

Basic use manual of FIMED clinical tool

SANDRO HURTADO, JOSÉ GARCÍA-NIETO, ISMAEL
NAVAS-DELGADO AND JOSÉ F. ALDANA-MONTES

KHAOS RESEARCH, UNIVERSITY OF MÁLAGA



What is Fimed?

FIMED *application for flexible integration of biomedical data* is a new software solution that facilitates the handling of large amounts of heterogeneous data in clinical research processes, thus improving the efficiency and quality of the data. It offers numerous benefits for the user in each of the aspects of the phases of clinical trials, including the possibility of inserting patient data dynamically and performing different studies. This software application has been designed to guarantee scalability, versatility and flexibility. In that way it can be adapted to multiple clinical trials. This tool has been tested with a real case for a clinical assay in Melanoma disease including two data analysis and visualization components for gene expression data: heatmap visualization and gene regulatory network inference. From its initial use to the collection of data analysis results, this tool eliminates the obstacles typical of clinical research by allowing the insertion and manipulation of data at any time in a simple way for the user.

Contents

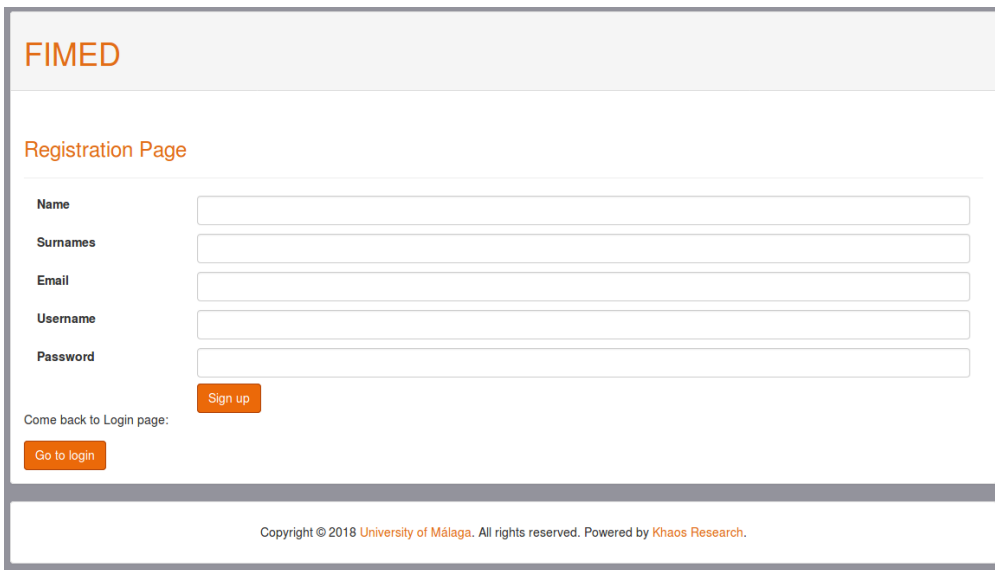
1	Overview of FIMED	3
1.1	Create an account	3
1.2	Application interface	4
1.3	FIMED Home Page	4
1.3.1	Navigation Bar	4
1.3.2	Body of Home page	5
2	Create Patient(s)	5
2.1	First step: Add new Fields for the patient	6
2.1.1	Create simple fields	6
2.1.2	Create compound fields	6
2.2	Second step: Attach samples to your patient	7
2.3	Third step: Attach files to your patient	8
3	Search Patient(s)	11
3.1	Search all the information about patient	12
3.2	Search patient by ID	14
3.3	Search patient by parameter	14
4	Update the patient	16
4.1	How to insert new fields?	16
4.2	How to modify existing fields?	17
4.3	How to delete fields?	18
4.3.1	Delete simple field	18
4.3.2	Delete compound field	18
4.3.3	Delete samples and files attached to the patient	19
5	Clinical Analysis	20
5.1	HeatMap	21
5.2	Gene Regulation Network (GRN)	24

1 Overview of FIMED

To access the application we just have to go to the next url: <http://khaos.uma.es/Fimed/> from our web browser.

1.1 Create an account

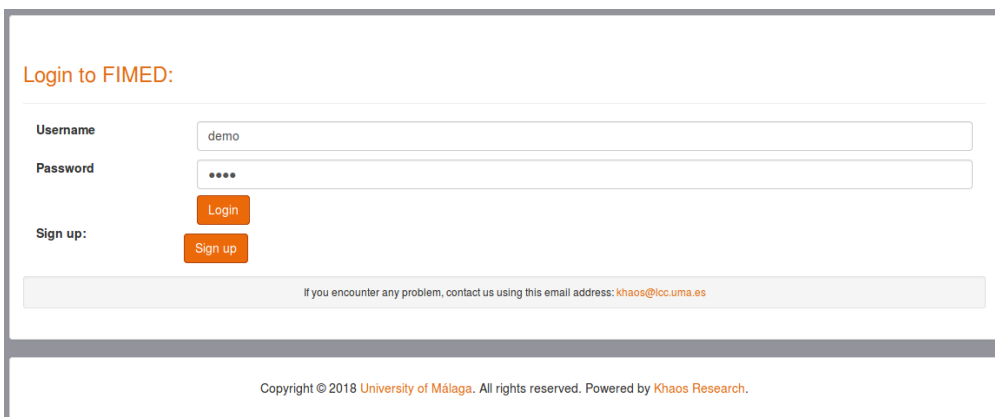
To access the application it is necessary to have a registered account. If you do not have one, you can register by going to the **Register** page (figure 1).



The screenshot shows the 'FIMED' registration page. It features a header with the 'FIMED' logo in orange. Below the header, the title 'Registration Page' is displayed in orange. The form contains five input fields: 'Name', 'Surnames', 'Email', 'Username', and 'Password'. A 'Sign up' button is located below the 'Password' field. A link 'Come back to Login page:' is followed by a 'Go to login' button. The footer contains the text: 'Copyright © 2018 University of Málaga. All rights reserved. Powered by Khaos Research.'

Figure 1: Registration Page

Then you must fill out the form with the fields that appear on the Register page. For this explanatory guide we are going to create a demo user, which will have a username: *demo* and password: *demo*



The screenshot shows the 'FIMED' login page. It features a header with the title 'Login to FIMED:' in orange. The form contains two input fields: 'Username' (with the value 'demo') and 'Password' (with masked characters '****'). A 'Login' button is located below the 'Password' field. A 'Sign up:' link is followed by a 'Sign up' button. A footer bar contains the text: 'If you encounter any problem, contact us using this email address: khaos@icc.uma.es'. The bottom footer contains the text: 'Copyright © 2018 University of Málaga. All rights reserved. Powered by Khaos Research.'

Figure 2: Log in Page

Once registered successfully we can access the application. Go to Login page again and enter in the application (figure 2).

1.2 Application interface

This application is developed for the uptake, intake and consolidation of clinical data, providing medical and biological information to researchers and physicians in this field and adding numerous advanced functionalities in each of the aspects of the phases of these trials. To demonstrate the viability of this proposal, a pilot scheme will be conducted in the context of a real clinical trial of Melanoma disease, which is presented as an emerging work among the Khaos research group ¹ of the University of Málaga in collaboration with the IBIMA ² group.

The user will be able to create your own database dynamically in a simple way, to later carry out the clinical analysis with the data of the patient's samples. Next, the different functionalities of the application will be shown and a quick guide on how to use it.

1.3 FIMED Home Page

FIMED Home page is the main page of the application. Is the first page user sees after log in. The home page provides links to functionalities and features in FIMED.



1.3.1 Navigation Bar

We'll start by explaining the functionality of the buttons in the navigation bar:

1. **Home:** redirection to the main page of the tool
2. **Insert:** insert a new patient to perform the clinical analysis

¹Khaos Research Group <http://khaos.uma.es/>

²IBIMA Biomedical Research Institute of Malaga www.ibima.eu/

3. **Find**: search for patients inserted in the database
4. **Analysis**: clinical data analysis tool
5. **About us**: additional information about Khaos Research Group
6. **Log out**: Log out button

1.3.2 Body of Home page

7. **2 Create Patient(s)**
8. **3 Search Patient(s)**

These functionalities are explained throughout the manual. Since the database is currently empty, we will start by inserting a new patient.

2 Create Patient(s)

Create the structure of the database in a personalized way. Thanks to the flexibility provided by the Mongo database, we can create attributes dynamically. In this way we can adapt our database to any case of study in the handling of data in clinical trials.

To start, click on the button **Create patient** (In the same way we can access by pressing the **Insert** button placed in the navigation bar).

FIMED

Create Patient

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Add new fields for the patient The patient will be created with the new parameters

Add new Field	Delete Field	Add new Subfield	Delete Subfield
---------------	--------------	------------------	-----------------

Next



Figure 3: Create Patient Page

The **Create Patient** page is divide in the following step:

1. First step: Add new Fields for the patient
2. Second step: Attach samples to your patient
3. Third step: Attach files to your patient

2.1 First step: Add new Fields for the patient

The application allows us to create two types of fields:

1. Simple fields
2. Compound fields

2.1.1 Create simple fields

Click the button **Add New Field** to create a simple field. We have to enter the name of the field and its value. For example, we could enter as name of the field *Name* and *Patient 1* as its value (figure 4). In the same way, we can press the **Delete field** button to delete the last created field.

FIMED

Create Patient

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Add new fields for the patient The patient will be created with the new parameters

Name	Patient 1
Code	1165
Sex	Male
Birth	Jun 8, 2000
Record	Demo Patient 1

Add new Field **Delete Field** **Add new Subfield** **Delete Subfield**

Next

● ● ●

Figure 4: Create Simple Field

2.1.2 Create compound fields

Click the button **Add New SubField** to create a compound field. First you have to enter the name of the compound field and then you can add simple fields associated to this by pressing the **+** button. For example, we can declare a compound field *Hospital* that has associated the simple fields *Name*, *Address*, *Zip Code* with their respective field value (Figure 5).

To delete a compound field first we will have to eliminate all its simple fields by pressing the button **-** and finally press the **Delete Subfield** button to erase it completely.

FIMED

Create Patient

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Add new fields for the patient The patient will be created with the new parameters

Name	Patient 1
Code	1165
Sex	Male
Birth	Jun 8, 2000
Record	Demo Patient 1
Hospital	<div><div>+</div><div>-</div></div>
<div><div>Name</div><div>Hospital Name</div></div>	
<div><div>Address</div><div>Street Name</div></div>	
<div><div>Zip Code</div><div>11001</div></div>	

Add new Field

Delete Field

Add new Subfield

Delete Subfield

Next

Figure 5: Create Compound Field

When the fields have been entered, press the next button to continue filling in the form.

2.2 Second step: Attach samples to your patient

In this second step, the samples associated with our patient are added, since this application is oriented to clinical data analysis. In our case we will attach clinical data of melanoma to analyze them later.

To insert a new sample of the patient, press the **browse** button and select a sample. We can also insert metadata associated to that sample in the same way that we previously added simple fields to our patient. Press the **add new metadata** button and fill the gaps with the name of the field and its value. For example, we can enter the name of the sample or the date of the sample together with its value, as shown in the figure 6.

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Insertion of Samples for the Patient Attach samples associated with your patient

Attach sample Elegir archivos Sample_1.txt

Insert Metadata Insert information associated with the attached Sample

Name	Sample 1
Experiment Date	Jan 15, 2018

New Metadata Delete Metadata

Prev Next

● ● ●

Figure 6: Attach Samples

When the sample have been entered, press the next button to continue filling in the form.

2.3 Third step: Attach files to your patient

This application allows you to attach files to your patient and insert metadata associated (figure 7).

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Insert Files Attach files associated with your patient

Attach new file Elegir archivos Manual_de_Uso.pdf

Insert Metadata Insert information associated with the attached file

Filename	documentation
----------	---------------

New Metadata Delete Metadata

Insert Patient

Prev

● ● ●

Figure 7: Attach Files

Finally we have to press the button **Insert Patient** to insert it in the Mongo database. When we press the button, a message *Your form has been successfully filled* and a menu to go to Home, Create another patient or search for your created patients will appear (figure 8)

Figure 8: Form successfully filled

If we press the button **Create new Patient** to create another patient, we will see that the fields that we have created previously appear as predetermined fields (figure 9), in this way we will configure our database as we create the patients.

Figure 9: Create new Patient with predetermined fields

In the same way it happens in the following pages to attach samples (figure 10) and files (figure 11) to the patient.

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Insertion of Samples for the Patient Attach samples associated with your patient

Attach sample

Elegir archivos

Ningún archivo seleccionado

Insert Metadata Insert information associated with the attached Sample

Experiment Date

Enter Value

Name

Enter Value

New Metadata

Delete Metadata

Prev

Next



Figure 10: Attach Sample with predetermined meta-data

Create Patients Dynamically ADDITIONAL INFORMATION ⓘ

Insert Files Attach files associated with your patient

Attach new file

Elegir archivos

Ningún archivo seleccionado

Insert Metadata Insert information associated with the attached file

Filename

Enter Value

New Metadata

Delete Metadata

Insert Patient

Prev



Figure 11: Attach File with predetermined meta-data

3 Search Patient(s)

FIMED allow the user searching for patients already registered in the database. In FIMED Home page we can search for a patient(s) by clicking on the **Search Patient(s)** button (or directly in the navigation bar by pressing the **Search** button), as shown in figure 12.



Figure 12: Search Patient

There are three different ways to search a patient (figure 13):

1. Find patient by ID
2. Find patient by parameter
3. Find all the patients

FIMED

Patient search

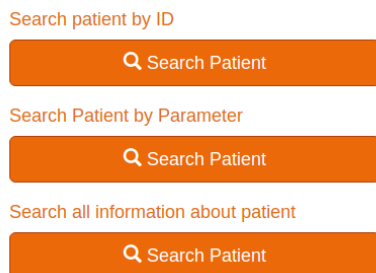


Figure 13: Search Patient

3.1 Search all the information about patient

To perform a search of all the patients in the database, click on the **Search Patient** button and you will be redirect to the following page: **list of patients** (figure 14)

List of Patients

Search: Select the patients' parameters:

Name

Code

Sex

Birth

Record

Search parameter:

Name

Value:

e.g: Psoriasis

FindPatient

Patient: 5cb06fd3c4aa767ad6fd2b6e	
Name	Patient 1
Code	1165
Sex	Male
Birth	Jun 8, 2000
Record	Demo Patient 1
Hospital	
Name	Hospital Name
Address	Street Name
Zip Code	11001

Display Samples

Display Files

Update Patient

Delete Patient

Figure 14: List of Patient

On this page we can see the list of patients that currently are in the database. The figure 15 shows a table with all the patient information that we have entered in the database previously. The patient identifier (ID created automatically by the Mongo database) is shown in the header of the table, and the data entered by the user are displayed in the table body.

Patient: 5cb06fd3c4aa767ad6fd2b6e	
Name	Patient 1
Code	1165
Sex	Male
Birth	Jun 8, 2000
Record	Demo Patient 1
Hospital	
Name	Hospital Name
Address	Street Name
Zip Code	11001

Display Samples

Display Files

Update Patient

Delete Patient

Figure 15: Patient table

Just under the table there are four buttons associated with the patient which

allow us to perform the following actions:

1. **Display Samples:** It allows to visualize the corresponding samples to the patient. We can also download the sample with the download button (figure 16)

Samples ×

Patient code: 5cb06fd3c4aa767ad6fd2b6e

Sample ID	Sample Name	Sample Date	Download
5cb06fd3c4aa767ad6fd2b74	Sample_1.txt	Fri Apr 12 04:00:35 PDT 2019	📄 Sample_1.txt
5cbd96b6c4aa767ad6fd2b77	Sample_2.txt	Mon Apr 22 03:25:58 PDT 2019	📄 Sample_2.txt
5cbd96dbc4aa767ad6fd2b7a	Sample_3.txt	Mon Apr 22 03:26:35 PDT 2019	📄 Sample_3.txt

Figure 16: Patient attached Samples

2. **Display Files:** This button allows you to view and download the files associated with this patient.

Attached Files ×

Patient code: 5cb06fd3c4aa767ad6fd2b6e

Attached File:	
Filename	Manual_de_Uso.pdf
Filename	documentation
Download File:	📄 Manual_de_Uso.pdf

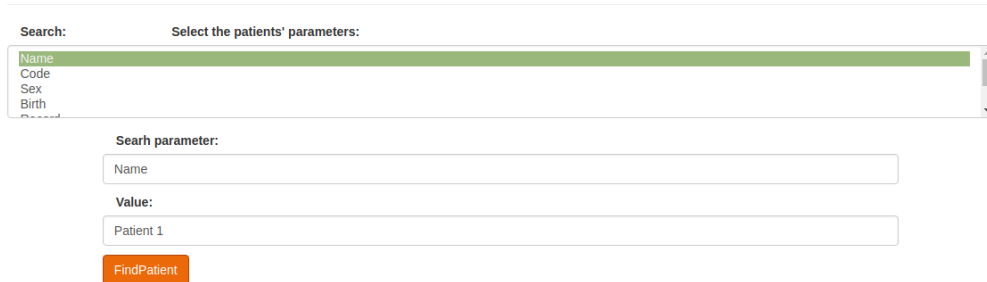
Figure 17: Patient attached Files

3. **Update Patient:** This button will redirect you to the patient's update page, where you can insert, modify or delete patient fields. (This point will be discussed in the following section 4: Update the patient)
4. **Delete Patient:** removes the patient from the database and all the samples and associated files.

In addition, there is a patient search engine at the top of the page, where we can search for a patient by the value of the parameters it contains. We

must choose one of the predetermined fields that the search engine emerges and introduce its value. Finally press the **FindPatient** button. For example, we can search for the patient that we have previously entered by choosing *Name* as the suggested parameter and then we will enter its value *Patient 1* (Figure 18). This query will return a list of those patients who meet the condition of the query.

List of Patients



Search: Select the patients' parameters:

Name
Code
Sex
Birth
Blood

Search parameter:

Name

Value:

Patient 1

FindPatient

Figure 18: Use search engine

3.2 Search patient by ID

To find a patient according to his ID, we must enter the identifier generated automatically by the Mongo database as shown in the figure 19 (this identifier can be found in the header of the tables that contain the patient's data, as we mentioned before).

FIMED

Patient search



Patient

Find by ID

5cb06fd3c4aa767ad6fd2b6e

FindPatient

Figure 19: Search patient by ID

3.3 Search patient by parameter

Selecting the button to search for a patient by its parameters, we will redirect to the following page. As we can see, the search method is the same as before (figure 20).

Search: **Select the patients' parameters:**

Name

Code

Sex

Birth

Gender

Search parameter:

Sex

Value:

Male

FindPatient

Figure 20: Search patient by Parameter

4 Update the patient

Update Patient page works in the same way as the Create Patient page, but in this case we are able to create new fields, modify existing ones and even delete them.

To update a patient we must first search for the patient that we want to update and then we will select the function to update it.

Search Patient \Rightarrow Update Patient

Insert, update or delete patient fields The selected fields will be deleted when the patient is updated

<input type="checkbox"/> Name	<input type="text" value="Patient 1"/>
<input type="checkbox"/> Code	<input type="text" value="1165"/>
<input type="checkbox"/> Sex	<input type="text" value="Male"/>
<input type="checkbox"/> Birth	<input type="text" value="Jun 8, 2000"/>
<input type="checkbox"/> Record	<input type="text" value="Demo Patient 1"/>
<input type="checkbox"/> Hospital ⓘ	
<input type="checkbox"/> Name	<input type="text" value="Hospital Name"/>
<input type="checkbox"/> Address	<input type="text" value="Street Name"/>
<input type="checkbox"/> Zip Code	<input type="text" value="11001"/>

Insert new Patient Fields The patient will be update with the new parameters.

<input type="button" value="Add new Field"/>	<input type="button" value="Delete Field"/>	<input type="button" value="Add new Subfield"/>	<input type="button" value="Delete Subfield"/>
--	---	---	--

Figure 21: Update Patient Page

4.1 How to insert new fields?

As previously on the patient creation page, we can add simple fields and compound fields, selecting the buttons **Add new Field** and **Add new SubField**. On the other hand, we can insert new subfields to the compound fields that the patient contains. For example, It is possible to include a new subField associated to Hospital pressing the **Add new Fields to Hospital** button, as shown in the figure 22:

☐ Hospital ⓘ

- ☐ Name: Hospital Name
- ☐ Address: Street Name
- ☐ Zip Code: 11001

Insert new Patient Fields The patient will be update with the new parameters.

Figure 22: Insert new SubField to compound Field *Hospital*

In the same way it happens with the samples and the files associated with the patient. We can add new samples and new files with their respective metadata.

4.2 How to modify existing fields?

To modify the existing fields we just have to delete the value of the field and replace it with the one we want. For example, we could decide to change the value of the patient code from 1165 to 1175 (figure 23).

Insert, update or delete patient fields The selected fields will be deleted when the patient is updated

- ☐ Name: Patient 1
- ☐ Code: 1175
- ☐ Sex: Male
- ☐ Birth: Jun 8, 2000
- ☐ Record: Demo Patient 1
- ☐ Hospital ⓘ
 - ☐ Name: Hospital Name
 - ☐ Address: Street Name
 - ☐ Zip Code: 11001

Insert new Patient Fields The patient will be update with the new parameters.

Figure 23: Modifying the value of *Code* Field

4.3 How to delete fields?

To eliminate patient fields we have to select the checkbox that is next to each field. This way when we finish completing the update of the form, the selected fields will be eliminated.

4.3.1 Delete simple field

Select the checkbox that is to the left of the field. When we select the checkbox, we see that the value of the field disappears from the application. For example, in the following figure 24 we observe how we can erase the Sex and Record fields.

Insert, update or delete patient fields The selected fields will be deleted when the patient is updated

<input type="checkbox"/> Name	Patient 1
<input type="checkbox"/> Code	1175
<input checked="" type="checkbox"/> Sex	
<input type="checkbox"/> Birth	Jun 8, 2000
<input checked="" type="checkbox"/> Record	
<input type="checkbox"/> Hospital	
<input type="checkbox"/> Name	Hospital Name
<input type="checkbox"/> Address	Street Name
<input type="checkbox"/> Zip Code	11001

Insert new Patient Fields The patient will be update with the new parameters.

Figure 24: Removing *Sex* and *Record* Fields from the form.

4.3.2 Delete compound field

With the compound fields we must pay special attention (Figure 25), because if we select the compound fields, all the associated simple fields will be eliminated as well (Figure 26).

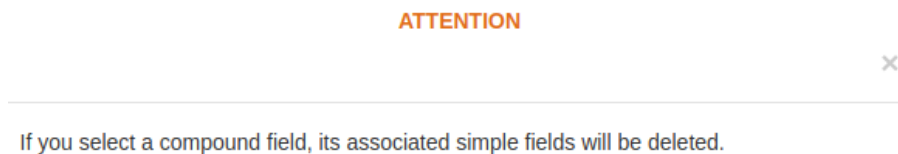


Figure 25: ATTENTION

☒ Hospital ⓘ

☐ Name

☐ Address

☐ Zip Code

-

Insert new Patient Fields The patient will be update with the new parameters.

Figure 26: Removing *Hospital* compound Field and all the associated simple fields (*Name*, *Address*, *Zip Code*) from the form.

On the other hand, we can eliminate simple fields associated with a compound field, without having to eliminate the completely composed field. We could remove the *Zip Code* from the *Hospital*, as shown in the figure 27

☐ Hospital ⓘ

☐ Name

☐ Address

☒ Zip Code

-

Insert new Patient Fields The patient will be update with the new parameters.

Figure 27: Delete *Zip Code* Field from the *Hospital* Compound Field

4.3.3 Delete samples and files attached to the patient

In addition, in the same way we can eliminate samples and files associated with the patient. We must bear in mind that their associated metadata will also be eliminated.

Finally we select the **Update Patient** button to finalize the form. Next we will look for the patient that we have just modified and we can see that all their fields have been updated successfully.

5 Clinical Analysis

FIMED current version also includes two data analysis and visualization components for gene expression data: heatmap visualization and gene regulatory network inference. These analyzes are focused on the study of gene expression in the case of the use of Melanoma cancer. In the demo user of this application we have created a patient (*Patient 1*), to which have been attached 4 samples of gene expression in different moments of time (figure 28).

The screenshot displays the FIMED application interface. A modal window titled "Samples" is open, showing a table of attached samples for a specific patient. The patient's code is 5cb06fd3c4aa767ad6fd2b6e. The table lists four samples with their IDs, names, dates, and download links. In the background, the "List of Patients" search interface is visible, including search parameters and a "Find Patient" button. Below the search interface, a patient details form for "Patient 1" is shown, containing fields for Name, Code, Sex, Birth, Record, Hospital, Address, and Zip Code. At the bottom of the interface, there are buttons for "Display Samples", "Display Files", "Update Patient", and "Delete Patient".

Sample ID	Sample Name	Sample Date	Download
5cb06fd3c4aa767ad6fd2b74	Sample_1.txt	Fri Apr 12 04:00:35 PDT 2019	Sample_1.txt
5cbd96b6c4aa767ad6fd2b77	Sample_2.txt	Mon Apr 22 03:25:58 PDT 2019	Sample_2.txt
5cbd96dbc4aa767ad6fd2b7a	Sample_3.txt	Mon Apr 22 03:26:35 PDT 2019	Sample_3.txt
5cc6e2c7c4aa0d35e7ba1a36	Sample_10114.txt	Mon Apr 29 04:40:55 PDT 2019	Sample_10114.txt

Patient: 5cb06fd3c4aa767ad6fd2b6e	
Name	Patient 1
Code	1165
Sex	Male
Birth	Jun 8, 2000
Record	Demo Patient 1
Hospital	
Name	Hospital Name
Address	Street Name
Zip Code	11001

Figure 28: Attached Patient Samples

For this case, the analysis component analyses the RCC files, starting from the data normalization following a housekeeping based method.

5.1 HeatMap

To select a clinical analysis of Heat Map, we will go to the navigation bar where Analysis is placed and select HeatMap (figure 29).

Select **Analysis** \Rightarrow **HeatMap**

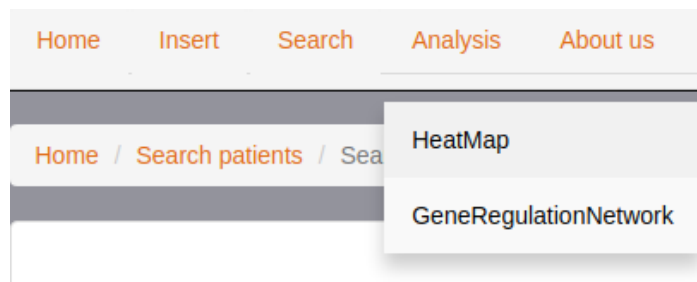


Figure 29: Select HeatMap

Here all the patients that we have in our database will appear (figure 30). In our case only the patient that we have previously introduced will appear.

List of Patients

Patient:5cb06fd3c4aa767ad6fd2b6e
Add Samples

Name	Patient 1
Code	1165

Analysis samples

Selected samples

Sample ID

Patient Code

✕ delete

Remove those you are not interested.

Select label to display:

Services

☐ Cluster heatmap

Select at least one service to be executed.

% of significantly altered gene expression levels

0.05%

Submit

Figure 30: HeatMap Page

The first step is adding the samples of the patients' genetic expression to be analyzed. To do this, we select the **Add Samples** button next to each patient (figure 31):

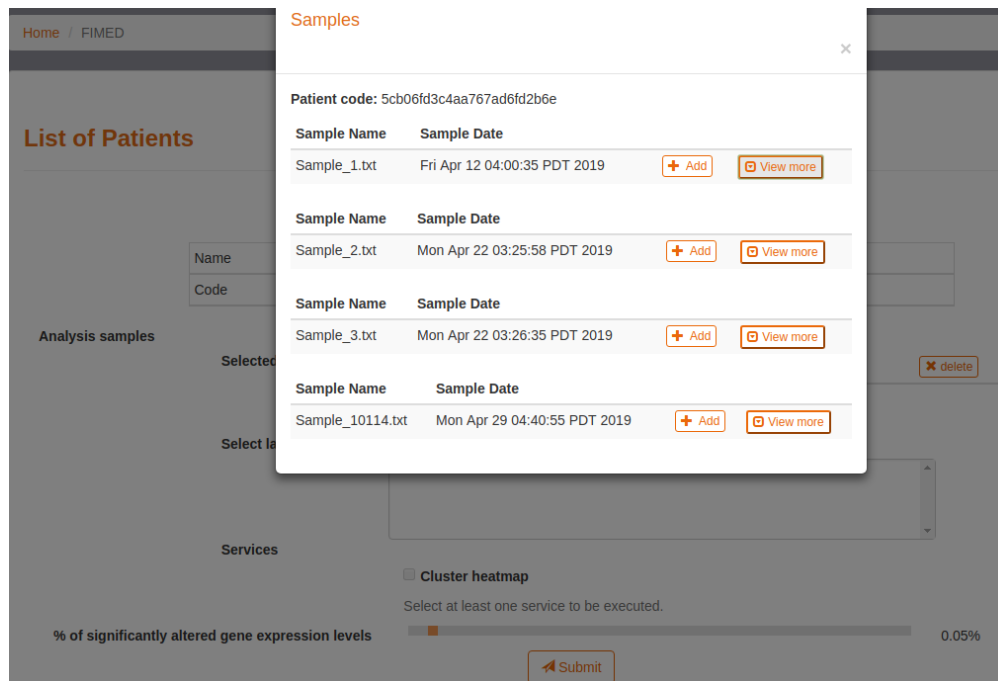


Figure 31: Patient Samples in HeatMap Page

We can observe the metadata associated with each sample by clicking on the **View More** button (figure 32)

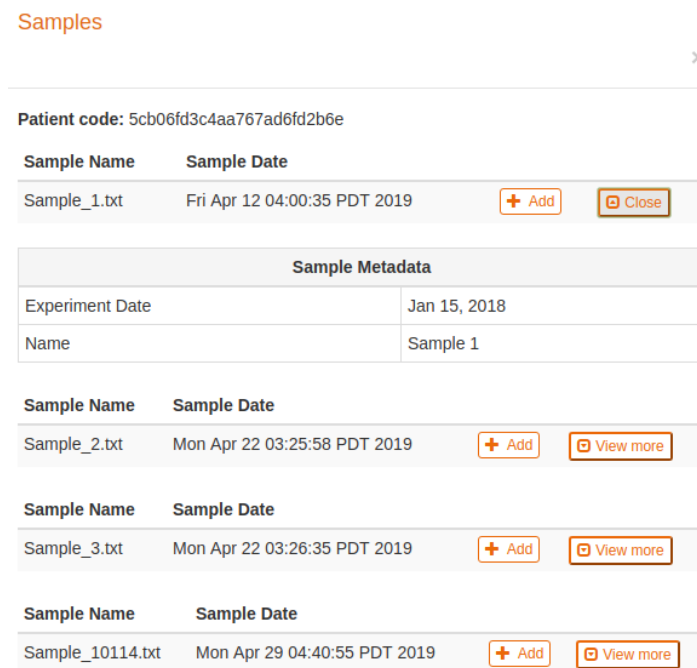


Figure 32: Clicking on the **View More** button

Then Click the **Add** button to add the samples you want to analyze. For our example we will add *Sample 1*, *Sample 2* and *Sample 3*. Below we can see that the selected samples have been added to Selected Samples table (figure 33).

Patient: 5cb06fd3c4aa767ad6fd2b6e [+ Add Samples](#)

Name	Patient 1
Code	1165

Analysis samples

Selected samples	Sample ID	Patient Code	✕ delete
1	5cb06fd3c4aa767ad6fd2b74	5cb06fd3c4aa767ad6fd2b6e	
2	5cbd96b6c4aa767ad6fd2b77	5cb06fd3c4aa767ad6fd2b6e	
3	5cbd96dbc4aa767ad6fd2b7a	5cb06fd3c4aa767ad6fd2b6e	

Remove those you are not interested.

Select label to display:

Experiment Date
Name

Services

☐ Cluster heatmap

Select at least one service to be executed.

% of significantly altered gene expression levels 0.05%

[Submit](#)

Figure 33: This image shows the samples selected for the analysis and the common metadata of the samples to be shown in the HeatMap graph (*Select label to display*)

Once the samples to be analyzed have been selected, we follow the following steps:

1. **Selected Samples:** We can delete some sample by pressing the delete button or add more samples as we have done previously (figure 35).

Selected samples	Sample ID	Patient Code	✕ delete
1	5cb06fd3c4aa767ad6fd2b74	5cb06fd3c4aa767ad6fd2b6e	
2	5cbd96b6c4aa767ad6fd2b77	5cb06fd3c4aa767ad6fd2b6e	
3	5cbd96dbc4aa767ad6fd2b7a	5cb06fd3c4aa767ad6fd2b6e	

Remove those you are not interested.

Figure 34: Here is the table of selected samples. We can eliminate or add more samples

2. **Select label to display:** the selected label will be represented on the HeatMap chart. in our case we will select *Experiment date*.

Experiment Date
Name

Figure 35: Select label to display

3. **HeatMap Service and percentage of significantly altered gene expression levels:** we have to click the checkbox of *Cluster Heatmap* and select the percentage of significantly altered gene expression levels, that it is normally adjusted in 0.05% (figure 36).

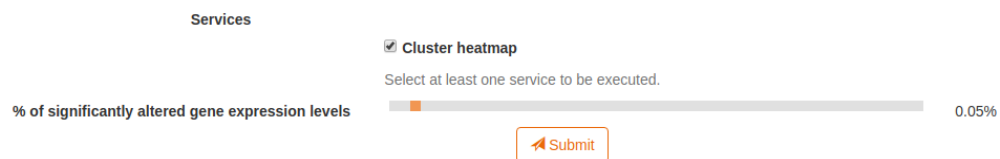


Figure 36: Select HeatMap Service

Finally we will select the Submit button to start the analysis:

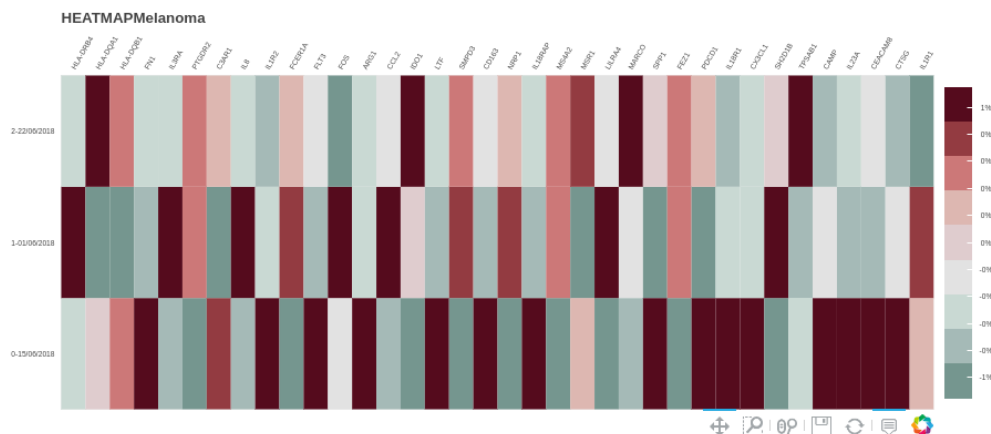


Figure 37: Cluster HeatMap plot

It can be observed how the genes are represented on the X axis and on the Y axis we represent the experiment date on which the clinical trial was performed, in this way we see how the expression of the genes evolves over time with each of the samples. This graphic allows you to zoom, scroll and even save the Heatmap in `textit.png` format.

5.2 Gene Regulation Network (GRN)

Second data analysis provided is the gene regulatory networks inference using GRNBoost and GENIE3 algorithms (from Arboreto Python package 1), producing a visualization of gene subsets and their interactions.

To select this clinical analysis, we will go to the navigation bar where Analysis is placed and select *GeneRegulationNetwork*.

Select **Analysis** \Rightarrow **GeneRegulationNetwork**

As in the previous analysis, the list of patients with all their associated samples appears. In this example we only have one patient with four samples (figure 38).

List of Patients

The screenshot shows the 'List of Patients' section. At the top, there is a patient entry: 'Patient:5cb06fd3c4aa767ad6fd2b6e' with an '+ Add Samples' button. Below this is a table with two rows: 'Name' with value 'Patient 1' and 'Code' with value '1165'. Under the 'Analysis samples' section, there is a 'Selected samples' table with columns 'Sample ID' and 'Patient Code', and a 'delete' button. Below this is a 'Services' section with a checkbox for 'Gene regulatory network'. A progress bar for '% of significantly altered gene expression levels' is shown at the bottom, with a 'Submit' button.

Figure 38: GRN Page

The first step is adding the samples of the patients' genetic expression to be analyzed. To do this, we select the Add Samples button next to each patient (figure 39).

The screenshot shows a modal window titled 'Samples' overlaid on the 'List of Patients' page. The modal displays the 'Patient code: 5cb06fd3c4aa767ad6fd2b6e'. It contains a table with columns 'Sample Name' and 'Sample Date'. There are four rows of sample data, each with an '+ Add' button and a 'View more' button. The background page shows the 'List of Patients' section with a 'delete' button and a 'Submit' button.

Figure 39: Patient Samples in GRN Page

To perform the analysis we will add the samples *Sample 1*, *Sample 2* and *Sample 3*, by clicking the **add** button. Below we can see that the selected samples have been added to Selected Samples table. We also select the *Gene Regulatory Network* service, the percentage of significantly altered gene expression levels and maximum of links of the Gene Regulatory Network (figure 40).

Patient:5cb06fd3c4aa767ad6fd2b6e [+ Add Samples](#)

Name	Patient 1
Code	1165

Analysis samples

Selected samples		Sample ID	Patient Code	✖ delete
1	5cc70ae9c4aa0d35e7ba1a40	5cb06fd3c4aa767ad6fd2b6e		
2	5cc70b0fc4aa0d35e7ba1a43	5cb06fd3c4aa767ad6fd2b6e		
3	5cc70b79c4aa0d35e7ba1a4b	5cb06fd3c4aa767ad6fd2b6e		

Remove those you are not interested.

Services

☒ Gene regulatory network

Select at least one service to be executed.

% of significantly altered gene expression levels 0.05%

maximum of links of the Gene Regulatory Network 5

[Submit](#)

Figure 40: Submit GRN analysis

Finally we press the **Submit** button. We will have to wait a few seconds to finish the analysis process (figure 41).

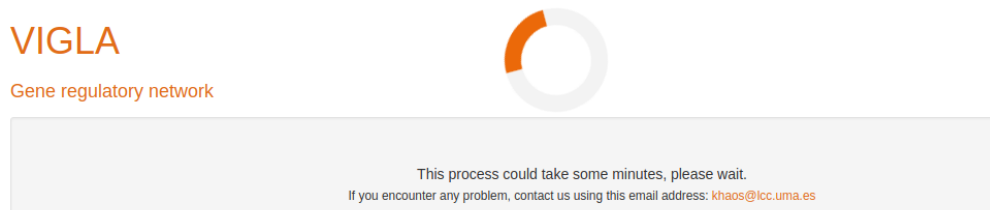


Figure 41: Loading GRN

Finally we obtain the result of the analysis, where we can observe the networks of genetic regulation and the inferences that occur in the expression of the genes.

Network (3D visualization)

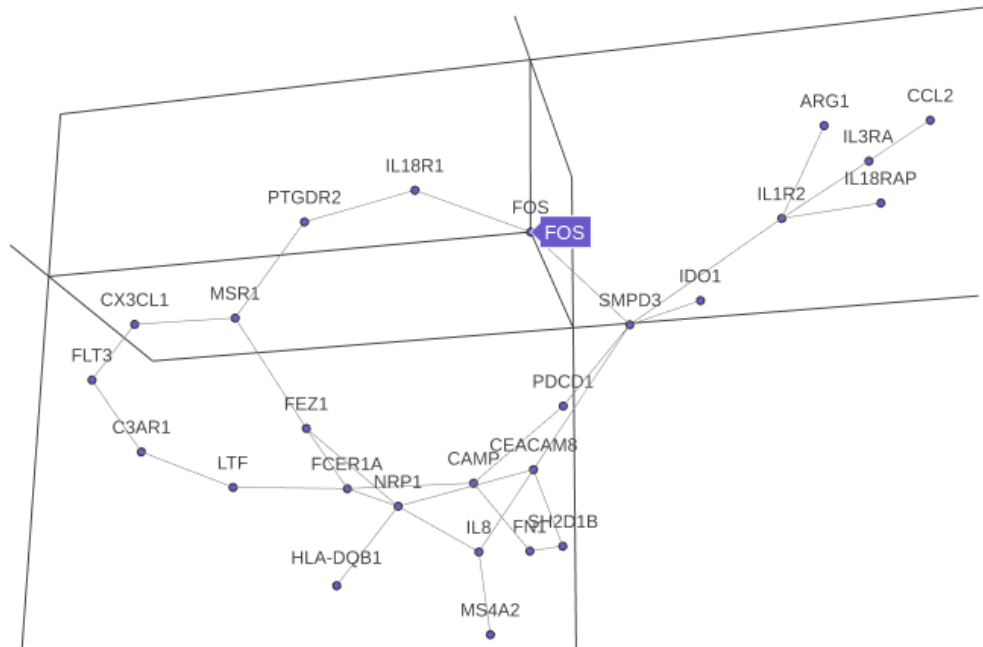


Figure 42: GRN Result