



## Shannon Human Splicing Pipeline Server Documentation

Last Revised: Mar 10, 2014

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# Account creation and types of accounts

## Registering a new account

You can create a new account from the Shannon pipeline server home page (<http://shannonpipeline.cytognomix.com>) by clicking the button “Register a new account”. An account creation screen will appear. Upon successful submission of the account creation form an e-mail will be sent to the e-mail address you provided. Clicking the activation link in this e-mail will grant you trial access to the server. Two types of accounts are available, a trial account and a subscription based account. Differences between the two account types are described below.

## Trial account

This is the account type you will be assigned upon standard account creation. You can run the pipeline any *reasonable* number of times to test and evaluate the resource. Basic server functionality is identical to subscription accounts, with the exception of the number of results reported. While viewing results, you are presented with a reduced subset of the full results. Trial users see fewer than 2% of leaky and inactivating variants and the maximum number of variants returned is capped. We hope you find the trial output useful and see enough potential in Shannon pipeline functionality to consider subscribing.

## Subscription

We thank you for considering purchasing a subscription. Your contributions allow us to keep the server running and improve the resource. A subscribe button is adjacent to the “Register a new account” button on the server home page. Clicking it will navigate your browser to a page describing the Shannon pipeline along with subscription pricing. Short-term subscriptions are currently available through PayPal, which provides the latest pricing. Other payment mechanisms are available by contacting us at [info@cytognomix.com](mailto:info@cytognomix.com). Subscribers gain the ability to view full Shannon pipeline output. Jobs submitted by subscribers are priority queued in front of trial users to ensure subscribers are not delayed by trial user submissions. For users who wish to run the Shannon pipeline locally or incorporate it into an existing pipeline, a standalone version of the pipeline may suit your needs. For more information on these options please visit the [Subscription webpage](#).

## Quick start and overview of site functionality

This section contains basic information on how to run the plugin, view your results, and check your messages. We assume you have registered and signed in to the Shannon pipeline server. Following these instructions will guide you through your first run and provide an overview of server functionality. After signing in you will see a page with three tabs at the top of your screen labeled “Execute a new analysis”, “View completed analyses”, and “View messages”.

### Running the pipeline with sample data

In the event you don't currently have a VCF file you would like to examine, sample data can be executed in order to see how results are presented on the server. To execute a sample job, simply navigate to the “Execute a new analysis” tab (see the screenshot below) and click the button “Try a sample run”.

### Running the pipeline using a VCF file

The Shannon pipeline server accepts files in VCF format for analysis. Information on this file format can be found [here](#). VCF files adhering to this format are understood by the server, however only the first five columns of each variant entry are taken into account. Other columns are ignored and may be left out while generating your own files in VCF format. For example the following data is an acceptable variant entry in a VCF file:

```
22      17237440      Dataset1_Group5      C      T
```

Note: The ID field (3<sup>rd</sup> column above) in a VCF file can be used as a label to facilitate separating multiple samples after a run. To label all variants from a sample, place the name of the sample in the ID field in a VCF file. Do this for all samples and place them in the same VCF file. When results are reported, the ID of each variant is preserved.

The number of variants in a VCF file is limited to 2,500,000. If a VCF file is submitted with a larger number of variants than this maximum, an error message will appear. To examine a VCF file with greater than 2,500,000 variants, it must be split into multiple files and submitted separately.

When you have your VCF file ready, navigate to the “Execute a new analysis” tab (see the screenshot below). Your data can be submitted to the server by clicking on “Choose File”, browsing your computer for the VCF file, then clicking “Submit”.

**Shannon Human Splicing Pipeline**  
Genome-Scale Information Theory Based Binding Site Analysis

CYTOGNOMIX

Execute a new analysis | View completed analyses | **View messages**

Welcome to the Shannon Human Splicing Pipeline online analysis suite. To use this website, please select a VCF file and click submit. **The VCF file must be properly formatted.** For more information on VCF format please visit [this website](#). It is important to note that this server only needs the first five columns for each entry (CHROM, POS, ID, RED, ALT) in the VCF file. Taking this into account, it is possible (but certainly not required) to submit a minimal VCF file with only the first five columns present for each variant. If you do not have a VCF file you would like to examine at the moment, you can "Try a sample run" by clicking the button below.

Upon submission, jobs will be executed in the order they are submitted. If no jobs are queued, execution will take less than 10 minutes. After clicking submit, you will be redirected to a page confirming your submission was received. You can view your results in the "View completed analyses" tab once they have been generated. Messages will appear in the "View messages" tab to inform you of the current status of your job. When a new message is received, an icon will appear beside "View messages" on the tab itself. Please note that if you are a trial user, filters selected below will not be applied to the results.

| Natural/Cryptic site filters   | Natural site filters   | Cryptic site filters   |
|--|--|--|
| <input checked="" type="radio"/> Display both positive and negative strands<br><input type="radio"/> Positive strand only<br><input type="radio"/> Negative strand only<br><br><input checked="" type="radio"/> Display both donors and acceptors<br><input type="radio"/> Donors<br><input type="radio"/> Acceptors<br><br><input type="radio"/> Do not filter by average heterozygosity<br><input checked="" type="radio"/> Hide variants with average heterozygosity > 5%<br><input type="radio"/> Hide variants with average heterozygosity > 1% | <input type="checkbox"/> Enable min. $\Delta R_i$ (use slider to select)<br><input type="text"/><br><input checked="" type="checkbox"/> Hide natural sites with increasing $R_i$ | <input type="checkbox"/> Enable min. $\Delta R_i$ (use slider to select)<br><input type="text"/><br><input checked="" type="checkbox"/> Hide cryptic sites with decreasing $R_i$<br><input checked="" type="checkbox"/> Hide cryptic sites with lower $R_i$ than nearest natural site<br><input checked="" type="checkbox"/> Hide intronic cryptic sites > 300bp from nearest natural site |

Upload a VCF file for analysis.

No file chosen

Please direct any questions or comments related to the Shannon Human Splicing Pipeline or this website to [info@cytognomix.com](mailto:info@cytognomix.com)

## After your job has been submitted

Upon clicking submit, your job will be queued on our server. If no other users are currently executing a job, it will begin execution immediately. The "View messages" tab will contain updates related to your job submission. For example, a message will be posted when the job first becomes queued, begins executing, and has finished. When you have received a new message a light bulb will appear beside "View messages" in the tab itself (see the "View messages" tab in the screenshot above to for an example of this icon). When you navigate to the "View messages" tab, the light bulb will disappear indicating you have read your new messages. An example of messages you will find in your messages tab can be found in the screenshot below.

**Shannon Human Splicing Pipeline**  
Genome-Scale Information Theory Based Binding Site Analysis

CYTOGNOMIX

Execute a new analysis | View completed analyses | **View messages**

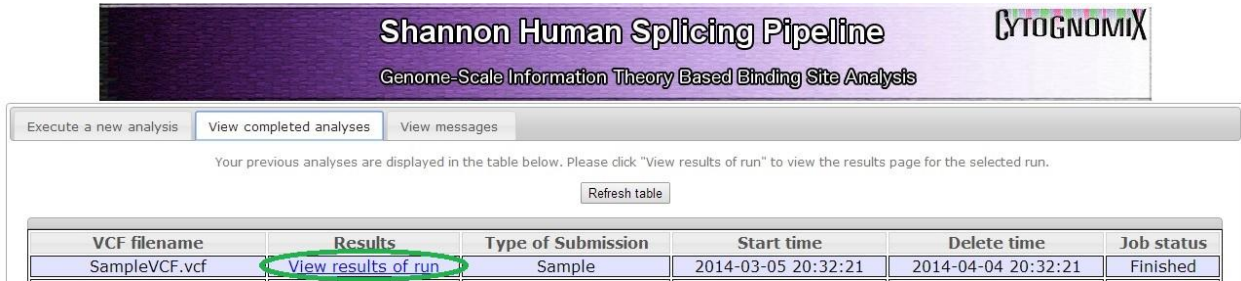
This table contains your messages. Messages can include: Job execution start/finish notifications, subscription notes, and server-wide messages.

| Time posted            | Message  | Notes  |
|------------------------|--|--|
| 2014-03-05<br>20:32:43 | Your job using VCF file: SampleVCF has completed execution | View results for this job in the 'View completed analyses' tab |
| 2014-03-05<br>20:32:23 | Your job using VCF file: SampleVCF is currently executing  | You will be notified when this job has completed               |
| 2014-03-05<br>20:32:22 | Your job using VCF file: SampleVCF has been queued         | You will be notified when this job begins execution            |

Jobs will generally take several minutes to execute. A job analyzing the maximum number of variants will execute in approximately 15 minutes. You do not have to wait online while your job is executing. Completed jobs are saved on the server for 30 days. Thus, you can submit your job and return later to view your results.

## Viewing results

Completed jobs can be found in the “View completed analysis” tab (see screenshot below). Click on “View results of run” to view results for the selected run.



**Shannon Human Splicing Pipeline** CYTOGNOMIX  
Genome-Scale Information Theory Based Binding Site Analysis

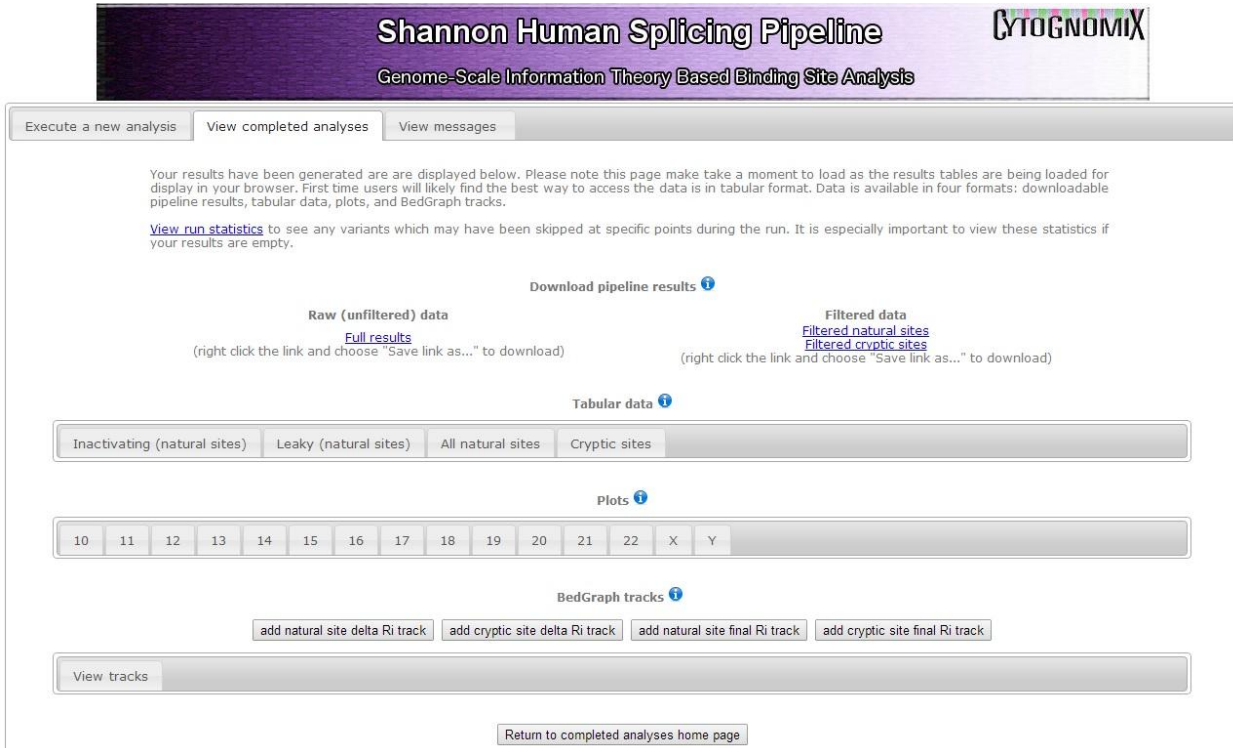
Execute a new analysis | **View completed analyses** | View messages

Your previous analyses are displayed in the table below. Please click "View results of run" to view the results page for the selected run.

[Refresh table](#)

| VCF filename  | Results                             | Type of Submission | Start time          | Delete time         | Job status |
|---------------|-------------------------------------|--------------------|---------------------|---------------------|------------|
| SampleVCF.vcf | <a href="#">View results of run</a> | Sample             | 2014-03-05 20:32:21 | 2014-04-04 20:32:21 | Finished   |

The screenshot below shows a typical results page. For more information about any of the types of data reported (downloading raw pipeline results, tabular data, plots, or BedGraph tracks) please refer to the appropriate sections within this document.



**Shannon Human Splicing Pipeline** CYTOGNOMIX  
Genome-Scale Information Theory Based Binding Site Analysis

Execute a new analysis | **View completed analyses** | View messages

Your results have been generated and are displayed below. Please note this page may take a moment to load as the results tables are being loaded for display in your browser. First time users will likely find the best way to access the data is in tabular format. Data is available in four formats: downloadable pipeline results, tabular data, plots, and BedGraph tracks.

[View run statistics](#) to see any variants which may have been skipped at specific points during the run. It is especially important to view these statistics if your results are empty.

**Download pipeline results** ⓘ

Raw (unfiltered) data

[Full results](#)

(right click the link and choose "Save link as..." to download)

Filtered data

[Filtered natural sites](#)

[Filtered cryptic sites](#)

(right click the link and choose "Save link as..." to download)

**Tabular data** ⓘ

Inactivating (natural sites) | Leaky (natural sites) | All natural sites | Cryptic sites

**Plots** ⓘ

10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | X | Y

**BedGraph tracks** ⓘ

[add natural site delta Ri track](#) | [add cryptic site delta Ri track](#) | [add natural site final Ri track](#) | [add cryptic site final Ri track](#)

[View tracks](#)

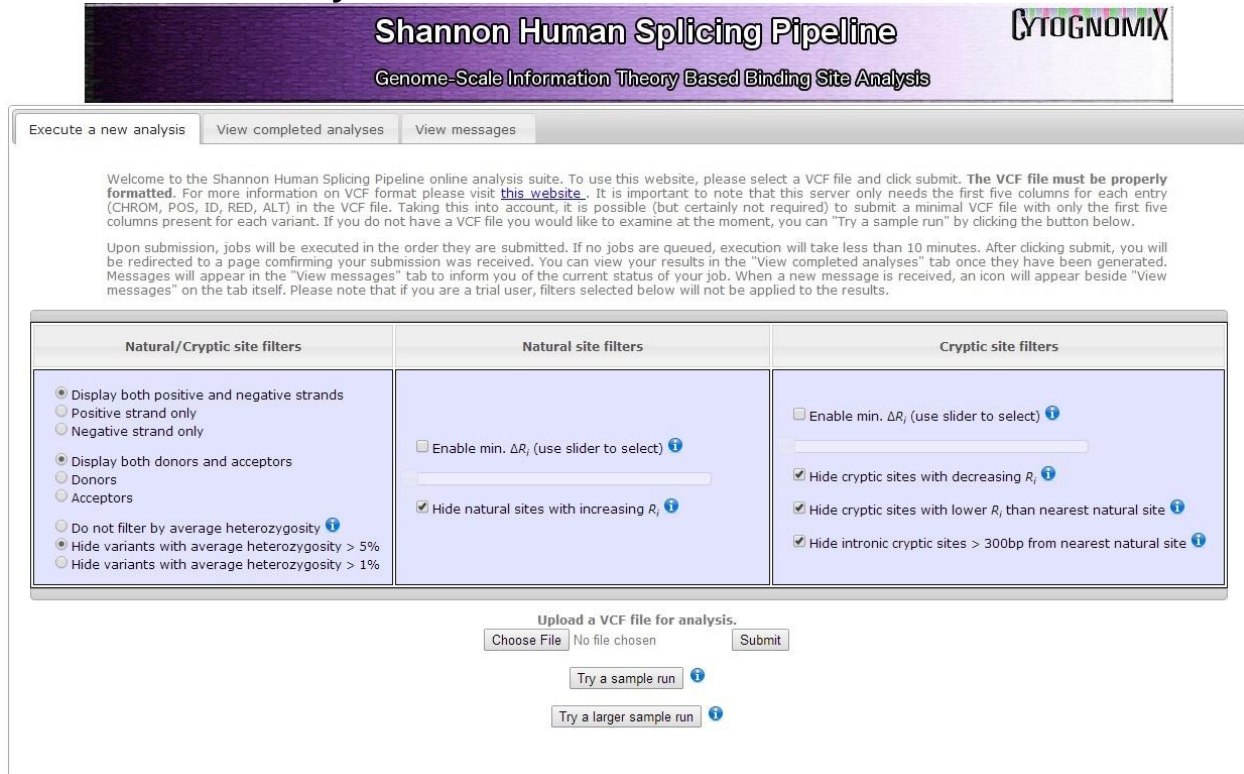
[Return to completed analyses home page](#)



# Navigating the Shannon pipeline server

After logging in, you are presented with three tabs on the Shannon pipeline server home page. All server functionality can be found within these tabs.

## Execute a new analysis tab



## Filters

Nine filters are currently available to help further reduce pipeline results to a tractable number of potentially deleterious variants or to hone in on specific types of variants. Default filters are depicted in the screenshot and were selected to greatly reduce the number of variants in pipeline results while removing as few relevant variants as possible. Reasoning behind the selection of these particular default values is discussed in greater detail in our [2013 paper](#).

### Strand

Default value: display both positive and negative strands.

Some targeted analyses may only be interested in variants on either the positive or negative strand.

### Splice site type

Default value: display both donors and acceptors.

Use this filter to display only donor or acceptor sites.

### Average heterozygosity

Default value: hide variants with average heterozygosity > 5%

dbSNP135 is examined to determine if a variant has been assigned an rsID. Although a variant may be a known variant in dbSNP, a known variant with low average heterozygosity may be potentially pathogenic. Generally, known variants with high average heterozygosity will not be of interest and thus this filter is set to hide variants with average heterozygosity > 5%.

### Natural site $\Delta R_i$

Default value: not used

To make use of this filter, the checkbox labeled “Enable min.  $\Delta R_i$ ” must be checked. Doing so will enable the slider below the checkbox which can be dragged to select the minimum  $\Delta R_i$  for filtering. This minimum limit applies to both positive and negative  $\Delta R_i$  values. For example, to view only those variants which increase natural splice site  $R_i$  by three or more bits or reduce natural splice site  $R_i$  by three or more bits, set the slider to 3.

Note: the slider begins at a value of 1.0 as splice sites with  $\Delta R_i < 1.0$  are not reported by the pipeline.

### Hide natural sites with increasing $R_i$

Default value: yes

An increase in natural site strength will likely serve only to widen the existing gap in  $R_i$  between the natural and nearby cryptic sites.

### Cryptic site $\Delta R_i$

Default value: not used

To make use of this filter, the checkbox labeled “Enable min.  $\Delta R_i$ ” must be checked. Doing so will enable the slider below the checkbox which can be dragged to select the minimum  $\Delta R_i$  for filtering. This minimum limit applies to both positive and negative  $\Delta R_i$  values. For example, to view only those variants which increase cryptic splice site  $R_i$  by three or more bits or reduce cryptic splice site  $R_i$  by three or more bits, set the slider to 3.

Note: the slider begins at a value of 1.0 as splice sites with  $\Delta R_i < 1.0$  are not reported by the pipeline.

### Hide cryptic sites with decreasing $R_i$

Default value: yes

A decrease in cryptic site strength will likely serve only to widen the existing gap in  $R_i$  between the cryptic site and any nearby natural sites.

### Hide cryptic sites with lower $R_i$ than nearest natural site

Default value: yes

Generally, if a cryptic site has not increased in strength to an  $R_i$  greater than a nearby natural site it will not be of interest.

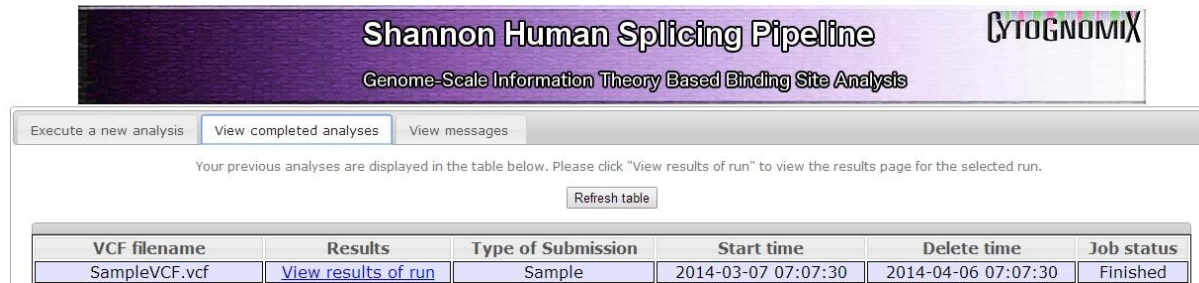
### Hide intronic cryptic sites > 300bp from nearest natural site

Default value: yes

Cryptic sites more distant than 300bp from a natural site are unlikely to form a viable exon.



## View completed analyses tab



Shannon Human Splicing Pipeline  
Genome-Scale Information Theory Based Binding Site Analysis

Execute a new analysis | **View completed analyses** | View messages

Your previous analyses are displayed in the table below. Please click "View results of run" to view the results page for the selected run.

Refresh table

| VCF filename  | Results                             | Type of Submission | Start time          | Delete time         | Job status |
|---------------|-------------------------------------|--------------------|---------------------|---------------------|------------|
| SampleVCF.vcf | <a href="#">View results of run</a> | Sample             | 2014-03-07 07:07:30 | 2014-04-06 07:07:30 | Finished   |

Information related to each job you have submitted to the Shannon pipeline server is displayed here. The "VCF filename" and "Start time" fields can be used to identify the job you wish to examine. Jobs are ordered by start time. To view job results click the hyperlink "View results of run". Times are displayed in Greenwich Mean Time (GMT). Jobs are removed from our servers at the "Delete time". The "Job status" field is set to one of three states 1) Queued, 2) Executing, or 3) Finished. The option to view results will appear only if the job is in a "Finished" state.

After clicking "View results of run" a results page will appear in the same tab (see the screenshot below). For more information about any of the types of data reported (downloading raw pipeline results, tabular data, plots, or BedGraph tracks) please refer to the appropriate sections in this document. The hyperlink "View run statistics" will open a new tab in your browser and display the number of variants examined in the run. The number of variants unable to be examined by the server will also be displayed. The vast majority of the time, variants are unable to be examined due to an improperly formatted VCF file or a reference nucleotide which does not match the reference genome. If variants were indeed unable to be examined, a hyperlink will be provided to view the list of variants skipped along with the reason why the server could not examine each variant.

**Shannon Human Splicing Pipeline**  
Genome-Scale Information Theory Based Binding Site Analysis

CYTOGNOMIX

Execute a new analysis | View completed analyses | View messages

Your results have been generated and are displayed below. Please note this page may take a moment to load as the results tables are being loaded for display in your browser. First time users will likely find the best way to access the data is in tabular format. Data is available in four formats: downloadable pipeline results, tabular data, plots, and BedGraph tracks.

[View run statistics](#) to see any variants which may have been skipped at specific points during the run. It is especially important to view these statistics if your results are empty.

Download pipeline results ⓘ

Raw (unfiltered) data  
[Full results](#)  
(right click the link and choose "Save link as..." to download)
Filtered data  
[Filtered natural sites](#)  
[Filtered cryptic sites](#)  
(right click the link and choose "Save link as..." to download)

Tabular data ⓘ

Plots ⓘ

BedGraph tracks ⓘ

## View messages tab and messaging system

**Shannon Human Splicing Pipeline**  
Genome-Scale Information Theory Based Binding Site Analysis

CYTOGNOMIX

Execute a new analysis | View completed analyses | View messages

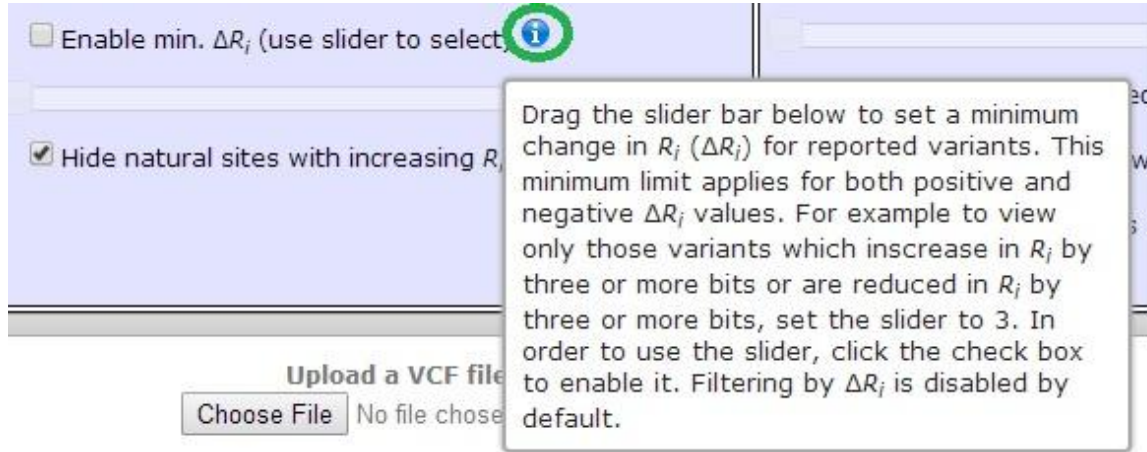
This table contains your messages. Messages can include: Job execution start/finish notifications, subscription notes, and server-wide messages.

| Time posted            | Message  | Notes  |
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| 2014-03-05<br>20:32:23 | Your job using VCF file: SampleVCF is currently executing  | You will be notified when this job has completed               |
| 2014-03-05<br>20:32:22 | Your job using VCF file: SampleVCF has been queued         | You will be notified when this job begins execution            |

The server provides a messaging system to inform you of changes in your submitted job status, account information, and server-wide notices. When you have received a new message a light bulb will appear beside "View messages" in the tab itself to inform you a new message has been received. Navigating to the "View messages" tab will remove the light bulb indicating you have read your new messages. The messaging system allows you to focus on submitting additional jobs or other tasks while your job is being processed. It is important to note it is not necessary to remain on the Shannon server website while your job is executing if it is inconvenient to do so. Your jobs are saved for 30 days after submission and can be viewed at a later date. The system generates a reminder message in advance of deletion of previously generated results.

## Getting additional help and bug reporting

Blue “information” icons can be found on most pages on the Shannon pipeline server. Hovering the mouse over one of these icons will cause additional information to be displayed in the form of a tooltip. An example of one of these icons and its related tooltip can be found in the screenshot below.



For additional assistance with the use of the server or to report a software bug, please contact [info@cytognomix.com](mailto:info@cytognomix.com).

## Tabular data

Tabular data

Inactivating (natural sites) Leaky (natural sites) All natural sites **Cryptic sites**

Show **25** entries Search:

| Splice site location |           | $R_i$ in bits |         |       | Splice site type and affected gene |      | dbSNP     |             | Cryptic site specific |               |                   |                             |                           | Submitted variant attributes |                            |                |           |           |                   |                  |     |
|----------------------|-----------|---------------|---------|-------|------------------------------------|------|-----------|-------------|-----------------------|---------------|-------------------|-----------------------------|---------------------------|------------------------------|----------------------------|----------------|-----------|-----------|-------------------|------------------|-----|
| Chr                  | Coord.    | Strand        | Initial | Final | $\Delta R_i$                       | Type | Gene name | rsID        | Av. het.              | Location type | Loc. Rel. to exon | Dist. from nearest nat site | Coord of nearest nat site | Ri of nearest nat. site      | Cryptic $R_i$ rel. to nat. | Variant coord. | Variant   | Input ID  | Variant type      |                  |     |
| 10                   | 135371600 | -             | 1.20    | 3.09  | 1.89                               | Acc. | SYCE1     |             |                       | Indel         | -                 | -177                        | 135371423                 | 6.42081                      | 0.00                       | -              | 135371602 | G/C/G     | _78018            |                  |     |
| 10                   | 135368199 | -             | -3.97   | 6.91  | 10.88                              | Acc. | SYCE1     | rs189831260 | 0                     |               | INTRONIC          | -                           | -366                      | 135367833                    | 5.81                       | GREATER        | 135368199 | T/C       | _77946            | SNV              |     |
| 10                   | 135352354 | +             | 7.23    | 8.32  | 1.09                               | Acc. | CYP2E1    |             |                       | EXONIC        | -                 | -71                         | 135352283                 | 8.21                         | GREATER                    | 135352344      | C/T       | _77918    | SNV               |                  |     |
| 10                   | 135345668 | +             | -9.20   | 5.62  | 14.71                              | Acc. | CYP2E1    | rs60452492  | 0.002634              |               | EXONIC            | -                           | -31                       | 135345627                    | 4.13                       | GREATER        | 135345667 | G/A       | rs60452492_77858  | SNV              |     |
| 10                   | 135209741 | +             | -1.20   | 0.17  | 1.37                               | Acc. | MTG1      | rs140558106 | 0.001317              |               | EXONIC            | -                           | -75                       | 135209666                    | -6.12                      | GREATER        | 135209729 | G/C       | rs140558106_77703 | SNV              |     |
| 10                   | 135193396 | -             | 2.41    | 3.60  | 1.09                               | Acc. | ECHS1     |             |                       |               | INTRONIC          | -                           | -339                      | 135192527                    | 2.18                       | GREATER        | 135193378 | G/A       | _77550            | SNV              |     |
| 10                   | 135123693 | +             | 0.26    | 1.38  | 1.12                               | Acc. | ZNF511    |             |                       |               | EXONIC            | -                           | -16                       | 135123667                    | -1.73                      | GREATER        | 135123681 | T/C       | _77345            | SNV              |     |
| 10                   | 135116264 | -             | -0.09   | 1.02  | 1.10                               | Acc. | TUBGCP2   |             |                       |               | INTRONIC          | -                           | -2646                     | 135113618                    | 0.98                       | GREATER        | 135116279 | C/G       | _77312            | SNV              |     |
| 10                   | 135113666 | -             | 8.04    | 9.45  | 1.41                               | Acc. | TUBGCP2   |             |                       |               | INTRONIC          | 3'-FLANKING                 | -48                       | 135113618                    | 0.98                       | GREATER        | 135113669 | T/T/A     | rs113322932_77307 | Indel            |     |
| 10                   | 135112865 | -             | 1.38    | 2.62  | 1.25                               | Acc. | TUBGCP2   |             |                       |               | INTRONIC          | -                           | -1249                     | 135111616                    | 1.86                       | GREATER        | 135112888 | C/A       | _77284            | SNV              |     |
| 10                   | 135103393 | -             | -10.86  | 0.03  | 10.88                              | Acc. | TUBGCP2   | rs149388663 | 0.001318              |               | EXONIC            | -                           | 121                       | 135103474                    | -1.44                      | GREATER        | 135103353 | T/C       | rs149388663_77199 | SNV              |     |
| 10                   | 135024213 | +             | -9.90   | 0.98  | 10.88                              | Acc. | KNDC1     | rs148648854 | 0.000439              |               | EXONIC            | -                           | -99                       | 135024114                    | 0.88                       | GREATER        | 135024213 | A/G       | rs148648854_76593 | SNV              |     |
| 10                   | 135020769 | +             | -7.13   | 4.83  | 11.87                              | Acc. | KNDC1     | rs147343928 | 0.000447              |               | EXONIC            | -                           | -129                      | 135020640                    | 1.86                       | GREATER        | 135020769 | C/G       | rs147343928_76581 | SNV              |     |
| 10                   | 134999870 | +             | -10.49  | 4.23  | 14.71                              | Acc. | KNDC1     | rs35998551  | 0.048702              |               | EXONIC            | -                           | -393                      | 134999477                    | 3.06                       | GREATER        | 134999869 | G/A       | rs35998551_76384  | SNV              |     |
| 10                   | 134664804 | -             | 1.47    | 2.50  | 1.03                               | Acc. | TTC40     |             |                       |               | EXONIC            | -                           | 6                         | 134664810                    | 0.18                       | GREATER        | 134664820 | C/G       | _75778            | SNV              |     |
| 10                   | 134660826 | -             | 1.42    | 2.70  | 1.27                               | Acc. | TTC40     |             |                       |               | Indel             | -                           | 0                         | 134660826                    | 1.42477                    | 0.00           | -         | 134660833 | A/C/A             | _75752           | SNV |
| 10                   | 134660650 | -             | 0.77    | 2.10  | 1.33                               | Acc. | TTC40     |             |                       |               | EXONIC            | -                           | 66                        | 134660616                    | 2.08                       | GREATER        | 134660571 | C/A       | _75736            | SNV              |     |
| 10                   | 134648305 | -             | -10.92  | 3.79  | 14.71                              | Acc. | TTC40     |             |                       |               | INTRONIC          | 3'-FLANKING                 | -25                       | 134648280                    | 0.24                       | GREATER        | 134648306 | C/T       | _75676            | SNV              |     |
| 10                   | 134628169 | -             | -13.22  | 1.50  | 14.71                              | Acc. | TTC40     |             |                       |               | INTRONIC          | 3'-FLANKING                 | -52                       | 134628117                    | -2.35                      | GREATER        | 134628170 | C/T       | _75621            | SNV              |     |
| 10                   | 134628124 | -             | -8.31   | 6.40  | 14.71                              | Acc. | TTC40     |             |                       |               | INTRONIC          | 3'-FLANKING                 | -7                        | 134628117                    | -2.35                      | GREATER        | 134628126 | C/T       | _75614            | SNV              |     |
| 10                   | 134628253 | -             | -8.41   | 6.30  | 14.71                              | Acc. | TTC40     |             |                       |               | INTRONIC          | -                           | -1717                     | 134624636                    | 2.66                       | GREATER        | 134628254 | C/T       | _75579            | SNV              |     |
| 10                   | 134623994 | -             | 2.53    | 4.16  | 1.64                               | Acc. | TTC40     |             |                       |               | Indel             | -                           | 0                         | 134623994                    | 2.62666                    | 0.00           | -         | 134624008 | TCCC/T            | rs76677206_75568 | SNV |
| 10                   | 134165113 | +             | -0.04   | 1.68  | 1.73                               | Acc. | LRRC27    |             |                       |               | EXONIC            | -                           | -3                        | 134165110                    | 0.16                       | GREATER        | 134165103 | A/C       | rs117614382_75084 | SNV              |     |
| 10                   | 134041674 | -             | 2.92    | 4.01  | 1.09                               | Acc. | STK32C    | rs144273062 | 0                     |               | INTRONIC          | 3'-FLANKING                 | -41                       | 134041633                    | 3.69                       | GREATER        | 134041684 | G/A       | rs144273062_74967 | SNV              |     |
| 10                   | 134038846 | -             | -6.47   | 4.45  | 10.92                              | Acc. | STK32C    | rs151066427 | 0                     |               | INTRONIC          | 3'-FLANKING                 | -5                        | 134038841                    | 3.86                       | GREATER        | 134038847 | G/A       | rs151066427_74899 | SNV              |     |

Showing 1 to 25 of 18,272 entries

First Previous 1 2 3 4 5 Next Last

## Types of tabular data

Tabular output is generated based on filters selected on the job submission page. Variants which do not meet the filtering criteria will not appear in tabular data and must be found in the raw pipeline output (full output). Four types of tables can be viewed in the tabular data section, these are:

### 1. Inactivating (natural sites)

Includes natural splice sites with an initial  $R_i$  greater than 1.6 bits and which drop below that value after the variant is introduced.

### 2. Leaky (natural sites)

Leaky sites are those natural splice sites which experience a drop in  $R_i$  after the variant is introduced but do not fall below an  $R_i$  of 1.6 bits.

### 3. All natural sites

All natural sites with  $\Delta R_i$  of at least 1.0 bit are included here.

### 4. Cryptic sites

All cryptic sites with  $\Delta R_i$  of at least 1.0 bit are included here.

## Description of column headers

**Each row in the table represents a single variant. The meaning of each column is described below:**

1. Chr

Chromosome where the splice site is located.

2. Coord

Genomic coordinate of the splice site experiencing a change in  $R_i$ .

3. Strand

Displayed as "+" for positive and "-" for negative strand.

4. Initial

$R_i$  of the splice site using the reference genome (hg19/GRCh37).

5. Final

$R_i$  of the splice site after introducing the variant specified in the input VCF file.

6.  $\Delta R_i$

The change in  $R_i$  before and after introducing the variant.

7. Type

The site is either an acceptor or a donor. Displayed as "Acc." or "Don.".

8. Gene Name

Name of the gene closest to the location of the variant. If multiple genes overlap the genomic coordinate of the variant, they will all be appear in a comma delimited list.

9. rsID

If the variant is found in dbSNP135 its rsID is displayed here. Otherwise the field is blank.

10. Av. het

If the variant has an rsID in dbSNP135, its average heterozygosity is displayed. Otherwise the field is blank.

### Columns displayed only for cryptic site variants

11. Location type

If the cryptic site is found within a known exon in RefSeq it is "EXONIC". If it is not, it is "INTRONIC".

12. Loc. Rel. to exon

If variant is downstream relative to the nearest exon it is "3'-FLANKING". Otherwise it is "5'-FLANKING".

13. Dist. From nearest nat site

The number of base pairs separating the cryptic splice site from its nearest natural site of the same phase (donor, acceptor).



14. Coord of nearest nat site

The genomic coordinate of the natural site closest to the cryptic site.

15.  $R_i$  of nearest nat site

The  $R_i$  of the natural site closest to the cryptic site.

16. Cryptic  $R_i$  rel. to nat

If a cryptic site has a higher final  $R_i$  than the nearest natural site we denote it "GREATER", otherwise it is "LESS".

**Additional columns displayed for all variants**

17. Variant coord

The genomic coordinate of the variant as specified in the input VCF file.

18. Variant

Reference and alternate nucleotides as specified in the input VCF file. Ex: A/G

19. Input ID

The ID column from the input VCF file. An additional "\_" followed by a number is appended to ensure each ID is unique.

20. Variant type

A variant is either an SNV (single nucleotide variant) or an Indel (insertion or deletion).

## Table functions

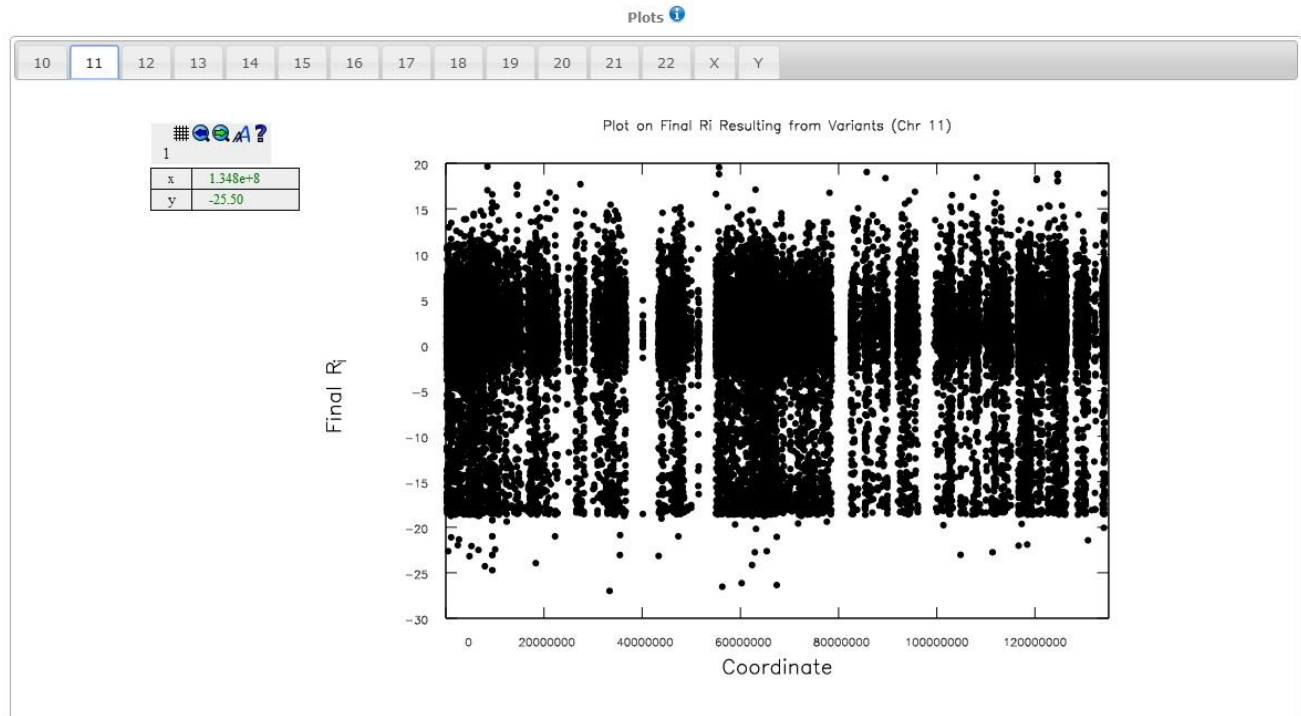
A dropdown box ("Show x entries") can be utilized to alter the number of variants displayed on the same page of the table. Ten, 25, 50, or 100 variants can be displayed at once. The search bar located at the upper-right of the table allows real-time searching for specific letters/numbers. Those variants matching a search term will be preserved while those which do not will be temporarily removed from the table. Pages of the table can be browsed by using the paging options located at the lower-right of the table.

## Table load times

Tables with a large number of variants will take a moment to load in your browser. To ensure tables load in a relatively timely manner, tables cannot display greater than 100,000 variants simultaneously. To obtain data unable to be displayed within a table because of this restriction, please download the raw pipeline output.



## Plots



An example of a plot generated by the pipeline.

Scatter plots provide a visual representation of the final  $R_i$  for each variant.

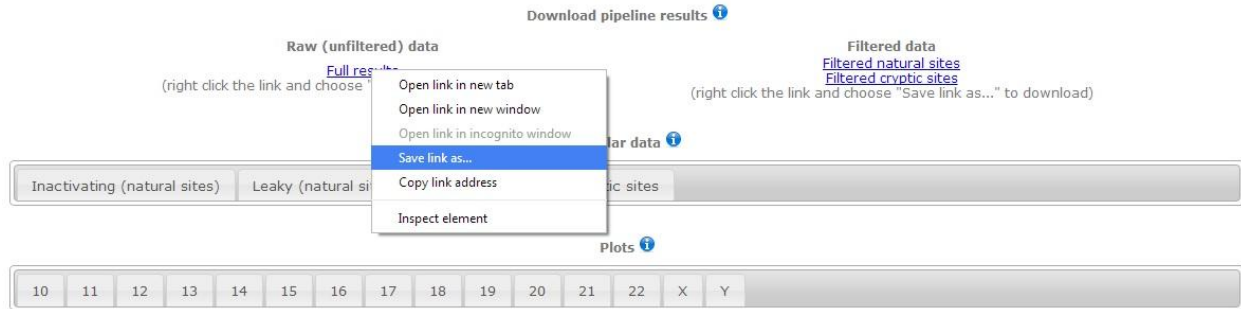
### Plot functions

Hovering the mouse over a plot point will produce a tool-tip containing the variant ID specified in the input VCF file. This ID can be used to find a variant of interest in the tabular output or raw pipeline output.

To zoom in to a specified location, hold right click and draw a box within the plot. Upon releasing right click, the plot will zoom to the boxed location. To zoom out, make use of the box to the left of the main plot. Clicking the icon of a magnifying glass with an arrow pointing left will zoom out to the previous level of zoom.

Clicking a location on the plot will display the genomic coordinate of the location followed by the final  $R_i$ .

## Downloading pipeline output



Three types of files are available for download. “Full results” contains the unfiltered raw pipeline output. Therefore any filters chosen before your job was submitted will not be represented here. Filters can be performed manually using a scripting language or spreadsheet software. “Filtered natural sites” and “Filtered cryptic sites” mirror the tabular data.

### How to download or view the pipeline output

Pipeline output files can be downloaded by right clicking on the appropriate output file and clicking “Save link as..” (or equivalent in your browser). To view the output online, simply click on the link and the output will appear in a new browser tab.

### Differences between raw pipeline output and “tidy” output

There are two formats in which pipeline output can be downloaded. Differences between these two formats are largely cosmetic. Column headers are present in “tidy” output. The “tidy” format can be used directly as input for [Veridical](#). Within raw pipeline output, positive strand is represented by a “0” and negative strand is represented by “1”.  $R_i$  values are not rounded to two decimal places and there is no  $\Delta R_i$  field in raw pipeline output. Acceptor sites are denoted “ACCEPTOR” instead of “Acc.”. Similarly, donor sites are denoted “DONOR” instead of “Don.”. The chromosome field contains a preceding “chr” in the raw output.

#### Column order in “tidy” pipeline output

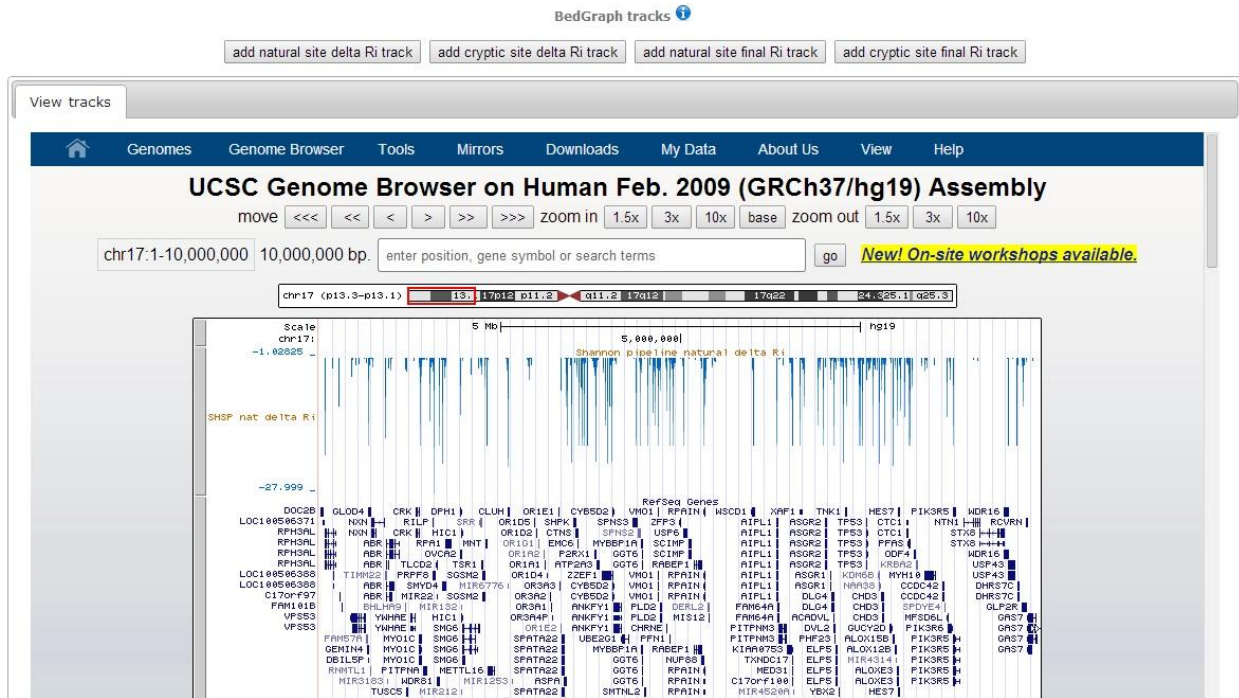
1. Chromosome
2. Splice site coord
3. Strand (+ or -)
4. Initial  $R_i$  (rounded to two decimal places)
5. Final  $R_i$  (rounded to two decimal places)
6.  $\Delta R_i$  (rounded to two decimal places)
7. Splice site type (donor or acceptor)
8. Gene name
9. CRYPTICSITE or NATURALSITE
10. Location type (intronic or exonic)
11. Loc. Rel. to exon (5'-flanking or 3'-flanking)
12. Dist. From nearest natural site
13. Coord of nearest natural site

14.  $R_i$  of nearest natural site (rounded to two decimal places)
15. Cryptic site  $R_i$  relative to nearest natural site  $R_i$
16. rsID
17. Average heterozygosity
18. Input variant coord
19. Input variant nucleotides
20. Input ID
21. Variant type

Column order in raw pipeline output

1. Input ID
2. Splice site coord
3. Strand (0 represents positive strand. 1 represents negative strand)
4. Initial  $R_i$
5. Final  $R_i$
6. Input variant coord
7. Input variant nucleotides
8. Chromosome
9. Splice site type (donor or acceptor)
10. Gene name
11. CRYPTICSITE or NATURALSITE
12. Location type (intronic or exonic)
13. Loc. Rel. to exon (5'-flanking or 3'-flanking)
14. Dist. From nearest natural site
15. Coord of nearest natural site
16.  $R_i$  of nearest natural site
17. Cryptic site  $R_i$  relative to nearest natural site  $R_i$
18. rsID
19. Average heterozygosity
20. Variant type

# BedGraph Tracks



Four BedGraph tracks are generated each time the pipeline is executed, these are:

1.  $\Delta R_i$  of all natural sites.
2.  $\Delta R_i$  of all cryptic sites.
3. Final  $R_i$  of all natural sites.
4. Final  $R_i$  of all cryptic sites.

## How to view tracks

The BedGraph tracks are automatically submitted to the UCSC Genome Browser and can be viewed there within a frame on the pipeline results page. Clicking the buttons labelled “add natural site delta  $R_i$  track”, etc. will upload the selected track to the UCSC Genome Browser. Any custom tracks previously uploaded from this site will also be visible. To remove tracks, click the button “manage custom tracks” on UCSC directly beneath the genome browser window, check the appropriate checkboxes of tracks to be removed and click delete. Uploading a new track will replace an older track of the same name. For example, if you uploaded the cryptic site delta  $R_i$  track from a previous run on this server, uploading it again by clicking the button “add cryptic site delta  $R_i$  track” will replace it.

Note: The UCSC Genome Browser is a separate resource managed by UCSC. As such, we are not responsible for maintaining this resource. As the functionality of the UCSC Genome Browser is quite extensive, it cannot be properly discussed in this document. For an introduction to the genome browser please visit [this tutorial](#) written by OpenHelix.

## FAQ

This FAQ will be updated with answers to common questions.

**Q: How fast is the Shannon human splicing pipeline server?**

A: The length of time needed to examine a VCF file is related to the number of different chromosomes in the VCF file being examined. As a general rule, if all chromosomes are present, a run will take at least 5 minutes. (3,000,000 variants in ~15min). Examining only chromosome 22 even with a large number of variants will take less than 1min.

**Q: How does the Shannon pipeline annotate the gene name field for a variant location overlapped by more than one gene?**

A: The gene name field will contain multiple genes separated by commas.

**Q: I performed an analysis on a VCF file I uploaded and I'm getting empty results. What can I do?**

A: In this situation it is important to make use of the "View run statistics" hyperlink on the results page. It is likely the server could not properly parse the VCF file you uploaded. Inside the "View run statistics" link, you can find more information about how many variants were unable to be examined by the server and a description of why they were skipped.

## Terms of use

You are welcome to use the Shannon human splicing mutation pipeline server (SMPS) as our guest. Guest (trial) access requires a valid email address and affiliation to test and evaluate the resource.

This resource is covered by US Patent #5867402 and other patents pending.

Subscriptions to obtain full pipeline results and increased job queue priority are available from Cytognomix. Pricing is tiered according to licensee, seat quantity, and license duration.

This resource is intended for research purposes only and is not intended for use in clinical diagnostics or selection of therapy. The technology has been peer reviewed in multiple scientific journals and has been widely cited. The results produced by this resource are based on these publications. No other warranty or guaranty is granted based on the results generated by the SMPS.

Analyses submitted by subscribers are executed before those submitted by trial users.

Disk space is limited on the Shannon human splicing pipeline sever. We reserve the right to remove uploaded VCF files or pipeline results in advance of the standard deletion schedule in the event files exceed our capacity to store them. Users will be notified by email in advance of file deletions that occur on non-standard deletion schedules.

Executing the same variants on the pipeline server repeatedly or other actions which may be disruptive to the server's functionality is considered to be a serious violation of these Terms of Use and is prohibited. This is a shared resource with finite resources. Any attempt to circumvent the limitations of trial server access or any failure to adhere to these restrictions will result in permanent suspension/removal of your account, and/or notification of administrators or officers at your institution or company. Uploading malicious code or other more serious attacks upon the website will incur legal liability for you and your employer for any damages sustained by Cytognomix.

Publications or presentations that use or describe results produced by this resource should reference the server web address (<http://shannonpipeline.cytognomix.com>), and Shirley et al. "Interpretation, stratification and evidence for sequence variants affecting mRNA splicing in complete human genome sequences.", Genomics Proteomics Bioinformatics, 11:77-85, 2013 [DOI: 10.1016/j.gpb.2013.01.008](https://doi.org/10.1016/j.gpb.2013.01.008).



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