RESEARCH ARTICLE

Differential CTCF binding in motor neurons and lymphocytes

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Abstract

Background: Diversity is critical to lymphocyte roles in the immune system and to neurons, which form complex network structures in the brain. Emerging evidence suggests that an increasing number of molecules associated with the immune system are also expressed in various central nervous system (CNS) regions and play crucial roles in brain development. Examination of shared molecular mechanisms underlying neurogenesis and lymphocyte differentiation may clarify relevant pathways, and suggests additional biomarkers in lymphocytes for neurological disorders. These results can contribute to find biomarkers that can be monitored through patient lymphocyte populations.

Methods: We analysed similarities and conserved regions in several genes regulated by CCCTC-binding factor (CTCF) during lymphocyte and neuronal developmental stages. We performed epigenetic analyses of CTCF binding *Trak1*, *Gabpa*, *Gabpb1*, *Gabpb2*, *Gfi1*, *Gfi1b* gene loci in T and B lymphocytes at different developmental stages, as well as in neural progenitor cells and motor neurons.

Results: Common and shared CTCF binding events at *Trak1* suggest additional transcriptional regulatory factors that control *Trak1* gene expression levels differ in neurons and lymphocytes. *Gabpb1* includes a common CTCF binding site shared with neurons and lymphocytes. Correlation of CTCF binding analysis and gene expression profile suggests that CTCF binding plays a role in epigenetic regulation of *Gabpb1* gene. While *Gfi1a* is phylogenetically well-conserved and CTCF sites are occupied in lymphocytes, there are no CTCF binding occupied in neurons and neural progenitor cells. Although *Gfi1b* is highly homologous to *Gfi1*, differences in expression levels suggest that *Gfi1b* is critical for both lymphogenesis and neurogenesis. Neurons and lymphocytes have multiple common CTCF binding sites in the *Gfi1b* gene.

Conclusions: The partial overlap in CTCF regulatory sites for some genes in neurons and lymphocytes suggests that there may be markers which can exhibit parallel changes in these cells and serve as biomarkers.

Keywords

CTCF, Trak1, Gabpa, Gabpb1, Gabpb2, Gfi1, Gfi1b, neurogenesis, lymphogenesis

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Abbreviations

CTCF: CCCTC-binding factor

ChIP-Seq: Chromatin immunoprecipitation coupled with deep sequencing

GEO: Gene Expression Omnibus

UCSC: University of California Santa Cruz

Introduction

Diversity is critical to lymphocyte roles in the immune system as well as to neurons, which form complex network structures in the brain (Morimoto and Nakajima, 2019). Emerging evidence suggests that an increasing number of molecules that are typically associated with the immune system are also expressed in various central nervous system (CNS) regions and play crucial roles in brain development (Morimoto and Nakajima, 2019). Examination of shared molecular mechanisms underlying neurogenesis and lymphocyte differentiation may give rise to a clearer definition of relevant pathways, and suggests additional biomarkers in lymphocytes for neurological disorders. These results can contribute to find biomarkers that can be monitored through patient lymphocyte populations.

In this study, we analysed similarities and conserved regions in several genes regulated by CCCTC-binding factor (CTCF) during lymphocyte and neuronal developmental stages. Genes of interest fell into two categories: a role in mitochondrial biology (*Trak1*, *Gabpa*, *Gabpb1* and *Gabpb2*) or differentiation factors (*Gfi1*, *Gfib*).

CTCF is a ubiquitously expressed zinc finger protein best known for its function in transcriptional insulation (Phillips and Corces, 2009). CTCF binds to insulator regions and physically blocks enhancer-promoter interactions (Holwerda and de Laat, 2013). Thus, it can be involved in either activation or repression of gene expression. Together with cohesin, CTCF is responsible for the regulation of higher order chromatin structure, allowing and/or blocking transcriptional machinery, gene rearrangements and enhancer-promoter activity (Lee and Iyer, 2012). CTCF is well known for its function in epigenetic regulation during lymphocyte differentiation (Gunal Sadik *et al.*, 2014), but has also been shown to play a role in the regulation of proliferation-differentiation equilibrium of neuroprogenitor cells during cortex formation (Watson *et al.*, 2014). As a result, examining the role of CTCF in regulating expression of specific genes in differentiation of neurons and lymphocytes may be informative.

Recent studies revealed that the co-localization of cohesin and CTCF at the variable IgH segments affects the usage of V gene segments during V(D) J recombination in pre-B cells. Cohesin and CTCF both facilitate long-range interactions between the V genes, the E μ enhancer and some 3' cohesin/CTCF binding sites (Gunal Sadik *et al.*, 2014; Guo *et al.*, 2011; Seitan *et al.*, 2012). CTCF is a key molecule playing critical roles in conformational changes in chromatin that determine cellular differentiation. It was found that significant changes in 390 transcripts of cortex and hippocampus occurred in CTCF knock-out mice (Hirayama *et al.*, 2012). To further investigate the potential role of CTCF in neuronal development, we analysed shared CTCF binding sites on several critical genes for neuronal and lymphocyte development using publicly available genomic data. We determined common as well as non-shared CTCF binding sites on these genes through developmental stages of neurons and lymphocytes. We also analysed changes in expression levels of these genes in neurons and lymphocytes and determined their sequence conservancy via phylogenetic analysis.

During brain development, changing local energy needs should be met during differentiation; thus, mitochondrial transport is critical for brain development (Ogawa *et al.*, 2013). These energy needs are fulfilled by mitochondria which facilitate ATP synthesis. Proper differentiation of cells depends on availability of required energy at times of necessity. In cells like neurons that show high levels of polarization, axonal transport mechanisms are dependent on proper mitochondrial function. One protein implicated in the transport of mitochondria in axons is *Trak1*, which is thought to play a critical role in the long-distance trafficking of mitochondria in axons (Melkov and Abdu, 2018; Ogawa *et al.*, 2013). However, *Trak1* is also expressed in lymphocytes, where distances traveled are shorter and the degree of polarization is lower. Can we gain insight into shared *Trak1* functions between neurons and lymphocytes by looking at its expression during differentiation of neurons and lymphocyte lineages?

Another transcription factor implicated in mitochondrial function is the GA binding protein (GABP) transcription factor, which is involved in mitochondrial biogenesis and expression of mitochondrial genes needed for ATP production (Yang *et al.*, 2014). This transcription factor binds to DNA sequences that are rich in the nucleotides guanine and adenine, and is composed of two subunits; GABP α and GABP β . GABP α comprises an ETS domain that binds to DNA. GABP β also contains four ankyrin repeats that mediate protein-protein interactions. GABP α /GABP β dimer contains a nuclear localisation signal for nuclear import. GABP regulates *Pax5* gene expression and plays role in B cell differentiation (Jing *et al.*, 2008), but little is known about its role in neuronal development.

Growth factor independence-1 (Gfi1), is a transcription factor which is involved in both neuronal and hematopoietic cell development. The deletion of Gfi1 in mice gives rise to defects in sensory neurons and developmental disorders in neuroendocrine cells and causes defective hematopoietic stem cells and neutrophil deficiency. Gfi1 mediates distinct stages of lymphocyte development due to its transcriptional repressor function, and is critical for early development of T lymphocytes (Kazanjian *et al.*, 2006). The role of Gfi1 in neuronal development is less well defined, but neurodegeneration due to mutations in Ataxin-1 (Spinocerebellar Ataxia type 1, SCA1) is thought to be mediated by interaction with Gfi1, and the loss of Gfi1 mimics the SCA1 phenotype (Tsuda *et al.*, 2005).

Gfi1b is 97% homologous to *Gfi1*. *Gfi1b* is fundamental for megakaryocytic and erythroid development (van der Meer *et al.*, 2010). Both are expressed in T-cell precursors as well (Kazanjian *et al.*, 2006). Gfi1 is a target for p53, and the regulation of hematopoietic stem cells via Gfi1 is mediated by p53. It is also involved in B cell differentiation, as *Gfi1* expression decreases in mature B cells (van der Meer *et al.*, 2010). *Gfi1b* is more widely expressed in adults than *Gfi1*, but little is known about *Gfi1b* function in neurons, and the deletion of *Gfi1b* in embryos is lethal (Wallis *et al.*, 2003). However, members of this family play an important role in neuronal development and maintenance. For example, the *Senseless* gene in *Drosophila melanogaster* and *Pag3* in *Caenorhabditis elegans* are orthologous to *Gfi1*. *Senseless* and *Pag3* are critical for neuronal development and sensory organ specification. Deletion of *Gfi1* causes deficiency in inner ear hair cells in mice, giving rise to hearing loss as well as reduced numbers of cochlear neurons. *Gfi1* also is expressed in cells of the peripheral nervous system, as well as inner ear hair cells, the eye, and rare pulmonary neuroendocrine cells (Kazanjian *et al.*, 2006).

To fully understand how differential expression of genes that direct development of both lymphocytes and neuronal cells can produce very different cell types, the mechanisms of functionally relevant regulatory genes should be analysed. Evaluating shared and lineage-specific mechanisms may shed light on common and cell type-specific control mechanisms in these distinct cell types. Genes that are controlled by shared regulatory mechanisms in different cell types might be major determinants of differentiation.

Methods

Comparative ChIP-Seq analysis

Publicly available CTCF ChIP-seq data files were downloaded from the Gene Expression Omnibus (GEO) online database as bed or bigwig files. Data was retrieved in University of California Santa Cruz (UCSC) Genome Browser as custom tracks. Visualisation of ChIP-seq peaks was performed using UCSC Genome Browser. GEO accession numbers of each data set are given in Table 1. UCSC gene references are used for gene annotations. Sequences of genes under investigation were annotated according to UCSC gene references. Data is analysed according to *Mus musculus* mm9 assembly.

Phylogenetic conservation analysis

Phylogenetic trees for genes were extracted from the Ensembl database by using the Gene Tree option under the Comparative Genomics section (Herrero *et al.*, 2016). *Mus musculus* gene IDs were given as query to create gene trees. Tree branches were collapsed at genus taxonomic rank and visualised accordingly. Gene Tree IDs are given in Table 2 for genes under investigation.

Phylogenetic gene trees depicting conserved domains for each gene were generated online using the Phylomedb pipeline (Huerta-Cepas *et al.*, 2014). The *Mus musculus* reference metatranscriptome model is chosen to visualise the mouse gene as seed.

Comparative gene expression analysis:

Gene expression values were retrieved from the murine gene atlas data set, GNF Mouse GeneAtlas V3, with GEO Accession number GSE10246 (Su *et al.*, 2004). The GEO2R tool under NCBI GEO website was used to visualise gene expression levels of selected genes expressed in two groups of samples: lymphocytes and neurons. GEO accession numbers are given in Table 3. Gene expression profile graphs were generated by submitting the identifier ID for each gene from the ID column of the Platform record.

Table 1. List of publicly available CTCF ChIP-Seq data.

Cells	GEO Accession Number
Neural progenitor cells	GSE65748
Differentiated motor neurons	GSM1468394
Pro B cells	GSM1023420
Double positive T cells	GSM1023418
Double negative T cells	GSM1023416

Table 2. Gene Tree IDs and accession links.

Gene	Gene Tree ID	Accession URL
<i>Trak1</i>	ENSGT00940000155697	https://identifiers.org/ensembl:ENSGT00940000155697
<i>Gabpa</i>	ENSGT00940000155799	https://identifiers.org/ensembl:ENSGT00940000155799
<i>Gabpb1</i>	ENSGT00940000157875	https://identifiers.org/ensembl:ENSGT00940000157875
<i>Gabpb2</i>	ENSGT00940000156794	https://identifiers.org/ensembl:ENSGT00940000156794
<i>Gfi1</i>	ENSGT00940000156166	https://identifiers.org/ensembl:ENSGT00940000156166
<i>Gfi1b</i>	ENSGT00940000160010	https://identifiers.org/ensembl:ENSGT00940000160010

Table 3. GEO accession number of tissues and cells used for gene expression analysis.

Cells	GEO Accession Number	Tissue
Neurons	GSM258617	Amygdala
	GSM258618	Amygdala
	GSM258637	Prefrontal cerebral cortex
	GSM258638	Prefrontal cerebral cortex
	GSM258671	Hippocampus
	GSM258672	Hippocampus
Lymphocytes	GSM258621	Marginal zone B cells
	GSM258622	Marginal zone B cells
	GSM258663	Follicular B cells
	GSM258664	Follicular B cells
	GSM258781	Double positive T cells
	GSM258782	Double positive T cells
	GSM258783	CD4 single positive T cells
	GSM258784	CD4 single positive T cells
	GSM258785	CD8 single positive T cells
	GSM258786	CD8 single positive T cells

Results and discussion

In this study, we performed epigenetic analysis of CTCF binding *Trak1*, *Gabpa*, *Gabpb1*, *Gabpb2*, *Gfi1*, *Gfi1b* gene loci at T and B lymphocytes at different developmental stages, as well as in neural progenitor cells and motor neurons. Genes of interest fell into two categories: a role in mitochondrial biology (*Trak1*, *Gabpa*, *Gabpb1* and *Gabpb2*) or differentiation factors (*Gfi1*, *Gfi1b*). Mitochondria play critical roles in both neuronal and lymphocytic lineages, but play different roles in the two lineages. Similarly, neuronal and lymphocytic lineages undergo multistep differentiation events leading to functionally diverse cell populations. Both lineages are affected by CTCF binding to genes that play a role in differentiation, so comparison of regulatory events in representative genes may begin to elucidate shared and distinct pathways.

We compared expression levels of these genes in the brain and lymphocyte populations using publicly available data and correlated these results with differential CTCF binding. Finally, phylogenetic analysis was performed for genes under investigation to identify highly conserved motifs. In these analyses, we observed common CTCF binding events as well as differential binding of CTCF in various cell types at different stages. When differential binding events were compared to gene expression levels, expression levels correlated with selective binding or non-binding of CTCF at these genes. Genes under investigation in this study play critical roles in the development of both lymphocytes and neurons. Significantly, some genes epigenetically regulated by CTCF exhibited similar control mechanisms during differentiation of neurons and lymphocytes, but these analyses also revealed the use of lineage-specific binding domains.

lineages, but not in B cells. In contrast, both B and T cells as well as mature motor neurons exhibited binding at site b, but there was no signal at site b in neuronal progenitors. Due to limitations of publicly available data, gene expression levels were only investigated in mature neurons in this study. Common and shared CTCF binding events on the *Trak1* gene suggest further transcriptional regulatory factors controlling *Trak1* gene expression levels that differ in neurons and lymphocytes. Identification of factors that bind at site c in neurons, neural progenitors and B cells, may reveal additional differentiation factors for *Trak1*.

This conclusion is reinforced by the phylogenetic analysis. When we analyzed CTCF binding sequences at sites a, b and c of the *Trak1* gene locus across species, we observed that site c is the most highly conserved sequence across species including *Rattus rattus* (Black rats), *Homo sapiens* (Humans), *Pan troglodytes* (Chimpanzees), *Pongo pygmaeus abelii* (Orangutans), *Canis familiaris* (Dogs) and *Equus caballus* (Horses). Sites a and b were also conserved, but conservation of site c as more prominent. This well-conserved site had specific CTCF binding in DN and DP T cells. In contrast, site a showed a high similarity in species *Homo sapiens*, *Pan troglodytes* and *Pongo pygmaeus abelii*. These two sites had differential CTCF binding profiles in B lymphocytes and neural progenitor cells. However, these three CTCF binding sites were not conserved in *Gallus gallus* and *Danio rerio* species, which suggests that this aspect appeared at the mammalian level and is absent in organisms whose immune system is regulated differently.

Unlike *Trak1*, *Gabpa* only had two CTCF binding sites (Figure 2A). Given the role of the GABP transcription factor in mitochondrial biogenesis (Yang et al., 2014) and its expression in all the lineages examined (Figure 2B), the limited extent of CTCF binding events was not expected. The CTCF binding sites were occupied for T lymphocyte differentiation, but not for neuronal or B cell lineages. In particular, the *Gabpa* gene exhibited a specific CTCF binding site in DP T cells shown in Figure 2A at site a and a specific binding event at site b in DN T cells. Transcriptional regulation of this gene might be of importance in T lymphocyte differentiation, given its higher expression levels in the T-cell lineage. However, there were no binding events observed in motor neurons, neural progenitor cells and proB cells. No differences were observed between *Gabpa* gene expression levels in DP and CD4+ and CD8+ T cells, although expression levels were generally higher in T cell lineages than in B cell and neuronal lineages. *Gabpa* gene expression in neurons and lymphocytes appears to be regulated independently of CTCF, which is consistent with limited conservation of CTCF binding sites in phylogenetic studies. Site b was only conserved between humans and *Equus caballus*. In contrast, site a was well conserved among *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii* and *Equus caballus* (Figure 2C).

Figure 2. A: Gene conservation and CTCF binding profile at *Gabpa* locus, B: *Gabpa* gene expression in neurons and lymphocytes, C: *Gabpa* gene phylogeny depicting conserved domains.

Although our phylogenetic analysis revealed that the *Gabpa* gene has the highest overall conservation profile amongst all genes under investigation, the absence of conserved CTCF binding is consistent with suggestions that *Gabpa* gene expression is regulated independently of CTCF.

In contrast to *Gabpa*, the *Gabpb1* gene included a common CTCF binding site shared with neurons and lymphocytes. Site a in **Figure 3A** was occupied in all cell types except proB cells, while site b was occupied in all cell types examined. Interestingly, *Gabpb1* gene expression was 2-to 3-fold higher in follicular B cells than thymocytes, and its expression in neurons was even lower (**Figure 3B**). CTCF binding at site a might regulate suppression of *Gabpb1* in T cells and neurons along with other transcription factors. The correlation between CTCF binding and gene expression profile suggests that CTCF binding plays a role in the epigenetic regulation of *Gabpb1* gene.

A common CTCF binding event (site b) at *Gabpb1* gene was well conserved in *Rattus rattus*, *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii*, *Canis familiaris* and *Equus caballus*. Site a, which was occupied in neurons and T cells, was conserved among *Rattus rattus*, *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii*.

Gabpb2 gene included a CTCF site common to all cells examined. There was only one CTCF site, site a which was only occupied in DP T cells. Like *Gabpa* and *Gabpb1*, *Gabpb2* was differentially expressed in neurons and lymphocytes (**Figure 4**). *Gabpb2* was highly expressed especially in B lymphocytes and moderately expressed in T lymphocytes, but showed almost no expression in the amygdala, hippocampus and prefrontal cortex. Similar to *Gabpb1*, *Gabpb2* expression was also suppressed more in neurons than lymphocytes. However, CTCF binding site at *Gabpb2* was conserved among more species than *Gabpb1*. This site was well conserved among *Rattus rattus*, *Cavia porcellus*, *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii*, *Canis familiaris* and *Equus caballus*. The role of CTCF binding in regulating *Gabpb2* in these cells was modest and may require interactions with other transcription factors.

Figure 4. A: Gene conservation and CTCF binding profile at *Gabpb2* locus, **B:** *Gabpb2* gene expression in neurons and lymphocytes, **C:** *Gabpb2* gene phylogeny depicting conserved domains.

Figure 5. A: Gene conservation and CTCF binding profile at *Gfi1* locus, **B:** *Gfi1* gene expression in neurons and lymphocytes, **C:** *Gfi1* gene phylogeny depicting conserved domains.

CTCF binding sites at *Gabp2* were evolutionarily more conserved than those at *Gabp1*, which may indicate that *Gabp1* has more specific roles in mediating neurogenesis and lymphocyte differentiation. Moreover, higher conservation of gene regulation via CTCF in primates suggest that the transcriptional suppression of the *Gabp1* gene might contribute to neuronal diversity in primates.

Gfi1 and Gfi1b are zinc-finger transcription factors which play a critical role in hematopoiesis (van der Meer *et al.*, 2010); however, *Gfi1b* was also expressed in neurons, while *Gfi1a* was low or absent from neurons (Figures 5 and 6). Both DP T lymphocytes and proB lymphocytes were occupied by CTCF. There were 3 CTCF binding sites at *Gfi1a* gene locus for DP T lymphocytes, but only one was shared with proB lymphocytes. *Gfi1a* gene expression was relatively higher in DP T lymphocytes than other lymphocytes and neurons. This might be due to several factors. Given the fact that CTCF plays a critical role in the differentiation of lymphocytes, elevated gene expression levels might be dependent on CTCF binding to these sites.

Unlike *Gfi1*, *Gfi1b* was expressed at moderate levels in both neuronal and lymphocyte lineages. Interestingly, there was only one conserved CTCF site at the *Gfi1b* gene locus, which was occupied in all cell types examined. Consistent with this, gene expression levels for *Gfi1b* were similar but not high in all cells. Both CTCF binding profile and gene expression levels were different than for *Gfi1*.

The CTCF binding event on the *Gfi1* gene which was shared in B and T cells was conserved among *Rattus rattus*, *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii*, *Canis familiaris* and *Equus caballus* as well as *Gallus gallus* and *Danio rerio*. A more in-depth analysis of these conserved sites in *Gallus gallus* and *Danio rerio* will shed light in understanding the potential roles of Gfi1 in the evolutionary variation of lymphocytes.

Figure 6. A: Gene conservation and CTCF binding profile at *Gfi1b* locus, B: *Gfi1b* gene phylogeny depicting conserved domains, C: *Gfi1b* gene expression in neurons and lymphocytes.

Gfi1a was phylogenetically well-conserved in many species. There were no CTCF binding occupying neurons and neural progenitor cells. Low expression levels of *Gfi1s* in neurons indicate that the regulation of this gene is CTCF-independent. Although *Gfi1b* is highly homologous to *Gfi1*, differences in expression levels suggest that *Gfi1b* is not only critical for lymphogenesis but also neurogenesis. The common CTCF site at *Gfi1b* gene was well conserved between *Rattus rattus*, *Homo sapiens*, *Pan troglodytes*, *Pongo pygmaeus abelii*, *Canis familiaris* and *Equus caballus*. *Gfi1a* domains were conserved in more species than *Gfi1b*, despite their homology, so it is considered to be the most ancestral gene.

Consequently, differences in the regulation mechanisms of neurogenesis and lymphopoiesis may contribute to the identification of new target and signaling pathways for neurodevelopmental diseases. In this case, there appears to be more parallels in transcriptional regulatory pathways between neuronal and B cell lineages than between T cell and neuronal lineages. This may reflect the common role of neurons and B cells as secretory cells. Regardless, this emphasizes the importance of selecting the appropriate targets and cell types in the search for plasma markers of neurodevelopmental and neurodegenerative diseases. In this context, specific transcriptional regulators that play a role in their different expression levels need to be identified, although they contain common CTCF binding sites in neurons and lymphocytes.

Data availability

Underlying data

CTCF ChIP-Seq:

- NCBI Gene Expression Omnibus: Genome-wide binding and mechanistic analyses of Smchd1 mediated epigenetic regulation [ChIP-Seq, MBD-Seq]. Accession number GSE65748, <https://identifiers.org/geo:GSE65748>
- NCBI Gene Expression Omnibus: CTCF.MN.WT [ChIP-Seq]. Accession number GSM1468394, <https://identifiers.org/geo:GSM1468394>
- NCBI Gene Expression Omnibus:CTCF_pro-B. Accession number GSM1023420, <https://identifiers.org/geo:GSM1023420>
- NCBI Gene Expression Omnibus:CTCF_DP ChIP_seq. Accession number GSM1023418, <https://identifiers.org/geo:GSM1023418>
- NCBI Gene Expression Omnibus:CTCF_DN ChIP_seq. Accession number GSM1023416, <https://identifiers.org/geo:GSM1023416>

Genes phylogenetic trees

- Ensembl Gene Tree: Trak1. Accession number ENSGT00940000155697; <https://identifiers.org/ensembl:ENSGT00940000155697>
- Ensembl Gene Tree: Gabpa. Accession number ENSGT00940000155799; <https://identifiers.org/ensembl:ENSGT00940000155799>
- Ensembl Gene Tree: Gabpb1. Accession number ENSGT00940000157875; <https://identifiers.org/ensembl:ENSGT00940000157875>
- Ensembl Gene Tree: Gabpb2. Accession number ENSGT00940000156794; <https://identifiers.org/ensembl:ENSGT00940000156794>
- Ensembl Gene Tree: Gfi1. Accession number ENSGT00940000156166; <https://identifiers.org/ensembl:ENSGT00940000156166>
- Ensembl Gene Tree: Gfi1b. Accession number ENSGT00940000160010; <https://identifiers.org/ensembl:ENSGT00940000160010>

Gene expression levels

- NCBI Gene Expression Omnibus: GNF Mouse GeneAtlas V3. Accession number GSE10246, <https://identifiers.org/geo:GSE10246>
- NCBI Gene Expression Omnibus: amygdala_4MJW061208119. Accession number GSM258617, <https://identifiers.org/geo:GSM258617>
- NCBI Gene Expression Omnibus: amygdala_4MJW061208120. Accession number GSM258618, <https://identifiers.org/geo:GSM258618>
- NCBI Gene Expression Omnibus: cerebral_cortex_prefrontal_4MJW061208177. Accession number GSM258637, <https://identifiers.org/geo:GSM258637>
- NCBI Gene Expression Omnibus: cerebral_cortex_prefrontal_4MJW061208178. Accession number GSM258638, <https://identifiers.org/geo:GSM258638>
- NCBI Gene Expression Omnibus: hippocampus_4MJW06120801. Accession number GSM258671, <https://identifiers.org/geo:GSM258671>
- NCBI Gene Expression Omnibus:hippocampus_4MJW06120802. Accession number GSM258672, <https://identifiers.org/geo:GSM258672>
- NCBI Gene Expression Omnibus: B-cells_marginal_zone_4MJW06120889. Accession number GSM258621, <https://identifiers.org/geo:GSM258621>
- NCBI Gene Expression Omnibus: B-cells_marginal_zone_4MJW06120890. Accession number GSM258622, <https://identifiers.org/geo:GSM258622>
- NCBI Gene Expression Omnibus: follicular_B-cells_4MJW06120849. Accession number GSM258663, <https://identifiers.org/geo:GSM258663>
- NCBI Gene Expression Omnibus:follicular_B-cells_4MJW06120850. Accession number GSM258664, <https://identifiers.org/geo:GSM258664>
- NCBI Gene Expression Omnibus: thymocyte_DP_CD4+CD8+_4MJW061208171. Accession number GSM258781, <https://identifiers.org/geo:GSM258781>
- NCBI Gene Expression Omnibus: thymocyte_DP_CD4+CD8+_4MJW061208172. Accession number GSM258782, <https://identifiers.org/geo:GSM258782>
- NCBI Gene Expression Omnibus: thymocyte_SP_CD4+_4MJW061208173. Accession number GSM258783, <https://identifiers.org/geo:GSM258783>
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- NCBI Gene Expression Omnibus: thymocyte_SP_CD8+_4MJW061208176. Accession number GSM258786, <https://identifiers.org/geo:GSM258786>

Competing interests

No competing interests were disclosed.

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