

# Tutorial of the online CLIME analysis portal

CLIME (CLustering by Inferred Models of Evolution) is a statistical algorithm that partitions an input gene set of interest into distinct, evolutionarily conserved modules (ECMs), and then expands each module with genes sharing an inferred evolutionary history. This is a step-by-step tutorial that introduces the users how to use the online CLIME analysis portal. For demonstration, we apply CLIME to analysis of 7 genes in the human WASH complex as an example.

1. First we visit the CLIME portal in a web browser ([www.gene-clime.org](http://www.gene-clime.org)). The front page is shown below. It contains a brief description of CLIME algorithm and provides the links for submitting online CLIME jobs and downloading pre-computed CLIME outputs for about 1025 classically defined human pathways. To submit a CLIME job, we click the “Submit a CLIME job” button.

**CLIME** Clustering by Inferred Models of Evolution

Home My CLIME Jobs Help Login

**CLIME** (Clustering by Inferred Models of Evolution) is an algorithm that partitions an input gene set of interest into distinct, evolutionarily conserved modules (ECMs), and then expands each module with genes sharing an inferred evolutionary history. CLIME accepts as input (i) a binary species tree, (ii) an input gene set, and (iii) a phylogenetic matrix of all genes in a reference genome across the species. CLIME software is available for download at this site, and we also provide a interactive interface for users to perform CLIME analysis on gene sets from within 10 model organisms (*H. sapiens*, *M. musculus*, *D. melanogaster*, *C. elegans*, *N. crassa*, *S. cerevisiae*, *A. thaliana*, *C. merolae*, *P. falciparum*, *T. brucei*). Also available at this site are pre-computed CLIME analyses of 1025 human pathways (GO cellular locations and KEGG pathways), the mitochondrial proteome (MitoCarta), cilia, and full-genome analysis of *P. falciparum*, *C. merolae*, and *S. cerevisiae*.

**Citing CLIME**

In review

**Run CLIME**

Submit a CLIME Job

**Downloads**

**CLIME software (including users' manual)**

CLIME v1.0 Beta - Linux 32-bit CLIME v1.0 Beta - Linux 64-bit

**Pre-computed CLIME analyses of published gene sets**

[PDF](#) [TXT](#) Human complex I  
[PDF](#) [TXT](#) Human MICU1  
[PDF](#) [TXT](#) Human ciliary genes  
[PDF](#) [TXT](#) Human mitochondrial genes  
[PDF](#) [TXT](#) All 5331 *P. falciparum* genes  
[PDF](#) [TXT](#) All 5013 *C. merolae* genes  
[PDF](#) [TXT](#) All 5882 *S. cerevisiae* genes

2. A registered account is required for submitting online CLIME jobs and viewing the results of previously submitted jobs (otherwise the user is directed to a login page). Here we enter:

- 1) Job name: used for future reference to this job. **Enter: WASH complex**
- 2) Organisms: use dropdown menu to select which of 10 precomputed phylogenetic profile matrices to input. **Select H. sapiens**
- 3) Gene list: list of input genes, with one gene symbol/Entrez ID per line. Entered names will be mapped to standard symbols using a static lookup table of gene aliases (NCBI Entrez ID, official gene symbol, other symbols listed in NCBI). Maximum 200 genes can be entered (users can analyze larger gene sets by downloading CLIME software available on the main web page).  
**Enter the gene symbols: CCDC53 WASH1 KIAA0196 23325 FAM21A FAM21B FAM21C**
- 4) Notes: optional annotation to a CLIME job. **Leave blank**

Next click "Submit CLIME job".

The screenshot shows the CLIME web interface. At the top, there is a navigation bar with the CLIME logo and the text "Clustering by Inferred Models of Evolution". To the right of the logo are four buttons: "Home", "My CLIME Jobs", "Help", and "Logout: scalvo". Below the navigation bar is the main heading "Submit a new CLIME Job". Underneath this heading is a section titled "Instructions" which contains text about submitting jobs, including a limit of 200 genes and a link to the home page. Below the instructions is a section titled "Job Parameters". This section contains a form with the following fields: "Name: (A short identifier for this gene set)" with the value "WASH complex"; "Organism" with a dropdown menu set to "H. sapiens"; "Gene List: One gene per line, Entrez gene IDs or symbols only" with a text area containing the following text: "CCDC53", "WASH1", "KIAA0196", "23325", "FAM21A", "FAM21B", "FAM21C"; and "Notes" with an empty text area.

3. The CLIME portal will validate the input gene symbols/IDs. If all genes exist in the selected organism, a CLIME job will be submitted to a compute queue, and the browser will be directed to the page shown below. A email will be received upon job completion, or you can check status on the My CLIME Jobs page.

The screenshot shows the CLIME portal interface. At the top, there is a navigation bar with the CLIME logo and the text "Clustering by Inferred Models of Evolution". The navigation bar includes links for "Home", "My CLIME Jobs", "Help", and "Logout: scalvo". Below the navigation bar, a message states: "WASH complex" was successfully submitted. It informs the user that they will receive an email upon completion and that results will load automatically. The job details are as follows:

- Name:** WASH complex
- Gene list:** CCDC53 , WASH1 , KIAA0196 , 23325 , FAM21A , FAM21B , FAM21C
- Organism:** H. sapiens
- Notes:**
- Submitted on:** 2014-04-01 15:02:45

The page also indicates it was last refreshed at 2014-04-01 15:02:45 and includes a "Back" link.

While waiting for the job to finish, users are free to close the web browser, and go back to check the job status by logging in again and visiting "My CLIME Jobs" page. As shown below, the "My CLIME jobs" page shows all jobs that are ever submitted by this user. Users can check the status of unfinished jobs by clicking "Get Status" button. For example, as shown below we are waiting our newly submitted job to be finished, and the "View Results"/"Download Results" buttons are not available yet.

4. When the job is done, an email containing the link to the results will be sent to the user (the email for our example is shown below). Alternatively, users can also log in the portal again, and visit "My CLIME Jobs" page. As shown below, for all finished jobs users can download their result files, view their PDF results in the web browser by clicking "View Results", or open the "Interactive Visualizer" of results.

The screenshot shows the "My CLIME Jobs" page. At the top, there is a navigation bar with the CLIME logo and the text "Clustering by Inferred Models of Evolution". The navigation bar includes links for "Home", "My CLIME Jobs", "Help", and "Logout: scalvo". Below the navigation bar, the page title is "My CLIME Jobs". There is a "Show 10 entries" dropdown and a "Filter Results: WAS" search box. The main content is a table of jobs:

| Name         | Date Submitted      | Notes | Organism   | Status | Gene list                      | View Results                 | Interactive Visualizer                 | Download Result Files                 |
|--------------|---------------------|-------|------------|--------|--------------------------------|------------------------------|--|---------------------------------------|
| WASH complex | 2014-04-01 15:02:45 |       | H. sapiens | Done   | <a href="#">View Gene List</a> | <a href="#">View Results</a> | <a href="#">Interactive Visualizer</a> | <a href="#">Download Result Files</a> |

The "View Results" and "Download Result Files" buttons are highlighted in blue, indicating they are available for this completed job. A red "X" icon is visible in the bottom right corner of the table row.

5. The downloadable CLIME outputs, compressed in a zip package, consist of a PDF file and a text file. The PDF file contains the visual representation of partitioning of the gene sets into ECMs, each ECM's evolutionary model, and the symbols and phylogenetic profiles of the genes in the ECM. The text file contains the same information as the PDF file, and can be useful to view in Excel and to link gene symbols to other annotations (see Help). The detailed description of PDF output can be found in the first page on PDF file and in the Help page.

| Name                   | Type                   | Size    |
|------------------------|------------------------|---------|
| CLIME.wash_complex.pdf | Adobe Acrobat Document | 415,592 |
| CLIME.wash_complex.txt | Text Document          | 9,419   |

6. Clicking the “Interactive Visualizer” in “My CLIME Jobs” page directs user to the interactive visualizer. The interactive visualizer provides an interactive HTML representation of the CLIME PDF output with some additional features. For our example gene set, the interactive visualizer on ECM 2 is shown below. Users can switch to view different ECMs by the “Select ECM” dropdown menu (highlight by red). The ECM genes are shown in blue rows and the ECM+ genes are shown in green/gray rows. The gene symbols are shown at left and can be click to direct to the corresponding NCBI gene page. See the Help page for instructions on using the CLIME Interactive Visualizer.

