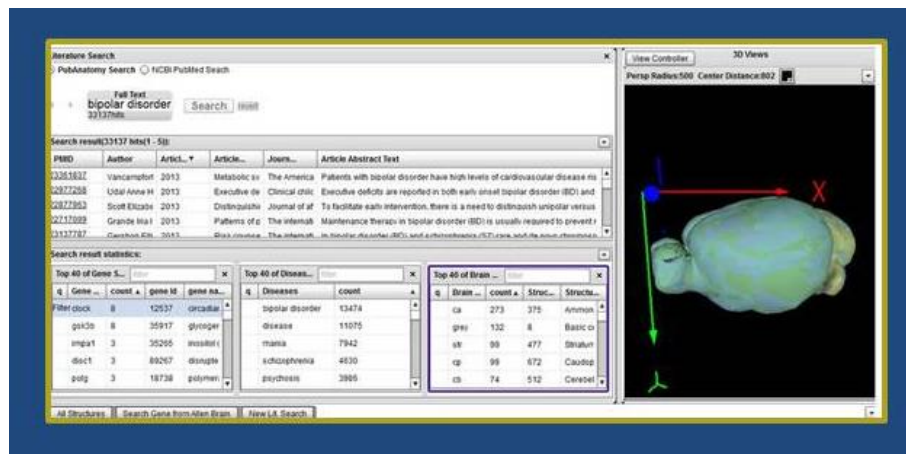


# PubAnatomy 3D User Guide



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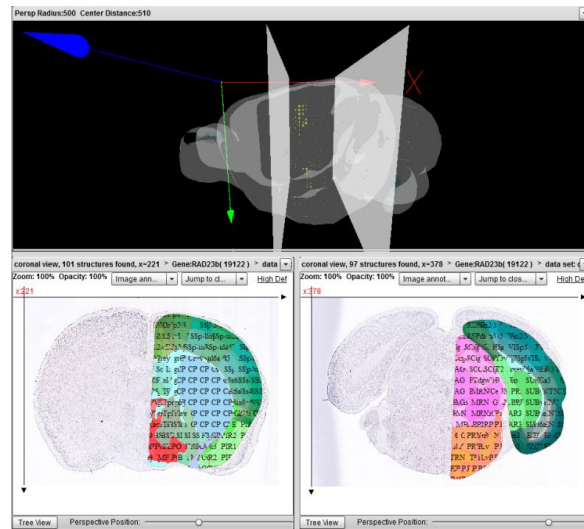
Quick guide to each panel display and its operations

- Search Screen
- Retrieved Results Screen
- 3D Display and View Controller Screens
- 3D Display with Selected Structures and Transparency
- Putting a Plane in a Select Area through the 3D Display
- 2D Plates Resulting from Putting a Plane through the 3D view

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## Overview

PubAnatomy 3D is a Flash-based web application. It uniquely integrates MEDLINE searching with gene expression data and images from Allen Brain Atlas with a 3D brain model. Pubanatomy3D can help researchers efficiently explore and evaluate hypotheses about genes' role in various neurobiological processes.



System requirements include:

- Mainstream browsers such as IE, Chrome, Firefox on Win/Mac
- Most current Adobe Flash Player
- 4+ GB memory is recommended
- Full HD ( 1920 by 1080 ) and full screen is recommended

For Help email: [brainarray@umich.edu](mailto:brainarray@umich.edu)

User Group: <https://groups.google.com/forum/?fromgroups=#!forum/pubanatomy3d>

## About data sources

PubAnatomy3D provides access to data from MEDLINE and the data and images from Allen Brain Atlas. With PubAnatomy3D you can search MEDLINE and get relevant articles and summarized tables of genes, diseases and brain structures mentioned in the articles. You can then filter to only articles referring to genes, diseases or brain structures in which you are interested. It automatically maps mouse genes to human homologues. PubAnatomy 3D also integrates additional annotations from the Unified Medical Language System (UMLS) and offers its own unique, highly interactive 3D model of the brain.

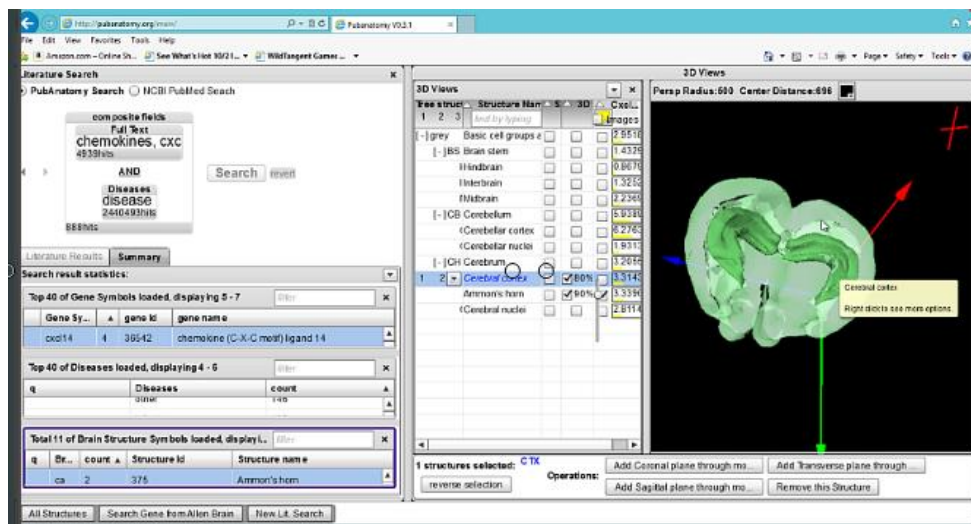
## Why use PubAnatomy 3D?

With PubAnatomy you can you can situate gene expression in specific structures and infer roles genes may play in diseases. PubAnatomy 3D helps you address questions such as the following:

- What unexpected genes are expressed in a brain structure of interest that are relevant to a disease of interest?
- Do gene expression patterns suggest unknown nuclei in particular structures?
- Are the expressions of a receptor and ligand of the receptor local or distal in a targeted brain structure?
- What genes are co-expressed in a structure of interest and how densely?
- What literature pertains to a disease and genes of interest in a specific brain structure?

PubAnatomy 3D lets neurobiologists explore gene expression in a literature-centric way. With it, neurobiologists work from the premise that literature supports their inquiries into expression in particular regions related to particular diseases.

PubAnatomy 3D integrates richly annotated results from literature searches with an ability to explore genes contained in search results in both the 3D and 2D visualizations of the brain. Exploratory insights can then be used to further query the MEDLINE database.



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## Workflow overview

<b>Search</b>	Search the literature for research and find genes, brain structures, and diseases to which results refer. You can enter simple or compound searches and nested searches ( AND, OR and NOT).
<b>Investigate gene expression in the brain in 3D and 2D</b>	<p>From the search results, quickly drag and drop 1-3 genes and/or any number of brain structures of interest into the 3D brain view. Select the all brain structures and gene expression in any of them that you want to analyze, using the 3D View Controller. PubAnatomy 3D then shows your selection.</p> <p>You can zoom in, view the 3D area with a coronal, sagittal or transverse plate cut through it, and change the transparency of various brain structures for better visibility. You can also hide brain structures and quickly bring back any structures that you want for surrounding context.</p>
<b>See expressions of 2-3 genes</b>	When you bring in two or three genes you can relate their respective expressions within and across brain structures.
<b>Examine corresponding 2D slides for detail</b>	When you put a plane through a structure or expression point in the 3D view, you see the closest corresponding 2D Nissl slide. The expression of your gene of interest is displayed in it. You can move sequentially through the slides. This movement is updated in the 3D view, as well. As you go through the series of slides, the annotations for brain structures included in the slides change accordingly.
<b>Refine search</b>	From 2D plates, run a NeuroBlast on selected datasets and structures. Drag and drop the genes that resulting it into your earlier literature search. Or use insights from the analysis to change or filter that search. Click the PMID to go directly to PubMed.

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## GETTING STARTED WITH PUBANATOMY 3D

### Open PubAnatomy 3D

1. Go to [pubanatomy3d.org](http://pubanatomy3d.org). The front page appears.



2. Click the icon. An empty Search box and 3D view of the mouse brain appear.

### Tips for accessing common functions and features

The user interface offers the following general interactions (alphabetically listed):

- **Add Search terms to a Query.** Open a new search box for each term or drag and drop items from the Results to the query area. By default the program connects terms with AND. Add any gene or brain structure directly from the 3D view. Right click it and select “Add structure to main search.”
- **Control the transparency of one item.** To make any one structure more or less transparent, mouse over the “100” or other number that appears next to a structure name in the 3D column. A slider appears, which is an opacity slider. Move it up or down to make it more or less transparent.
- **Control the transparency of 2+ items.** When 2 or more items are selected (highlighted in blue), click the Adjust Opacity button to get a slide that will control the transparency of all items at once.
- **Display Brain Structures into the 3D View.** PubAnatomy contains 828 brain structures and maps expression data to them. All the structures are not read into and displayed in the 3D display by default. Only some select, high level structures are displayed by default. You can bring whatever structures you want into the 3D view in one of four ways:
  - Drag and drop structures in Search Results to the 3D view.
  - Interact with the hierarchical tree view of all 828 brain structures in the panel named All Structures. Open the tree view of all brain structures by clicking All Structures (button at the bottom of the screen). Find structure(s) of interest. Drag and drop them into the 3D view or the View Controller.
  - Click the arrow next to a high level structure in the View Controller that is the

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“parent “ of your structure of interest. From the pull down list of functions, select “Load all Children” or “Load Children one level down.” The lower level structures will be read in. You need to select them to display them.

- **Drag and Drop.** Move items efficiently from one panel of the program to another by dragging and dropping them. A green circle with + in the middle shows that the item can be dropped at the intended spot. A red circle with X indicates that it cannot.
- **Get a drop down list:** Arrows appear on the screen, and some appear when you mouse over a row of data . Click the arrow to get a drop down list of additional operations to perform.



- **Get a drop down list:** In the 3D view, right click on a structural area of the brain to get drop down list of additional operations to perform. You can perform a number of actions either for the exact position on which you click or for the structure more generally.
- **Reorder column headings.** Drag and drop column headings to rearrange their order.
- **Rotate.** Rotate the 3D view with your mouse, pressing the left mouse down.
- **Search.** Search in the View Controller, Tree Structure panels, and/or 2D slice structure column to quickly find brain structures, Type the structure term into the search box at the top of the table. Retrieved items are indicated in red (e.g. “3 found” written in red). Click on the red text and the tree will open to show the results.
- **Select items.** Click on a row of a table to select the item in it. Keyboard shortcuts work for (1) Selecting 2+ adjacent items (Shift + Mouse click; (2) Selecting non-adjacent items (Ctrl + Mouse click); and (3) Selecting all (Ctrl+ A)
- **Selected items - confirm.** In the 3D View Controller, selected rows are highlighted in blue. Y and N in the boxes next to structure and gene names indicate whether or not the structure and/or gene are displayed in the 3D view. They do not indicate “selection.”
- **Sort columns.** In any table other than the Literature search results, PubAnatomy 3D only sorts by a column when it is in the far left position of a table. Drag and drop any column by which you want to sort (e.g. gene expression) to the farthest-most left position of the table. The green X appears. Then press the white arrow (black arrow in Literature search tables).
- **Take actions on Selections.** Buttons on the bottom of the screen specify allowable actions.
- **Zoom.** Click Center Distance in the title bar of the 3D view. A slider appears. Move it up or down to zoom in and out in the 3D view. You can also zoom in and out with a mouse wheel.



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## SEARCHING THE RESEARCH LITERATURE

1. Enter terms in the Search box on the Search and Results panel.

“Full Medline record” (the default field) is the broadest category. It searches the whole MEDLINE record. It does not do a search on the full text available in PubMed Central articles.

✘ **NOTE:** If you do not want to search Full record but prefer a narrower category, click the arrow on the title bar of the search box. Select “Change term to...” and select a field.

An auto-completion drop down provides choices as you type. Choices show the number of article associated with specific terms. Select the term closest to your intentions.

Add as many terms as you want by following these steps:

- a. Click the arrow on the field name title of the search box. Select “Add a new term” from the drop down list.
- b. Select the field name of the term you want to enter. A new search box appears, automatically jointed to the prior term with AND.
- c. Fill in the term on which you want to search.
- d. If you want to change AND to another Boolean operator, click it. Change it to OR or NOT.

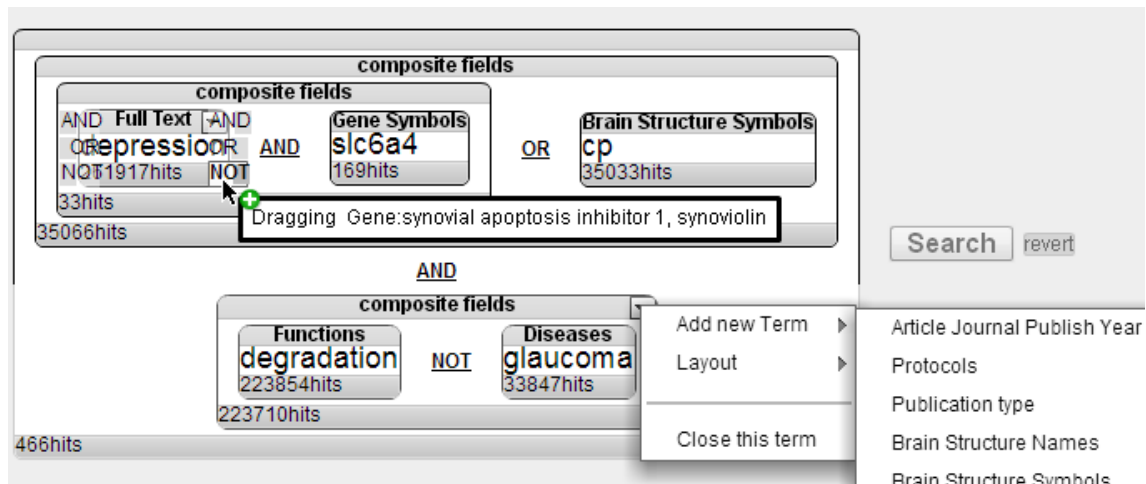
✘ **NOTE:** You *must* enter a term in a newly opened search box *before* changing the Boolean operator or before attempting to close a previous search box. Otherwise the box will close.

✘ **NOTE:** To close a previously entered search box, click the arrow at the top of the field name title. In the drop down list, select Close This term. You cannot close a search box if only one search box is displayed. In this case, change the search by typing a new term over the prior term.

Therefore, if you search on a term – e.g. depression - in the default Full Record search and decide that you want to only search on a gene in a Gene Symbol search box you must take the following steps:

- After typing in depression, open a new search box for Gene Symbol with the steps above.
- Enter the symbol of the gene

- Click the Full Record title bar arrow and select Close the term. Only the filled in Gene Symbol search box remains.
2. In the bottom of each search box, Pubanatomy 3D shows you how many hits each term and the search statement of combined terms produce.
  3. Construct a search statement with as many terms as needed.



**NOTE:** Pay attention to the counts of hits indicated in each search box and in the overall search box. It will let you know if your query produces hits before pressing Search. In the figure above this search statement produces 466 hits.

4. Submit your search by clicking Search. Alternatively, click twice after entering the term.

## INTERACTING WITH SEARCH RESULTS

### What the Results view shows

Retrieved articles and annotations of them appear from your search.

The screenshot shows the PubAnatomy search results interface. The search term is "depression", resulting in 263,415 hits. The main table displays search results with columns for PMID, Author, Article title, Journal title, and Article Abstract. Callouts provide instructions: "Number of hits for this term" points to the hit count; "Hover over to see the whole abstract" points to the abstract column; "Click a PMID to access the article in PubMed." points to a PMID; "View and sort by the count of retrieved articles referring to each term." points to the "count" column in the "Top 40 of Diseases" table; and "Search a tab. Type in your term." points to the search input in the "Top 40 of Brain" table. A 3D brain model is visible on the right side of the interface.

**NOTE:** You may get a display that is not spread out like the screen shot above. It may have 2 tabs, one named Literature and the other named Summary or it may have the Gene, Disease and Structure tabs positioned vertically (instead of horizontally as above). To get a more spread out view, make more space by pulling the panel border to the right.

### Change displays

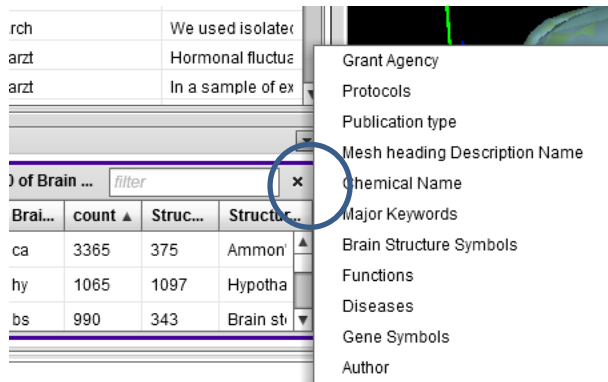
Add new fields to the table displaying the articles.

1. Click the arrow at the end of the title bar of the Literature Results tab. A list appears.
2. Select the field you want to add. It appears in the table.

The screenshot shows the dropdown menu for adding fields to the search results table. The menu lists various fields such as Author affiliations, Grant Agency, Article inclusive pages, Major Keywords, and others. A red circle highlights the "Major Mesh heading Description Name" field, which is being added to the table. The table below shows the updated columns: q, Brai..., count, Struc..., and Structur... with corresponding data rows.

## Add new tabs of annotations

1. Click the arrow at the end of the Results Statistics title bar. A list appears.  
PubAnatomy 3D maps annotations from established sources to articles. Sources include MEDLINE records (e.g. MeSH and Keywords), Gene Ontology, Allen Brain Atlas, and UMLS.
2. Select the field for which you want a tab. It appears in the display.



## Manage the display space: Close and resize tabs; resize and sort columns

1. Move the borders between the tabs to resize them.
2. Close a tab by clicking the X in its title bar. It is removed. To restore it, click the arrow at the end of the Results statistics title bar. On the drop down list, choose it to display it again.
3. Widen or narrow columns by adjusting their borders, as with the tabs in Step 1.
4. Sort a column by clicking the column name.



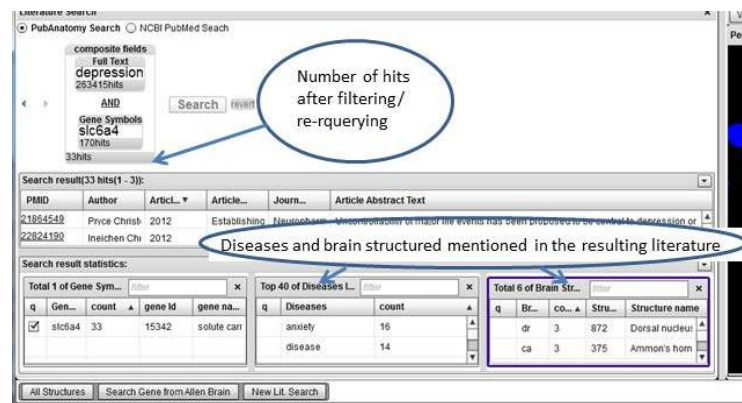
✘ **NOTE:** In this version, you cannot change the order of the columns in the tabs.

✘ **NOTE:** For search results you are able to sort columns *without* moving them to the left.

## Filter and alter the Search statement

Add terms to your search statement in three ways:

1. To add a number of search fields. Add fields as described in SEARCHING THE LITERATURE.
2. To add a number of fields based on retrieved result annotations, drag and drop each term to the search statement box.
  - a. Change the AND as desired. Click the AND and change it to NOT or OR.
  - b. When done building a query, click Search. The program updates results to this query.
3. . To add a term, filter all results by it, and add another use the Results q (filter) column.
  - a. Click on the “q” column in the row with your term of interest. A check box appears.
  - b. Pubanatomy 3D automatically adds the term to the search statement and filters results.
  - c. If you want to filter to everything *but* the selected term, click the AND. A list appears. Select NOT. (If you search to OR the results will be the same as before you filtered). Click Search and the program updates results to this query.



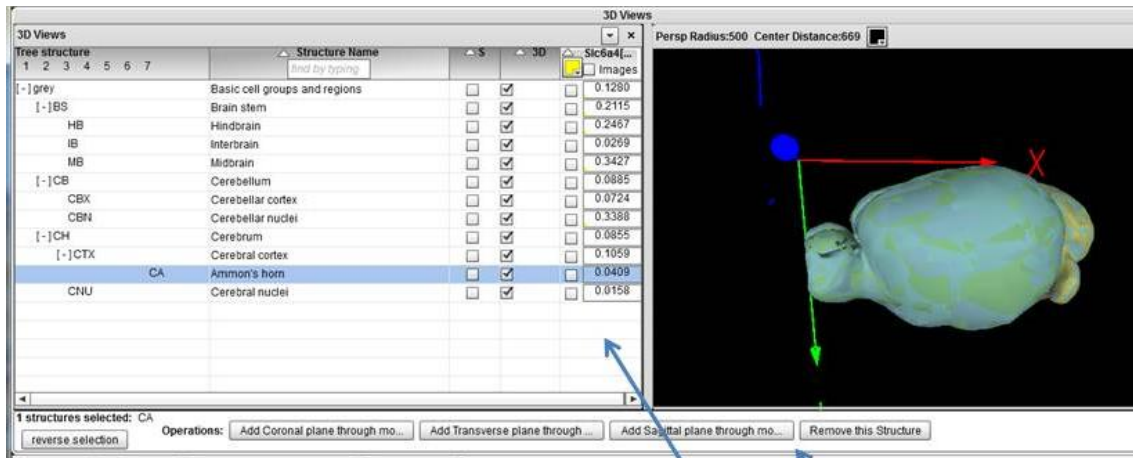
## Show selected genes and brain structures in the 3D Views

Drag and drop any gene and/or brain structure to the 3D view. Those gene expressions and structures are now read into the 3D view, and you can manipulate them.

The View Controller opens listing structures and genes that are read into the 3D brain display. The gene columns shows relative gene expression values across the brain.

Widen the border of the View Controller. If you close it, you can open it again at any point by clicking the View Controller button in the title bar of 3D views. The content stays the same.

⚠ **NOTE:** Only a subset of brain structures are read into the 3D display by default to keep the processing size manageable. You can bring in whatever other structures you want. To do so, either drag and drop from the Search Results or use the All Structures panel by clicking the All Structures button on the left bottom corner of the screen. See the All Structures instructions.



A user dragged Slc6a 4 and Ammon's horn to the 3D View.  
 A user clicked the View Controller button on the 3D Views title bar.  
 The 3D Views screen opened.  
 The relative gene expression for each structure loaded in the 3D view is listed on the right.  
 Ammon's horn is selected (highlighted in blue). Selection means that a user can perform the actions in the buttons on it.  
 All listed brain structures are displayed in the view (indicated in the boxes in the 3D column).  
 No gene expression is displayed yet in the 3D view (indicated by the boxes in the Gene expression column).

⚠ **NOTE:** Ammon's horn is not visible because it is covered by the higher level brain structures.

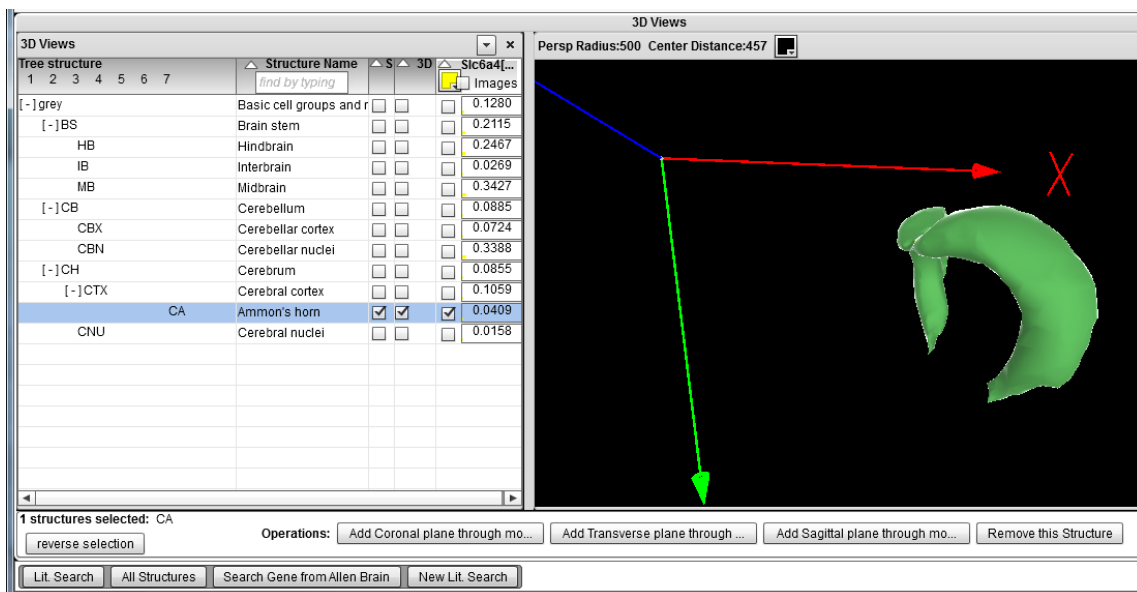
Move now to interacting with the 3D views to explore genes and structures of interest.

## INTERACTING WITH GENES AND BRAIN STRUCTURES IN 3D

After loading genes and brain structures of interest into the 3D Views panel, manipulate the 3D visual and the View Controller table to show meaningful view for your research purposes.

### Show only a structure of interest in the 3D View

1. Using the example from the previous section - dragging and dropping Ammon's horn:
2. With the Ammon's horn row selected (highlighted in blue) click Reverse selection. All structures but Ammon's horn will be selected
3. Click Hide Selected (make them invisible). All structures but Ammon's horn disappear from the 3D visual. They remain in the View Controller (with N in their 3D column box), and you can bring back any that you want by checking their boxes in the 3D column.
4. Click the box in the "S" column (Structure selection) to put a white outline around the displayed structure, as shown below for Ammon's horn.

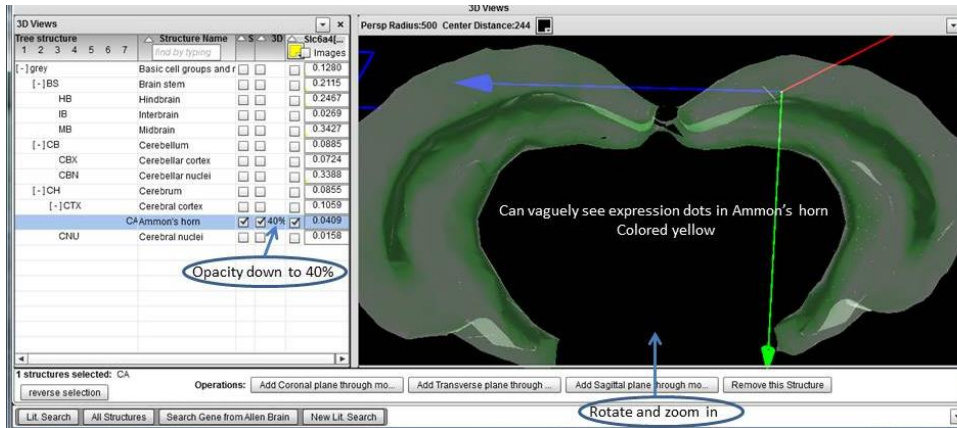


### Arrange the view

1. **Zoom to see a structure more closely.** Click the "Center Distance" button (located right under the 3D Views title bar). A slider appears. Move the slider to zoom in.
2. **Rotate.** Hold down the left mouse on the 3D view and move the mouse to rotate.
3. **Adjust the opacity.** Click the 100% on the structure row, 3D column, of the View Controller. A slider appears. Slide it to fix the opacity level.

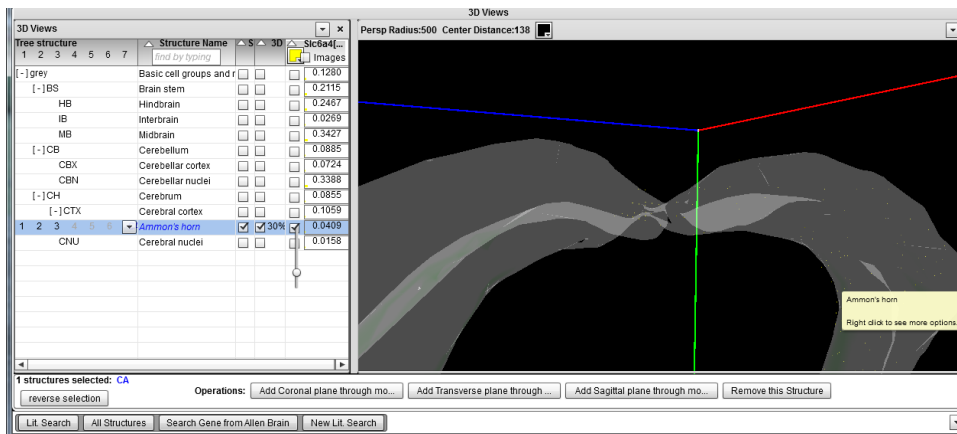
**Change the opacity of two or more structures at once.** Select the 2+ structures that you want to adjust in opacity. Click the “Adjust Opacity” button at the bottom of the screen. A slider appears. Set all the structures to the same opacity by moving the slider.

**NOTE:** Gene expression shows best when opacity is set very low (e.g. 0 - 20%).



The next figure shows the same view with less opacity and zoomed in to see expression better.

Expression is represented as small dots on the brain structure. The representation reflects the location of expression and the density of grouping. The size of the dots corresponds to relative strength of expression. Larger dots represent higher expression values.



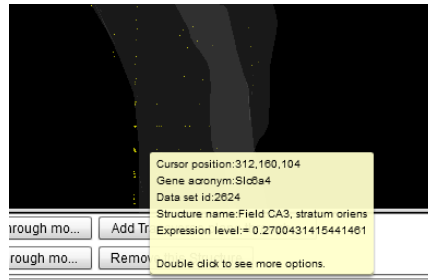
1. **Center the structure of interest.** Right click on the structure or expression point of interest. A list appears with various functions you can perform. Click either Structure or Cursor position to get an additional menu pertaining to either the general structure or exact cursor position. Click “Point Camera to the Center...” The center point of the view now becomes either the structure or cursor point (depending which you choose in the menu).



Adjust the opacity for this new centered focus by clicking “Center Distance.”

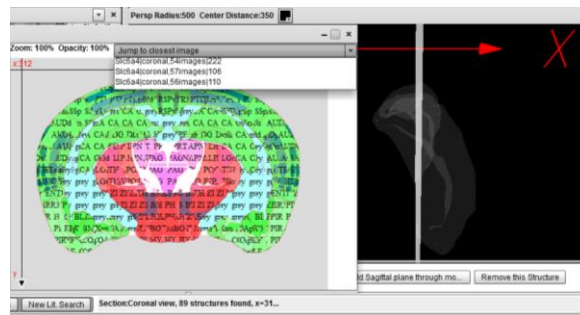
## Narrow to a gene within a structure & examine its expression

1. Zoom into a structure. Use the mouse, mouse wheel or the Center Distance slider.
2. Hover over a gene in the structure until its information displays.



3. Right click on the gene. A list appears with functions to perform.
4. Click Cursor hit position (i.e. the cursor click positioned on the gene). A sub-menu appears.
5. On the sub-menu, click “ Add coronal plane through model.” You can choose whichever plane you want to use for a slices. Coronal slices are usually the most highly curated.
6. A plane cuts through the 3D view and a corresponding 2D slice appears.

**✗ NOTE:** For more screen space, you can close panels that you are not using right now. They are minimized, and you can re-open them easily (through buttons) as needed.



The 3D view shows the coronal plane and next to it the corresponding 2D plate.

- a. If the 2D plate says “Jump to closest image”, pull down the list.
- b. Select the nissl slide that you want to display. It contains the expression of the gene of interest.

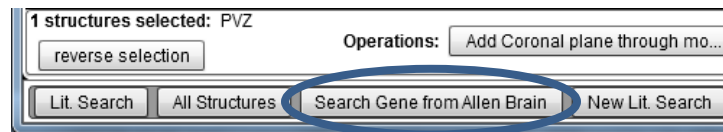
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## Show the expression of two or more genes at once

1. Bring the genes of interest into the 3D view in one of two ways:
  - a. Drag each gene from the search Results Gene tab into the 3D view.

Or

  - b. Click the “Search Gene From Allen Brain” button on the bottom of the screen.



- c. A search box opens. Click the radio button for Gene Name or Symbol.
- d. Enter the gene name or symbol. From the resulting list, drag and drop your desired genes to the 3D view.
- e. Close the search box when done.

## Adjust the view to see the two expressions of interest

In the next two screen shots, two pertaining to neuroimmune issues are read into the 3D view.

**Screen shot 1** shows a zoomed out view and annotates the actions users can take to adjust the controls in the View Controller to optimize the visibility of the gene expression. These actions include:

In the view controller, check only the structures you want visible in the 3D view.

In the brain structure row, check the box next to the expression if you want to see gene expression in that structure.

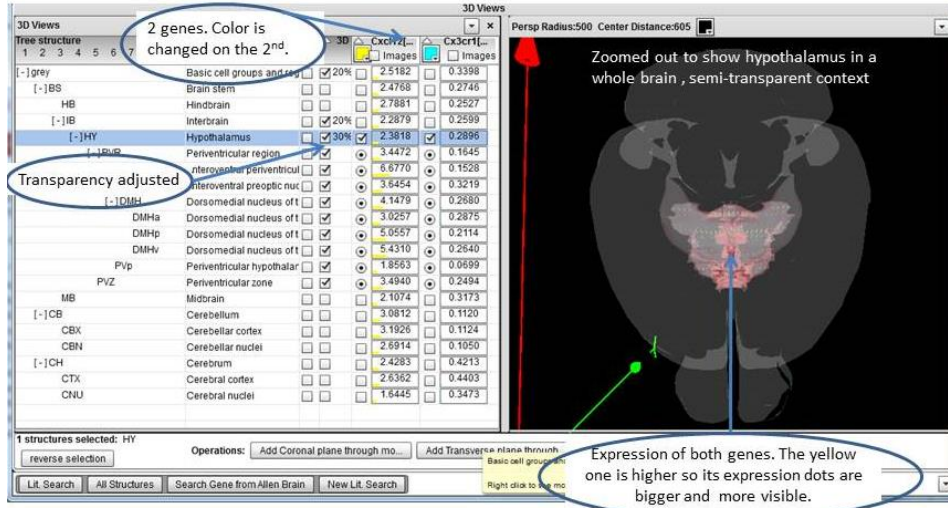
Rotate the 3D view to the angle you want to see.

Adjust the transparency with the transparency slider to show the structure and context that are important to see.

Change the color of one of the genes to easily differentiate them from each other in the 3D view. Click the color box next to the work Images in the gene expression column. A color palette appears. Select a different color.

Right click on the structure of main interest. In the drop down list select Point Camera to the Center. The focus point for the 3D view now centers on this structure.

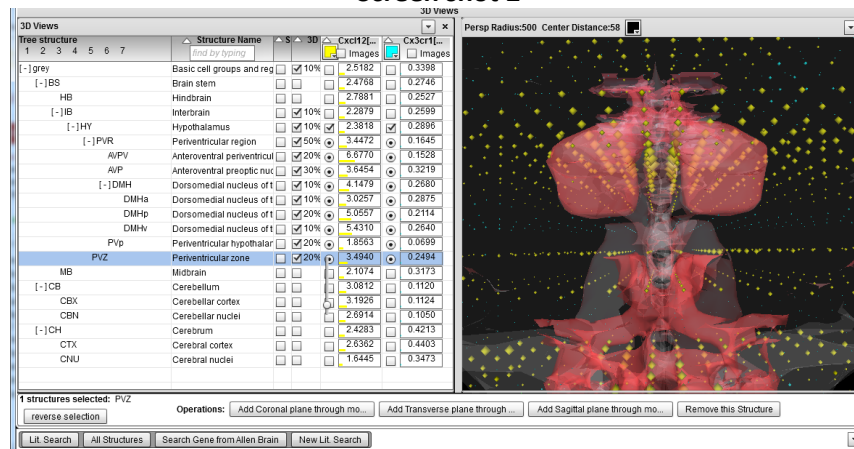
Screen shot 1:



Screen shot 2 zooms in. It lets you better differentiate the expression of the two genes (yellow and blue). The size of the dots represent relative expression values (small to large) across the brain. To get to the zoomed in view:

Use your mouse wheel or Center Distance button and slider to zoom in.

Screen shot 2



At this point, right click to put a plane through any selected point (either gene) to see a 2D slide

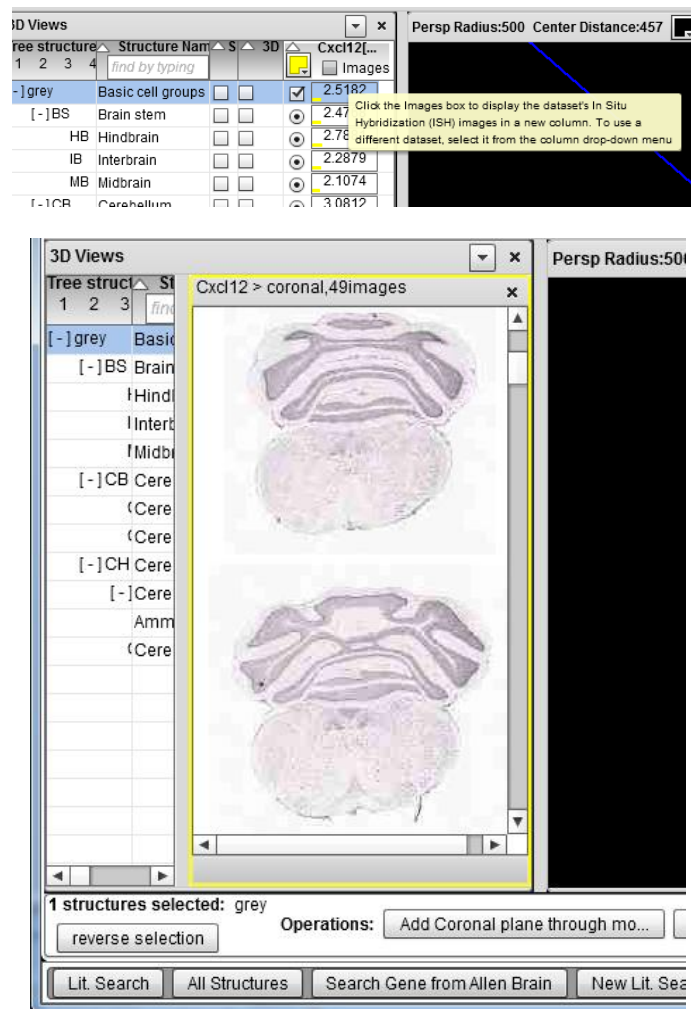
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## INTERACTING WITH 2D IMAGES

### Call up a 2D slide to examine gene expression

You can call up a 2D slide showing the expression of a select gene in one of two ways.

1. Option 1: Interact with the View Controller after bringing a gene into the 3D View.
  - a. In the View Controller, click the Images box in the Gene column title bar in the View Controller. A column of images appears



If you want to close the image column click the X in the Gene name title bar.

The images are the available Nissl slides for the dataset currently loaded in the 3D View. They include, as well, the expression of the gene of interest at serial slices of the brain.



e. On the sub-menu, click “ Add coronal plane through the model.” You can choose whichever plane you want to use for a slices. Coronal slices are usually the most highly curated.

6. A plane cuts through the 3D view and a corresponding 2D slice appears.

**NOTE:** For more screen space, you can close panels that you are not using right now. They are minimized, and you can re-open them easily (through buttons) as needed.

## Adjust the view on the 2D slide to examine expression more clearly

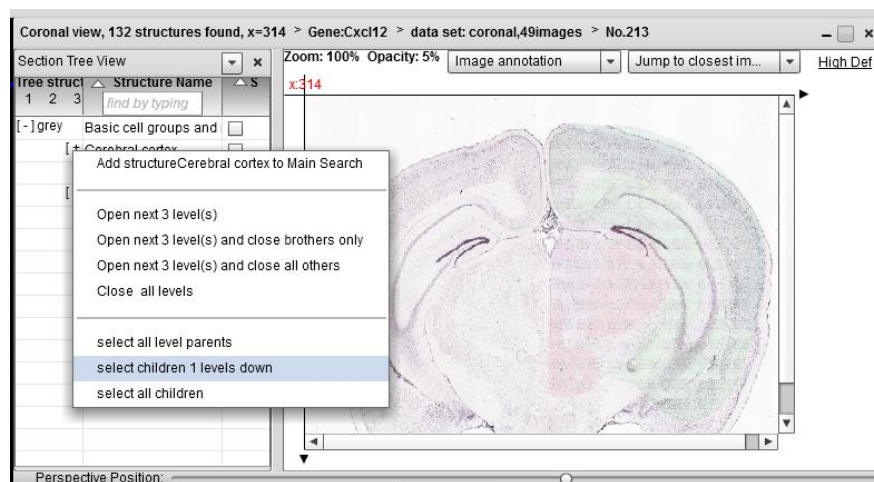
1. Jump to the closest available slide. If you see this message in the 2D slide pull down the drop down list and select an image. The 2D view now shows an available image for this gene and its expression.

2. Make the annotation more transparent to see the actually staining better. Click “Opacity 100” at the top of the 2D image (floating) window. A slider appears. Adjust it to the % opacity that you want. 0% will show only the slide with no annotation.

**NOTE:** In this version the annotation shows abbreviations for each region of the brain. The colors are used only to show different regions. They do not have any meaning otherwise and do not tie in with any other colors used in the program (e.g. in the 3D view or gene expression).

3. Outline regions of interest.

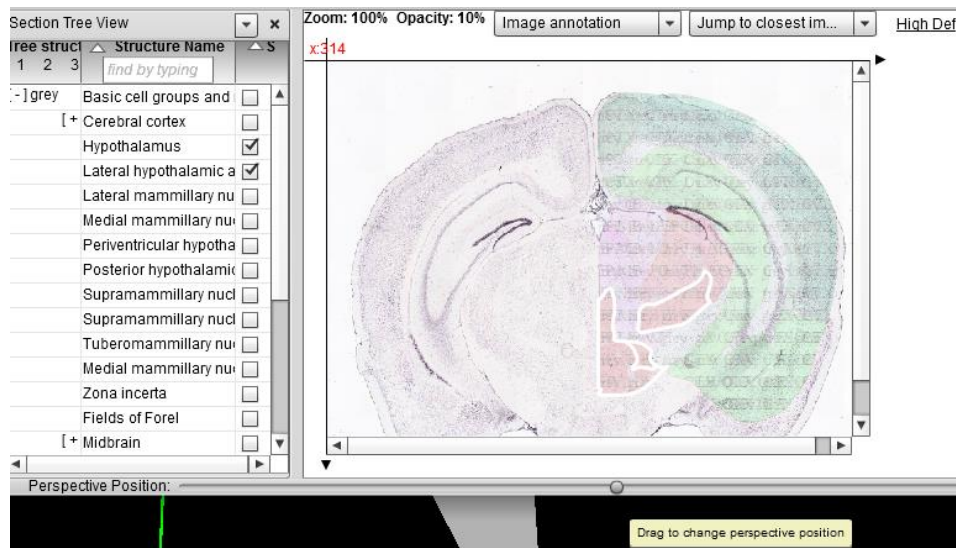
Display all regions included in the image that are relevant to you. Click the + next to a structure in the list of structures in the left panel of the 2D view. A drop down list of options appears. Click Open next three levels.



The substructures appear in the list.

Select areas of interest. Click an area of interest in the 2D image. Its name in the left hand list automatically gets checked. Alternately, you can check the box next to the name of a targeted structure in the left hand list. In both cases, the structures you select get outlined in white. The screen shot below shows 2 structures selected.

To show sub-structures in the left hand list, click the + next to a structure name. In the pull down list select the option that lets you open the structure's sub-structures/children.



⚠ **NOTE:** When you hover over an area, it gets outlined in black - whether it is selected (white outline) or not. The black outline goes away when you move your cursor.

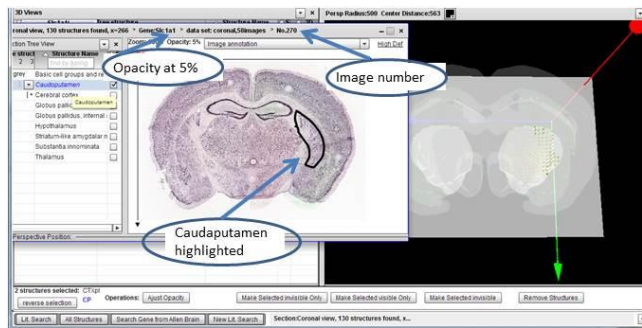
⚠ **NOTE:** The white outline of selected structures persists across sequential slides you view.

## Examine expression serially on successive slides

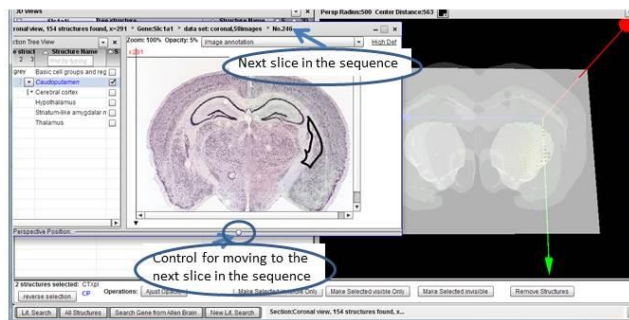
1. At the bottom of the 2Dslide is a small slider with a ball (small round button) that you can move side to side. Put your mouse on the ball and move it.



When you stop moving the slider, a new 2D slide replaces the previous one. The new one reflects a new location. For coronal images, as you move the slider from left to right, the images go from the front to the back of the brain. For sagittal images, as you move the slider from left to right, the images go from the left part of the brain to the right.



Two 2D slice s in sequence with expression of gene of interest



## View a 2D slide and serial views in high definition

1. Click on the [High Def](#) hyperlink at the right hand, top corner of the 2D ISH image. A high resolution image appears that lets you see detail very closely. This action opens a new tab and takes you out of PubAnatomy. Close it by closing its web browser tab.
2. The sequential images are available from this view, as well. Click through the sequence of images to view high resolutions of each successive slide.





## Examine expression on two slides side by side

PubAnatomy 3D lets you see 2D slides side by side, which facilitates comparing images. You can compare sequential slides of the same gene or slides of different genes. You can view side by side slides in two ways: either as free floating windows or docked images in the 3D view space.

1. Set up side by side 2D slides as free standing windows.
  - a. Open the first image by right clicking on a gene expression dot in the 3D view and putting a plane through the cursor position or structure.
  - b. Open additional images by returning to the 3D view. In the 3D View click on a gene expression dot – the same or a different one. Right click and put a plane through this position.

Windows open with the different 2D slides for each inserted plane. You can perform different actions on each. You can move the slider on each one to see its distinct sequential slides. You can arrange the free floating windows as you like.

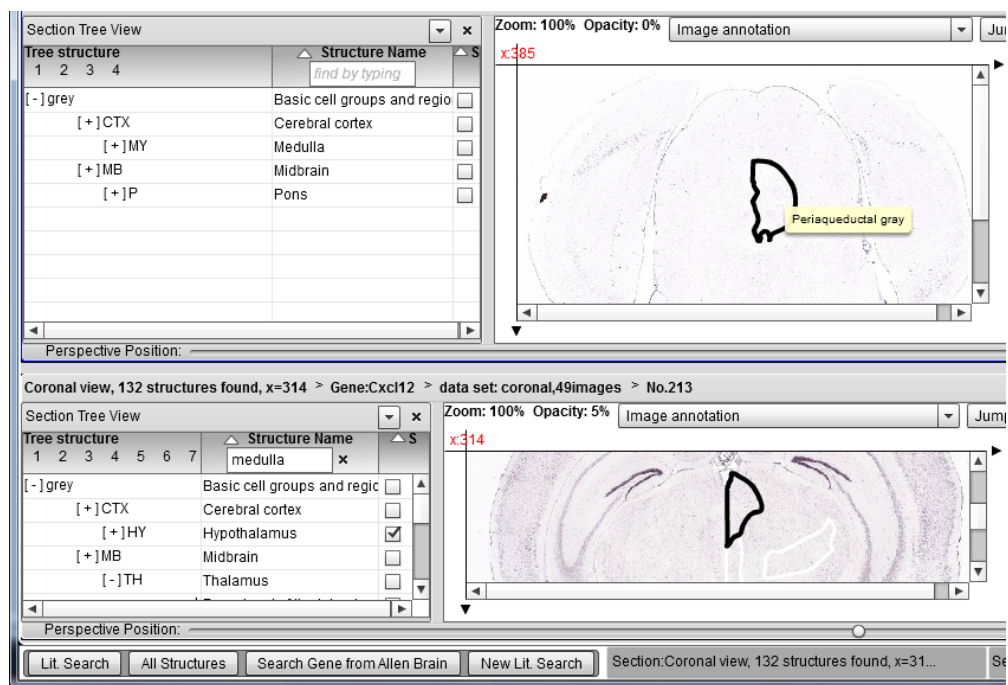
2. Set up side by side 2D slides as stationary (docked) images in the 3D view space.

**NOTE:** The slides cannot be undocked if you choose this option.

- a. On the title bar of the 2D slide image, find the information telling you the Gene Name > Dataset> and slide number.

Coronal view, 43 structures found, x=480 > Gene:Cxcl12 > data set: coronal,56images > No.22

- b. Drag the Image number (No.22 in the screen shot above) and drop it into the 3D view. The 2D slide opens within the 3D screen space. It also remains as a free floating window.
- c. Close (X) or minimize (-) the free floating window to make more space.
- d. Drag another image number from another open 2D image/ISH slide into the 3D space. Its 2D view opens in the 3D space as well. Close or minimize its free floating window.
- e. Arrange the views so that you can see them as you like. When you hover over and highlight (black outline) areas in one the same areas in the other get highlighted (I.e. if they are present in both images).



Close views by clicking on the arrow under the title bar of each image. A pull down list appears. Click "Close this View."

If you have minimized the same images earlier, you can re-open them by clicking on their names on the tabs at the bottom of the screen.

Productive steps to take after this detailed view are to refine your literature search based on insights or new genes/structures of interest that you have uncovered so far.

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## USING GENES/ BRAIN STRUCTURES FROM 2D OR 3D TO SEARCH MEDLINE

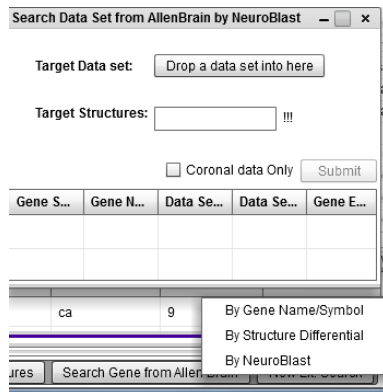
After examining details, you may have new ideas for searches you'd like to conduct in the literature – either by refining your original search, adding a new term, or changing your previous search statement. For example, you may have found a brain sub-structure of interest relevant to the gene expression you are examining that you had not thought about before. PubAnatomy's quick drag and drop options let you move any number of items/terms to a MEDLINE search.

### Refine or change an existing literature search

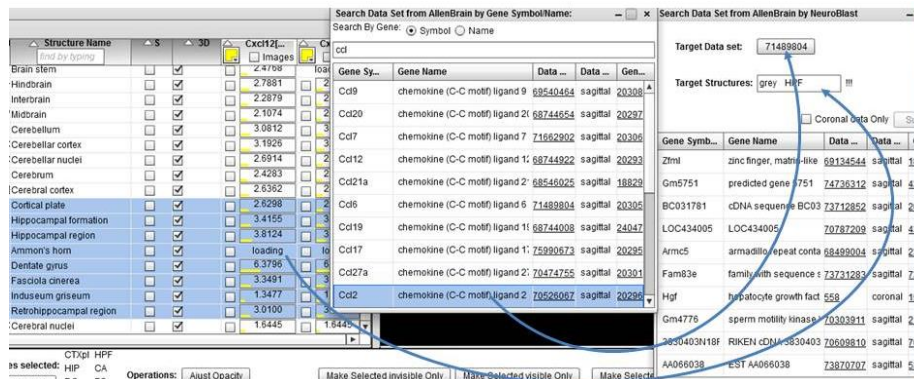
1. Open the literature search panel. If you have closed it, click the Lit Search button at the bottom of the screen. The panel opens. It still displays the last search you executed and its results. Build your searches by using either of the two options that follow.
2. **Option 1. Use the 3D View, 2D view or View Controller.** Drag and drop (one at a time) any number of items to the search statement area. If you drag and drop gene symbols or brain structures PubAnatomy automatically opens a search box relevant to the respective field (gene name, brain structure).

Dragged Items from the 3D and 2D views and View Controller may include:

- Structure names from the structure name row of the View Controller or 2D image panel
  - Gene names from the 2D slide title bar (where it says Gene Name > Dataset> and slide number)
3. **Option 2: Use results from a NeuroBlast run.** Drag genes resulting from a NeuroBlast that you run within PubAnatomy 3D.
    - a. Click the button that says “Search from Allen Brain” at the bottom of the PubAnatomy 3D screen. A list appears. Click “By NeuroBlast.” A dialogue box appears.



- b. Fill in the Target Structures box. To do so, drag structures of interest from the View Controller or 2D slide You may drag multiple structures into this dialogue box. Select multiple structures at once from a list with Shift+mouse click or Ctrl+ mouse click. Drag them all at once to the Target Structures box in the NeuroBlast dialogue box.
- c. Click to put your cursor in the box that says Drag a dataset here. Two choices appear in a pop up list. You can either choose to get a data set by gene name (searching Allen Brain for a data set related to a gene of interest) or by structure differential. Select one of the two options and fill out the dialogue box that appears for that option.
- d. Results from either an Allen Brain gene search or a structure differential search appear. Results list genes according to specific datasets.
- e. Drag and drop one of the results of interest into the NeuroBlast field that says Drag a dataset here. Press Submit.
- f. Results appear from the NeuroBlast run. From the results you can get an idea of other genes that may be related to your genes and structures of interest. Find out more about potential functional relationships by searching the research literature.



- g. Drag and drop selected results from the NeuroBlast run to the literature search space. Submit the search.

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## BRINGING MORE STRUCTURES INTO VIEW USING THE INTERACTIVE BRAIN STRUCTURE TREE VIEW

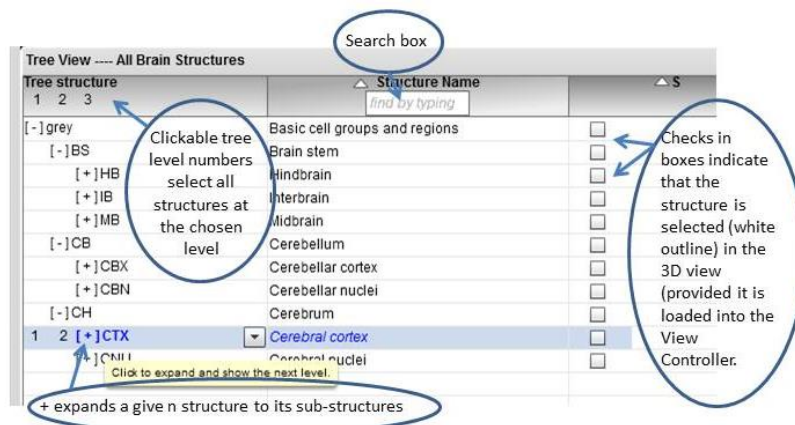
The default displays of the PubAnatomy 3D brain and associated structures (listed in the View Controller) do not show all 828 brain structures that are in the Allen Brain database. But you can quickly bring in any structure or group of structures that you want. Use the interactive brain structure tree view – called “All Structures.”

By default the “All Structures” panel is hidden until you want to open it to find brain structures and drag and drop them into view.

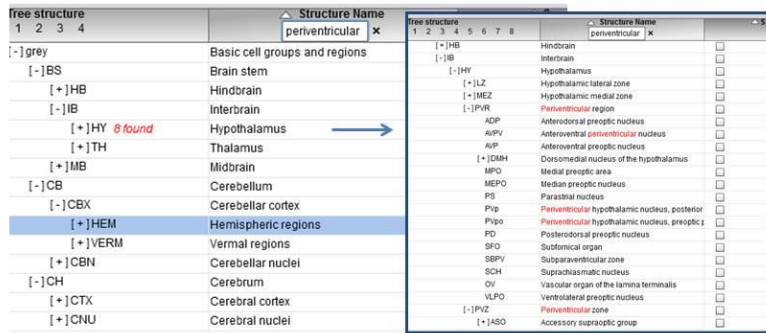
1. Call up the “All Structures” panel. Click the “All Structures” button at the bottom of the screen. The “All Structures” panel appears with a tree view of all brain structures.

**NOTE:** In this version of PubAnatomy3D the list is organized by the system that Allen Brain Atlas uses. Next versions will have options that may be more intuitive to some neurobiologists

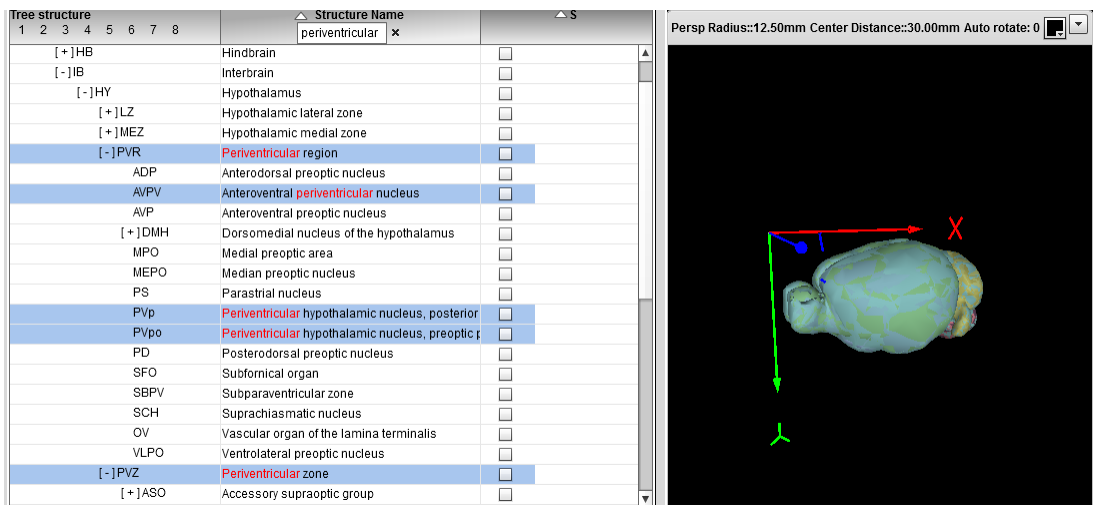
2. Adjust the panel that appears as needed by moving its border.
3. Find a desired structure by typing its name in the search box or by clicking the + to find it.



If you search, PubAnatomy 3D retrieves and shows results. Click the red number of results found and PubAnatomy 3D opens the tree list to them.



4. Select one or many structures with your mouse. Drag and drop them into the 3D view or View Controller. They load into the 3D view, ready for you to adjust views accordingly.



5. Select any structures that you want outlined in white in the 3D view in the S column. You can also do this selection in the View Controller's S column.
6. Close the All Structures panel by clicking the X in the top right corner.

## Appendix

### Quick guide to each panel display and its operations

#### Search Screen

Enter search word here

Click arrow on Full text title  
Add a new term & field

Select the field for the next term

Click here to do a PubMed search

Click here to get only a gene to examine in 3D

Literature Search  
PubAnatomy Search  NCBI PubMed Search

Full Text  
bipolar disorder  
33137hits

Add new Term  
Layout  
Close this term

Article Journal Publish Year  
Protocols  
Publication type  
Brain Structure Names  
Brain Structure Symbols  
Brain Structure IDs  
Gene Names  
Gene Symbols  
Gene IDs  
Author  
Article Abstract Text  
Article title  
Major Keywords  
Functions  
Diseases  
Mesh heading Description Name  
Chemical Name  
Full Text

All Structures Search Gene from Allen Brain New Lit. Search

View Controller 3D Views  
Persp Radius:500 Center Distance:329

3D view of a brain structure with axes.

#### Retrieved Results Screen

Click arrow to close a box

Click AND to change it to OR or NOT

Widen panel as needed to view results

Click search

Literature -- sortable columns

Click arrow to select more tabs

Drag and drop any item from any tab into the search box to continue building a query.

Click here to start a new search

Literature Search  
PubAnatomy Search  NCBI PubMed Search

Full Text  
slc1a1 AND glutamate  
84hits 91383hits  
67hits

Search Search revert

Search result (67 hits(1 - 5)):

PMID	Author	Articl...	Article...	Journ...	Article Abstract Text
22776887	Real E E. Gr	2013	Interaction o	The pharma	Genetic and environmental factors seem to interact and influence bo
23341099	Myles-Worst	2013	Deletion at t	American io	Growing evidence for genetic overlap between schizophrenia (SCZ)
23564280	Wu Haisu H.	2013	Association	Journal of m	Obsessive-compulsive disorder (OCD) is a common and severe me
23695234	Porton B B. C	2013	Isoforms of t	Translatona	The SLC1A1 gene, which encodes the neuronal glutamate transport

Search result statistics:

Total 2 of Gen...					Total 76 of Dis...			Total 9 of Bra...				
q	Gen...	co...	gen...	gen...	q	Diseases	count	q	Bral...	co...	Stru...	Struct...
	slc1a1	23	20272	solute		disease	30		ctx	4	688	Cereb
	pdpk1	1	18373	3-phos		brain	11		cbpl	4	695	Cortic

All Structures Search Gene from Allen Brain New Lit. Search

View Controller 3D Views  
Persp Radius:500 Center Distance:1200

3D view of a brain structure with axes.

## 3D Display and View Controller Screens

**3D Views**

Tree structure	Structure Name	3D	Slc1a1...
1			
2			
3			
4			
5			
6			
[-] grey Basic cell groups and regions <input type="checkbox"/> <input checked="" type="checkbox"/> 5.7025			
[-] BS Brain stem <input type="checkbox"/> <input checked="" type="checkbox"/> 4.6044			
HB Hindbrain <input type="checkbox"/> <input checked="" type="checkbox"/> 4.2537			
IB Interbrain <input type="checkbox"/> <input checked="" type="checkbox"/> 5.6145			
MB Midbrain <input type="checkbox"/> <input checked="" type="checkbox"/> 4.0536			
[-] CB Cerebellum <input type="checkbox"/> <input checked="" type="checkbox"/> 1.3249			
CBX Cerebellar cortex <input type="checkbox"/> <input checked="" type="checkbox"/> 1.1772			
CBN Cerebellar nuclei <input type="checkbox"/> <input checked="" type="checkbox"/> 3.2555			
[-] CH Cerebrum <input type="checkbox"/> <input checked="" type="checkbox"/> 7.3837			
CTX Cerebral cortex <input type="checkbox"/> <input checked="" type="checkbox"/> 7.8200			
[-] CNU Cerebral nuclei <input type="checkbox"/> <input checked="" type="checkbox"/> 5.8538			
CP Caudoputamen <input type="checkbox"/> <input checked="" type="checkbox"/> 6.6476			

1 gene was dragged and dropped into the 3D view (Slc1a1).  
1 structure was dragged and dropped (Caudoputamen)

The structure appears in the brain (but is not visible due to outer layers of the brain). The gene appears in the 3D View panel (View Controller) but not yet in the 3D display. You have to click the box next to the gene expression that you want to display. Values in the Slc1a1 gene column are its relative expression values for different brain structures.

1 structures selected: CP

reverse selection    Operations: Add Coronal plane through mo...    Add Transverse plane through ...    Add Sagittal plane through mo...    Remove this Structure

Lit. Search    All Structures    Search Gene from Allen Brain    New Lit. Search

## 3D Display with Selected Structures and Transparency

**3D Views**

Slc1a1...	Tree structure	Structure Name	3D
<input type="checkbox"/>	1		
<input type="checkbox"/>	2		
<input type="checkbox"/>	3		
<input type="checkbox"/>	4		
<input type="checkbox"/>	5		
<input type="checkbox"/>	6		
<input type="checkbox"/>	7.8200	[-] CTX Cerebral cortex	<input type="checkbox"/>
<input type="checkbox"/>	7.6670	1 2 3 CTXpl (31403) Cortical plate	<input checked="" type="checkbox"/> 20%
<input type="checkbox"/>	7.3837	[-] CH Cerebrum	<input type="checkbox"/>
<input type="checkbox"/>	6.6476	CP Caudoputamen	<input checked="" type="checkbox"/>
<input type="checkbox"/>	5.8538	[-] CNU Cerebral nuclei	<input type="checkbox"/>
<input type="checkbox"/>	5.7025	[-] grey Basic cell groups and rec	<input type="checkbox"/>
<input type="checkbox"/>	5.6145	IB Interbrain	<input type="checkbox"/>
<input type="checkbox"/>	4.6044	[-] BS Brain stem	<input type="checkbox"/>
<input type="checkbox"/>	4.2537	HB Hindbrain	<input type="checkbox"/>
<input type="checkbox"/>	4.0536	MB Midbrain	<input type="checkbox"/>
<input type="checkbox"/>	3.2555	CBN Cerebellar nuclei	<input type="checkbox"/>
<input type="checkbox"/>	1.3249	[-] CB Cerebellum	<input type="checkbox"/>
<input type="checkbox"/>	1.1772	CBX Cerebellar cortex	<input type="checkbox"/>

Move the gene column to the left. Click the arrow to sort, high to low.

So far, no genes are displayed in 3D. None is checked yet.

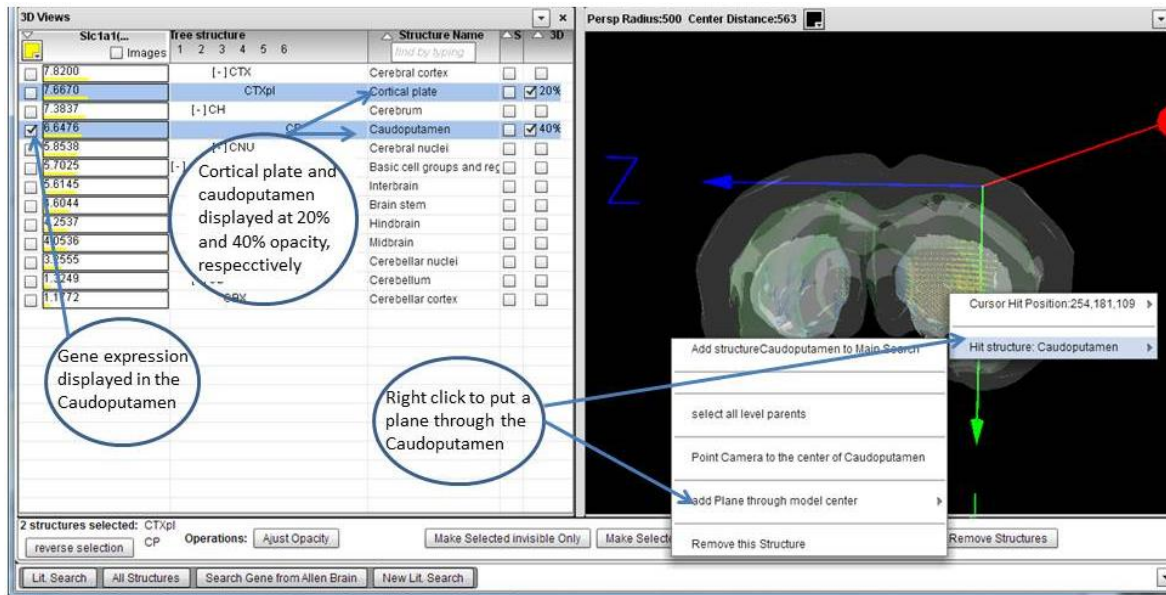
2 structures selected: CTXpl CP

reverse selection    Operations: Adjust Opacity    Make Selected invisible Only    Make Selected visible Only    Make Selected invisible    Remove Structures

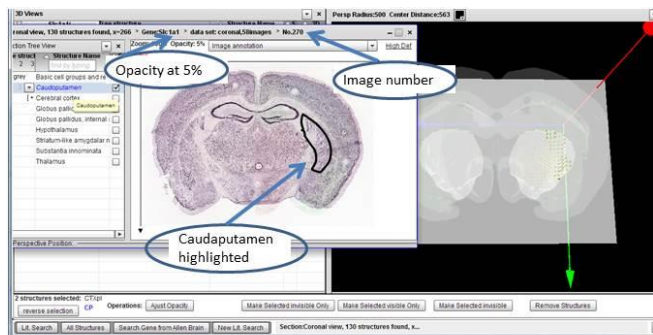
Lit. Search    All Structures    Search Gene from Allen Brain    New Lit. Search



## Putting a Plane in a Select Area through the 3D Display



## 2D Plates Resulting from Putting a Plane through the 3D view



Two 2D slice in sequence with expression of gene of interest

