

Interactive visualization with MetaRelSubNetVis

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03/30/2022

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1 MetaRelSubNetVis

MetaRelSubNetVis allows the comparison the integrated networks of patients within patient groups with respect to the individuals' contained biological data. The previously created and to the NDEx uploaded network contains all the necessary information and description of the data attribute. It is available on NDEx as "Combined patient-specific breast cancer subnetworks" at <https://www.ndexbio.org/viewer/networks/a420aaee-4be9-11ec-b3be-0ac135e8bacf>

The MetaRelSubNetVis website is available at <https://frankkramer-lab.github.io/MetaRelSubNetVis/>:

The screenshot shows the homepage of the MetaRelSubNetVis website. At the top, there is a navigation bar with links for "About", "NDEx", and "Getting started". Below this is a section titled "Find a network on NDEx" with a search bar. A list of networks is displayed, with the first item being highlighted: ★ [OFFICIAL DEMO] Combined patient-specific breast cancer subnetworks. This item has a detailed description box below it, mentioning it's a protein-protein interaction (PPI) network from the Human Protein Reference Database (HPRD) used for training and generating subnetworks. It includes statistics like mean, standard deviation, 25%, 50%, and 75% quartile of gene expression for each gene, and relevance scores from GCNN and GLRP. Buttons at the bottom of this box allow users to "Open the app with this network" or "Open this network on NDEx".

FAQ

With MetaRelSubNetVis we provide a visualization tool that allows users to inspect differences between two groups of patients by directly loading the network from the NDEx platform. Our previous network is already available as sample network on the website, but NDEx platform can be queried for any other publicly available networks. Additionally, the network not only has to be set to be public, but explicitly marked as searchable to be found by the search.

2 Network data requirements

To make sure, your network is compatible as input for this class comparison, it has to fulfill the specific properties.

The network needs to conform to the [CX data model](#) (which should already the case if it passed validation on the NDEx platform) and contain the aspects `nodes`, `edges`, `nodeAttributes`, and `networkAttributes`.

2.1 Nodes

Each node has to have an id (property `@id`) and a name (property `n`).

2.2 Edges

Each edge has to have an id (property `@id`), a source (property `s`) and a target (property `t`).

2.3 NodeAttributes

Each node can have multiple attributes. A node attribute's relation to a node is indicated by the node attribute's property `po`. The name of the node attribute (property `n`) always starts with a patient identifier, followed by `_`. After that the attribute is described. The following are required for each patient:

- `Score`: Relevance score, a numeric value
- `GE`: Gene expression, a numeric value
- `GE_Level`: Gene expression level, one of the following values: (`LOW`, `HIGH`, `NORMAL`)

Optional attributes are:

- `MTB`: a boolean value

2.4 NetworkAttributes

NetworkAttributes are used to describe the patient samples. Please note: The order within each of these attributes is crucial.

- `Patients`: String list of patient identifiers
- `PatientSubtype`: String list of each patient's cancer subtype
- `PatientSurvivalYears`: Double list of each patient's metastasis free survival
- `PatientGroups`: String list of each patient's group (in sum there can only be two different types of groups!)

Furthermore the property name contains the network's name (property `name`) that will be used as a headline for this application.

3 Interactive exploration

Clicking the “Open the app with this network” for the “Combined patient-specific breast cancer subnetworks” will open it in for exploration:

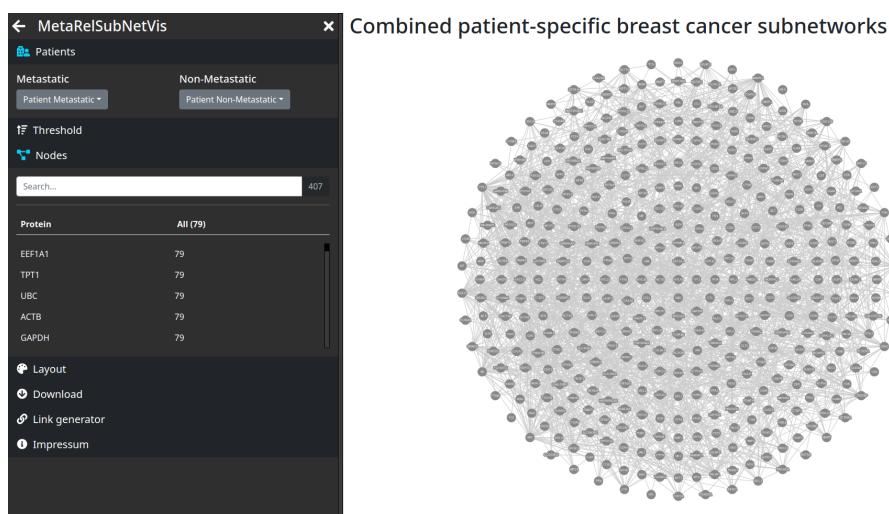


Figure 1: “Combined patient-specific breast cancer subnetworks” network loaded in MetaRelSubNetVis (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&col=0&size=1&all=false&shared=false&mtb=true&sb=0&cP=1&cT=1&cN=1&cL=1&cD=1&cG=1&cIm=1>)

Interactive visualization with MetaRelSubNetVis

By default all nodes are displayed in a concentric layout. The graph is interactive, meaning the nodes are draggable and preserve their position, even when the patient selection or visualization parameters change. The graph can also be zoomed in and moved to adjust the investigation of the content as wanted.

A specific patient can be investigated by selecting one from the metastatic or non-metastatic patients in the patients tab. For the single available patients their cancer subtype is displayed along their identifier. Selecting for example the patient GSM615368 with Basal cancer subtype from the metastatic group displays only the relevant genes to this subnetwork.

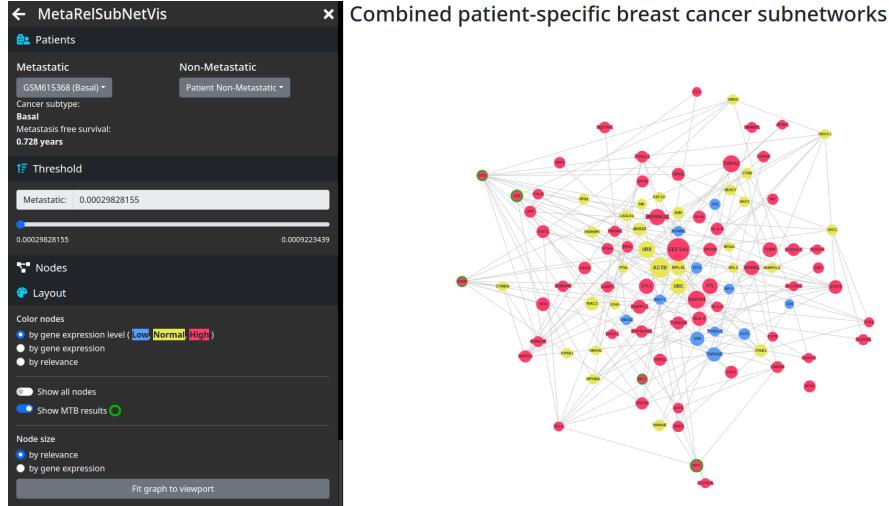


Figure 2: Visualization of patient GSM615368 colored by gene expression level and sized by relevance score (<https://frankkramer-lab.github.io/MetaRelSubNetVis/?uid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pa=GSM615368&th=0.00029828155&col=0&size=1&all=false&shared=false&mtb=true&sb=0&cP=0&cT=0&cN=1&cL=0&cD=1&cG=1&cIm=1>)

By default the subnetwork is colored by its gene expression level, and sized by the relevance score. The results of the molecular tumor board analysis are marked by a green border around the corresponding nodes. The coloring and sizing of the nodes can easily be adjusted, for example by changing it to gene expression and relevance score respectively. The displayed nodes can be filtered to lie above a certain threshold.

Interactive visualization with MetaRelSubNetVis

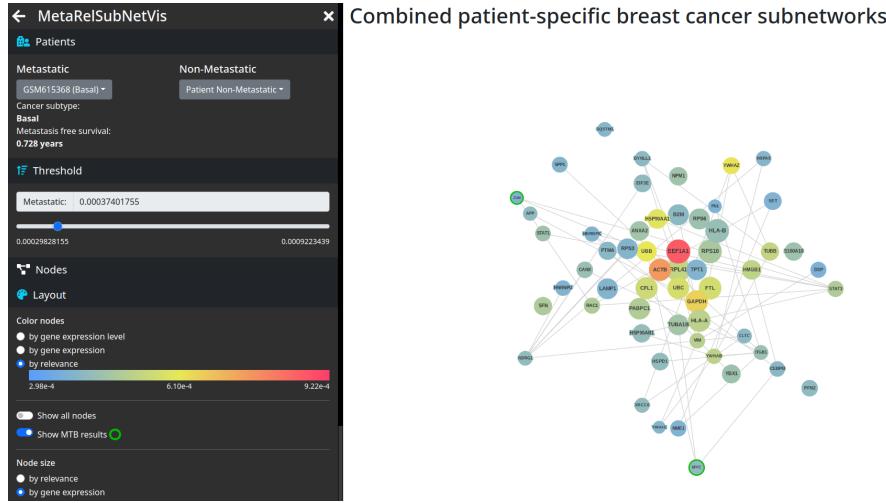


Figure 3: Visualization of patient GSM615368 colored by relevance score and sized by gene expression, and adjusted threshold (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pa=GSM615368&th=0.00037401755&col=2&size=0&all=false&shared=false&mtb=true&sb=0&cP=0&cT=0&cN=1&cL=0&cD=1&cG=1&clm=1>)

The coloring follows a gradient consistent over the relevance scores of all patients. It is also notable, that lower values of the relevance score for genes does not necessarily imply the lack of relevance: the selected genes still represent the top 140 relevant genes.

To display the subnetwork in the context of all genes combined by all patients, it is possible to include those genes within the visualization. Since not being relevant to this subnetwork, they are displayed in gray. The adjustment of the threshold (although here reset to include all relevant genes) then still includes otherwise no longer applicable nodes as default gray nodes.

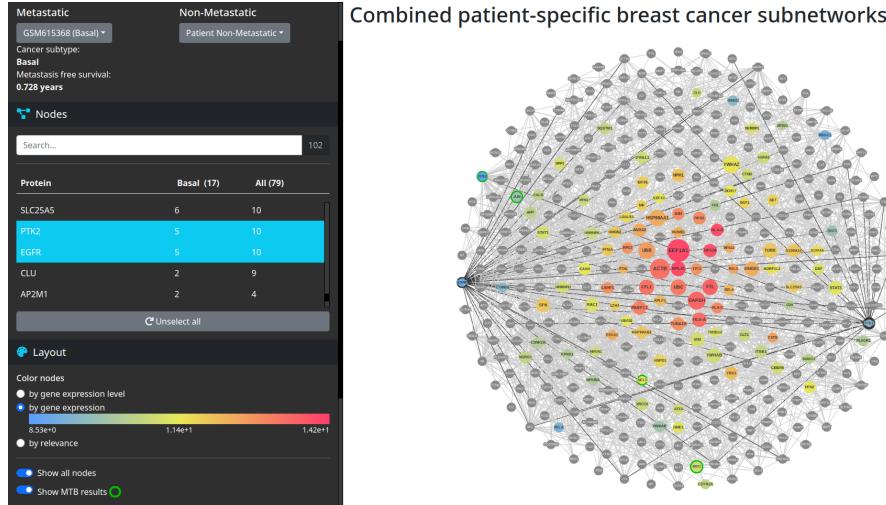


Figure 4: Visualization of patient GSM615368 colored by gene expression and sized by relevance score including genes present in remaining subnetworks (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pa=GSM615368&th=0.00029828155&sel=3406,1106&col=1&size=1&all=true&shared=false&mtb=true&sb=0&cP=0&cT=1&cN=0&cL=0&cD=1&cG=1&clm=1>)

Additionally the available nodes can be searched and highlighted within the graph. All the adjacent edges are highlighted as well to put focus on the interaction with the remaining nodes.

Interactive visualization with MetaRelSubNetVis

Selecting an additional patient from the non-metastatic group, e.g. GSM615184, as well from the Basal cancer subtype, the relevance scores (or other data if selected) are displayed for both patients in the corresponding half of the node (left for metastatic, right for non-metastatic). Gene only present in the patient of one group are colored gray for the other group. The size of the nodes is set to small for nodes only present in one group and double the size when present in both groups to make it easily distinguishable.

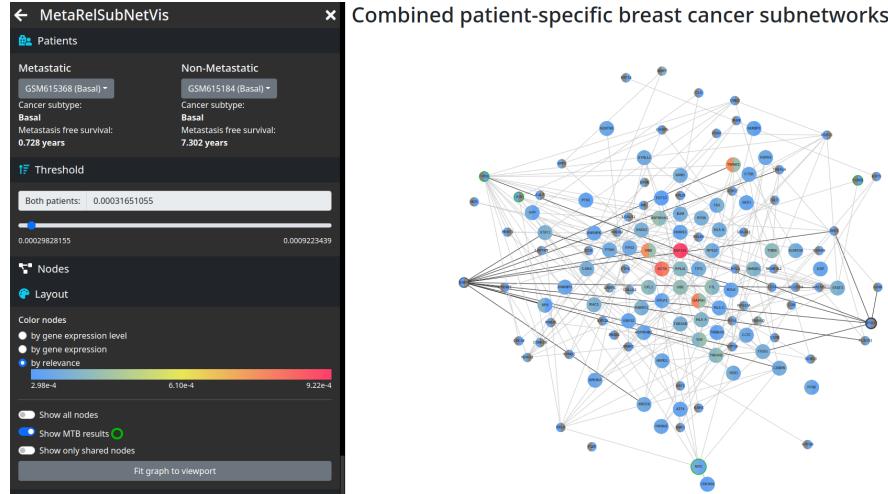


Figure 5: Comparative visualization of patient GSM615368 and GSM615184 colored by relevance score (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pa=GSM615368&pb=GSM615184&th=0.00031651055&sel=3406,1106&col=2&size=1&all=false&shared=false&mtb=true&sb=0&cP=0&cT=0&cN=1&cL=0&cD=1&cG=1&cIm=1>)

However, it is also possible to only display the nodes shared between both patients.

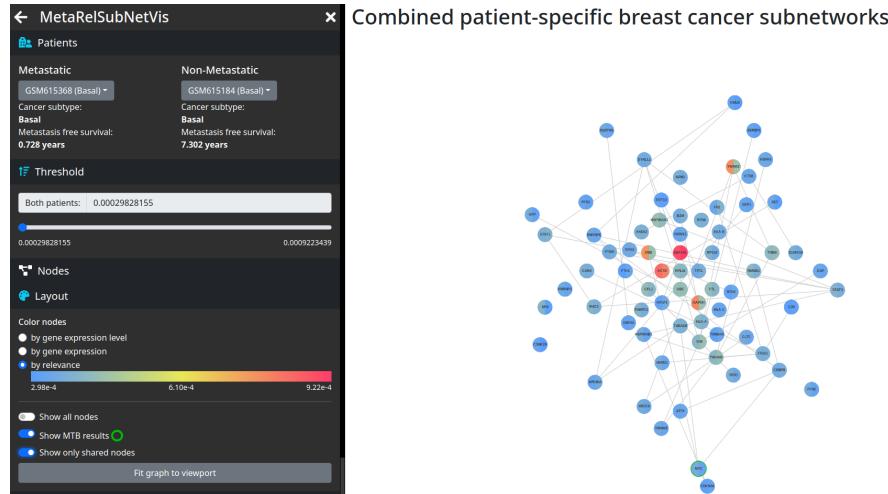


Figure 6: Comparative visualization of common genes between patient GSM615368 and GSM615184 colored by relevance score (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pa=GSM615368&pb=GSM615184&th=0.00031651055&sel=3406,1106&col=2&size=1&all=false&shared=true&mtb=true&sb=0&cP=0&cT=0&cN=1&cL=0&cD=1&cG=1&cIm=1>)

Disselecting the patient from the metastatic group leaves only the remaining patient visualized, here with marked genes MYC and CCND1.

Interactive visualization with MetaRelSubNetVis

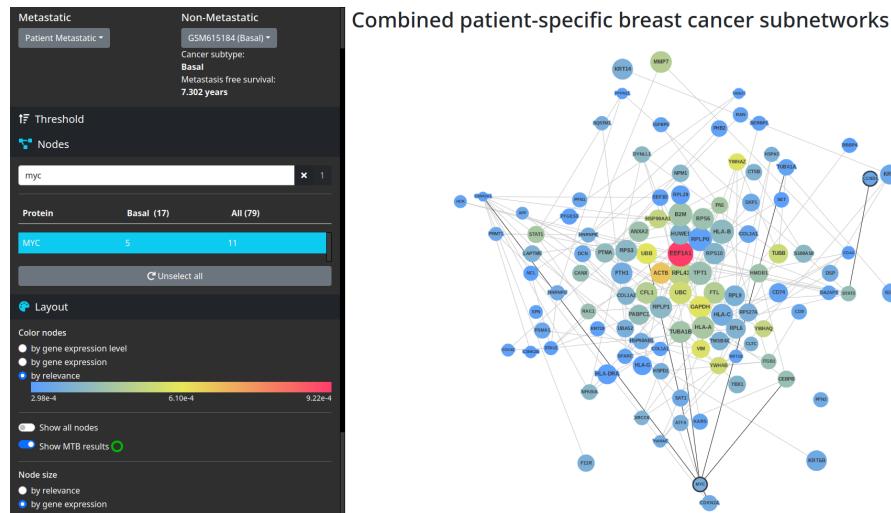


Figure 7: Visualization of patient GSM615184 colored by relevance score and sized by gene expression (<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pb=GSM615184&th=0.00030449335&sel=1016,1251&col=2&size=1&all=false&shared=true&mtb=true&sb=0&cP=0&cT=1&cN=0&cL=0&cD=1&cG=1&clm=1>)

The visualizations generated by setting the various parameters can easily be exported as images in different formats for further use or publication.

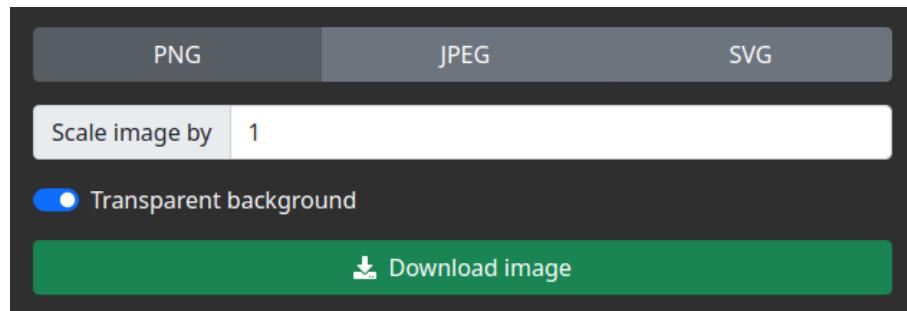


Figure 8: Image export options

The exported image in PNG format with transparent background from the current visualized network then can be included everywhere, even here:

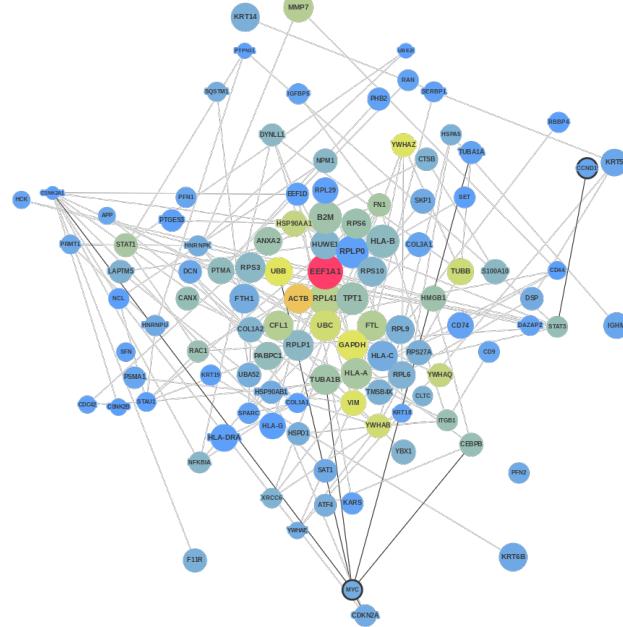


Figure 9: Shareable visualization of interactive patient comparison on MetaRelSubNetVis (<https://frankkramer-lab.github.io/MetaRelSubNetVis/?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pb=GSM615184&th=0.00030449335&sel=1016,1251&col=2&size=1&all=false&shared=true&mtb=true&dwn=true&img=PNG,1,true&sb=0&cP=0&cT=1&cN=0&cL=0&cD=1&cG=1&cIm=1>)

4 Sharing the network by visualization link

The results of the data integration with networks, and its visualization are useful information to collaborators. However, sharing the data needs the receiver to be able to handle the tools for exploration and visualization. Sharing the visualization only as images omits much of the otherwise included information.

MetaRelSubNetVis combines both to an advanced, but simple to use web-based visualization and exploration tool. One can generate links for sharing a specific subnetwork including the settings from current visualization.

Furthermore it is possible to set the options for automatic image download or display of the sidebar and its components.

Interactive visualization with MetaRelSubNetVis

Link generator	
Current settings	
Variable	Value
UUID	a420aaee-4be9-11ec-b3be-0ac135e8bacf
Patient Metastatic	
Patient Non-Metastatic	GSM615184
Threshold	0.00030449335
Selected nodes (2 selected)	<ul style="list-style-type: none">• MYC• CCND1
Node's color	Relevance
Node's size	Gene expression
Show all nodes	no
Show only shared nodes	yes
Show MTB results	yes

Figure 10: Exported PNG image of patient GSM615184 colored by relevance score and sized by gene expression with transparent background

The current visualization is summarized to comprehend and review the current settings.

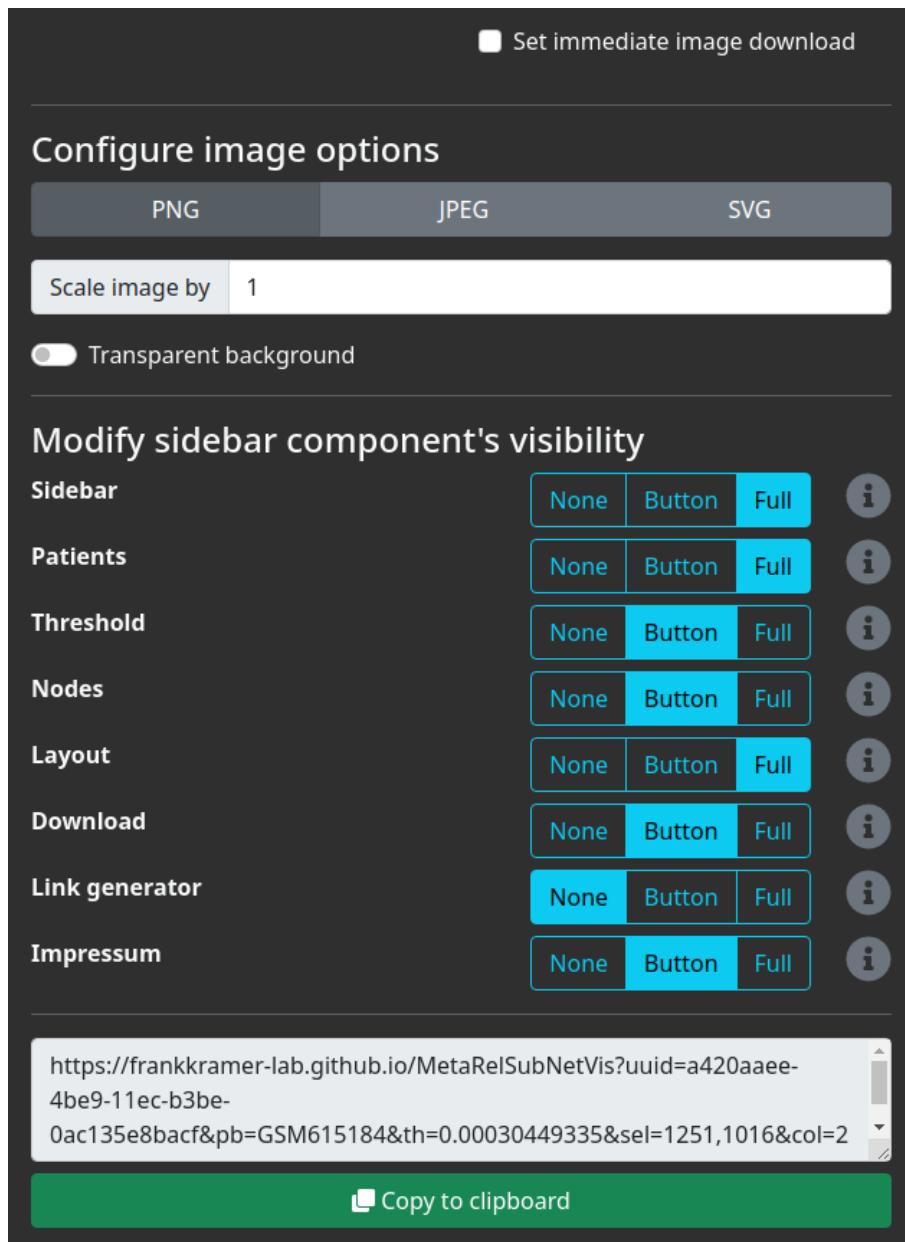


Figure 11: Set options for image download or display of the sidebar and its components

The remaining options can force the rendering of the network visualization and trigger an download dialogue, or determine the behaviour of the exploration panel. It is possible to set different options for the sidebar and the components: - *None*: hides the element completely - *Button* displays the element collapsed - *Full* displays the element in expanded form.

The here used options show the sidebar, patients and layout tab expanded, hides the link generator tab, and displays the remaining elements collapsed.

The link to share the current network with the set options and current visualization is as follows:

Interactive visualization with MetaRelSubNetVis

<https://frankkramer-lab.github.io/MetaRelSubNetVis?uuid=a420aaee-4be9-11ec-b3be-0ac135e8bacf&pb=GSM615184&th=0.00030449335&sel=1251,1016&col=2&size=0&all=false&shared=true&mtb=true&sb=0&cP=0&cT=1&cN=1&cL=0&cD=1&cG=2&clm=1>

This link starts the MetaRelSubNetVis app to display the network, and the selected patient the same way as when the link was generated. The link then can be used to share custom visualization with collaborators to point out certain specifics to discuss. Furthermore, it can be provided along the image used within a publication to enable the reader additional investigation and exploration of the studied network integration.

With this link, also an interactive visualization of the network can be embedded on a distinct website:

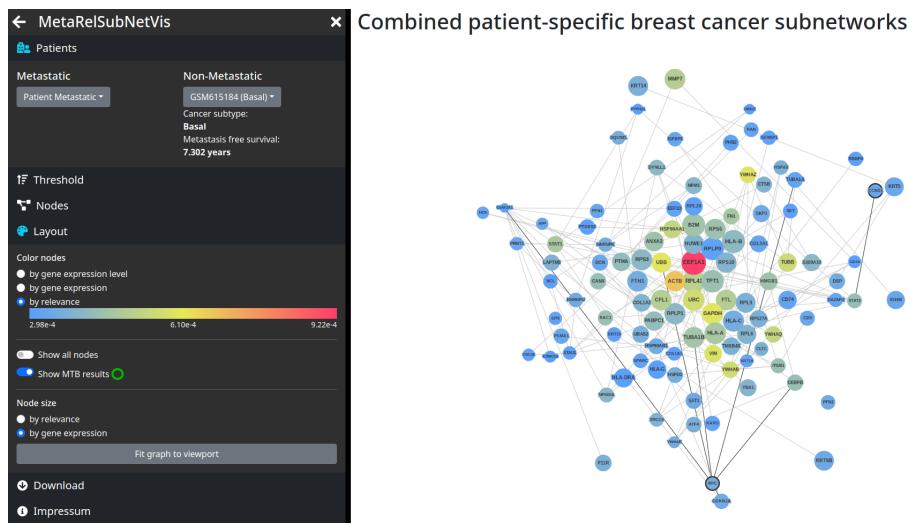


Figure 12: Shareable visualization of interactive patient comparison on MetaRelSubNetVis