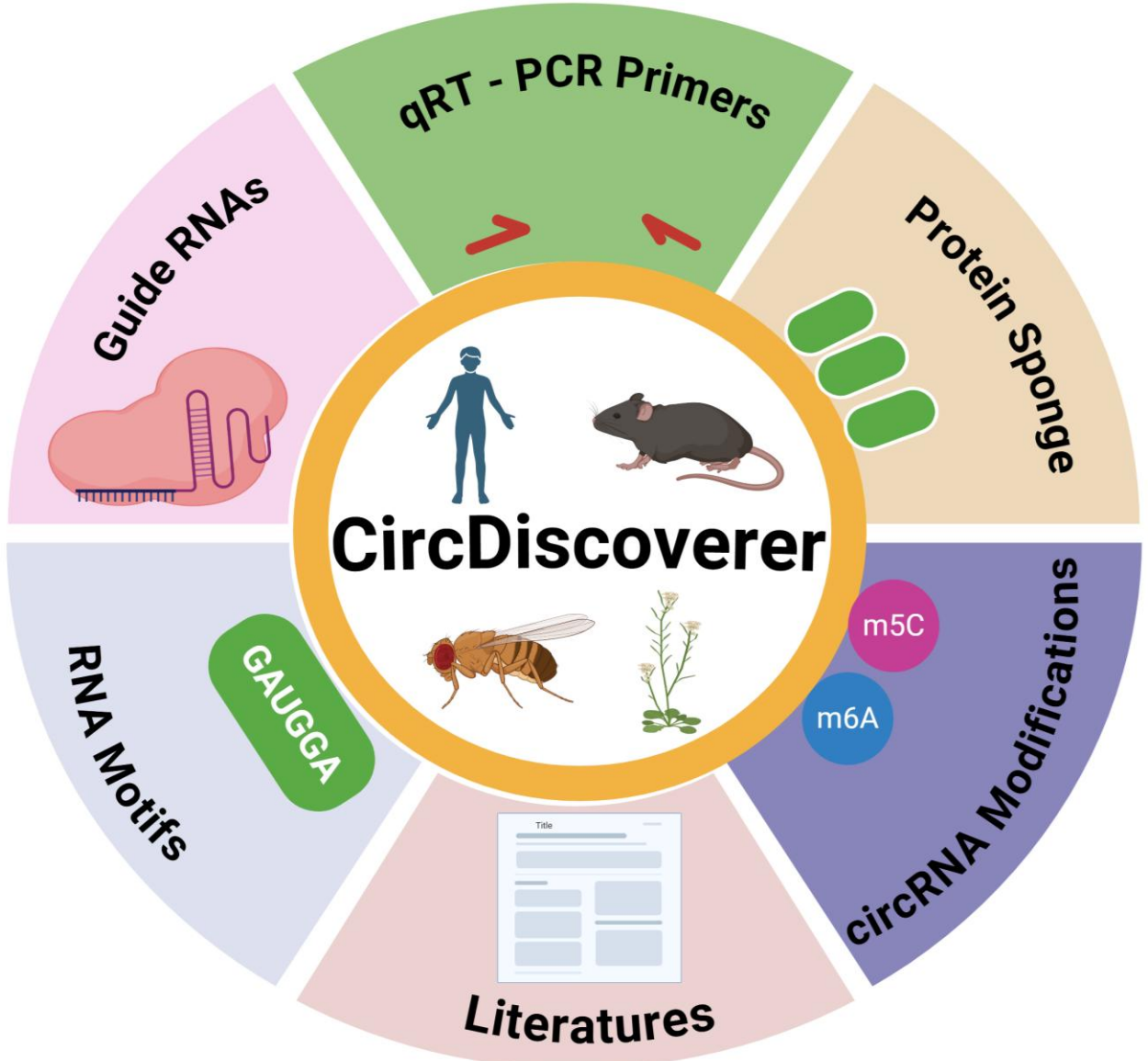
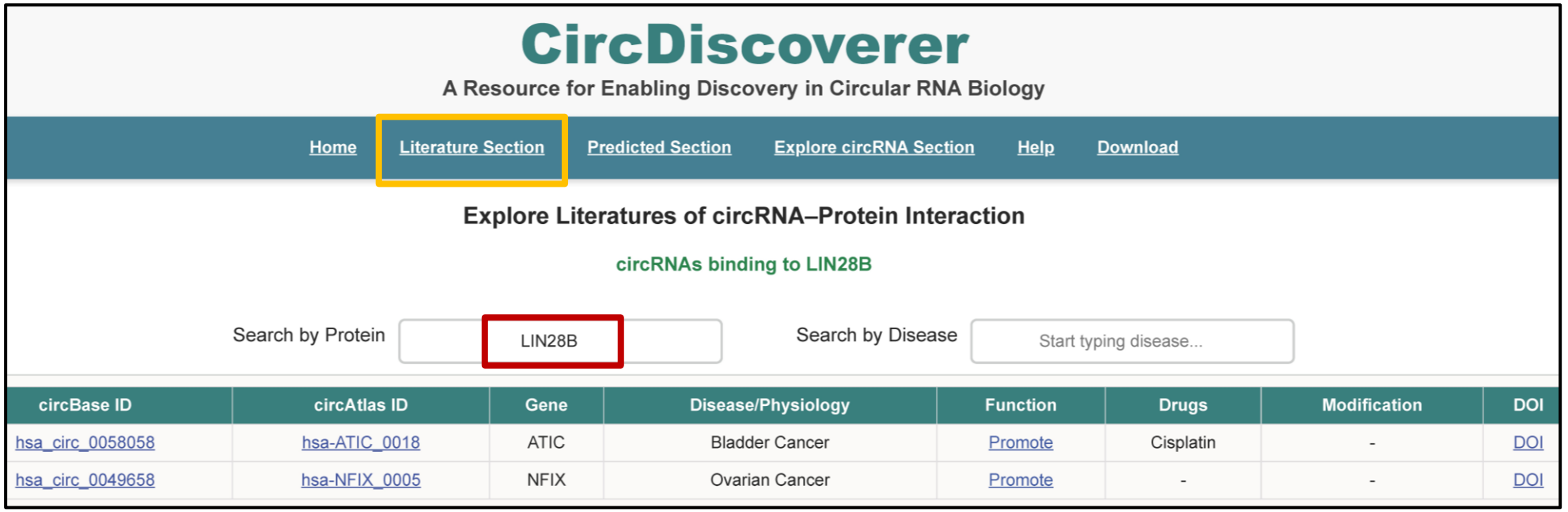
# Welcome To CircDiscoverer



# Literature Section

Explore the circRNA-Protein Interaction reported in the literatures

- Enter the name of protein to get the following details (Page 2-5) :
- E.g. Search by Protein, i.e. ***LIN28B*** in this case




| circBase ID | circAtlas ID | Gene | Disease/Physiology | Function | Drugs | Modification | DOI |
|---|---|---|---|---|---|---|---|
| hsa_circ_0058058 | hsa-ATIC_0018 | ATIC | Bladder Cancer | Promote | Cisplatin | - | DOI |
| hsa_circ_0049658 | hsa-NFIX_0005 | NFIX | Ovarian Cancer | Promote | - | - | DOI |

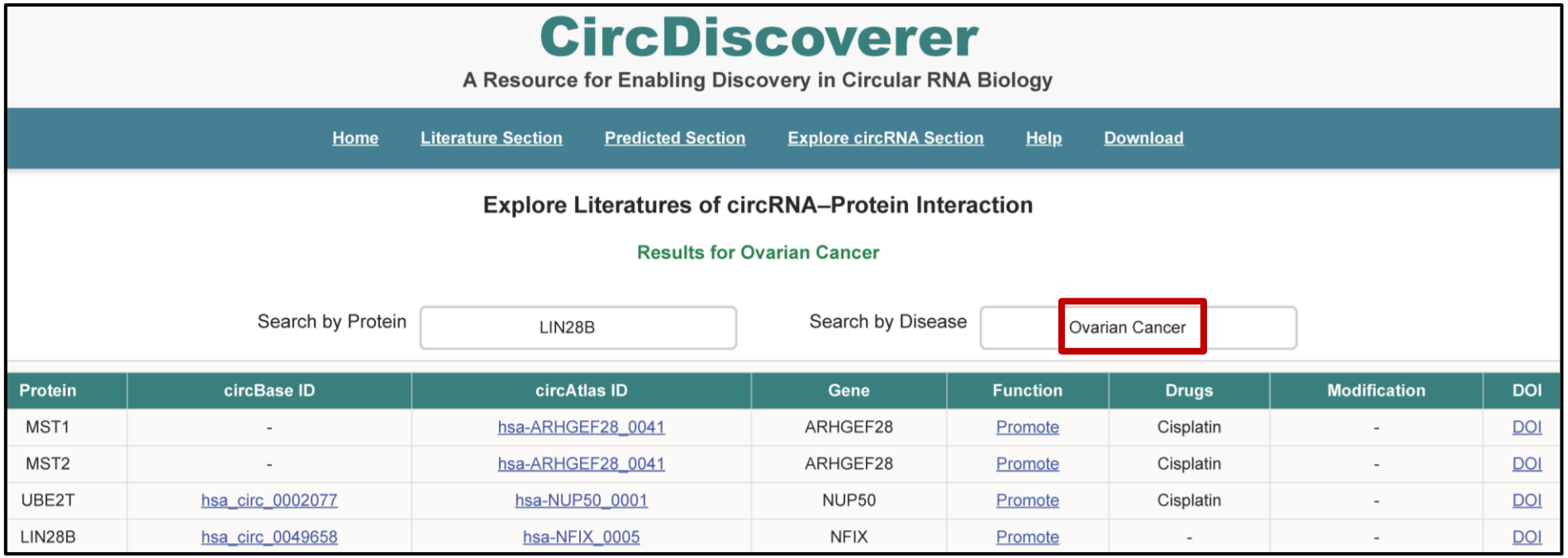
# Details of Literature Section

- **hg19** : The ***circBase*** ID of the binding circRNA.
- **hg38** : The ***circAtlas 3.0*** ID of the binding circRNA.
- **Gene** : The gene from which the circRNA is derived.
- **Disease** : The disease in which this circRNA-Protein Interaction is reported.
- **Function** : Function of this circRNA-Protein interaction in the respective disease, whether the circRNA-Protein interaction either promotes or inhibits the respective disease. Clicking this will open a pop up, describing the mechanism of the CPI in the respective disease.
- **Drugs** : The drugs, whose response is affected in the disease by this circRNA-Protein Interaction.
- **Modifications** : The modifications found in the interacting circRNA.
- **DOI** of the literature.

# Literature Section …. Continued

Enter the name of a diseases  to get the following details (Page 4-5) :

E.g. Search by Protein, i.e. ***Ovarian Cancer*** in this case.



CircDiscoverer

A Resource for Enabling Discovery in Circular RNA Biology

Home | Literature Section | Predicted Section | Explore circRNA Section | Help | Download

Explore Literatures of circRNA–Protein Interaction

Results for Ovarian Cancer

Search by Protein: LIN28B  Search by Disease: Ovarian Cancer

| Protein | circBase ID | circAtlas ID | Gene | Function | Drugs | Modification | DOI |
|---|---|---|---|---|---|---|---|
| MST1 | - | hsa-ARHGEF28_0041 | ARHGEF28 | Promote | Cisplatin | - | DOI |
| MST2 | - | hsa-ARHGEF28_0041 | ARHGEF28 | Promote | Cisplatin | - | DOI |
| UBE2T | hsa_circ_0002077 | hsa-NUP50_0001 | NUP50 | Promote | Cisplatin | - | DOI |
| LIN28B | hsa_circ_0049658 | hsa-NFIX_0005 | NFIX | Promote | - | - | DOI |

# Literature Section …. Continued

- **Protein** : List of Proteins interacting with the circRNAs, involved in the disease.
- **hg19** : The ***circBase*** ID of the binding circRNA.
- **hg38** : The ***circAtlas 3.0*** ID of the binding circRNA.
- **Gene** : The gene from which the circRNA is derived.
- **Function** : Function of this circRNA-Protein interaction in the respective disease, whether the circRNA-Protein interaction either promotes or inhibits the respective disease. Clicking this will open a pop up, describing the mechanism of the CPI in the respective disease.
- **Drugs** : The drugs, whose response is affected in the disease by this circRNA-Protein Interaction.
- **Modifications** : The modifications found in the interacting circRNA.
- **DOI** of the literature.

# Predicted Section

This sections displays the list of possible circRNAs binding to the selected protein and organism of interest.

This sections enables users to explore circRNAs binding to the given protein of interest either at the individual Bioproject level (Fig A) or across all protein samples analysed in this study (Fig B), as shown below.

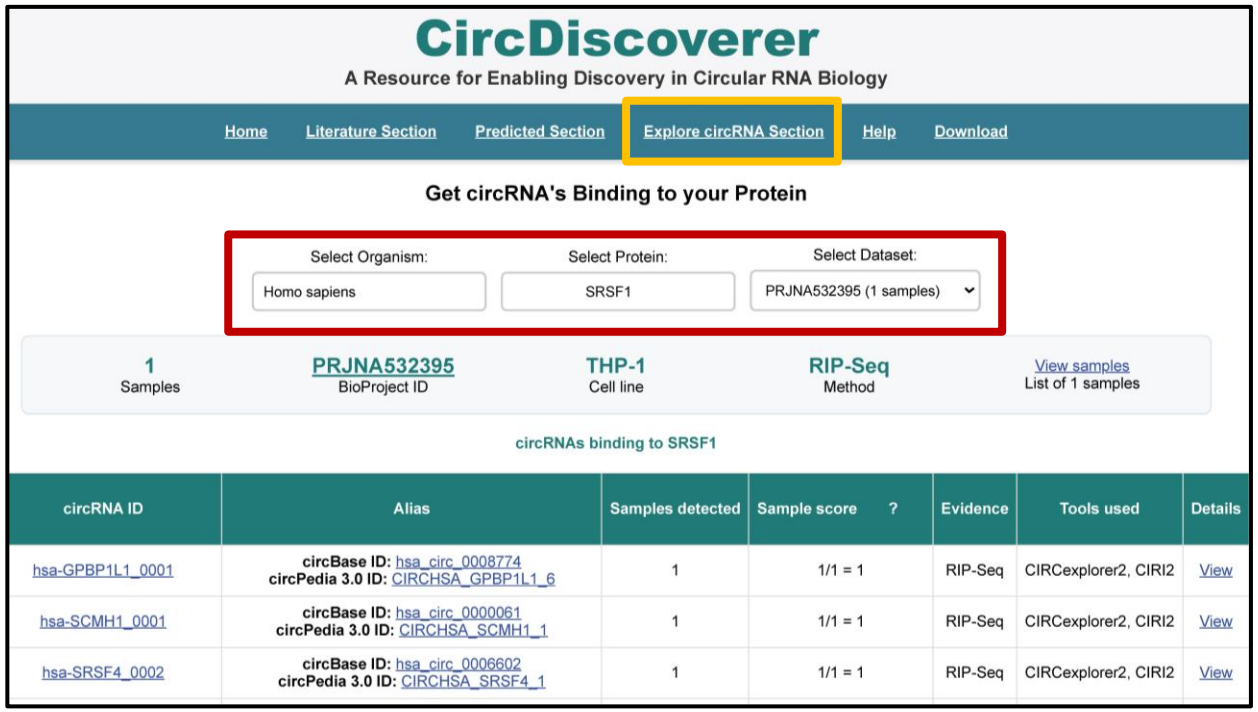



Fig A

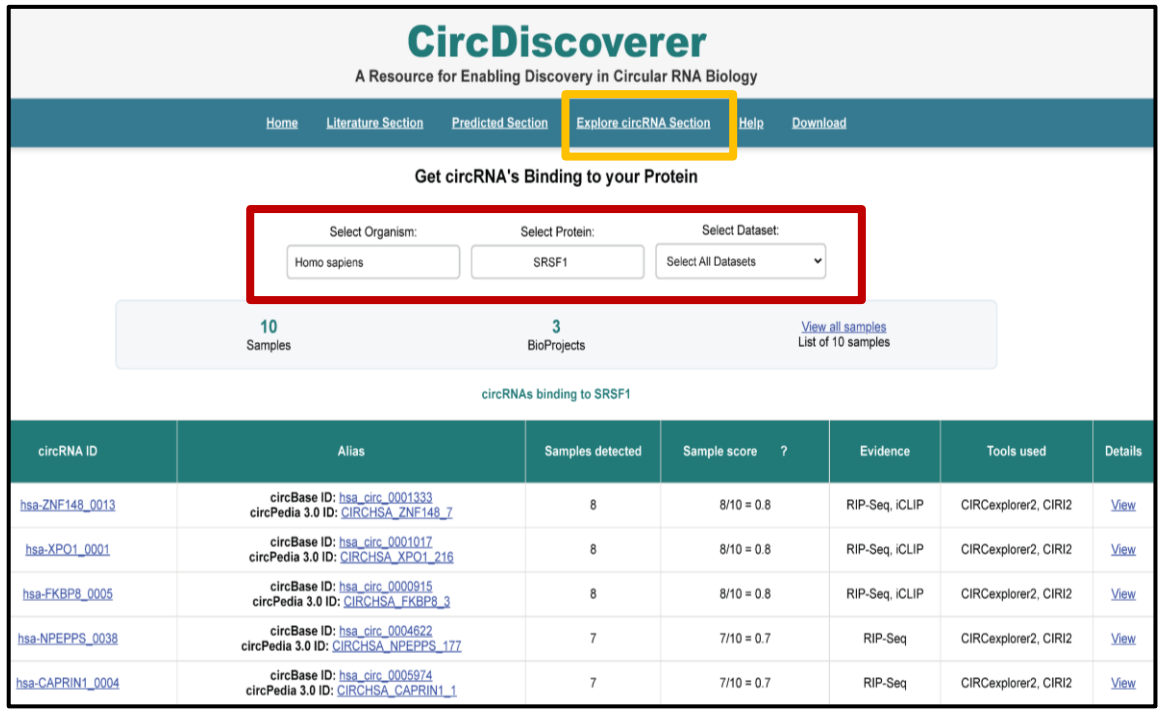



Fig B

# Details of the Predicted Section

- **circRNA ID** : circRNAs binding to the selected protein and organism of interest. For *Homo sapiens* and *Mus musculus,* circRNAs are mapped to the circAtlas 3.0 ID, CIRCPedia 3.0 for *Drosophila melanogaster* and PlantCircRNA for *Arabidopsis thaliana.*

- **Alias**: The other circRNA IDs for a given circRNA ID. Only for *Homo sapiens* and *Mus musculus,* alias are present i.e. circBase and CIRCPedia 3.0 IDs.

- **Sample Detected** : The number of samples in which a particular circRNA of interest is found.

- **Sample Score** : A metric used to measure the detection frequency of a circRNA. It tells in how many samples out of the total samples analysed, that particular circRNA is found.

- **Evidence Type** : Evidences or strategies used to infer the circRNA-Protein Interactions(CPIs).

- **Tools** : The respective tools used to analyse the CPIs.

- **Details :** Clicking on the View displays the list of protein samples, in which the circRNAs were detected, followed by the details of the tools used, and the respective raw counts detected by those tools.

# Explore circRNA Section

This section allows users to explore a circRNA of the selected organism in detail, either through its circRNA ID or by entering the coordinates as shown below. This section displays four tabs, i.e. ***Get Proteins***, ***Get Guide RNA***, ***Get Modifications*** and ***Get Primers,*** which will be discussed further ahead.

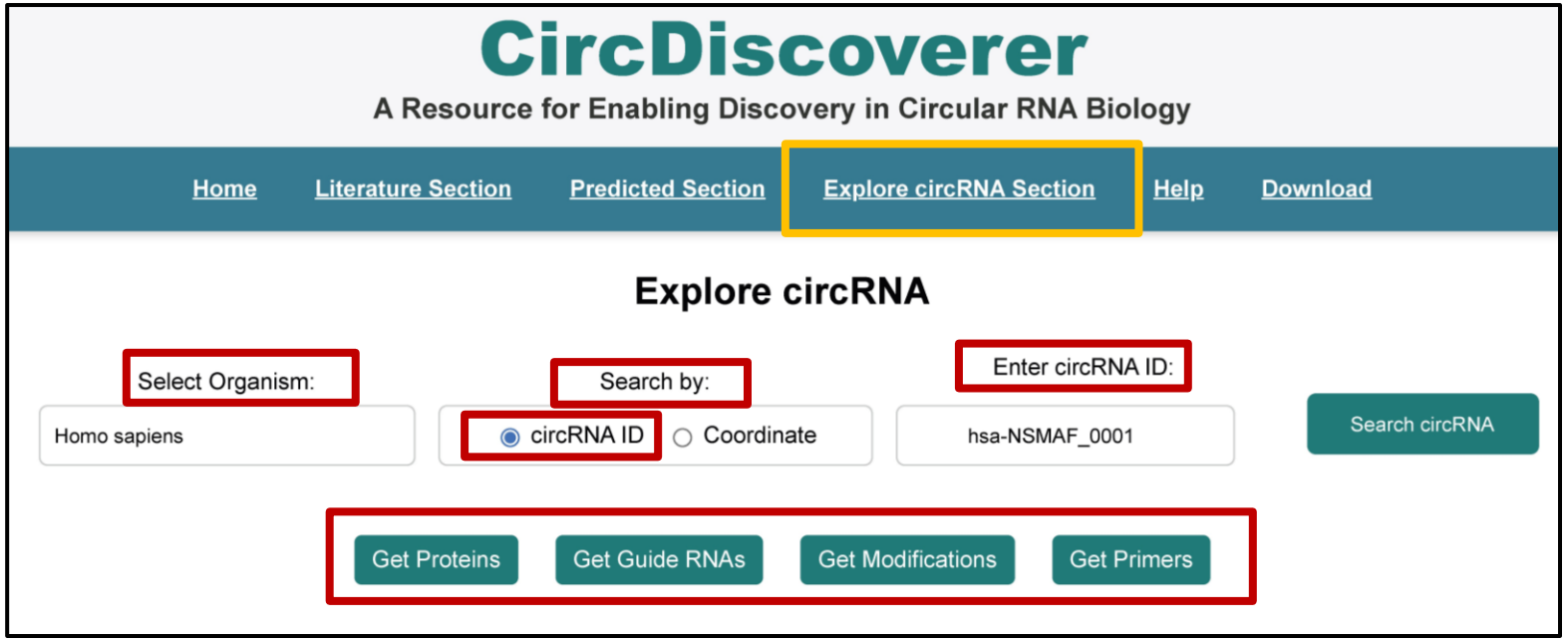
The circRNAs are mapped to their respective organism specific databases, i.e.,

- *Homo sapiens* : **circAtlas 3.0 (hg38)**
- *Mus musculus* : **circAtlas 3.0 (hg38)**
- *Drosophila melanogaster* : **CIRCPedia 3.0 (dm6)**
- *Arabidopsis thaliana* : **PlantCircRNA**

# Explore circRNA Section

## Search by circRNA ID

- First select the organism of interest.
- Then click on the radio button of circRNA-ID, this aill automatically load all circRNAs in the dropdown.
- Click on the search button, which will automatically display the four tabs, clicking on any of these will display the respective results as discussed ahead.



# Explore circRNA Section

## Search by Coordinate

- First select the organism of interest.
- Then click on the radio button of **Coordinate.**
- The circRNAs are mapped to their respective organism specific databases, i.e., **circAtlas 3.0** for *Homo sapiens* and *Mus musculus*. CIRCPedia 3.0 and PlantCircRNA for *Drosophila melanogaster* and *Arabidopsis thaliana*.

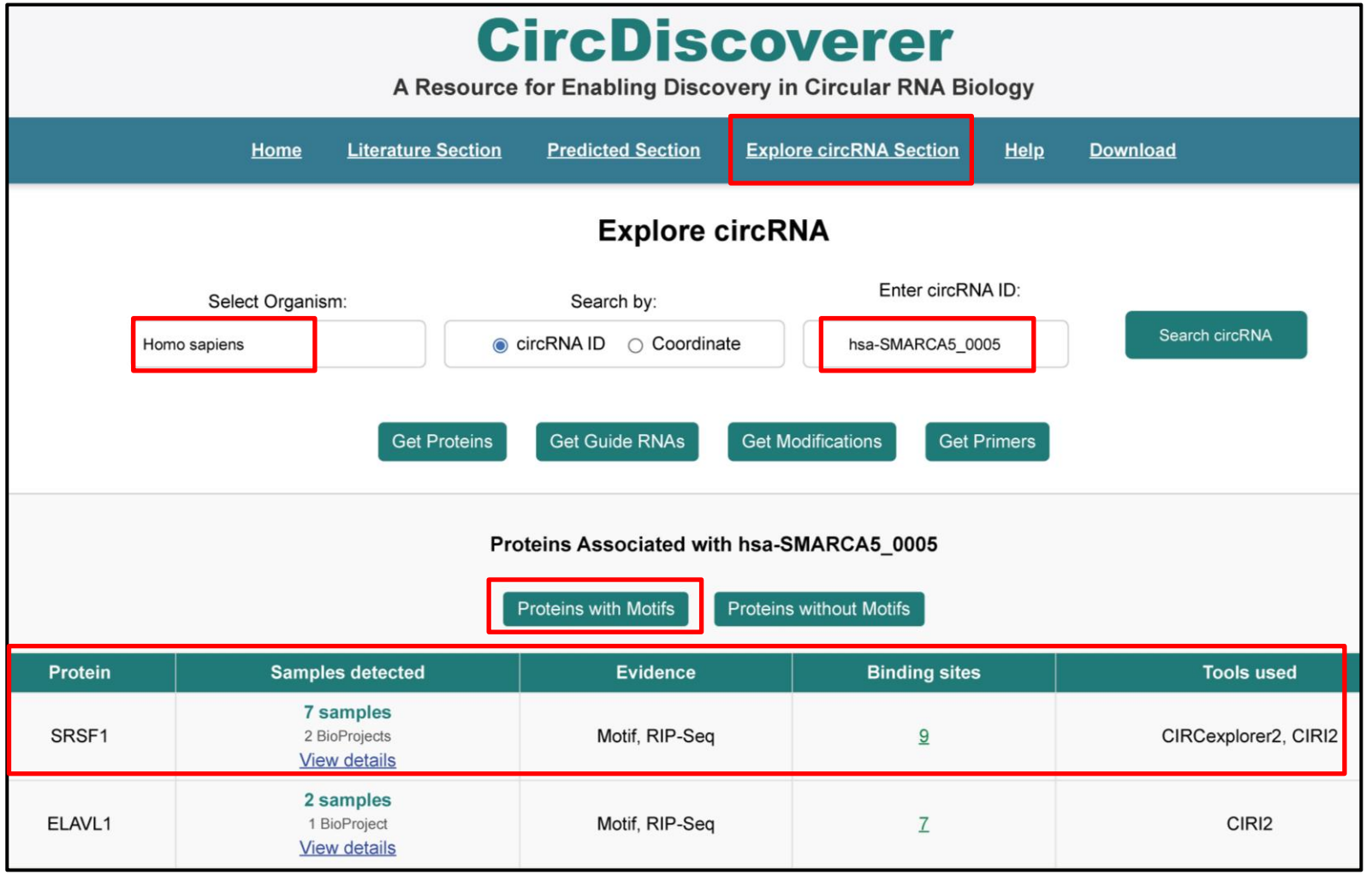
## Rules for entering coordinates

- All coordinates for ***Homo sapiens*** and ***Mus musculus*** are mapped in 1 based format, whereas for ***Drosophila melanogaster*** and ***Arabidopsis thaliana*** its in 0 based format, so the coordinates should be typed as follows:

**chromosome:Start|End(Strand) e.g. chr4:143543509|143543972(+).**

# Explore circRNA Section – Get Proteins

Select the organism and circRNA of interest, followed by clicking on the Get Proteins.



# Explore circRNA Section – Get Proteins Details

## Protein with Motifs

Clicking on the **“Protein with Motifs”** gives the list of proteins interacting with the circRNA of interest, having known RNA binding motifs with the following information.

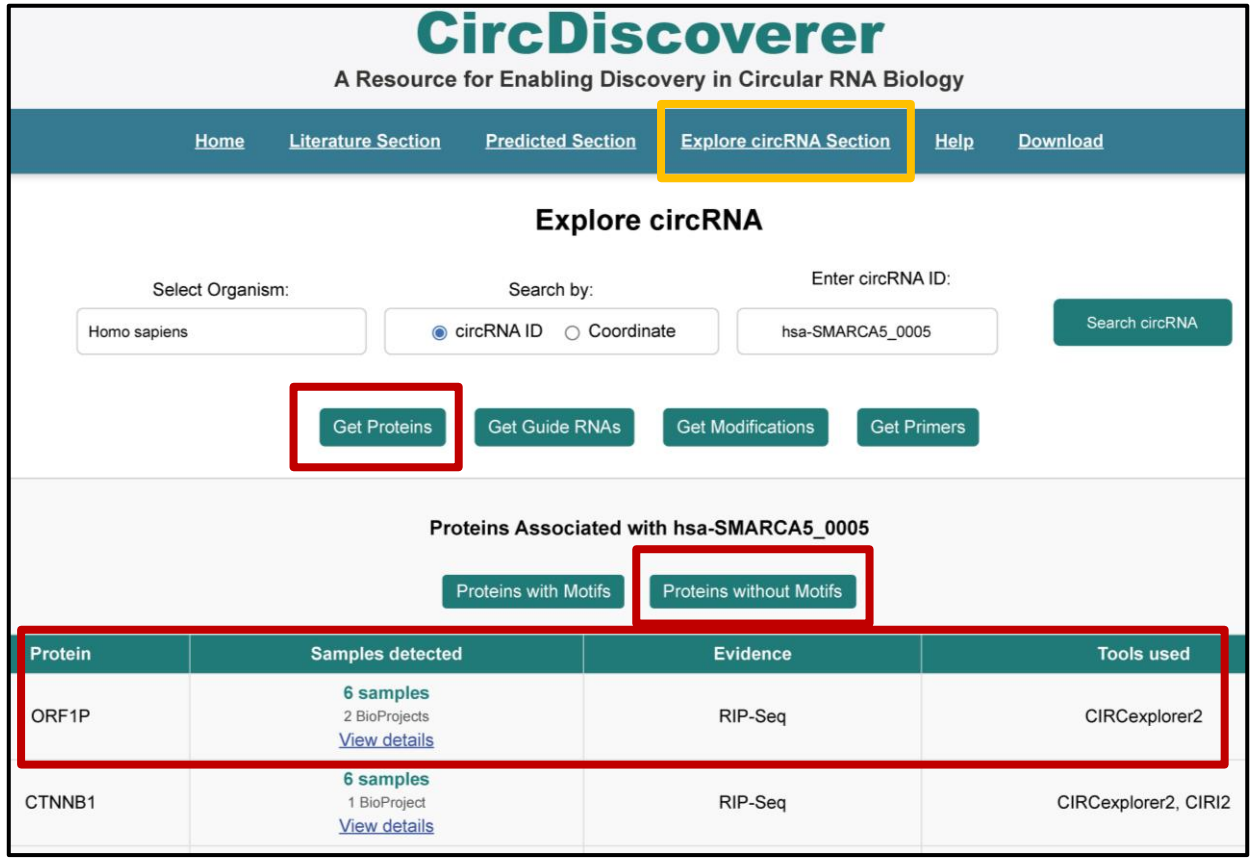
**Sample Detected :** List of all samples and the bioproject in which the circRNA of interest was found.

**Binding Sites** : Total number of binding sites for that protein in the given circRNA, clicking which opens a pop up, that displays details of that RNA binding motif.

**Evidence :** The respective strategy used to infer the given circRNA interacting with the protein of interest.

**Tools used :** The tools used to infer the CPI overall across all samples for the given protein.

# Protein without Motifs

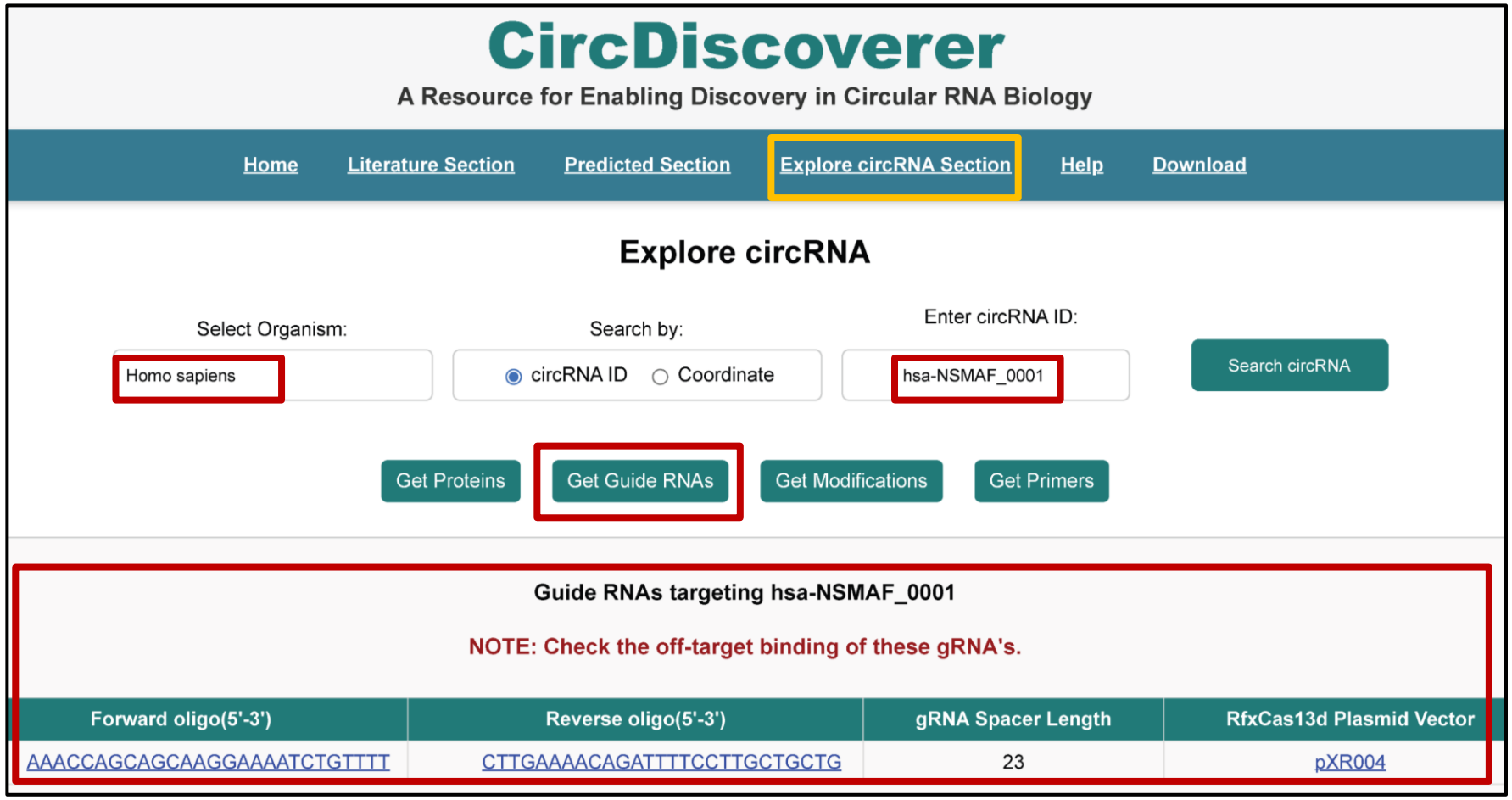



Clicking on the **"Protein without Motifs"** gives the list of proteins interacting with the circRNA of interest, but with no RNA binding motifs known.

**Sample Detected, Evidence and Tools Used** are same as for Protein with Motifs**.**

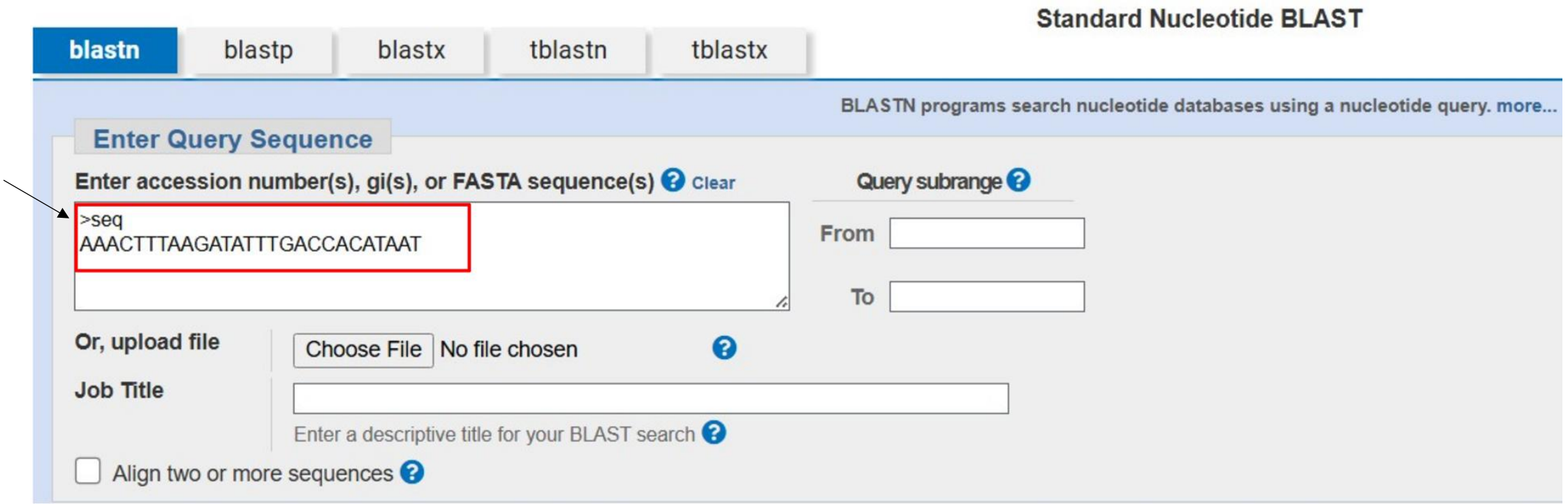
# Get Guide_RNA

Gives list of Forward & the Reverse oligos for cloning the gRNA's in RfxCas13d expressing plasmid vector called pXR004




Clicking the guide RNA's will land into the NCBI-BLAST page with the sequence pasted directly, allowing users to check the off-targets in their own settings(Page 15), i.e.

# Guide_RNA Results Page



# Get Primers

Get primers amplifying the backsplicing junction

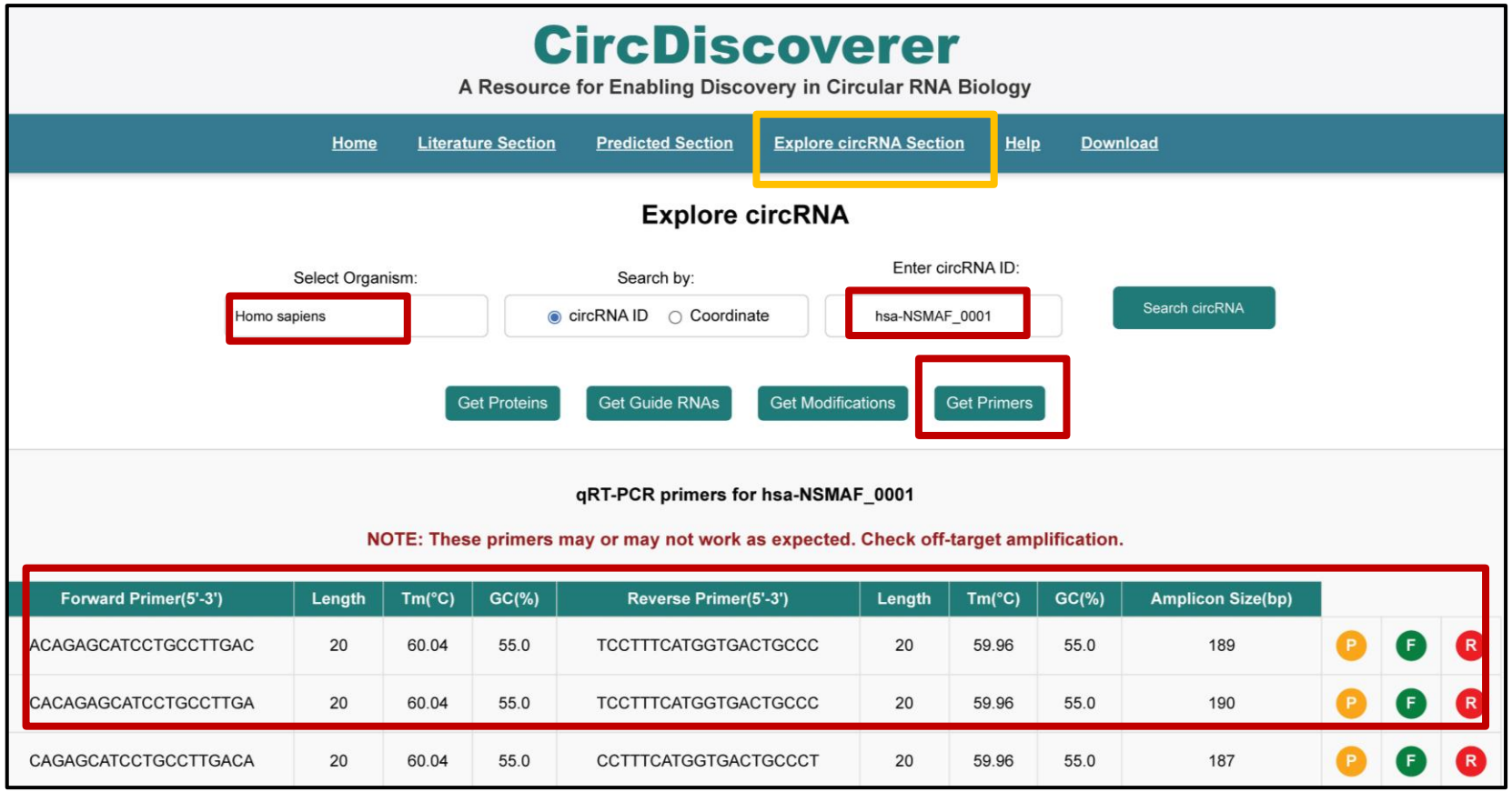
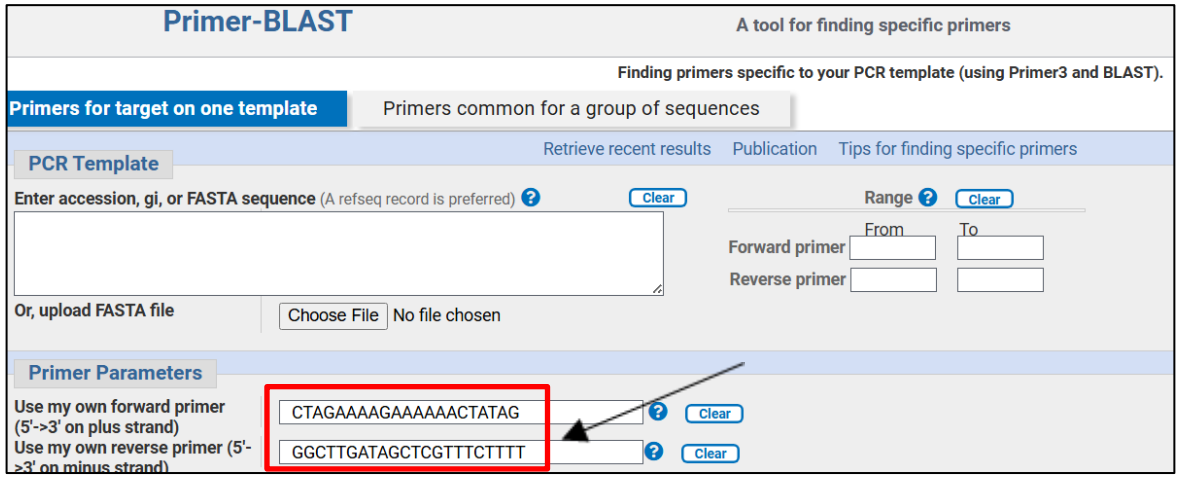



**Figure 8**

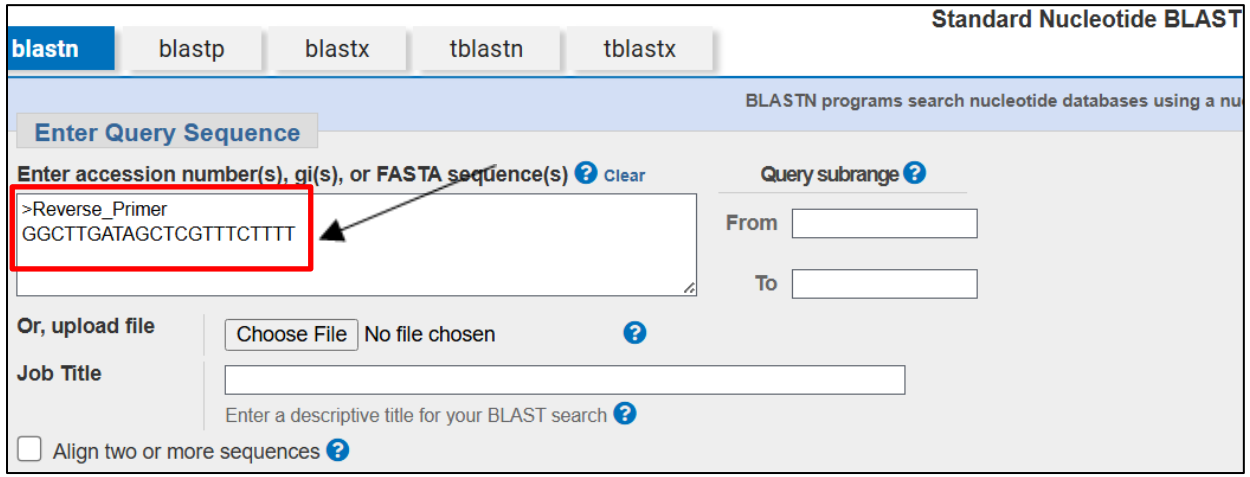
Clicking the buttons, i.e. P(Primer pair), F(Forward primer) ,R(Reverse primer) lands onto the NCBI-primer BLAST page with the primer sequence pasted, where the users can check for the off-targets (Page 11-A,B,C).

# NCBI-Primer BLAST Page

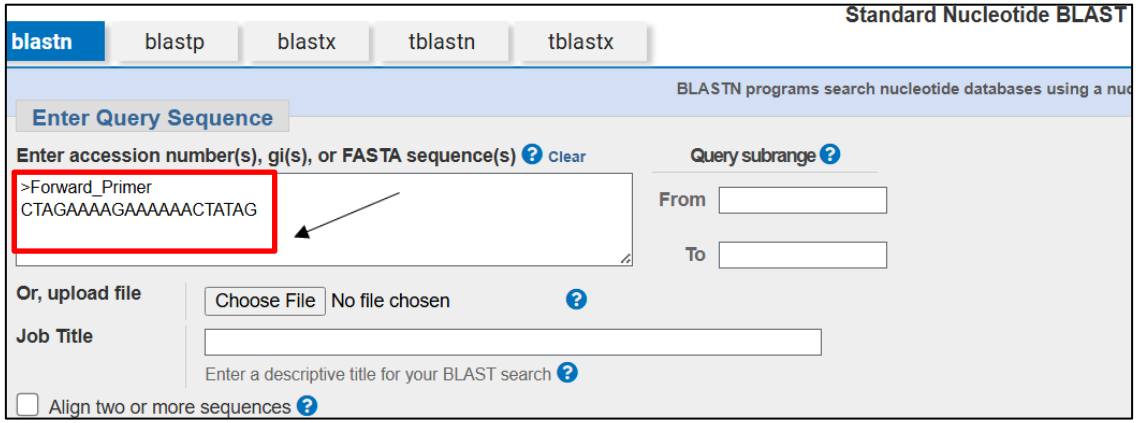
A)




B)

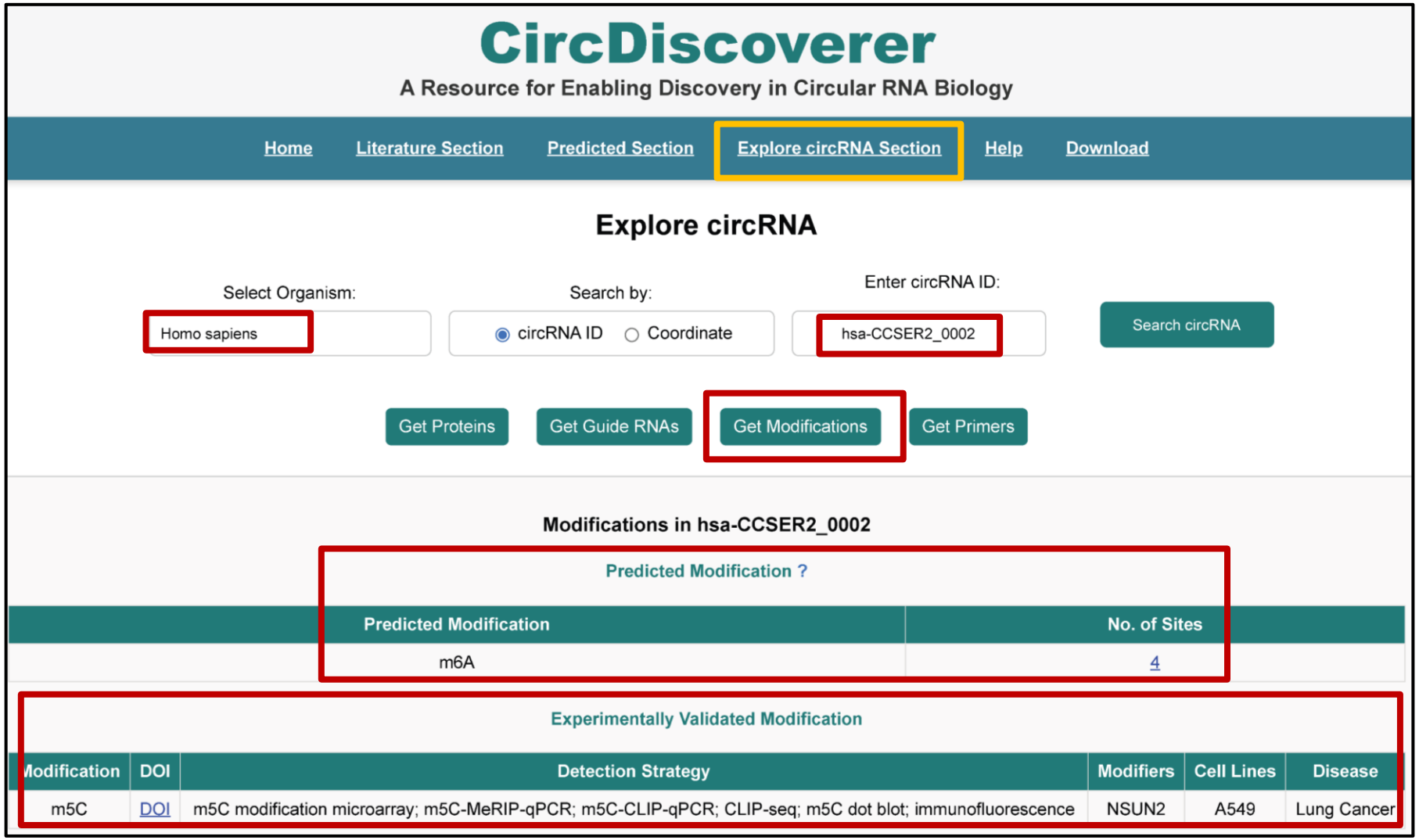



C)



# Get Modifications

Displays the possible modifications along with the experimentally known modifications wherever available



# Get Modifications …. Continued

## Predicted Modifications

These are inferred by overlapping the modification sites from RMBase v3.0 to the respective circRNA coordinates.

**The results of predicted modification displays :**

- The respective predicted modification
- **No. of sites :** This includes the total number of modification residues in the circRNA, clicking on which opens a pop-up, which displays the RMBase 3.0 sites overlapping in the circRNA, and the cell lines in which these sites were reported.

## Experimentally Validated Modifications

These modifications are collected from the respective literatures, and the information includes:

- **Modification** : The respective modification reported in the literature for the circRNA.
- **DOI** : The link to the literature covering the modification report.
- **Detection Strategy** : The strategies & methods inferred to find the modification in the circRNA.
- **Modifiers** : The enzymes adding the modification onto circRNA.
- **Cell Lines** : The cell lines reported in the literature, in which the modification were reported.
- **Diseases** : The disease context in which the circRNA modifications were reported.