MOAHIT: A Web Tool for visualizing tumormulti-omics data with human anatomy heatmaps

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Abstract

Multi-omics data plays an important role in cancer research, helping clinicians to better explore drug targets and biomarkers. At present, there exist several databases including TCGA (the Cancer Genome Atlas) and GDSC (Genomics of Drug Sensitivity in Cancer), which contain multi omics data on multiple cancer species, as well as various web tools for analyzing the multi-omics data, which are widely used in oncology research. Tumor heterogeneity is a widespread phenomenon, reflected by differences in multi-omics data of cancers originating from different tissues and organs. However, there is a lack of convenient analysis and visualization tools to explore tumor heterogeneity. As a result, we developed a web tool called Multi-Omics Anatomy Heatmap in Tumors (MOAHIT) based on shiny programming. This tool enables users to analyze and visualize the heterogeneity of human tissues. In addition, MOAHIT enables users to produce a beautiful human anatomy heatmap to visualize the heterogeneity between distinct cancers in the multi-omics data.

Introduction

Multi-omics data includes genomic, proteomic, transcriptome, metabonomic, and epigenetic data[1]. Bioinformatics analysis based on multi-omics data can be used to explore complex biological problems, including development, cell response and disease. By linking genotypes with phenotypes, it can also be used to discover drug targets and biomarkers[2]. Multi-omics analysis is a popular approach in tumor research that can help researchers better connect the tumor phenotypes with observations of tumor tissue, supporting the identification of new tumor therapeutic targets and screen related markers[3][4].

Tumor heterogeneity is a common condition, where tumors originating from different sites can show different morphological and surface characteristics such as differing cell morphology, gene expression, cell metabolism, proliferation and metastasis[5]. This heterogeneity can be observed across different cells within a tumor, and also exists between tumors of a different tissue or organ origin. Multi-omics data is a good representation of tumor heterogeneity, reflecting differences between cancers in different tissues and organs[6]. However, there is a lack of an intuitive and convenient analysis and visualization tool for the study of tumor heterogeneity

between different tissues and organs.

With the recent extensive development of tumor multi-omics research, many public databases have been created to store the multi-omics data collected from both cancer patients and normal human tissues. Some major examples include the TCGA database (the Cancer Genome Atlas), which stores tumor samples of more than 20000 individuals representing 33 different cancer types[7], the ICGC (International Cancer Genome Consortium) database for large-scale genomic research, which coordinates 76 cancer projects in 21 primary cancer sites from more than 20000 donors[8], the CCLE (Cancer Cell Line Encyclopedia) database, which stores multi-omics data and drug sensitivity data for several cancer cell lines[9], and the GDSC database (Genomics of Drug Sensitivity in Cancer)[10]. In addition, several databases collect tumor multi-omics data, such as METRBIC (Molecular Taxonomy of Breast Cancer International Consortium)[11] and TARGET[12]. Currently, there are many kinds of online web analysis tools or databases available for tumor multi-omics data, which are widely used in cancer research. A few examples of these include UCSC Xena[13], cBioPortal[14], HPA (Human Protein Atlas) [15], Gene Expression Profiling Interactive Analysis (GEPIA) [16] and GEPIA2[17]. These web tools can be used for multi-omics data analysis and visualization based on published tumor multi-omics data, with applications such as differential gene expression analysis, gene set enrichment analysis (GSEA) and immune infiltration analysis. However, these tools are not fully suitable for the analysis or visualization of the heterogeneity of cancer multi-omics data in different tissues and organs.

As a result, we have developed a multi-organ visualization tool named Multi-Omics Anatomy Heatmap in Tumor (MOAHIT), which can be used to visualize the heterogeneity between cancers originating from different tissues or organs.

Methods

MOAHIT web tool is an online analysis web tool based on R language and Shiny programming[18]. It is completely free and does not require a login or registration. Users can visualize published multi-omics data, such as multi omics data stored from TCGA[7], GTEx[19] or GDSC[10] through MOAHIT, or they can upload their own data to the web and customize the visualization results. The User Interface (UI) of MOAHIT is built based on the DashBoard framework, with the server and interactive data constructed using R. Data tables in MOAHIT are displayed using the DT package, which enables viewing, filtering, and downloading of data. Images are generated using the renderplot function, and users can download PDF files of the visualization results. All the code and visual images are built using R software (version. 4.0). Figure 1 shows the architecture flow chart of MOAHIT.

For published oncology multi-omics data, we collect and download data from the GTEXx database [19] and TCGA Pan-Cancer data [21]. The data included gene expression data, DNA methylation data, copy number variation data, genomic data, and proteome data. All data was stored in the form R.data and stored on our own server.

The human anatomy map in MOAHIT is an original creation by our team, which provides the image basis for MOAHIT to provide exquisite human anatomy heatmap with multi omics data. Its function mainly includes three parts: Single Omics Data, Comparison Analysis, and Custom Analysis. Each part can achieve unique functions and provide users with more analysis options to better meet the requirements of analyzing and visualizing tumor heterogeneity.

Results

Welcome

MOAHIT includes a simple graphical interface to introduce the usage of each part of the function, so that users can quickly learn how to use the web tool. The Welcome interface provides version update information, as well as contact information for the development team. This makes it easier for users to understand what changes have taken place in each version and how to give feedback or suggestions to the development team (Figure 2).

Single Omics Data

In the "Basic Analysis" interface of MOAHIT, users first need to select the type of multi-omics data to be displayed and the organ, then select the target gene or protein to determine the target molecule to be studied. By clicking the analysis button, users can obtain the single-omics expression data of the target gene in the selected cancer type, as well as an anatomical heat map of different human organs. This analysis can visualize multiple types of multi-omics data from the TCGA database including gene expression, gene mutation frequency, gene copy number variation, and gene methylation and protein expression, with 16 organs corresponding to 33 cancer species available for visualization. Users can then further customize the visualization results, changing the title, color and other image parameters. Once satisfied with the result, users can then download the data corresponding to the selected content as well as the visualization results by clicking on the “Download” button (Figure 3).

Comparison Analysis

In the “Comparison Analysis” interface of MOAHIT, users first select the desired target omics type from the multi-omics data for grouping. Using gene mutation data, target genes are selected, and samples are then divided into mutation type (MT) and wild type (WT); alternatively, target molecules can be selected, with the samples then divided into high expression and low expression based on the median expression value of the molecules. Once the grouping results have been obtained, the user can select the data type and target molecule to be displayed. Finally, the user chooses the category of tissues or organs to be displayed. After clicking the “Analysis” button, human organ anatomy heatmaps of the single-omics data of the selected gene are produced based

on the grouping result (MT vs WT or high expressed vs low expressed) (Figure 4).

Custom Analysis

In this module, users can organize their own data into a table (xlsx or csv format only
) containing the specific organ name along with the expression values of the corresponding multi-omics data. Next, the user can click the "Upload" button to upload the data to the server. After previewing the data, users can then click the "Analysis" button to visualize their data. It is also possible for the user to modify the visualization details in the "Customize" column, enabling them to alter features such as color, title and anatomy outline color. Once analysis and visualization are complete, the user can download the image by clicking the "Download" button (Figure 5).

Discussion

MOAHIT is an interactive web tool that enables the integration and analysis of tumor multi-omics data and its visualization in human organs, addressing a research need to more easily analyze the heterogeneity between tumors of different origins. Via the “Basic Analysis” module of MOAHIT, researchers can easily explore and visualize the heterogeneity presented in a certain omics data from different tumor types, obtaining a beautiful interactive human anatomy heatmap. Using the “Comparison Analysis” module, samples can be divided into groups according to gene expression or mutation status. It can not only conveniently compare multi-omics expression data in different human tissues and organs in a specific group vertically but can also compare the differences in multi-omics data between two distinct groups horizontally. The “Custom Analysis” module of MOAHIT can solve the research requirement of visualizing the heterogeneity of multi-omics data in tumors originating from different tissues and organs in Pan-cancer analysis. The user image modification function also enables high interactivity with the data and diversity in produced results. As well as its applications in Pan-cancer analysis, this function can also be extended to any situation requiring the mapping of expression values onto human organs. For example, the function could be used to display the number of samples of advanced cancer metastasized to each organ, or to sample the distribution of organs or systems affected by drug-induced adverse events. These functions can enable researchers to explore the heterogeneity between tumors from different tissues and organs using public databases, as well as exploring their own data for Pan-cancer research. It should be noted that MOAHIT can also be used in other scenarios for the visualization of human organ anatomy. A key innovation of this tool, which is currently lacking in other web tools, is the ability of these functions to analyze heterogeneity between tumors from different tissues and organs.

In addition to providing functional advantages in the study of tumor heterogeneity, the human anatomy visualization provided by MOAHIT is an original development of our team, producing simple and beautiful figures. The details of the visualization results can be modified in each functional module to meet the aesthetic needs of researchers and produce figures suitable for

publication. The anatomy plot of the human body produced by MOAHIT is similar to the "interactive bodymap" of GEPIA2[17] but is more conveniently organized, provides more visual choices for organ visualization, and is highly customizable.

The current version of the MOAHIT web tool can meet the basic multi-omics data visualization requirement to produce a human organ anatomy map. However, as a newly developed web tool, there is still a lot to improve. We welcome users to contact us to provide any suggestions that enable us to improve this web tool.

Data Availability

R studio is a language and environment for statistical computing available in https://www.r-project.org/. Shiny is an open source collaborative initiative available in the GitHub repository (https://github.com/rstudio/shiny).

Acknowledgement

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Ethics approval and consent to participate

Not applicable.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict.

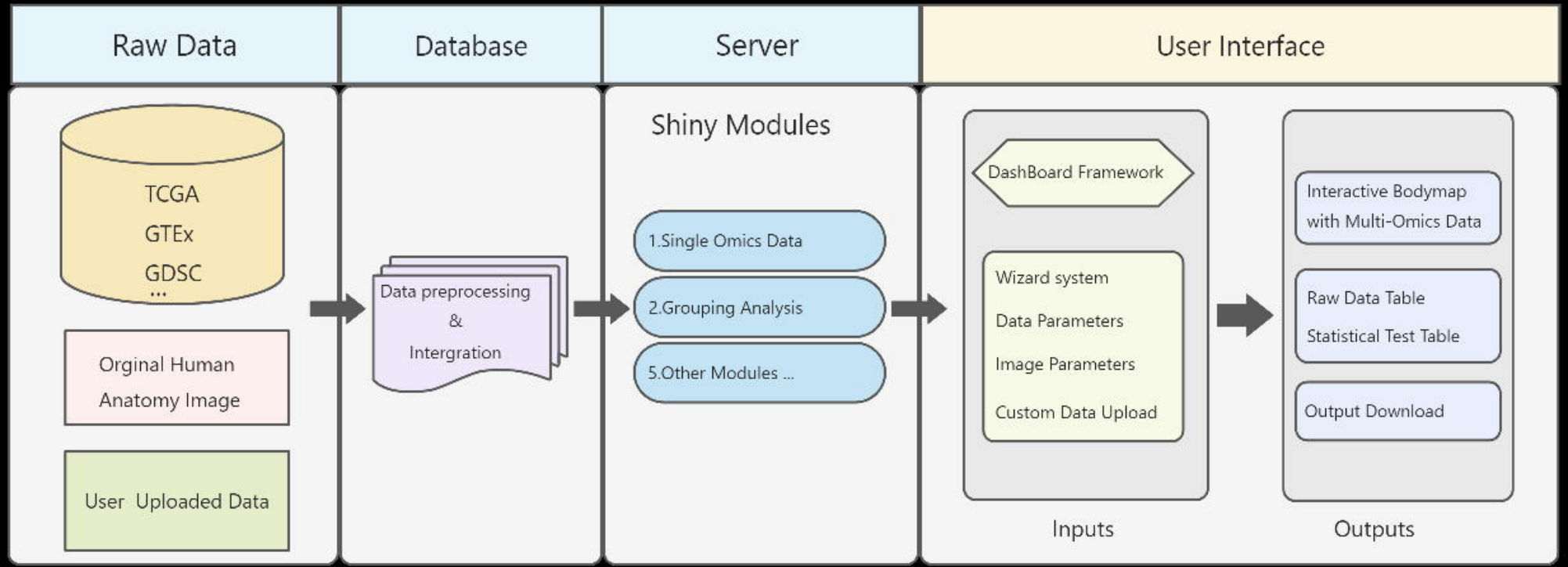
Figure Legend

- Figure 1: The framework and technical route of MOAHIT.
- Figure 2: Welcome interface with version information and contact information in the lower left corner.
- Figure 3: Functional display of the Basic Analysis module. In the example, the expression data in the data parameters box is first selected, then the cancer types to be displayed as PCPG (Pheochromocytoma and Paraganglioma) representing adrenal gland, BLAC (Bladder Urothelial Carcinoma) representing bladder, BGM (Glioblastoma Multiforme) representing brain, BRCA (Breast Invasive Carcinoma) representing breast, and KIRP (Kidney Renal Papillary Cell Carcinoma) representing kidney. Finally, the target gene TP53 is selected, and the Analysis button can be clicked to display the visualized results in the plot box, showing the expression level of the TP53 gene in the organs represented by the four cancer species.

Users can modify the visualization results in the plot parameter box. A data frame showing the selected data is visible on the top right.

- Figure 4: Functional display of Comparison Analysis module. In the example, the samples were divided into mutation group and wild group according to the mutation status of TP53 gene. The cancer types to be displayed are PCPG representing adrenal gland, BLCA representing bladder, BGM representing brain, BRCA representing breast, and KIRP representing kidney. After clicking the Analysis button, the visualized results can be seen in the plot box, showing the expression level of the BRCA1 gene in the organs represented by the four cancer species with different TP53 mutation status. The statistical test results of the differences between the two groups of data are shown in the top right side of the test table.

- Figure 5: Functional display of Custom Analysis module. Click Upload in the upper left corner to upload the custom data in CSV format. After uploading, the uploaded data can be previewed in the data table in the upper right corner. By clicking the Analysis button, the human organ anatomy heat map can be obtained, and the visualization results can then be modified through the customize box.


Raw Data
Database
Server
User Interface
TCGA
GTEx
GDSC
...
Orginal Human Anatomy Image
User Uploaded Data
Data preprocessing & Intergration
Shiny Modules
1.Single Omics Data
2.Grouping Analysis
5.Other Modules ...
DashBoard Framework
Wizard system
Data Parameters
Image Parameters
Custom Data Upload
Inputs
Interactive Bodymap with Multi-Omics Data
Raw Data Table
Statistical Test Table
Output Download
Outputs

MOAHIT Welcome Basic Analysis Comparison Analysis Custom Analysis

Welcom to MOAHIT

A Web Tool for Visualizing Tumor Multi-Omics Data with Human Anatomy Heatmap

MOAHIT

MOAHIT Version 1.0.0 | Contract Us: luopeng@smu.edu.cn

MOAHIT

Welcome | Basic Analysis | Comparison Analysis | Custom Analysis

Data Parameters

Choose data type

Gene Expression

Choose organs you want to display

PCPG, BLCA, GBM, BRCA, KIRP

Choose one gene to analysis

TP53

Plot Parameters

Show Outline

Fill based on color or value

value

Select a filling color for contour

#FFFFFF

Value colour

RdBu

Title

TP53

Parameters

Show 10 entries

Search:

	organ	system	value	color	cancer_type	Gene Symbol
17	adrenal_gland	adrenal_gland	10.56	#3DBEAB	PCPG	TP53
24	bladder	bladder	32.83	#8FACE0	BLCA	TP53
23	brain	brain	43.861	#7DB0DD	GBM	TP53
1	breast	breast	40.99	#E495A5	BRCA	TP53
16	kidney	kidney	26.835	#49BEA0	KIRP	TP53

Showing 1 to 5 of 5 entries

Previous 1 Next

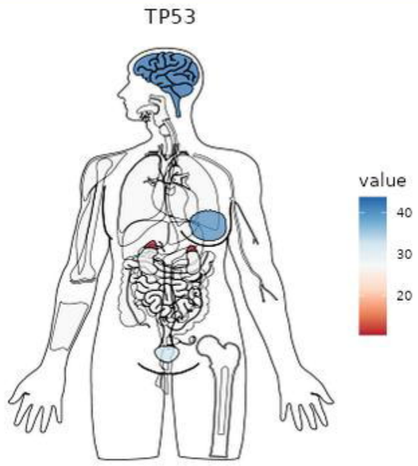
Analysis&Download

Analysis

Download Plot

Download Table

Plot



MOAHIT

Welcome | Basic Analysis | Comparison Analysis | Custom Analysis

Data Parameters

Choose type for analysis

Gene Mutation

Choose data for display

Gene Expression

Choose organs you want to display

PCPG, BLCA, GBM, BRCA

Choose one gene to analysis

TP53

Choose one gene to display

BRCA1

Plot Parameters

Show Outline

Fill based on color or value

value

Select a filling color for contour

#FFFFFF

Value colour

RdBu

Title

Enter the title of the plot

Parameters

Data Table | Test Table

Show 10 entries

Search:

	organ	system	color	gene_show	gene_group	value	group	Cancer Type
17	adrenal_gland	adrenal_gland	#3DBEAB	BRCA1	TP53	2.61	mutate	PCPG
24	bladder	bladder	#8FACE0	BRCA1	TP53	8.02	mutate	BLCA
23	brain	brain	#7DB0DD	BRCA1	TP53	7.72	mutate	GBM
1	breast	breast	#E495A5	BRCA1	TP53	5.65	mutate	BRCA
171	adrenal_gland	adrenal_gland	#3DBEAB	BRCA1	TP53	1.43	wild	PCPG
241	bladder	bladder	#8FACE0	BRCA1	TP53	5.995	wild	BLCA
231	brain	brain	#7DB0DD	BRCA1	TP53	6.825	wild	GBM
11	breast	breast	#E495A5	BRCA1	TP53	5.605	wild	BRCA

Showing 1 to 8 of 8 entries

Previous 1 Next

Analysis&Download

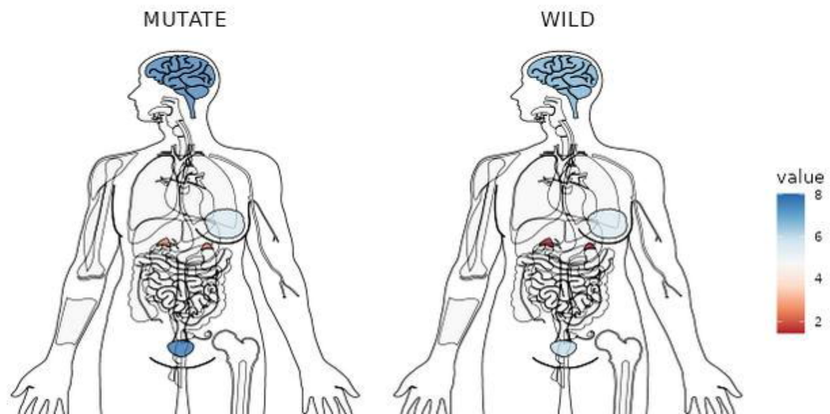
Analysis

Download Plot

Download Data Table

Download Test Table

Plot



MOAHIT

Welcome | Basic Analysis | Comparison Analysis | Custom Analysis

Upload Data

Upload... data_key.csv

Upload complete

Costomize

Show Outline

Fill based on color or value

value

Select a filling color for contour

#FFFFFF

Value colour

RdBu

Title

Enter the title of the plot

Data Table

Example Data | Custom Data

Show 10 entries

Search:

	organ	system	value	color
1	breast	breast	12	#E495A5
2	prostate	prostate	0.1	#E29899
3	ovary	ovary	17.2	#DE9A8E
4	large_intestine	large_intestine	20.9	#D99E82
5	uterus	uterus	1.4	#D3A178
6	cervix	cervix	2.7	#CBA56F
7	small_intestine	small_intestine	0.3	#C3A869
8	heart	heart	0	#B9AC65
9	trachea	trachea	0.4	#AEB064
10	lymph_nodes	lymph_nodes	0	#A2B367

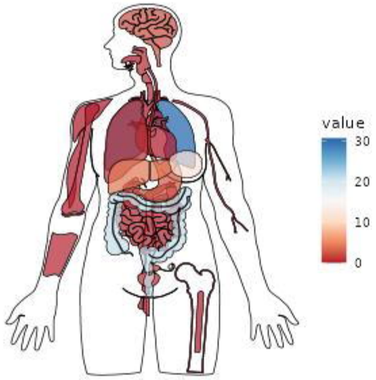
Showing 1 to 10 of 32 entries

Previous 1 2 3 4 Next

Analysis&Download

Analysis

Download Plot

Download Table

Plot