

ANNOTATION REPORT



MOTOR NUCLEUS OF THE TRIGEMINAL NERVE (V)

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Introduction

This report contains a summary of expression patterns for genes that are enriched in the motor nucleus of the trigeminal nerve (V) of the pons. All data is derived from the <u>Allen Brain Atlas</u> (ABA) in situ hybridization mouse project. The structure's location and morphological characteristics in the mouse brain are described using the Nissl data found in the <u>Allen Reference Atlas</u>. Using an established algorithm, the expression values of the motor nucleus of the trigeminal nerve were compared to the values of its larger parent structure, in this case the pons, for the purpose of extracting regionally selective gene expression data. The highest ranking genes were manually curated and verified. 50 genes were then selected and compiled for expression analysis. 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 <u>ABA</u>. Correlations between gene expression in the motor nucleus of the trigeminal nerve 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: 101-108 Allen Reference Atlas Sagittal Levels: 11-14

Shown below is a plate from the Allen Reference Atlas, depicting the motor nucleus of trigeminal (level 104):



Description of Structure:

LOCATION and STRUCTURAL ANATOMY:

The hierarchical relationship within the brain is depicted below in the structure <u>legend</u>. The Allen Reference Atlas (based on Nisslstained sections scanned at 10X) was the primary resource for the following descriptions.

For additional information please refer to the <u>Allen Reference Atlas white paper</u>. <u>BrainInfo</u> houses a search engine that allows searches for structure name aliases.

The motor nucleus of the trigeminal nerve (V) is located in the lateral region of the pons, within the lateral aspect of the pontine reticular nucleus (PRN). In the coronal plane, it first emerges at the level at which the trigeminal nerve root exits the pons, and terminates caudally at the border between the pons and the medulla. Laterally, the nucleus is bordered by the motor root of the trigeminal nerve (moV), which separates the motor nucleus from the principal sensory nucleus of the trigeminal nerve (PSV). It is bordered ventrocaudally by the facial motor nerve (VIIn), and dorsally by the supratrigeminal nucleus (SUT).

In the sagittal plane, at medial aspects of the motor nucleus, V sits within the posterior aspect of the PRN, ventral to the SUT. The facial nerve is positioned caudal to the motor nucleus, providing orientation as to the placement of V. At more lateral aspects, prior to the emergence of the SUT, it is located in the rostral portion of the PRN.

The neurons within the motor nucleus are larger than the neurons in the neighboring PSV and PRN. They are more densely packed than the large neurons of the PRN, making it easy to distinguish between these two structures. The motor nucleus of the trigeminal nerve is easily identified in both the coronal and sagittal NissI-stained sections.

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

	Allen Brain Atlas: Structural Relationships
	 Click on a row to see what structures it contains
sh	ow all hide all
	Basic Cell Groups and Regions
	Cerebellum [CB]
	Brain stem [BS]
	■ Interbrain [IB]
	m Midbrain [MB]
	E Hindbrain [HB]
	B Pons [P]
	Pons, sensory related [P-sen]
	B Pons, motor related [P-mot]
	Accessory abducens nucleus [ACVI]
	Accessory facial motor nucleus [ACVII] Deviated a subleme (D)
	■ Barrington's nucleus [B]
	■ Dorsal tegmental nucleus [DTN]
	Lateral tegriental nucleus [LTN] Dentine control grov [PCC]
	Pontine central gray [PC0] Pontine gray [PC1]
	■ Fontine gray [FO] ■ Pontine raticular puelous, caudal part [PPNe]
	Pontine reticular nucleus, caudar part [PRNv] Pontine reticular nucleus, ventral part [PRNv]
	Supranenual nucleus [SG]
	Superior salivatory nucleus [SSN]
	Supratrigeminal nucleus [SUT]
	■ Tegmental reticular nucleus [TRN]
	Motor nucleus of trigeminal [V]
	■ Abducens nucleus [VI]
	■ Facial motor nucleus [VII]
	■ Pons, behavioral state related [P-sat]
	medulla [MY]

Atlas and Nissl: Coronal:





In Situ Hybridization Expression Patterns of 50 Select Genes:

The in situ hybridization (ISH) data below presents the motor nucleus of the trigeminal nerve's 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 motor nucleus of the trigeminal nerve. 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 <u>Data Production Processes white paper</u>. To read about heat map conversion, refer to the <u>Informatics Data Processing white paper</u>. The expression data presented can be further explored, in coronal and sagittal planes, at <u>brain-map.org</u>.

The majority of the 50 Select Genes express with high density and high intensity throughout the motor nucleus of the trigeminal nerve. This type of expression, combined with the large motor neurons that comprise the nucleus, make it a readily discernable structure. For these 50 genes, expression was seen in almost all cells within the motor nucleus, with no evidence of either gradients or additional subdivisions of the nucleus itself. A small population of cells that only span a few coronal sections appear ventromedially to the main body of the nucleus and the vast majority of the 50 Select Genes express in this area.

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 the expression pattern of the motor nucleus of the trigeminal nerve.

ISH Dffa

Coronal: Expression of *Dffa* is widespread and intense, demonstrating the oblong shape of the nucleus. Note the small population of ventromedial cells.

Heat map

Coronal: Very high intensity labeling is obvious in the heat map image.



50 SELECT GENES:

This gene list was generated by manual curation of an <u>algorithmically</u> derived list that compared gene expression values of the motor nucleus of the trigeminal nerve to those of the pons. Categories of expression are subjectively grouped by relative expression characteristics.

Curation of 50 Select Genes List: July 2008

Widespread Expression		Pattern		
Number	Gene Symbol	Gene Name	Expression Pattern	
1	Hspb1	heat shock protein 1	High density, medium intensity	
		a disintegrin and metallopeptidase domain		
2	Adam19	19 (meltrin beta)	High density, medium intensity	
3	Layn	layilin	High density, very high intensity	
4	Pacro	Park2 co-regulated	High density, high intensity	
		potassium inwardly-rectifying channel, sub-		
5	Kcnj14	family J, member 14	High density, very high intensity	
6	Calcb	calcitonin-related polypeptide, beta	High density, very high intensity	
7	Ninj1	ninjurin 1	High density, medium intensity	
		cholinergic receptor, nicotinic, alpha poly-		
8	Chrna3	peptide 3	High density, high intensity	
9	Trhr	thyrotropin releasing hormone receptor	High density, medium intensity	
10	Pappa	pregnancy-associated plasma protein A	High density, high intensity	
		serine (or cysteine) peptidase inhibitor,		
11	<u>Serpina3k</u>	clade A, member 3K	High density, medium intensity	
12	Rspo2	R-spondin 2 homolog (Xenopus laevis)	High density, high intensity	
		solute carrier family 5 (choline transporter),		
13	<u>Slc5a7</u>	member 7	High density, very high intensity	
		protease, serine, 12 neurotrypsin		
14	Prss12	(motopsin)	High density, high intensity	
15	Lgals1	lectin, galactose binding, soluble 1	High density, very high intensity	
16	<u>Dmp1</u>	dentin matrix protein 1	High density, medium intensity	
47		serine (or cysteine) peptidase inhibitor,		
17	Serpinbba	clade B, member 6a	High density, very high intensity	
10	Cominala	serine (or cysteine) peptidase innibitor,	llish depait, madium interait,	
18	Serpinasc Om 500		High density, medium intensity	
19	GIII528 Cub5r1	gene model 528, (NCBI)	High density, high intensity	
20				
		activated channel subfamily M beta mem		
21	Kcnmh4	ber 4	High density, high intensity	
21	Tev261	testis expressed gene 261	Medium density, medium intensity	
23	<u>Slc41a3</u>	solute carrier family 41 member 3	High density, very high intensity	
20	Nrn1	neuronilin 1	High density, very high intensity	
		ectonucleoside triphosphate diphosphohy-		
25	Entpd3	drolase 3	High density, high intensity	
26	Anxa2	annexin A2	High density, high intensity	
27	Trim16	tripartite motif protein 16	High density, medium intensity	
28	Dffa	DNA fragmentation factor, alpha subunit	High density, very high intensity	
29	Cda	cvtidine deaminase	High density, medium intensity	
30	Cd59a	CD59a antigen	High density, high intensity	
31	2610019F03Rik	RIKEN cDNA 2610019F03 gene	High density, high intensity	
32	Sox14	SRY-box containing gene 14	Medium density, low intensity	
		calcitonin/calcitonin-related polypeptide.	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
33	Calca	alpha	High density, very high intensity	
34	Tmem74	transmembrane protein 74	High density, medium intensity	
		GTP binding protein (gene overexpressed		
35	Gem	in skeletal muscle)	High density, high intensity	
36	Lxn	latexin	High density, very high intensity	
37	Paqr8	progestin and adipoQ receptor family mem-	High density, medium intensity	

Widespread Expression Pattern					
Number	Gene Symbol	Gene Name	Expression Pattern		
		loss of heterozygosity, 11, chromosomal			
38	Loh11cr2a	region 2, gene A homolog (human)	Medium density, high intensity		
39	Dpysl3	dihydropyrimidinase-like 3	High density, high intensity		
40	<u>Msn</u> Ibrada O	moesin	High density, very high intensity		
41		IBR domain containing 2	Viedium density, medium intensity		
42	<u>VVISI</u>	solute carrier family 18 (vesicular monoam			
43	SIc18a3	ine), member 3	High density, very high intensity		
44	D930040M24Rik	RIKEN cDNA D930040M24 gene	Medium density, low intensity		
		RIKEN cDNA A330043P19 gene (non-			
45	A330043P19Rik*	RefSeq)	High density, very high intensity		
		DNA segment, Chr 13, Brigham & Womer	's		
46	D13Bwg1146e	Genetics 1146 expressed	High density, medium intensity		
47	Slc35f3	solute carrier family 35, member F3	High density, high intensity		
48	Rrad Tmom62a	Ras-related associated with diabetes	High density, IOW Intensity		
49	I Memb3C Slitek	transmembrane protein 63c	High density, high intensity		
UC 1 Heeb1	<u>SIIII K4</u>				
4.Pacrg		5.Kcnj14	6.Calcb		
<u>7.Ninj1</u>		8.Chma3	9.Trhr 1		



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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 (4376) was performed by comparing the expression value of the motor nucleus of the trigeminal nerve to expression values in other regions of the brain. Following <u>image analysis</u>, the data values for each experiment were mapped to a 3-D reference brain at $(200\mu m)^3$ 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 motor nucleus of the trigeminal nerve and other brain regions, expression values from all voxels within the motor nucleus of the trigeminal nerve were aggregated to form a single expression value. Two types of comparisons were then made. First, the aggregate expression values of the motor nucleus of the trigeminal nerve 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 motor nucleus of the trigeminal nerve 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 motor nucleus of the trigeminal nerve 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 motor nucleus of the trigeminal nerve and macro/parent-structures are presented, as well as correlation between the motor nucleus of the trigeminal nerve 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.

Correlation of the motor nucleus of the trigeminal nerve with macrostrue	ctures:
Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Constant Const	
(Contention of V with substructures	Correlation
Motor nucleus of trigeminal (V)	1
Facial motor nucleus (VII)	0.953486
Supratrigeminal nucleus (SUT)	0.952182
Lateral vestibular nucleus (LAV)	0.946214
Vestibular nuclei (VNC)	0.945164
Nucleus raphe magnus (RM)	0.942989
Inferior salivatory nucleus (ISN)	0.942613
Nucleus ambiguus (AMB)	0.939657
Paragigantocellular reticular nucleus (PGRN)	0.93956
Magnocellular reticular nucleus (MARN)	0.937785
Medial vestibular nucleus (MV)	0.934316
Hypoglossal nucleus (XI)	0.93378
Principal sensory nucleus of the trigeminal (PSV)	0.932107
Subceruleus nucleus (SLC)	0.929866
Red Nucleus (RN)	0.929273
Spinal nucleus of the trigeminal, interpolar part (SPVI)	0.929095
Linear nucleus of the medulla (LIN)	0.925068
Tegmental reticular nucleus (TRN)	0.924885
Superior olivary complex (SOC)	0.92226
Nucleus x (x)	0.920489
Spinal nucleus of the trigeminal, oral part (SPVO)	0.918403
Oculomotor nucleus (III)	0.918268
Lateral reticular nucleus (LRN)	0.918265
Cerebellar nuclei (CBN)	0.913978
Interposed nucleus (IP)	0.911639

STRUCTURE vs. VOXEL:

Correlation between the motor nucleus of the trigeminal nerve and all other $(200 \mu m)^3$ 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.



Gene Ontology (GO) Analysis:

GO TABLE:

Below is an ontological analysis of the 50 Select Genes, using <u>DAVID</u> 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 ≤ 0.05	
Gene Count	The minimum number of genes that must fall into an onto- logical category to be considered a group	5 genes per term group	
GO Level	The level of functional specificity for GO functional cate- gories: 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	49 DAVID gene IDs/ 50 input genes	

Date of table completion: July 2008

GO Category	GO Term	Gene Count	% of Genes	p-value
GOTERM_MF_ALL	enzyme inhibitor activity	6	12.24%	2.55E-04
GOTERM_MF_ALL	endopeptidase inhibitor activity	5	10.20%	6.85E-04
GOTERM_MF_ALL	protease inhibitor activity	5	10.20%	7.31E-04
GOTERM_BP_ALL	developmental process	15	30.61%	0.003049
GOTERM_BP_ALL	anatomical structure development	12	24.49%	0.003393
GOTERM_CC_ALL	membrane	30	61.22%	0.005016
GOTERM_BP_ALL	system development	10	20.41%	0.011239
GOTERM_BP_ALL	anatomical structure morphogenesis	8	16.33%	0.013500
GOTERM_CC_ALL	plasma membrane	12	24.49%	0.017106
GOTERM_CC_ALL	cell projection	5	10.20%	0.020549
GOTERM_BP_ALL	multicellular organismal development	11	22.45%	0.020719
GOTERM_MF_ALL	enzyme regulator activity	6	12.24%	0.025659
GOTERM_MF_ALL	cation transmembrane transporter activity	5	10.20%	0.032803
GOTERM_CC_ALL	extracellular region	12	24.49%	0.035155
GOTERM_BP_ALL	cell development	7	14.29%	0.049930

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

MOTOR NUCLEUS OF THE TRIGEMINAL NERVE Summary:

Anatomy

- The motor nucleus of the trigeminal nerve (V) is located in the lateral region of the pons, and is bordered by the pontine reticular nucleus (PRNc), the supratrigeminal nucleus (SUT), and the motor root of the trigeminal nerve (moV).
- The proximity of the motor nucleus of trigeminal to the facial nerve (VIIn) can be appreciated in the sagittal plane.
- Large, densely packed motor neurons comprise the motor nucleus of the trigeminal nerve and aid in distinguishing it from surrounding structures.

Expression Patterns of the 50 Select Genes

- All fifty genes examined showed widespread expression throughout the nucleus.
- Some genes, such as *Tex261* and *Loh11cr2a*, were expressed at a lower density, (i.e. scattered population of cells); however, no gradients or obvious subdivisions of the nucleus are revealed by this gene set.

Correlation

- The motor nucleus of the trigeminal nerve shows highest correlation with nuclei of the midbrain, the pons, the medulla, and the cerebellum.
- Additionally, within these areas, there is correlation with regions of the periaqueductal grey matter and subregions of the superior colliculus.
- Correlation of the motor nucleus of the trigeminal nerve with individual voxels throughout the cerebrum reveals gene expression in the globus pallidus and the zona incerta.

We encourage you to reply with any comments or questions by email to <u>!Annotation@alleninstitute.org</u>. To further explore the gene expression data and analytical tools referred to in this report, please access our genome-wide data set at <u>brain-map.org</u>.

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 <u>NeuroBlast white paper</u>.

BRAIN EXPLORER:

To compare gene expression levels across anatomical structures in 3-D detail, download the <u>Brain Explorer</u> 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.