How to use SITVIT2

This is a user manual helping researchers how to navigate and analyze their data through the SITVIT2 database.

Keywords: *Mycobacterium tuberculosis*, Database, Spoligotyping, Mycobacterial Interspersed Repetitive Units-Variable Number of Tandem Repeats (MIRU-VNTRs) typing, Evolution, Phylogeny, Demographics, Statistics, Epidemiology.

Homepage

Homepage briefly introduces the SITVIT2 database which is dedicated to study genotyping markers (phylogenetical information based on Spoligotyping and MIRU-VNTRs typing) of *Mycobacterium tuberculosis* complex (MTBC) isolates. SITVIT2 also allows to get demographic (sex, age, origin of patients), clinical (drug resistance, HIV serology) information alongside with the phylogenetical data, and establish statistical correlations between the different variables. The main functionalities of the Website are shown in figures below.



Figure 1: Homepage and brief description of main functionalities.

Users can easily navigate from one webpage to another. Please note that only the two first pages (titled 'Home' and 'Description') are translatable into French or English (**Figure 1**). The language of the other pages is English, however, the user is free to use another service (such as 'Google translate') to translate pages if wanted.

Description

This section describes the main contents of the database (Figure 2).



Figure 2: Description of main contents of SITVIT2.

Utility of the different thumbnails

The database: this part gives general information about genotyping molecular markers contained in the database.

Quantitative description: a quantitative description of molecular markers used is also provided.

Publications: list of publications which are in relation to the subject.

Contributors: a list of contributors will be available upon request.

Global Distribution: Map showing the global distribution of isolates in SITVIT2 vs. SITVITWEB.

Lineages: Map showing the distribution of main lineages contained in SITVIT2.

List of countries: the list of countries represented in the database (either regarding isolation of isolates or the origin of the patients).

<u>Search</u>

This section allows users to query SITVIT2 database according to several criteria (such as Spoligotype, 12-loci MIRU, SIT, 12-MIT, Lineage, Isolation Country, Drug resistance, HIV serology, etc....) used alone or in combination each other. Note that you can use regular expression or REGEXP (<u>http://en.wikipedia.org/wiki/Regular_expression</u>) in each field except fields "Drug resistance", "Sex", and "HIV Serology" (for which you can select directly the value).

The DHTMLX columns (see website: <u>http://dhtmlx.com/</u>) can be extended, and there is a scroll bar facilitating the navigation (**Figure 3**). The total number of isolates corresponding to the query is visible at the right bottom. The results can be exported as an Excel file.

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Figure 3: Snapshot of 'Search' tool taking the example of strains isolated in France.

Brief description of main search fields

- IsoNumber (ID): code allowing the identification of each isolate contained in the database. The code is generated thanks to the following information: country of isolation, laboratory code, year of isolation, code of drug-resistance, and a code generated by our database to protect anonymity of patients.
- Spoligotype: octal code containing **15 digits** (e.g. 0000000003771).
- 12-loci MIRU: 12 digits representing the MIRUs 2-4-10-16-20-23-24-26-27-31-39- and 40.
- *15-loci MIRU*: **15 digits** representing MIRU 4, 10, 16, 26, 31, and 40, ETR-A, ETR-C, QUB-11b, QUB-26, QUB-4156, Mtub04, Mtub21, Mtub30, and Mtub39.
- 24-loci MIRU: 24 digits corresponding to classical 12-loci MIRUs followed by ETR-A, ETR-B, ETR-C, QUB-11b, QUB-26, QUB-4156, Mtub04, Mtub21, Mtub29, Mtub30, Mtub34, and Mtub39.
- 5-locus ETRs (VNTR): 5 digits representing Exact Tandem Repeats (ETRs) A, B, C, D, E.
- *SIT*: an integer representing the shared-types in the database.
- 12-MIT: an integer identifying the 12-loci MIRU shared types.
- 15-MIT: an integer identifying the 15-loci MIRU shared types.
- 24-MIT: an integer identifying the 24-loci MIRU shared types.
- *VIT*: an integer identifying the 5-locus ETRs shared types.
- Lineage: phylogenetical lineage as describe in SITVIT2 database (Beijing, LAM, T, H, etc.).

- *Isolation Country*: the country in which strains were isolated (note that Country information must be written as country name not as a code: e.g. you must write Mexico instead of MEX).
- Origin Country: the country of origin of patients. As the '*Isolation Country*' field, the country of origin must be written as country name.
- Year: year of isolation of the strain.
- *Drug resistance*: code between 0 and 4 indicating the kind of resistance (see <u>http://www.pasteur-guadeloupe.fr:8081/SITVIT2/submit.jsp</u>).
- Sex: this field corresponds to the patient's sex (either 'F' for female or 'M' for male).
- Age: this field corresponds to the patient's age (as an integer).
- *HIV Serology*: this field corresponds to the patient's HIV status (either 'Negative' or 'Positive').
- Investigator: the name of the Contributor who has submitted isolates to SITVIT2 database.

<u>Analysis</u>

This section allows you to analyze your own data, following the example file provided (freely downloadable; **Table 1**). Note that you can let a cell empty when the information is not available. Your datafile must also include the same headings as presented in **Table 1**. Make sure to prepare your analysis file as shown in the example, and do not let spaces between the characters used for molecular markers (Spoligotype43, MIRU12, MIRU15, MIRU24, and VNTR).

Table 1: Example excel	file for analysis of data
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STRAIN	SPOLIGOTYPE43	MIRU12	MIRU15	MIRU24	VNTR	YEAR	ISOLATION COUNTRY
SITVIT001	00000000003771	224115153324	231533344323223	2141251133223241B3434433	22433	2007	RUS
SITVIT002	00000000003771	224315153323	231533344323223	2141251133223241B3434433	32234	2008	RUS
SITVIT003	777777777760771	224325153423	231533344323223	2141251133223241B3434433	32432	2006	GLP
SITVIT004	777777737760771	254326223633	231533344323223	2141251133223241B3434433	22235	2009	USA
SITVIT005	777777777720771	254326223633	231533344323223	2141251133223241B3434433	21443	2010	GLP

One you have followed the instructions to design and upload your file, the results of your analysis will be displayed on the webpage (**Figure 4**). This analysis tool allows you to identify your strains and see whether they already exist in the SITVIT2 database (if this is the case, your strains will be identified by International-Types or IT). You can also export the results as an excel document.

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Figure 4: Snapshot of the 'Analysis' tool.

Online Tools

This webpage (**Figure 5**) allows users to get information on distribution/cartographies of isolates in function of several characteristics. The distributions could be visualized at various scales/levels (worldwide, UN-subregion, country, or city level).

This section contains other 'sub-thumbnails' permitting the following functionalities:

- *Globally*: provides a global visualization of isolates recorded in SITVIT2
- *Genotyping markers*: provides a set of tools allowing to visualize data related to genotyping markers (see example in Figure 6)
- Lineages: provides information and distribution of phylogenetical lineages in SITVIT2
- Drug Resistance: provides information and distribution of drug resistance data in SITVIT2
- *HIV*: provides information on HIV serology of patients isolates recorded in the database
- Sex/Age: provides information on sex or age groups of patients isolates recorded in SITVIT2
- *Evolution of Genotypes*: provides SpoligoLogos (performed with WebLogo application), as well as phylogenetical analyses representing the genotypes present in SITVIT2
- Connection with other databases: proposes a corresponding nomenclature between our database and MIRU-VNTRplus (<u>http://www.miru-vntrplus.org/MIRU/index.faces</u>), and a correlation in designating lineages in the SITVIT-KBBN tool (<u>http://tbinsight.cs.rpi.edu/run_tb_lineage.html</u>)



Figure 5: Snapshot of the 'Online Tools'.



Figure 6: Example of use of 'Genotyping markers' function.

Other Statistics

This section allows users to get an overview on the distribution/evolution of isolates over time and space in function of various characteristics such as the kind of drug resistance, the lineages, and the sex or age groups of patients (**Figure 7**).

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Figure 7: Snapshot of webpage 'Other Statistics'.

Submit Your Data

This section shows users how to do to submit their data.

<u>TB Unit</u>

This webpage briefly introduces the team working at the lab: "Unité de la Tuberculose et des Mycobactéries, Institut Pasteur de la Guadeloupe".

<u>Links</u>

This section contains various supplemental information and interesting links of softwares or web tools.