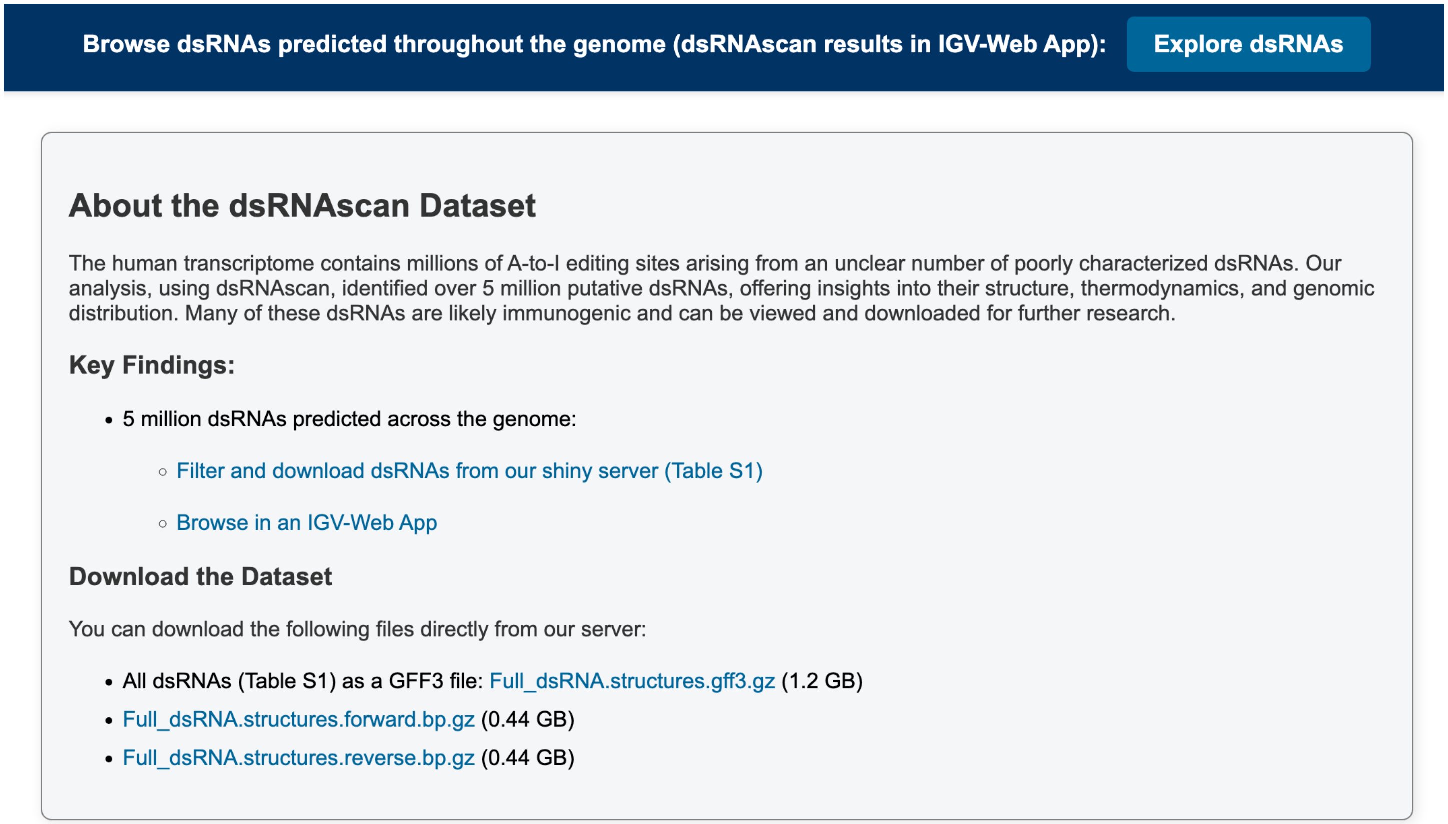
Introduction

Welcome to dsrna.chpc.utah.edu! This resource offers a unique way to dive into the **human dsRNAome**, helping you explore potential functional implications of dsRNAs, whether it's regulating gene expression or activating immune responses. Let's walk through how to make the most of this platform and discover dsRNAs that matter for your research.

Step 1: Getting Started IGV-Web App

- Open your preferred web browser and go to dsrna.chpc.utah.edu.

    1. Click on the **"Explore dsRNAs"** to view results in the IGV-Web App.



Browse dsRNAs predicted throughout the genome (dsRNAscan results in IGV-Web App): Explore dsRNAs

About the dsRNAscan Dataset

The human transcriptome contains millions of A-to-I editing sites arising from an unclear number of poorly characterized dsRNAs. Our analysis, using dsRNAscan, identified over 5 million putative dsRNAs, offering insights into their structure, thermodynamics, and genomic distribution. Many of these dsRNAs are likely immunogenic and can be viewed and downloaded for further research.

Key Findings:

- 5 million dsRNAs predicted across the genome:
    - Filter and download dsRNAs from our shiny server (Table S1)
    - Browse in an IGV-Web App

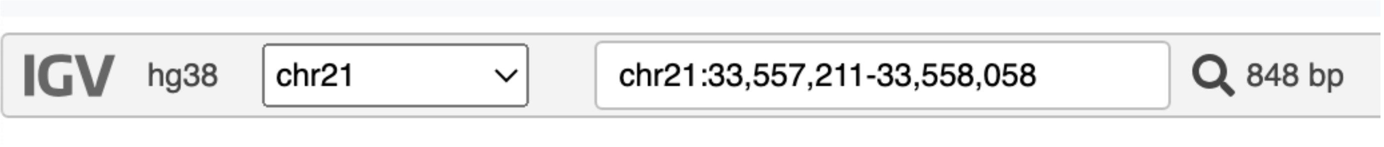
Download the Dataset

You can download the following files directly from our server:

- All dsRNAs (Table S1) as a GFF3 file: Full_dsRNA.structures.gff3.gz (1.2 GB)
- Full_dsRNA.structures.forward.bp.gz (0.44 GB)
- Full_dsRNA.structures.reverse.bp.gz (0.44 GB)

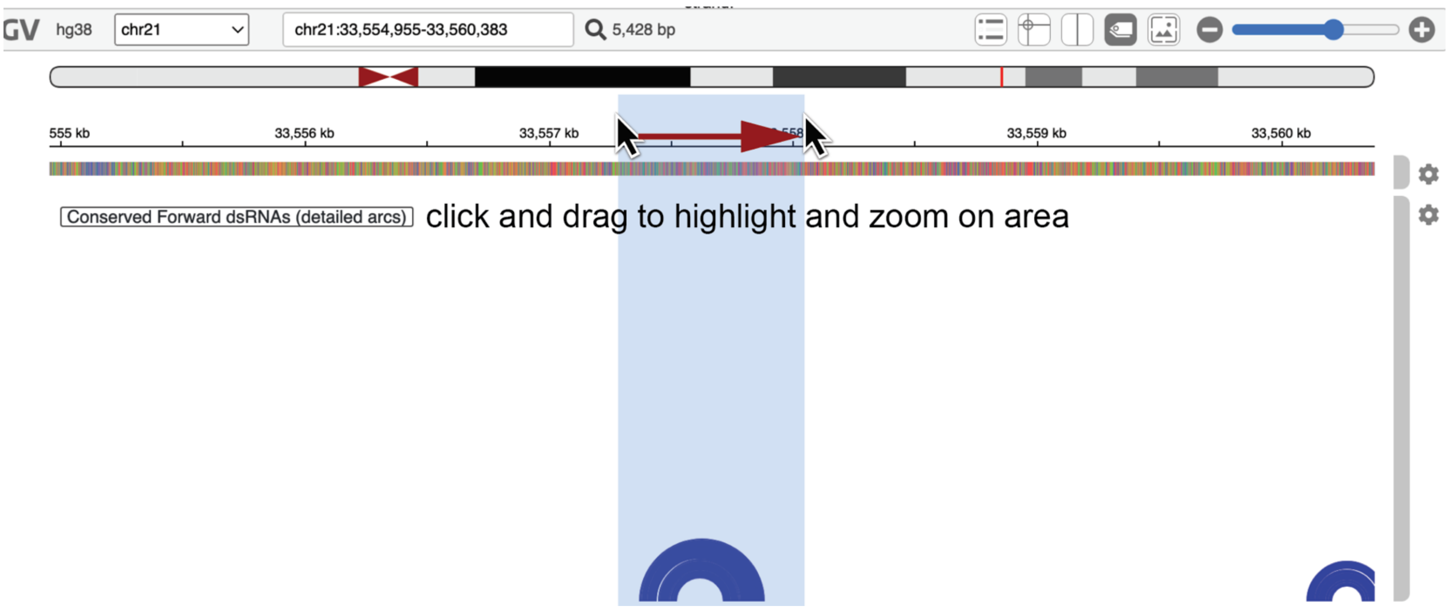
Step 2: Selecting a Region or Gene of Interest

- At the top of the page, you'll find a search bar where you can enter the gene name, transcript ID, or genomic coordinates of interest (e.g., "ZNF426" or "chr1:100000-200000").



- You can also browse dsRNAs across the entire genome by navigating through the chromosome map. This is a great way to see the bigger picture before diving into specifics.

- Zoom in or out by clicking the + or – buttons here
    - -or-

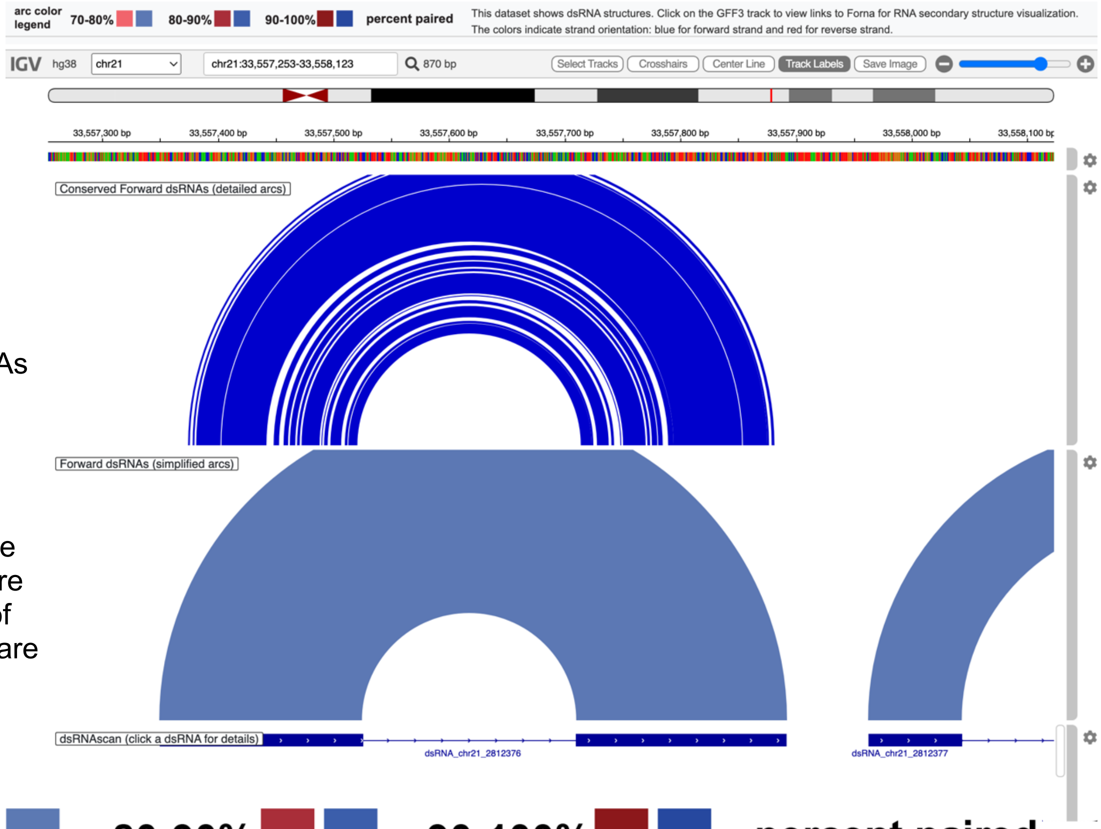


click and drag to highlight and zoom on area

- Moving around the genome:
    - Hold a click and drag left or right to move upstream or downstream
    - -or- Click on a chromosome position (red line shows position)

Step 3: Understanding dsRNA Predictions

- Once you've selected a region, the **dsRNA Viewer** will appear, displaying predicted dsRNAs as arcs or tracks.



This dataset shows dsRNA structures. Click on the GFF3 track to view links to Forna for RNA secondary structure visualization. The colors indicate strand orientation: blue for forward strand and red for reverse strand.

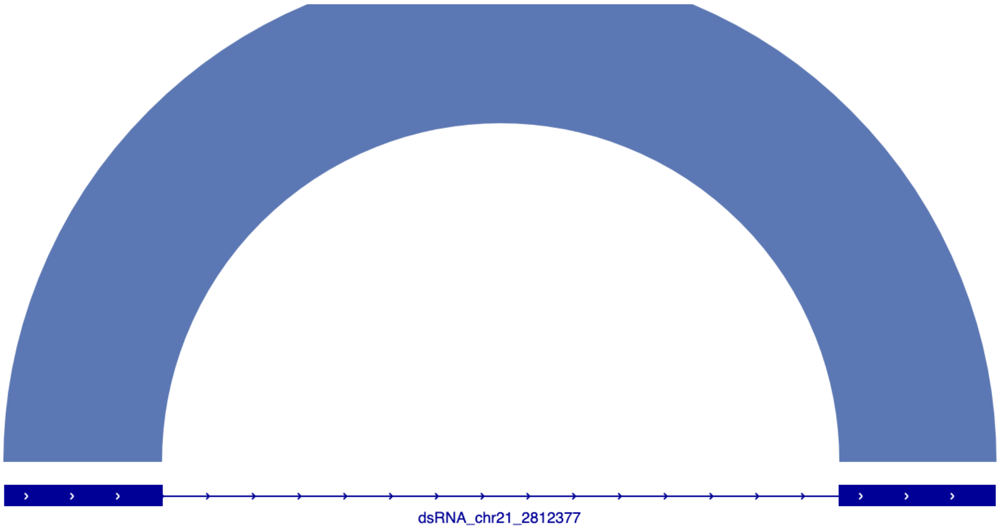
Arcs represent base-paired dsRNA regions, with larger arcs indicating longer dsRNAs.

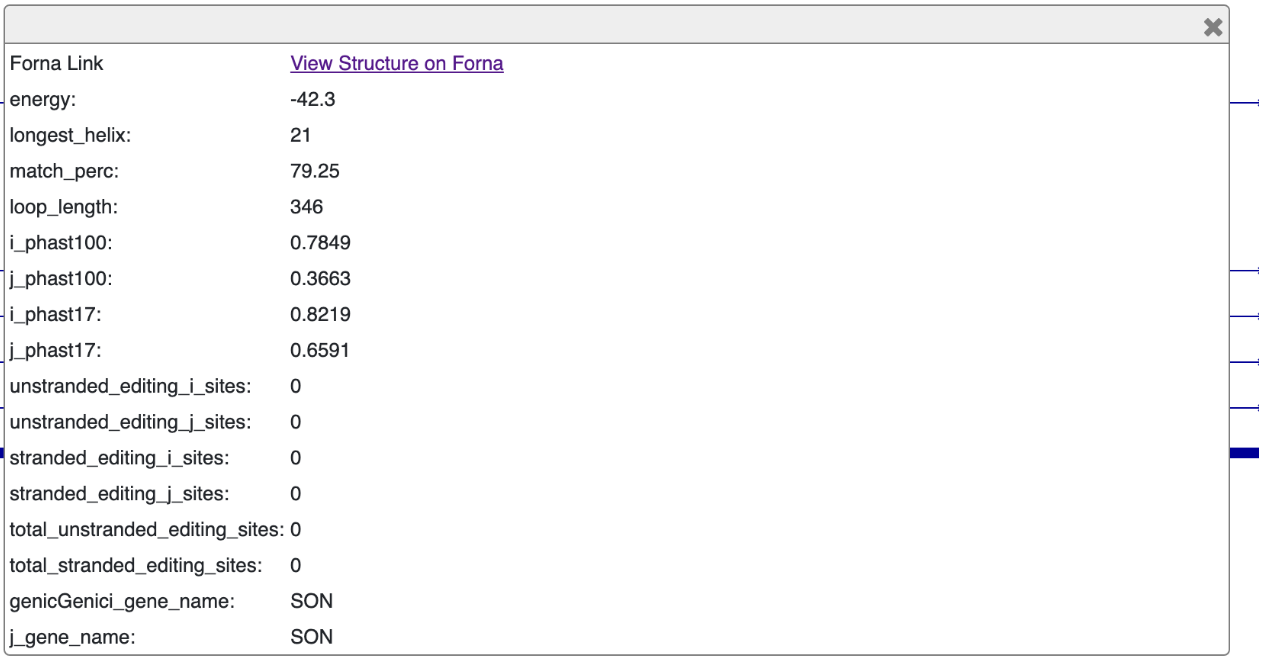
Detailed arcs show individual base pairs. This track is only available for conserved dsRNAs (for now)

Simplified arcs show where the dsRNA was predicted. They are colored based on how much of the nucleotides in the dsRNA are paired.


arc color legend 70-80% 🟥 🟦 80-90% 🟥 🟦 90-100% 🟥 🟦 percent paired

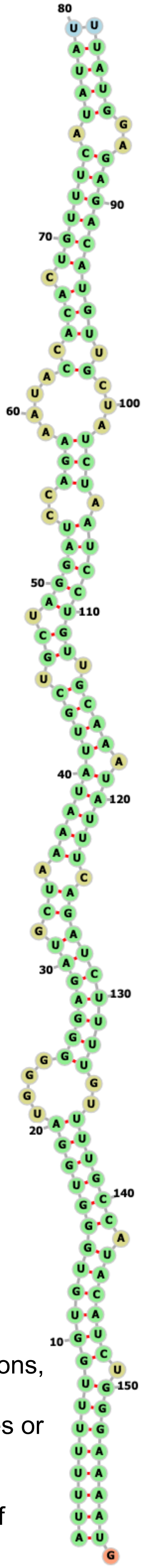
- **GFF3 Track.** Each arc has a corresponding gff3 entry which can be clicked on.
- These tracks show the dsRNA as its two arms, connected by a thin line (the loop). They are colored blue for forward strand and red for reverse strand.





Forna Link	View Structure on Forna
energy:	-42.3
longest_helix:	21
match_perc:	79.25
loop_length:	346
i_phast100:	0.7849
j_phast100:	0.3663
i_phast17:	0.8219
j_phast17:	0.6591
unstranded_editing_i_sites:	0
unstranded_editing_j_sites:	0
stranded_editing_i_sites:	0
stranded_editing_j_sites:	0
total_unstranded_editing_sites:	0
total_stranded_editing_sites:	0
genicGenici_gene_name:	SON
j_gene_name:	SON

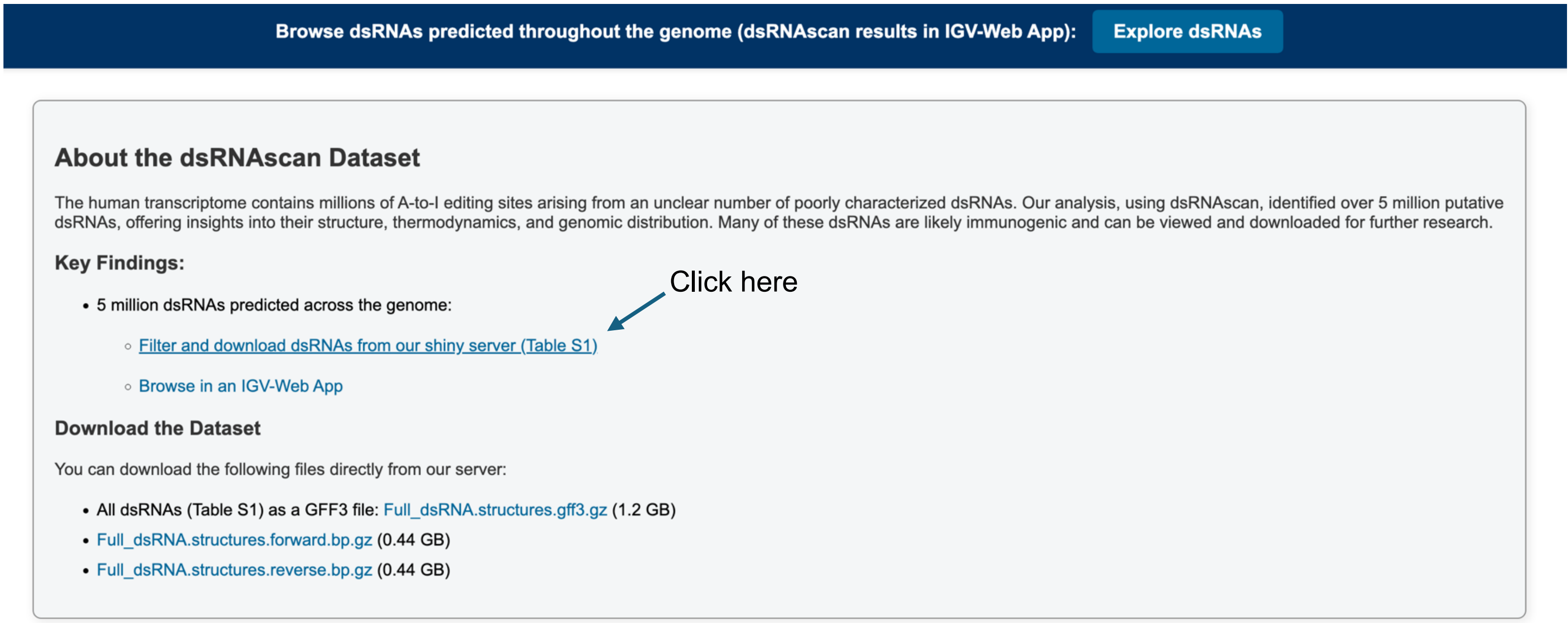
- When you click on these you get all the details about the dsRNA:
  - Start and end positions.
  - Base-pairing percentages.
  - Predicted thermodynamic stability (ΔG).
  - A link to view the structure on FORNA (example image on right)



Step 4: Interpreting the Data

- Now let's add some context. We have added relevant datasets, such as GENCODE annotations, RNA editing sites or repetitive elements (e.g., Alu sequences).
- Look at other features like **REDIportal Editing Sites** or **Repeats** to visualize how editing sites or repetitive elements intersect with dsRNA structures.
- But you can add more. To do this, select **"Tracks"** from the panel on the left.
- This is your chance to connect dsRNAs with other layers of genomic data and make sense of potential functional roles.

Using the SHINY data table to filter and download dsRNAscan data



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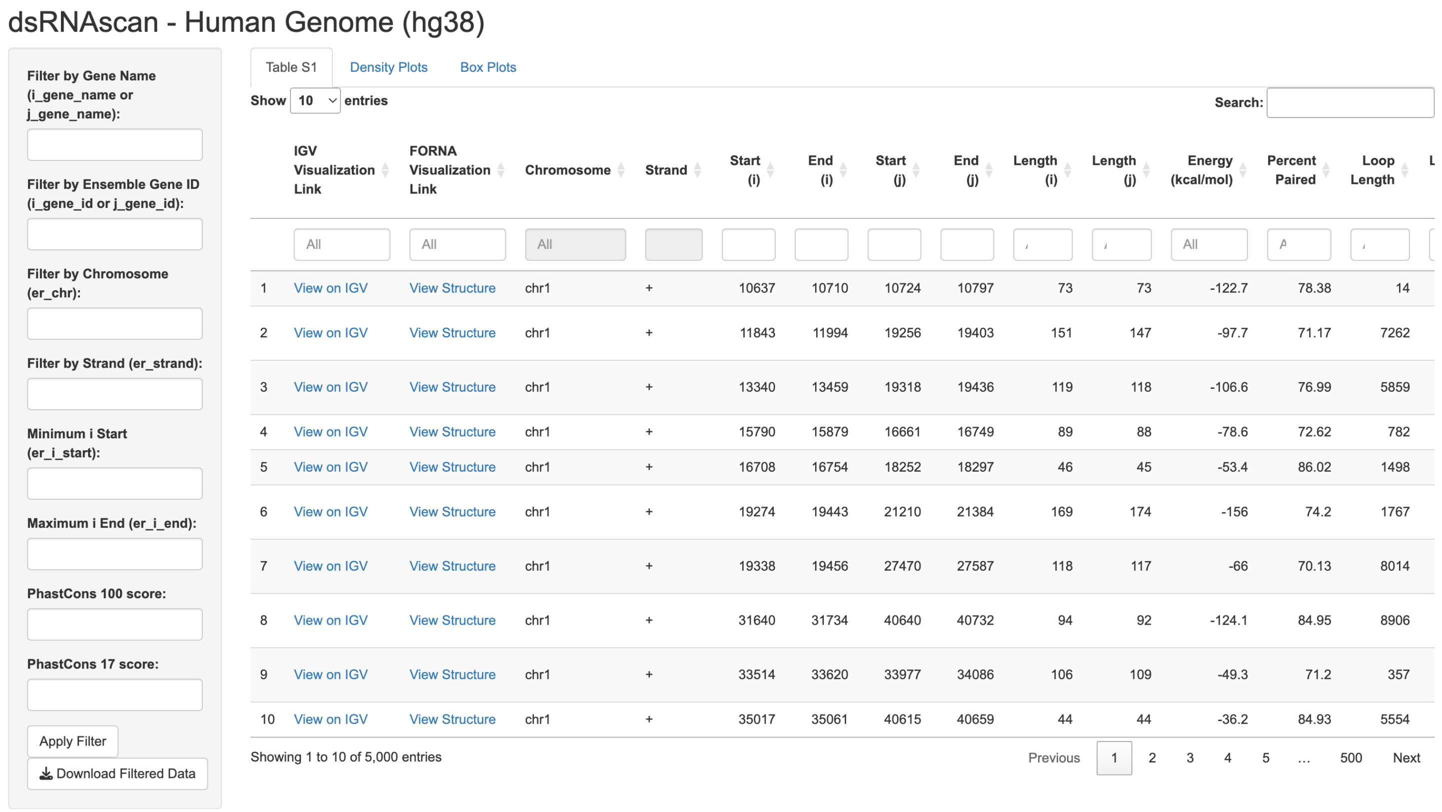
- The shiny platform allows you to browse the data as a table and includes information like our machine learning models to classify dsRNAs by their likelihood of being edited by ADARs on both arms.
- Use the **"Filters"** on the left to sort dsRNAs by gene name, location, or conservation.
- -or- Use the filters at the top of each column after doing an initial filter
- These filters make it easier to zero in on dsRNAs that might be functionally relevant, whether that's for gene regulation or immune activation.

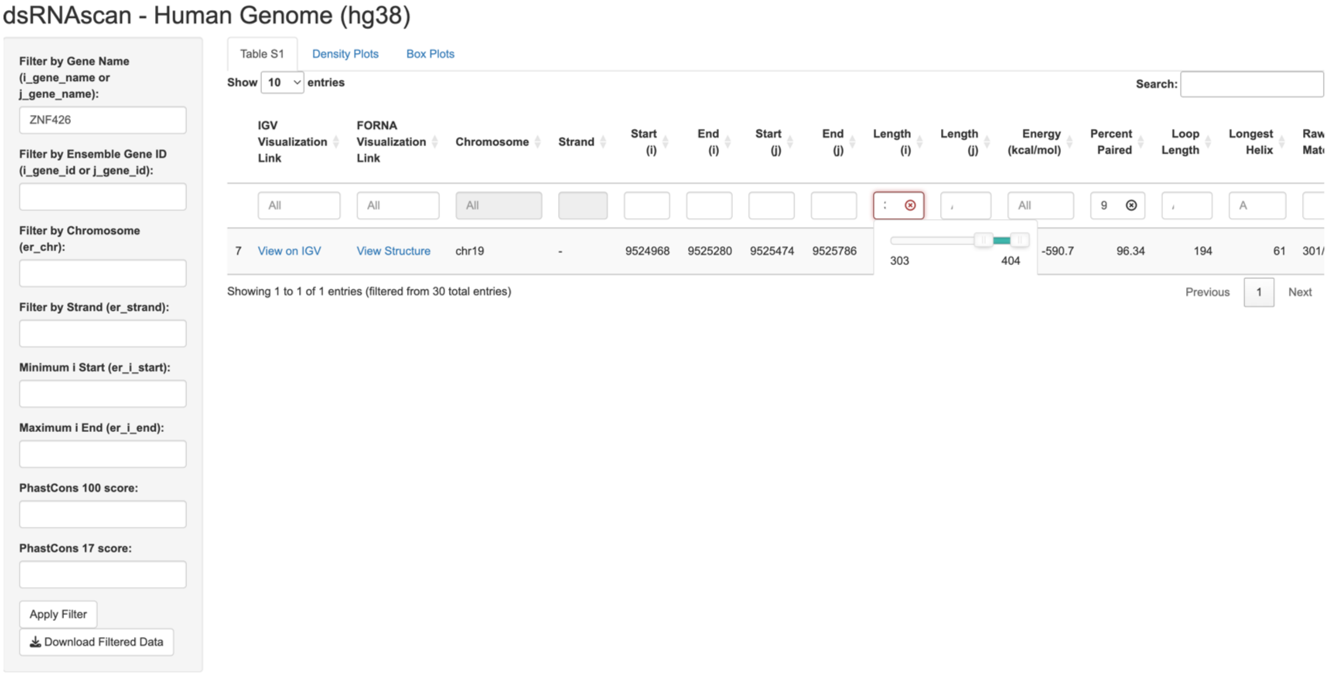


	IGV Visualization Link	FORNA Visualization Link	Chromosome	Strand	Start (i)	End (i)	Start (j)	End (j)	Length (i)	Length (j)	Energy (kcal/mol)	Percent Paired	Loop Length	L
	All	All	All								All			
1	View on IGV	View Structure	chr1	+	10637	10710	10724	10797	73	73	-122.7	78.38	14	
2	View on IGV	View Structure	chr1	+	11843	11994	19256	19403	151	147	-97.7	71.17	7262	
3	View on IGV	View Structure	chr1	+	13340	13459	19318	19436	119	118	-106.6	76.99	5859	
4	View on IGV	View Structure	chr1	+	15790	15879	16661	16749	89	88	-78.6	72.62	782	
5	View on IGV	View Structure	chr1	+	16708	16754	18252	18297	46	45	-53.4	86.02	1498	
6	View on IGV	View Structure	chr1	+	19274	19443	21210	21384	169	174	-156	74.2	1767	
7	View on IGV	View Structure	chr1	+	19338	19456	27470	27587	118	117	-66	70.13	8014	
8	View on IGV	View Structure	chr1	+	31640	31734	40640	40732	94	92	-124.1	84.95	8906	
9	View on IGV	View Structure	chr1	+	33514	33620	33977	34086	106	109	-49.3	71.2	357	
10	View on IGV	View Structure	chr1	+	35017	35061	40615	40659	44	44	-36.2	84.93	5554	

Showing 1 to 10 of 5,000 entries

Example 1: Focusing on Potentially Immunogenic dsRNAs

- Want to find dsRNAs that might activate immune responses? We've got you covered!
  - Filter by your gene of interest.
    - Lets use the gene symbol *ZNF426* as an example
- Use the **length and percent paired filter** at the top of they table to narrow down results to long (>300), and highly paired (>96%) dsRNAs, which are likely substrates for immune sensors like MDA5.



dsRNAscan - Human Genome (hg38)

Filter by Gene Name (i_gene_name or j_gene_name): ZNF426
Filter by Ensemble Gene ID (i_gene_id or j_gene_id):
Filter by Chromosome (er_chr):
Filter by Strand (er_strand):
Minimum i Start (er_i_start):
Maximum i End (er_i_end):
PhastCons 100 score:
PhastCons 17 score:

	IGV Visualization Link	FORNA Visualization Link	Chromosome	Strand	Start (i)	End (i)	Start (j)	End (j)	Length (i)	Length (j)	Energy (kcal/mol)	Percent Paired	Loop Length	Longest Helix	Raw Mat
	All	All	All								All	9		A	
7	View on IGV	View Structure	chr19	-	9524968	9525280	9525474	9525786			-590.7	96.34	194	61	301/

Showing 1 to 1 of 1 entries (filtered from 30 total entries)

- You'll quickly spot the single long, highly-paired dsRNA.
- You can click on links to view it in the IGV browser or View Structure in FORNA to see the specific base paired structure.

Exporting Results

- Once you've identified interesting dsRNAs, you can easily export the data for further analysis.
- Click the **"Download"** button to export dsRNA data as a csv file to open in Excel or other spreadsheet software.

Conclusion

The resources provided here (at https://dsrna.chpc.utah.edu) are designed to be your gateway to explore human dsRNAome. Our hope is that you can uncover dsRNAs that may play key roles in gene regulation, immune activation, and more. Whether you're investigating a specific gene or exploring the broader genome, we hope this guide helps you make meaningful discoveries!

If you have any questions let us know:

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