



## DENTATE GYRUS (DG)

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### Introduction

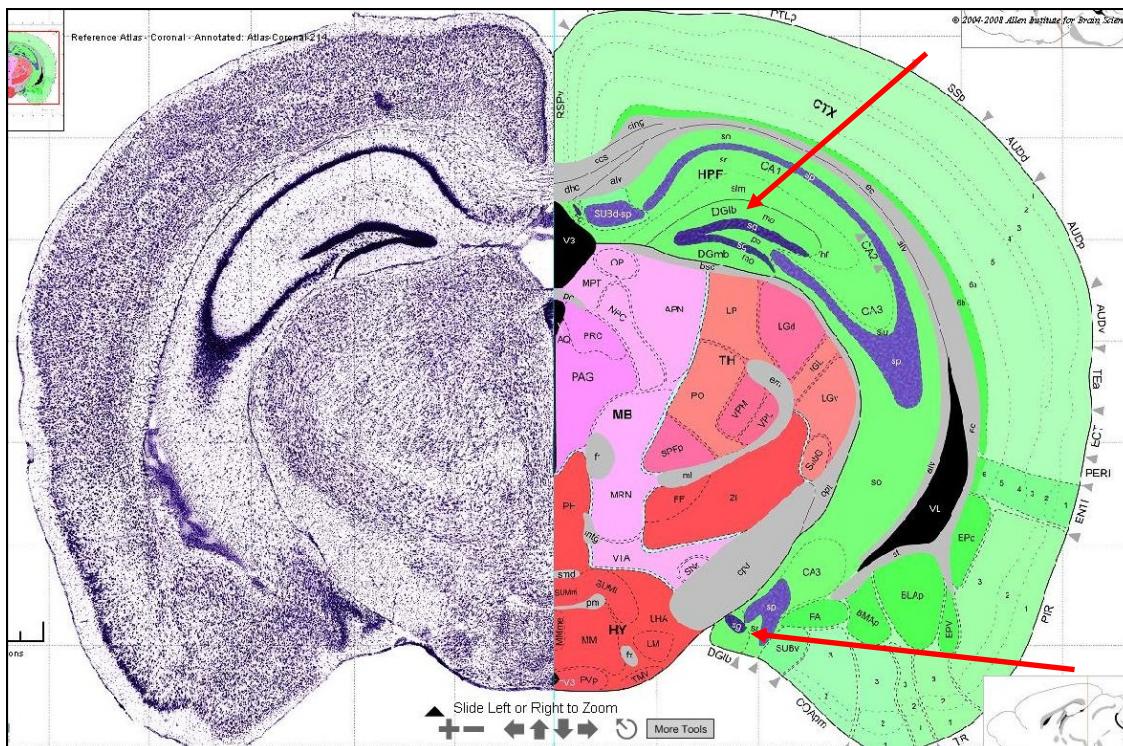
This report contains a gene expression summary of the dentate gyrus (DG), derived from the [Allen Brain Atlas](#) (ABA) *in situ* hybridization mouse data set. The structure's location and morphological characteristics in the mouse brain are described using the Nissl data found in the [Allen Reference Atlas](#). Using an established algorithm, the expression values of the dentate gyrus were compared to the values of the macro/parent-structure, in this case the hippocampal region, for the purpose of extracting regionally selective gene expression data. The genes with the highest ranking selectivity ratios were manually curated and verified. 50 genes were then selected and compiled for expression characterization. The experimental data for each gene may be accessed via the links provided; additional data in the sagittal plane may also be accessed using the [ABA](#). Correlations between gene expression in the dentate gyrus and the rest of the brain, across all genes in the coronal dataset (~4300 genes), were derived computationally. A gene ontology table (derived from DAVID Bioinformatics Resources 2007) is also included, highlighting possible functions of the 50 genes selected for this report.

To read more about how our 50 Select Genes list is derived, please refer to the [Fine Structure Annotation white paper](#).

Allen Reference Atlas Coronal Levels: 64-93

Allen Reference Atlas Sagittal Levels: 2-19, 21

Shown below is a plate from the Allen Reference Atlas, depicting the dentate gyrus (level 79):



# Description of Structure:

## LOCATION and STRUCTURAL ANATOMY:

The hierarchical relationship within the brain is depicted below in the structure [legend](#). The Allen Reference Atlas (based on Nissl-stained sections scanned at 10X) was the primary resource for the following descriptions.

For additional information please refer to the [Allen Reference Atlas white paper](#).

[BrainInfo](#) houses a search engine that allows searches for structure name aliases.

The dentate gyrus (DG) is a substructure of the hippocampal formation. In most coronal and sagittal views, the dentate gyrus appears as a V-shaped structure enveloping the end of the pyramidal cells of CA3. The dentate gyrus is composed of three regions: crest, lateral blade (suprapyramidal portion) and medial blade (infrapyramidal portion). In the coronal view, the medial blade appears first rostrally, while the lateral blade appears superior and more caudal to the medial blade. Continuing caudally, the blades meet and form a V-shaped structure. At the most caudal aspect of the hippocampus, the medial and lateral blades join at each end to form the crest.

The dentate gyrus is also divided into three layers: molecular, granule and polymorph (also referred to as the hilus). A relatively cell sparse area with varying cell sizes, the molecular layer (DGmo) is located superficial to the granule cell layer (DGsg), which contains an extensive number of small, densely packed and uniformly sized cells. The molecular and granule cell layers partially enclose the polymorph layer (DGpo), which contains sparsely distributed large polymorphic cells. At the interface of the DGsg and the DGpo lies the subgranular zone, one of the few regions in the brain in which adult neurogenesis occurs.

In the ABA, the dentate gyrus can be viewed throughout most sagittal sections. In the most lateral of views the dentate gyrus is seen as one entity, but moving medially one can see both dorsal and ventral parts of the dentate gyrus. Proceeding medially, the ventral portion can no longer be seen, while the dorsal portion remains visible through to the midline. Although not delineated in the Allen Reference Atlas sagittal view, all three layers (molecular, granule and polymorph) of the dentate gyrus can be easily identified and the description of their location relative to one another is the same as in the coronal view.

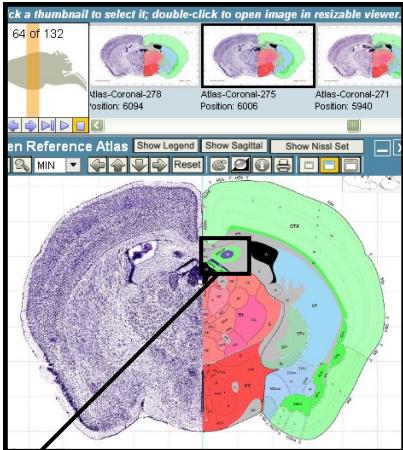
The appearance and location of the dentate gyrus can be appreciated on the following two pages. Nissl-stained sections and Allen Reference Atlas plates reveal the cytoarchitecture and extent of the dentate gyrus, and its location in relation to surrounding structures.

Alphabetically	By Structure
<b>Allen Brain Atlas: Structural Relationships</b> Click on a row to see what structures it contains.	
show all   hide all	
■ Basic Cell Groups and Regions	
■ Cerebrum [CH]	
■ Cerebral cortex [CTX]	
■ Cortical plate [CTXpl]	
■ Isocortex [Isocortex]	
■ Olfactory areas [OLF]	
■ Hippocampal formation [HPF]	
■ Hippocampal region [HIP]	
■ Ammon's Horn [CA]	
■ Dentate gyrus [DG]	
■ Dentate gyrus crest [DGcr]	
■ Dentate gyrus crest, molecular layer [DGcr-mo]	
■ Dentate gyrus crest, polymorph layer [DGcr-po]	
■ Dentate gyrus crest, granule cell layer [DGcr-sg]	
■ Dentate gyrus lateral blade [DGlb]	
■ Dentate gyrus lateral blade, molecular layer [DGlb-mo]	
■ Dentate gyrus lateral blade, polymorph layer [DGlb-po]	
■ Dentate gyrus lateral blade, granule cell layer [DGlb-sg]	
■ Dentate gyrus medial blade [DGmb]	
■ Dentate gyrus medial blade, molecular layer [DGmb-mo]	
■ Dentate gyrus medial blade, polymorph layer [DGmb-po]	
■ Dentate gyrus medial blade, granule cell layer [DGmb-sg]	
■ Dentate gyrus, granule cell layer [DG-sg]	
■ Fasciola cinerea [FC]	
■ Induseum griseum [IG]	
■ Retrohippocampal region [RHP]	
■ Cortical subplate [CTXsp]	
■ Cerebral nuclei [CNU]	
■ Cerebellum [CB]	

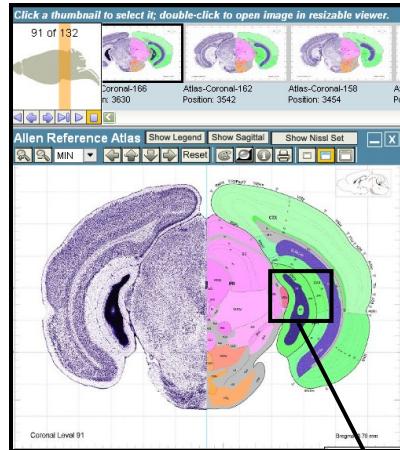
# Atlas and Nissl:

## Coronal:

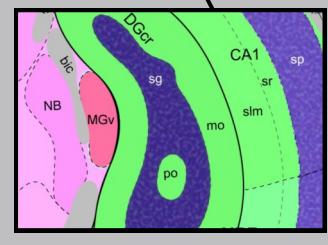
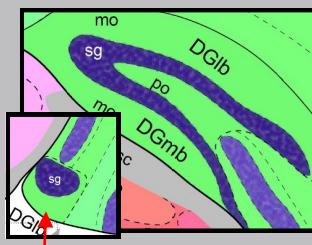
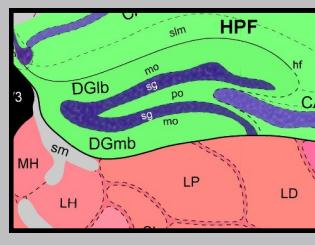
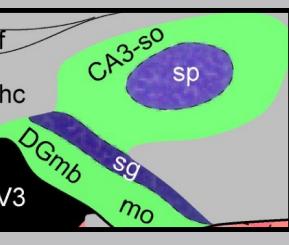
**Rostral**



**Caudal**



**Reference  
Atlas**

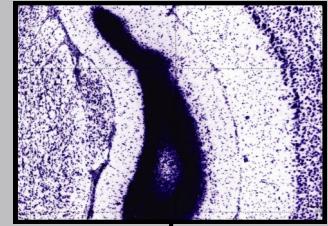
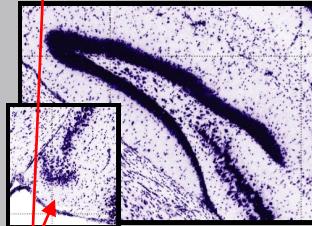
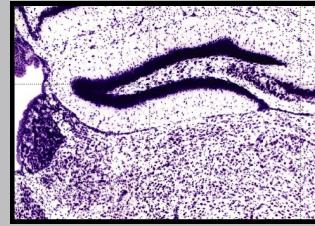
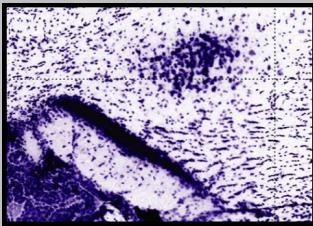


**Level 64**

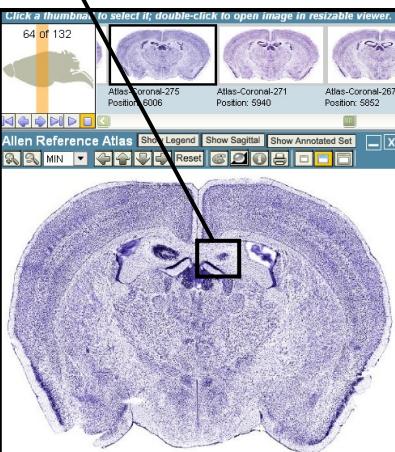
**Level 73**

**Level 83**

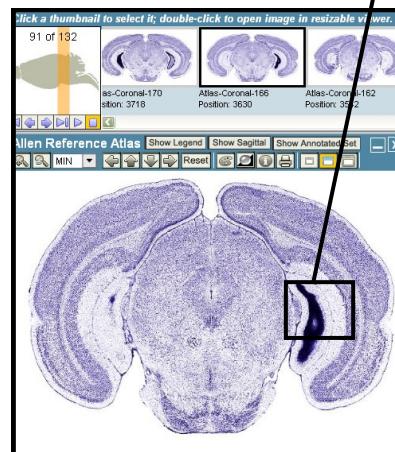
**Level 91**



**Ventral portion**



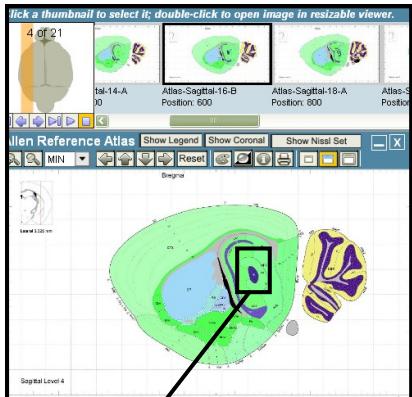
**Nissl**



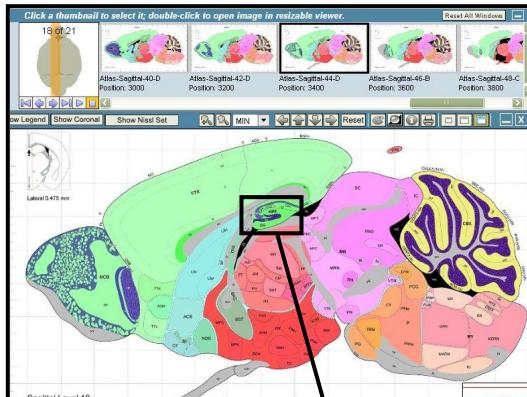
# Atlas and Nissl:

## Sagittal:

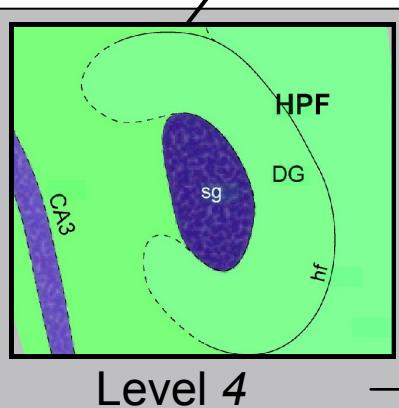
**Lateral**



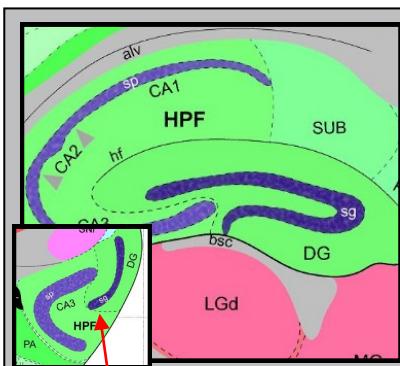
**Medial**



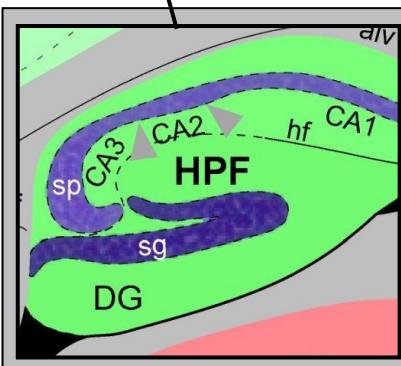
**Reference  
Atlas**



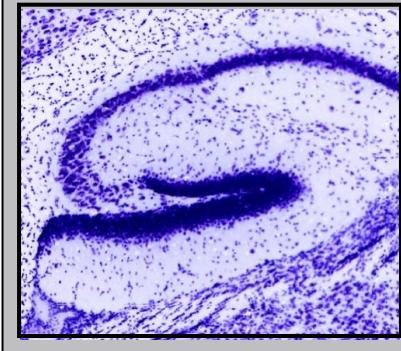
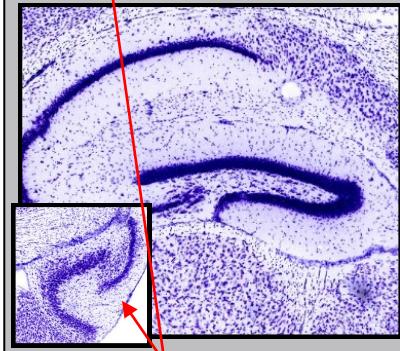
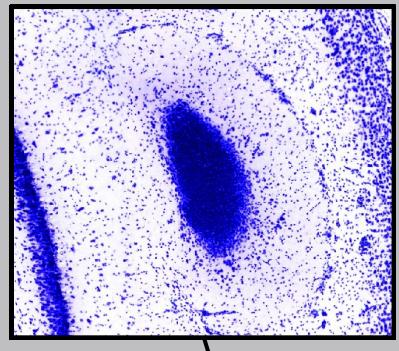
**Level 4**



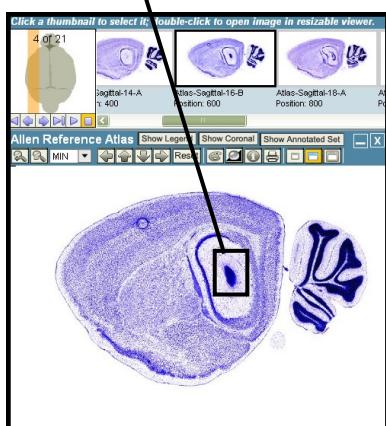
**Level 9**



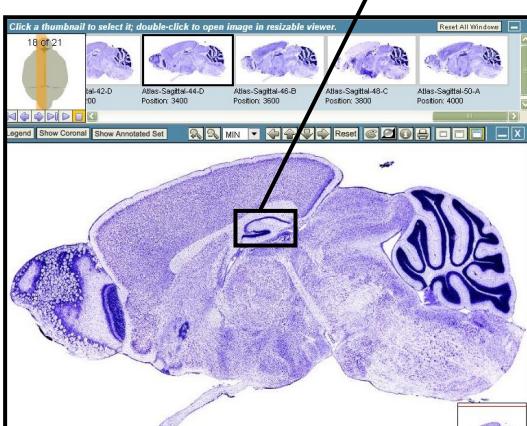
**Level 18**



**Ventral portion**



**Nissl**



# In Situ Hybridization Expression Patterns of 50 Select Genes:

The *in situ* hybridization (ISH) data below presents the dentate gyrus' anatomical and cytoarchitectural characteristics in the context of actual gene expression. In addition to presenting molecularly defined borders, ISH gene expression patterns also aid in phenotyping cell populations that otherwise can not be differentiated on purely morphological grounds.

The 50 genes in this section were selected based on a mathematical algorithm to identify gene expression patterns that allow selective identification of the dentate gyrus. The gene expression patterns were then verified manually. As such, these genes do not represent the only genes found in this structure, genes specific to this structure, or genes expressing at the highest level within this structure.

Please refer to our protocol in the [Data Production Processes white paper](#).

To read about heat map conversion, refer to the [Informatics Data Processing white paper](#).

The expression data subsequently presented can be further explored, in coronal and sagittal planes, at [brain-map.org](#).

A survey of selected gene expression shows three distinct categories of expression. The forty-five genes falling into the first category show preferential expression in DGsg with little to no expression in the DGpo and/or DGmo. Although a few genes showing minimal expression in DGpo and/or DGmo do fall within this group, the notable feature is the frequent high density and intensity expression within the granule cell layer. The second category contains two genes that show distinct enrichment in the subgranular zone. The last and most distinct category highlighted by these select genes contains three genes that show restricted expression in DGpo.

Using ISH data, the layers within the dentate gyrus can be just as easily distinguished as in the Nissl stained sections. Additionally, the border between CA3 of Ammon's horn and the polymorph layer, somewhat indistinguishable on Nissl stained sections, can be highlighted by specific gene expression patterns.

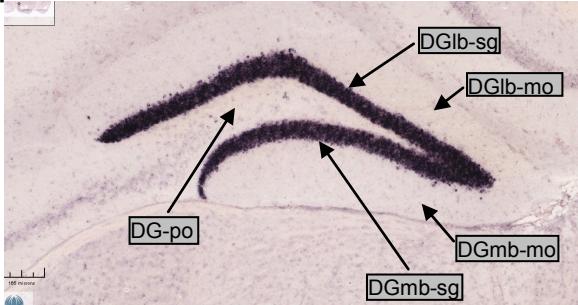
Cellular density expression key		Cellular intensity expression key	
None	No expression	No color	Very low intensity
Sparse	Very few cells expressing	Blue	Low intensity
Scattered	Less than 10% of cells expressing in scattered pattern	Green	Medium intensity
Medium	10-80% of cells expressing	Yellow	High intensity
High	Greater than 80% of cells expressing	Red	Very high intensity

To view heat map at [brain-map.org](#), right click on the ISH image and select "Show Expression Analysis."

**ISH DATA** The images below were selected to highlight various expression patterns of the dentate gyrus.

## ISH [C1ql2](#)

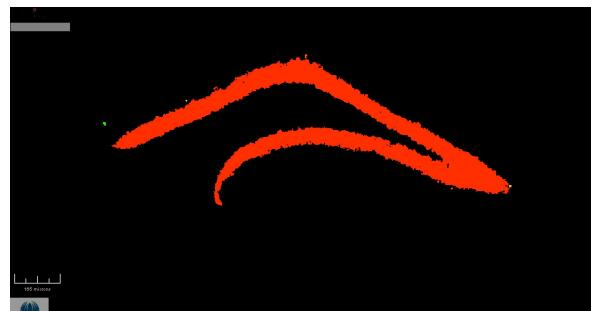
Coronal: The coronal view of C1ql2 shows preferential expression in DGsg with little to no expression in DGpo and/or DGmo.



## Heat map

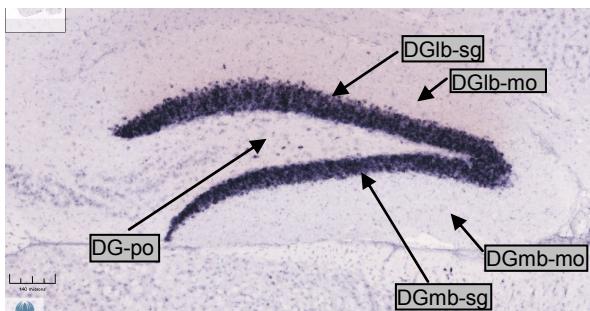
### [C1ql2](#)

Coronal: The coronal view of C1ql2 shows high density and very high intensity in the granule layer.



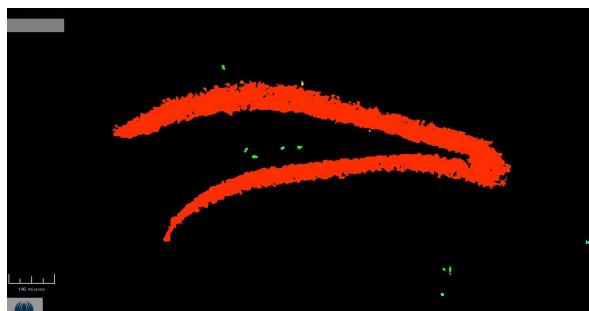
**ISH  
*C1ql2***

Sagittal: The sagittal view of C1ql2 shows preferential expression in DGsg with little to no expression in DGpo and/or DGmo.



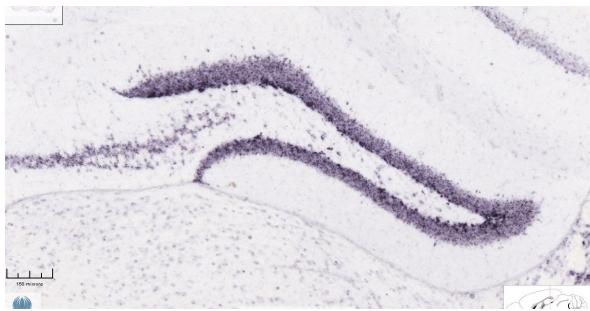
**Heat map  
*C1ql2***

Sagittal: The sagittal view of C1ql2 shows high density and very high intensity in the granule layer.



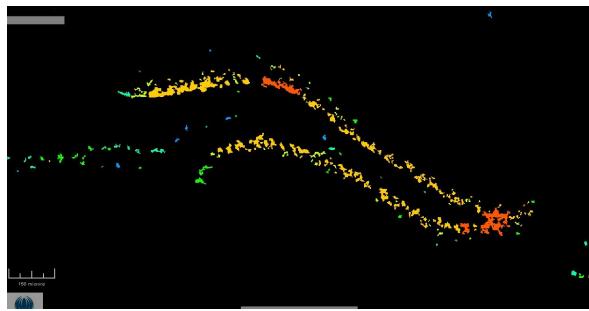
**ISH  
*Neurod1***

Coronal: The coronal view of Neurod1 shows enrichment in the subgranular zone.



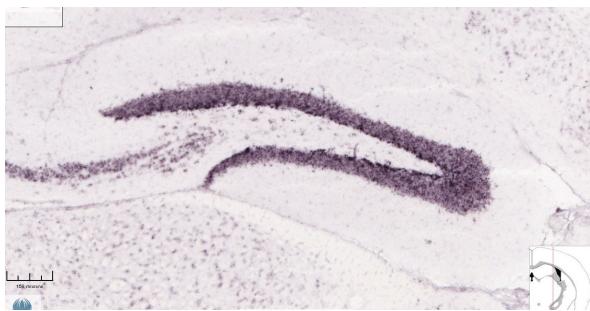
**Heat map  
*Neurod1***

Coronal: The heat map of the same view shows high density and intensity in the subgranular zone.



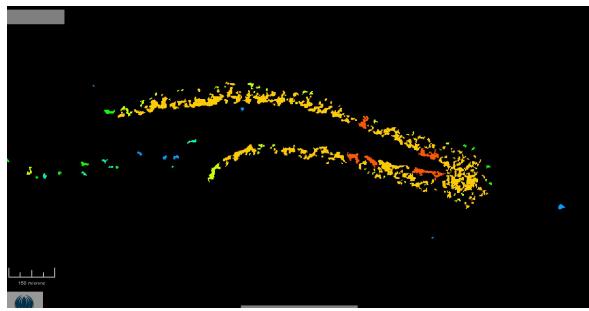
**ISH  
*Neurod1***

Sagittal: The subgranular zone is also highlighted in the sagittal view by Neurod1.



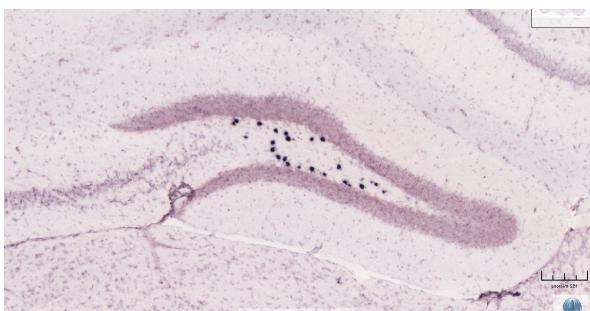
**Heat map  
*Neurod1***

Sagittal: The sagittal view of Neurod1 shows high density and intensity in the granule layer.



**ISH  
Csf2rb2**

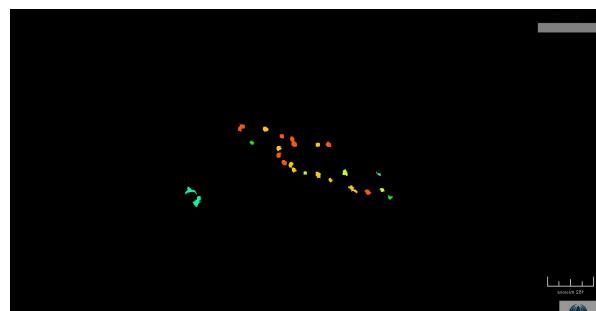
**Coronal:** Within the DG, expression of Csf2rb2 is restricted to the polymorph layer.



**Heat map**

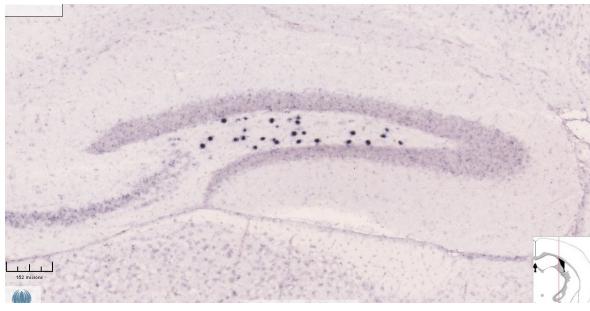
**Csf2rb2**

**Coronal:** The coronal view of Csf2rb2 shows scattered density and very high intensity.



**ISH  
Csf2rb2**

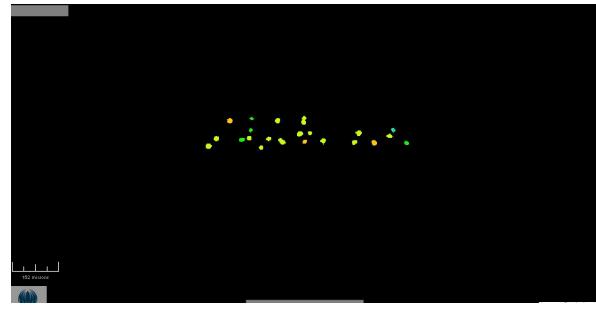
**Sagittal:** The polymorph layer is highlighted in the sagittal section as well.



**Heat map**

**Csf2rb2**

**Sagittal:** The sagittal view of Csf2rb2 shows scattered density and high intensity.



**50 SELECT GENES:**

This gene list was generated by manual curation of an [algorithmically](#) derived list that compared gene expression values of dentate gyrus to those of the hippocampal region. Categories of expression are subjectively grouped by relative expression characteristics.

Curation of 50 Select Genes List: April 2008

**Enriched Expression in DGsg with little to no Expression in DGpo and/or DGmo**

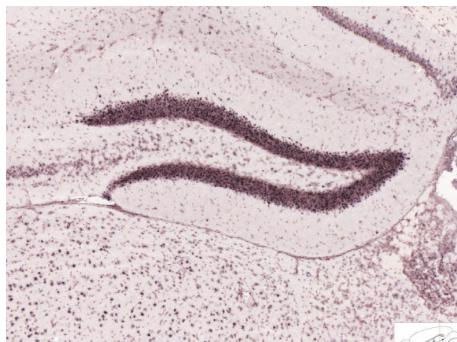
Number	Gene Symbol	Gene Name	Expression Pattern
1	<a href="#">C1ql2</a>	complement component 1, q subcomponent-like 2	High density, very high intensity
2	<a href="#">6430709H04Rik</a>	RIKEN cDNA 6430709H04 gene	High density and intensity
3	<a href="#">Sipa1l2</a>	signal-induced proliferation-associated 1 like 2	High density and intensity
4	<a href="#">C630035N08Rik</a>	RIKEN cDNA C630035N08 gene	High density, very high intensity
5	<a href="#">Btg1</a>	B-cell translocation gene 1, anti-proliferative	High density, very high intensity
6	<a href="#">Dsp</a>	desmoplakin	High density, very high intensity
7	<a href="#">Trpc6</a>	transient receptor potential cation channel, subfamily C, member 6	High density, very high intensity
8	<a href="#">Cyp7b1</a>	cytochrome P450, family 7, subfamily b, polypeptide 1	High density, very high intensity
9	<a href="#">Foxo1</a>	forkhead box O1	Medium density and high intensity
10	<a href="#">Pitpnm2</a>	phosphatidylinositol transfer protein, membrane-associated 2	High density, very high intensity
11	<a href="#">Abcb10</a>	ATP-binding cassette, sub-family B (MDR/TAP), member 10	Medium density and high intensity
12	<a href="#">Krt9</a>	keratin 9	Medium density and high intensity
13	<a href="#">Mcm6</a>	minichromosome maintenance deficient 6 (MIS5 homolog, <i>S. pombe</i> ) ( <i>S. cerevisiae</i> )	High density, very high intensity
14	<a href="#">Npy1r</a>	neuropeptide Y receptor Y1	High density, very high intensity
15	<a href="#">Plekha2</a>	pleckstrin homology domain-containing, family A (phosphoinositide binding specific) member 2	High density, very high intensity
16	<a href="#">A330019N05Rik</a>	RIKEN cDNA A330019N05 gene	High density, very high intensity
17	<a href="#">Lct</a>	lactase	High density, very high intensity
18	<a href="#">Pdyn</a>	prodynorphin	High density, very high intensity
19	<a href="#">Gabrd</a>	gamma-aminobutyric acid (GABA-A) receptor, subunit delta	Medium density and high intensity
20	<a href="#">Btbd3</a>	BTB (POZ) domain containing 3	High density, very high intensity
21	<a href="#">Tdo2</a>	tryptophan 2,3-dioxygenase	Medium density and high intensity
22	<a href="#">C78409</a>	expressed sequence C78409	Medium density and very high intensity
23	<a href="#">LOC432928</a>	similar to PAPIN	Medium density and high intensity
24	<a href="#">Spag5</a>	sperm associated antigen 5	Scattered density and high intensity
25	<a href="#">3110082D06Rik</a>	RIKEN cDNA 3110082D06 gene	Medium density and high intensity
26	<a href="#">Zim2</a>	zinc finger, imprinted 2	Scattered density and high intensity
27	<a href="#">2700045P11Rik</a>	RIKEN cDNA 2700045P11 gene	High density, very high intensity
28	<a href="#">Adamts17</a>	ADAM metallopeptidase with thrombospondin type 1 motif, 17	Medium density and high intensity
29	<a href="#">Npnt</a>	nephronectin	High density and intensity
30	<a href="#">Slc39a6</a>	solute carrier family 29 (nucleoside transporters), member 4	High density and intensity
31	<a href="#">Slc29a4</a>	solute carrier family 39 (metal ion transporter), member 6	High density, very high intensity
32	<a href="#">Al841794</a>	expressed sequence Al841794	High density and intensity
33	<a href="#">Crif1</a>	cytokine receptor-like factor 1	High density, very high intensity
34	<a href="#">Gm837</a>	gene model 837, (NCBI)	High density and intensity
35	<a href="#">Tiam1</a>	T-cell lymphoma invasion and metastasis 1	High density, very high intensity
36	<a href="#">Stxbp6</a>	syntaxin binding protein 6 (amisyn)	High density, very high intensity
37	<a href="#">Dock10</a>	dedicator of cytokinesis 10	High density, very high intensity
38	<a href="#">C230030N03Rik</a>	RIKEN cDNA C230030N03 gene	Medium density and high intensity
39	<a href="#">6330514A18Rik</a>	RIKEN cDNA 6330514A18 gene	High density, very high intensity
40	<a href="#">Igsf3</a>	immunoglobulin superfamily, member 3	High density, very high intensity
41	<a href="#">BC056349</a>	cDNA sequence BC056349	High density and intensity
42	<a href="#">Syn3</a>	synapsin III	High density and intensity
43	<a href="#">Prox1</a>	prospero-related homeobox 1	High density and intensity
44	<a href="#">Cblb</a>	Casitas B-lineage lymphoma b	Medium density and high intensity
45	<a href="#">Rreb1</a>	ras responsive element binding protein 1	High density and intensity

## Enriched Expression in DGsg with little to no Expression in DGpo and/or DGmo

1.C1ql2



2.6430709H04Rik



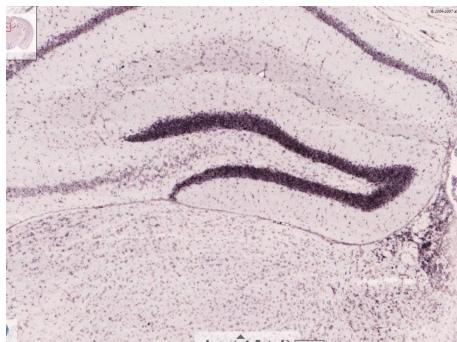
3.Sipa1l2



4.C630035N08Rik



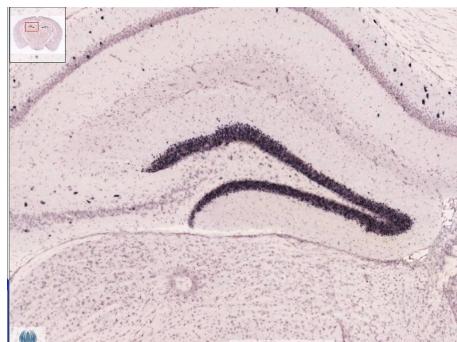
5.Btg1



6.Dsp



7.Trpc6



8.Cyp7b1



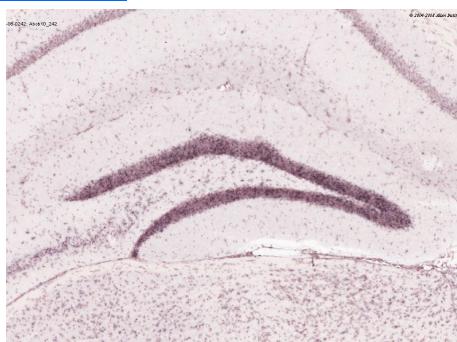
9.Foxo1



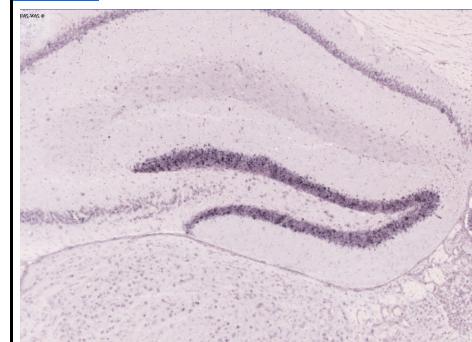
10.Pitpnm2



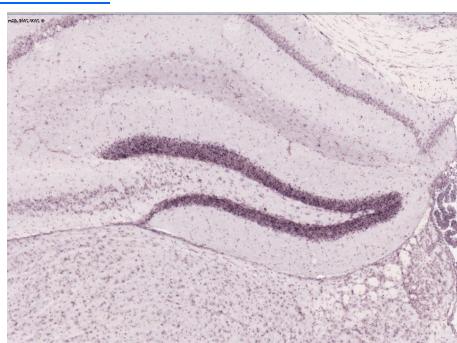
11.Abcb10



12.Krt9



13.Mcm6



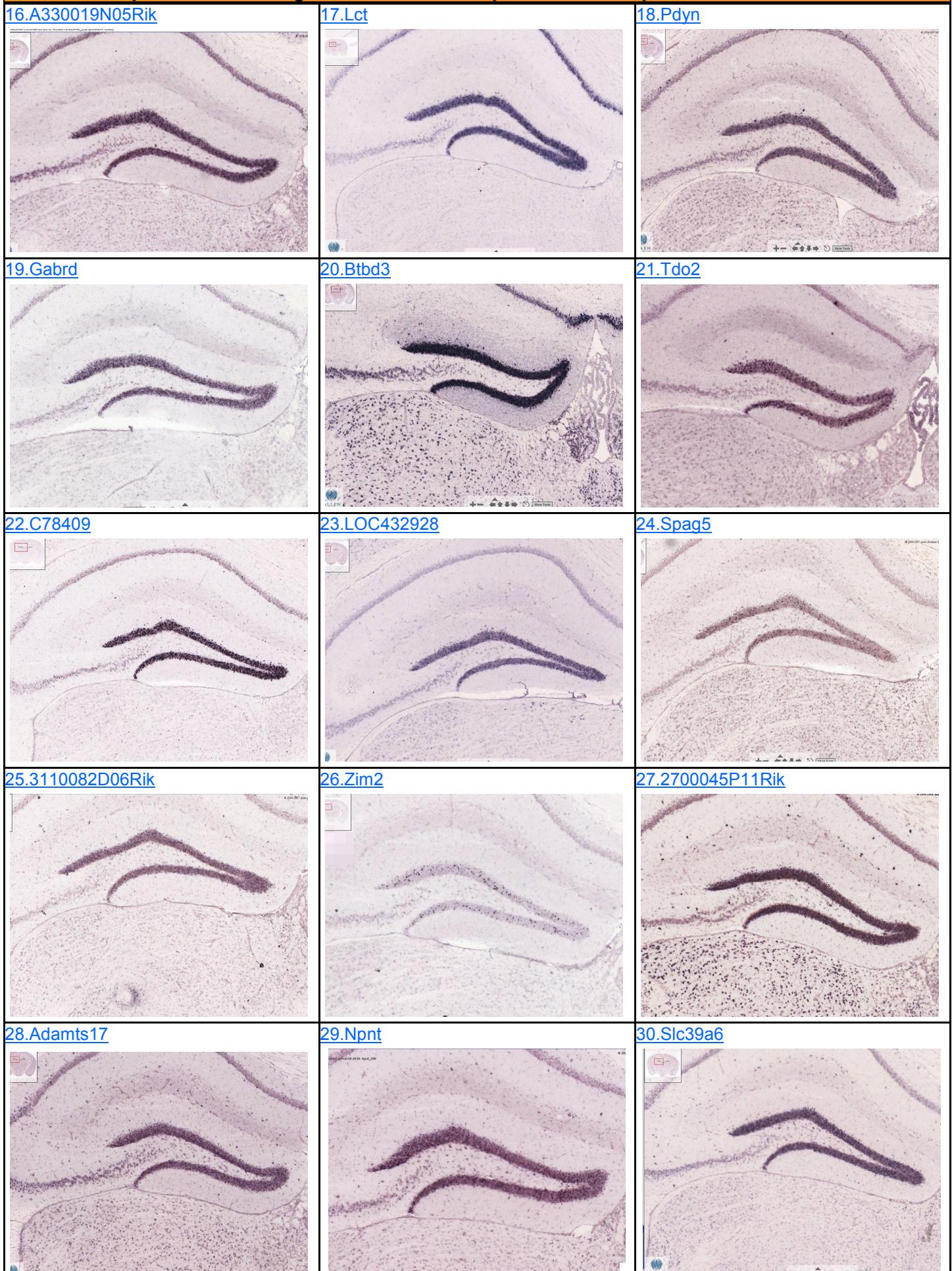
14.Npy1r



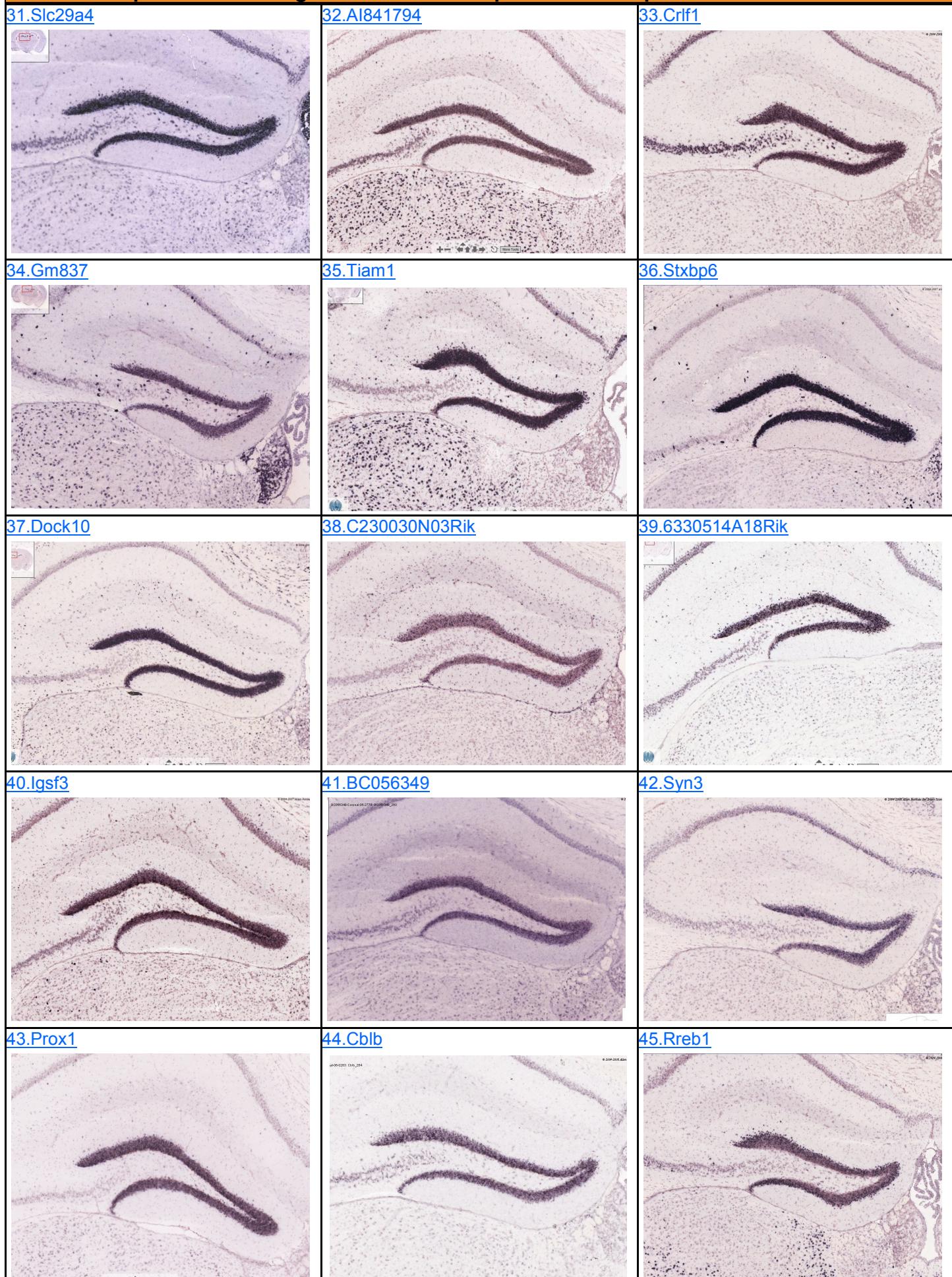
15.Plekha2



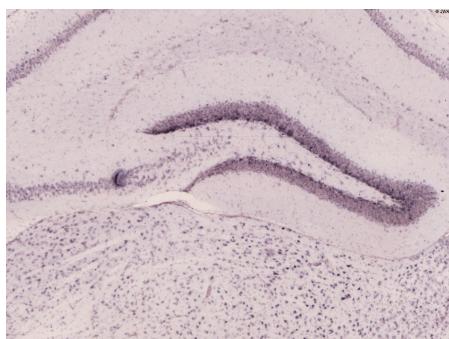
## Enriched Expression in DGsg with little to no Expression in DGpo and/or DGmo



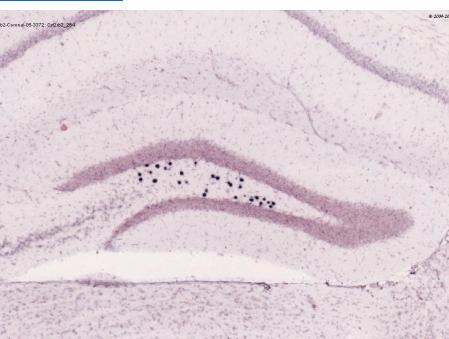
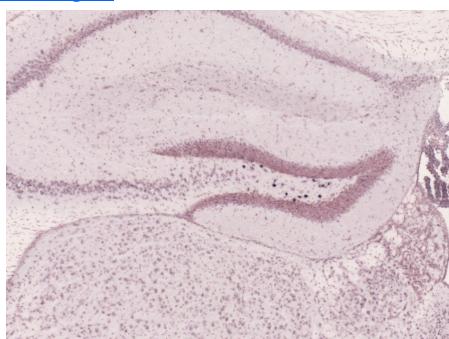
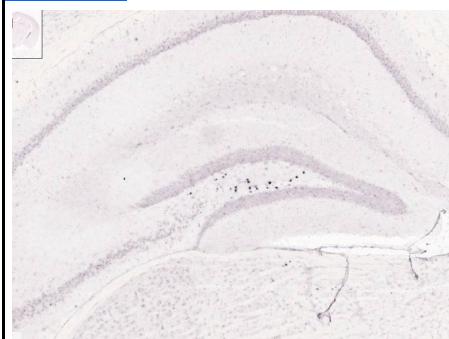
## Enriched Expression in DGsg with little to no Expression in DGpo and/or DGmo



## Subgranular Zone Enrichment

Number	Gene Symbol	Gene Name	Expression Pattern
46	<a href="#">Neurod1</a>	neurogenic differentiation 1	High density and intensity
47	<a href="#">D0H4S114</a>	DNA segment, human D4S114	Medium density and high intensity
46.Neurod1	47.D0H4S114		
			

## Expression Restricted to the Polymorph Layer

Number	Gene Symbol	Gene Name	Expression Pattern
48	<a href="#">Csf2rb2</a>	colony stimulating factor 2 receptor, beta 2, low-affinity (granulocyte-macrophage)	Scattered density and very high intensity
49	<a href="#">Cage1</a>	cancer antigen 1	Scattered density and very high intensity
50	<a href="#">Col6a3</a>	procollagen, type VI, alpha 3	Scattered density and very high intensity
48.Csf2rb2	49.Cage1	50.Col6a3	
			

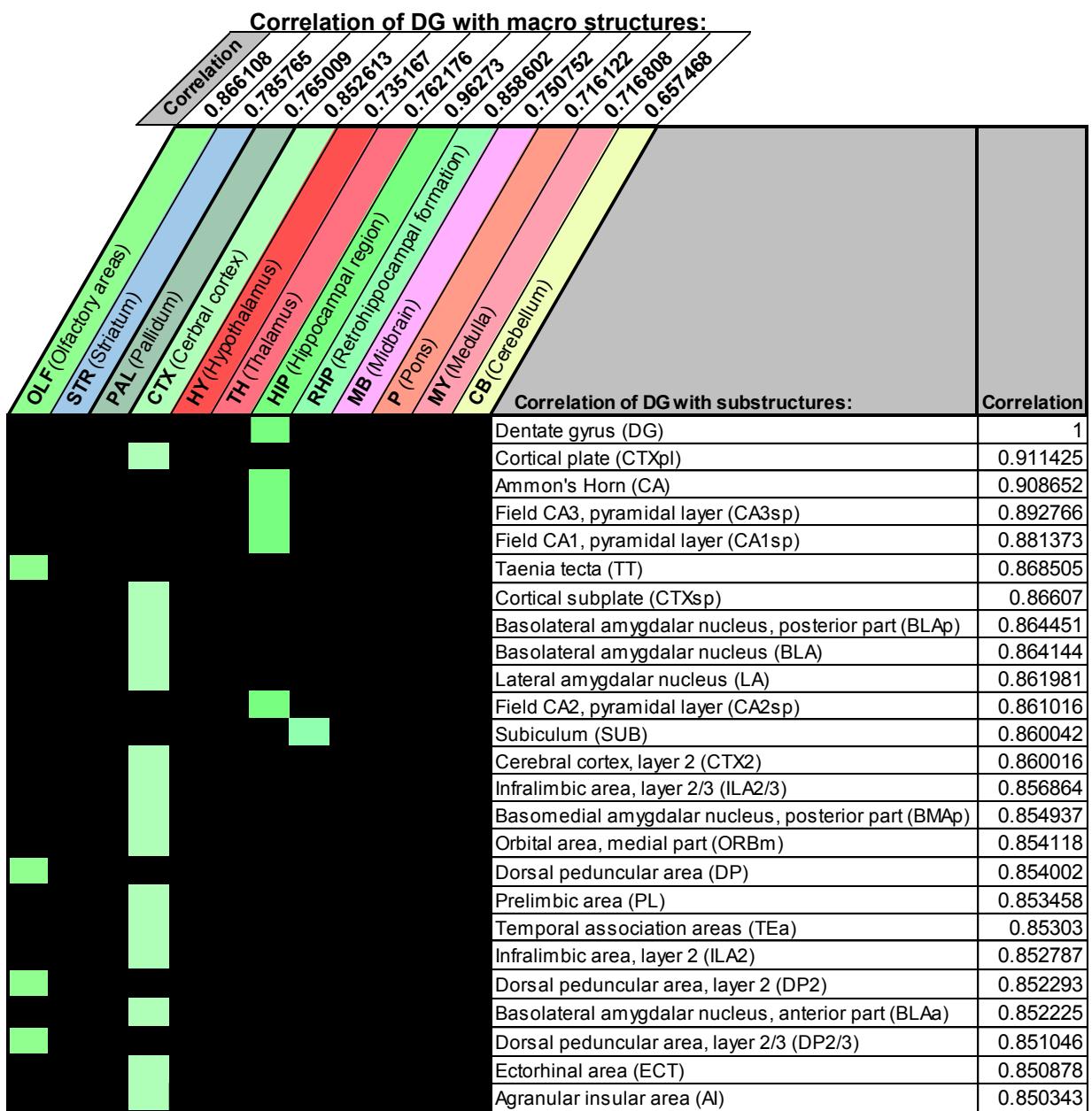
## Correlated Expression:

The ABA coronal set contains many genes of known scientific interest as well as genes exhibiting combinatorial or unique expression patterns. A correlation analysis of all available ABA coronal experiments ( $n=4376$ ) was performed by comparing the expression value of the dentate gyrus to expression values in other regions of the brain. Following [image analysis](#), the data values for each experiment were mapped to a 3-D reference brain at  $(200\mu\text{m})^3$  voxel resolution. Then, each voxel was assigned a single expression value based on the product of density and intensity of expression. Values from all 4376 experiments were computed, and the likelihood of co-expression between any two voxels or regions are reported as a Pearson's correlation coefficient.

For the purposes of determining correlated expression between the dentate gyrus and other brain regions, expression values from all voxels within the dentate gyrus were aggregated to form a single expression value. Two types of comparisons were then made. First, the aggregate expression values of the dentate gyrus and those of other anatomically defined regions (~200 structures) were compared within the 3-D reference brain (structure vs. structure; table below). Second, a color map was then generated to display the correlation between the dentate gyrus and each of the ~53,000 voxels of the reference volume (structure vs. voxel; correlation map on the following page).

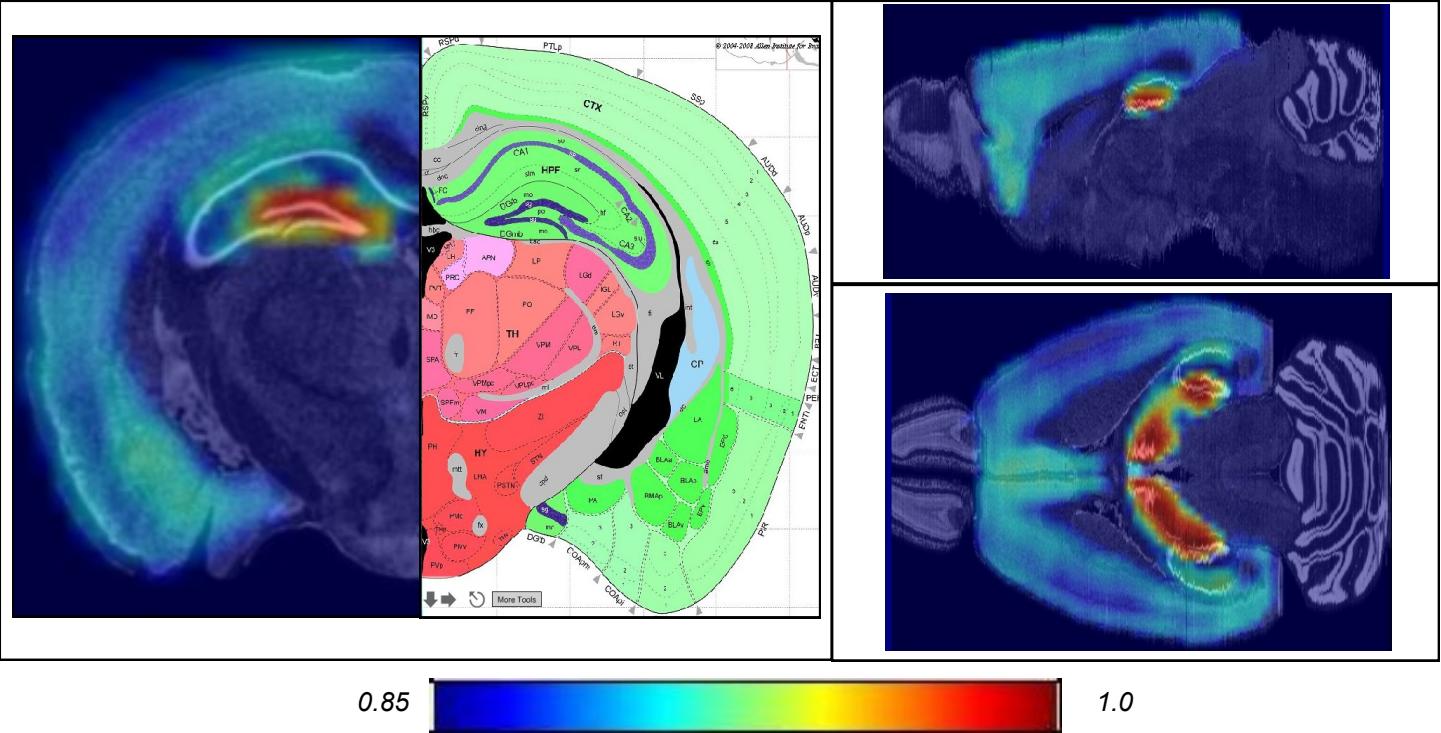
### STRUCTURE vs. STRUCTURE

The expression value of the dentate gyrus was compared to expression values for all other defined atlas regions. Degree of correlation is displayed as a comparative fraction, with self-correlation = 1.000. Correlation between the dentate gyrus and macro/parent-structures are presented, as well as correlation between the dentate gyrus and the 25 highest ranking substructures. The most highly correlated macro/parent-structures don't always contain the 25 top most correlated substructures. Columns match the Allen Reference Atlas palette.

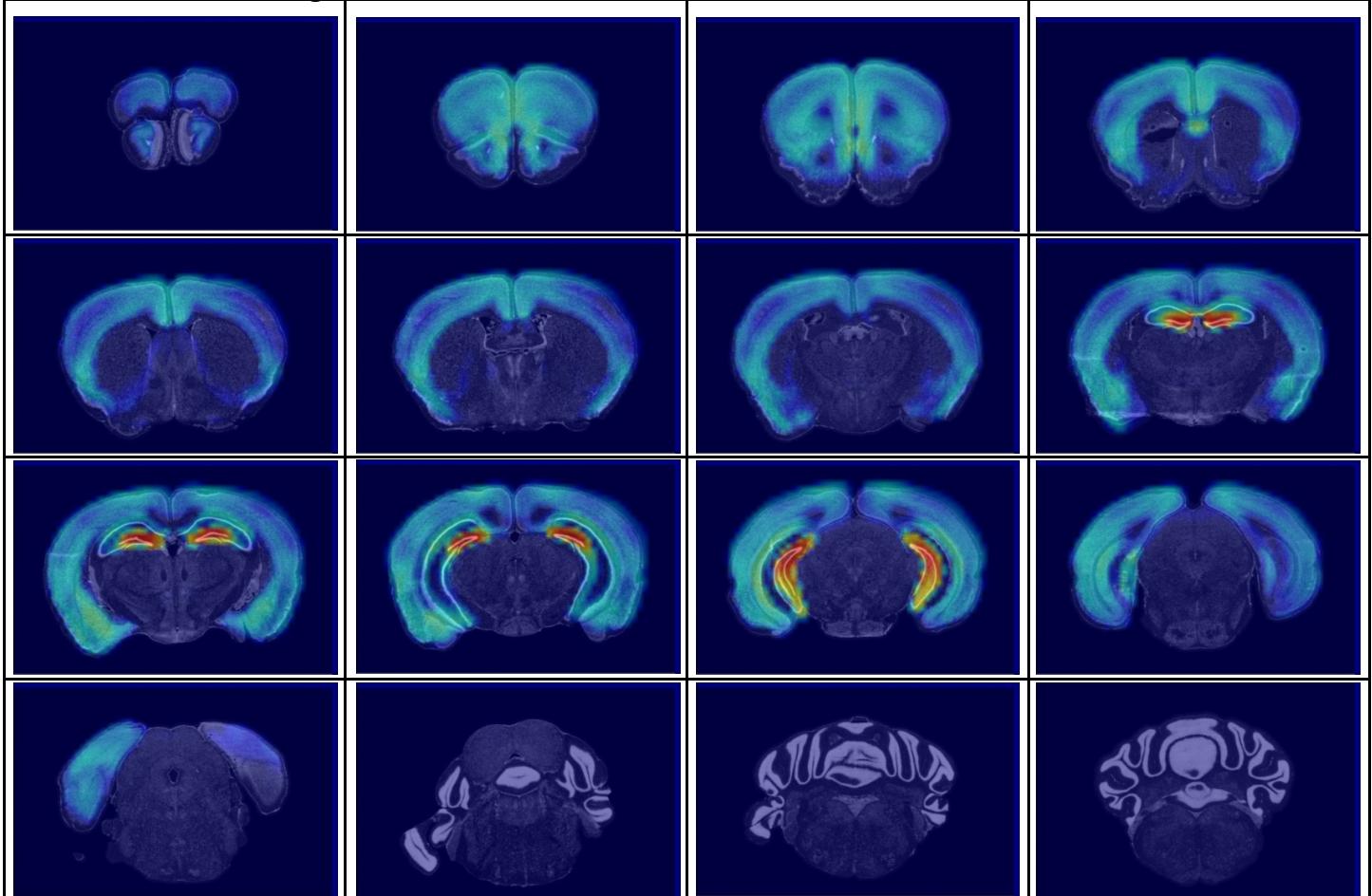


## STRUCTURE vs. VOXEL:

Correlation between the dentate gyrus and all other ( $200\mu\text{m}$ )<sup>3</sup> voxels in the brain. Degree of correlation assessed for each voxel is provided visually (lower value = the correlation value of the 25th ranked substructure reported on the previous page) using the "jet" color scale at rostrocaudal levels throughout the brain.



Coronal series through brain:



# Gene Ontology (GO) Analysis:

## GO TABLE:

Below is an ontological analysis of the 50 Select Genes, using [DAVID](#) Bioinformatics Resources. The functional terms that follow were returned using these constraints:

Category	Definition	Constraints
P-value	Probability that the term is over-represented in this 50 Select Genes list relative to the mouse genome	when $p \leq 0.05$
Gene Count	The minimum number of genes that must fall into an ontological category to be considered a group	5 genes per term group
GO Level	The level of functional specificity for GO functional categories: Molecular Function (mf), Biological Process (bp) and Cellular Components (cc)	Level GO_All
# of DAVID IDs	Number of unique DAVID gene IDs from user's input list	47 DAVID gene IDs/ 50 input genes

Date of table completion: April 2008

GO Category	GO Term	Gene Count	% of Genes	p-value
GOTERM_BP_ALL	establishment of localization	15	31.91%	0.0019
GOTERM_BP_ALL	localization	15	31.91%	0.002064
GOTERM_BP_ALL	transport	14	29.79%	0.002594
GOTERM_MF_ALL	transporter activity	8	17.02%	0.037463

Glynn Dennis Jr., Brad T. Sherman, Douglas A. Hosack, Jun Yang, Michael W. Baseler, H. Clifford Lane, Richard A. Lemicki. "DAVID: Database for Annotation, Visualization, and Integrated Discovery." *Genome Biology*. 2003 4(5): P3.

## DENTATE GYRUS Summary:

### Anatomy

- The dentate gyrus is composed of three regions (crest, lateral blade and medial blade) and three cell layers (molecular, granule and polymorph).
- The granule layer contains many small, densely packed and uniformly sized cells. The molecular layer, superficial to the granule cell layer, is a cell sparse area with cells of varying sizes. The polymorph layer, positioned between the two blades, contains a sparse distribution of large polymorphic cells.
- The borders between the layers within the dentate gyrus are clear and distinct, however the border between the polymorph cell layer and the pyramidal cells of CA3 is harder to discern in Nissl stained sections.
- The subgranular zone, one of the few regions in which adult neurogenesis occurs, is located at the interface of the granule and polymorph layers.

### Expression Patterns of the 50 Select Genes

- The most common expression pattern seen in these selected genes shows enriched expression in the DGsg with little to no expression in DGpo and/or DGmo.
- Heterogeneous expression in the granule cell layers can be observed across the septotemporal extent of the dentate gyrus for some genes, including *Dsp* and *Lct*, which exhibit septal enrichment.

### Correlation

- Gene expression patterns in the DG are highly correlated with expression in other hippocampal regions.
- Gene expression is also correlated with expression in the cerebral cortex, particularly with other limbic and paralimbic regions.
- Correlation of the gene expression in DG with individual voxels highlights regional differences in gene expression within the cortex.

We encourage you to reply with any comments or questions by email to [Annotation@alleninstitute.org](mailto:Annotation@alleninstitute.org). To further explore the gene expression data and analytical tools referred to in this report, please access our genome-wide data set at [brain-map.org](http://brain-map.org).

## Other Tools:

### NEUROBLAST:

Many of the 50 genes listed in this report can be used to explore the NeuroBlast tool. This unique mining tool works seamlessly from within brain-map.org to produce a list of genes that share similar expression patterns to any gene in the coronal data set. Search for and select any gene, then select one of several brain regions from the NeuroBlast drop-tab to explore a ranked list of similarly expressed genes for that region.

To learn more about this function, please refer to the [NeuroBlast white paper](#).

### BRAIN EXPLORER:

To compare gene expression levels across anatomical structures in 3-D detail, download the [Brain Explorer](#) desktop application. This program is used to view gene expression in 3-D view (coronal, sagittal, horizontal and everywhere in between) across all brain structures and allows for simultaneous viewing of multiple expression profiles.

The NeuroBlast spatial homology function and an anatomic search tool are also available from within Brain Explorer to allow the user to search for and visualize genes with similar expression patterns.