Cell type-specific transcriptome profiling in mammalian brains

Peter R. LoVerso¹, Feng Cui¹

¹Thomas H. Gosnell School of Life Sciences, Rochester Institute of Technology, One Lomb Memorial Dr., Rochester, NY 14623

TABLE OF CONTENTS
1. Abstract
2. Introduction
3. Identification and isolation of cell type-specific populations in a mammalian brain
   3.1. Common neural cell types
   3.2. Experimental techniques to isolate specific neural cell types
      3.2.1. LCM/LDM
      3.2.2. FACS
      3.2.3. PAN
      3.2.4. TRAP
4. Cell-type specific transcriptome profiling
   4.1. Expression profiling of acutely-isolated cells
   4.2. Expression profiling of cultured cells
5. Conclusions and future perspectives
6. Acknowledgement
7. References

1. ABSTRACT

A mammalian brain contains numerous types of cells. Advances in neuroscience in the past decade allow us to identify and isolate neural cells of interest from mammalian brains. Recent developments in high-throughput technologies, such as microarrays and next-generation sequencing (NGS), provide detailed information on gene expression in pooled cells on a genomic scale. As a result, many novel genes have been found critical in cell type-specific transcriptional regulation. These differentially expressed genes can be used as molecular signatures, unique to a particular class of neural cells. Use of this gene expression-based approach can further differentiate neural cell types into subtypes, potentially linking some of them with neurological diseases. In this article, experimental techniques used to purify neural cells are described, followed by a review on recent microarray- or NGS-based transcriptomic studies of common neural cell types. The future prospects of cell type-specific research are also discussed.

2. INTRODUCTION

The brain is one of the most complex and important organs in a mammal's body. A typical mammalian brain contains 10^8 (mouse) to 10^11 (human) neurons and even larger numbers of glia (1). It has been the subject of a great deal of research, due to its importance with respect to behavior, perception, thought, and emotion. It is also the root of a number of serious diseases, including dementia, epilepsy, strokes, headache disorders, Parkinson’s disease, and Alzheimer’s disease. The World Health Organization (WHO) published a report in 2007 estimating that up to 1 billion people, or one in six of the world’s population, suffer from neurological disorders (2). This indicates that these diseases pose a great threat to public health. Responding to this threat, the United States has launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative to develop new tools and technologies for deepening our understanding of the brain (3-5).

Neural tissues in mammals include a large number of cell types. Although much progress has been made in the development of techniques to identify common neural cell types, the total number of neural cell types and subtypes is still far from clear. As such, one of the priority research areas of the BRAIN Initiative is to differentiate neural cell types and determine their roles in health and disease (5). Successful implementation of the Initiative would facilitate a better understanding of various neurological diseases, aiding in their diagnosis and treatment.

High-throughput technologies, including microarrays (6, 7) and next-generation sequencing (NGS) (8, 9), have helped dissect numerous neurological diseases (reviewed in ref. 10-12) and allow brain functional
Transcriptomic profiling of mammalian neural cells

annotations at different levels. For instance, at the level of brain regions (e.g., prefrontal area), several studies have provided a comprehensive atlas of gene expression across the brain (13-15). At the level of single cells, expression profiling of tens of thousands of genes (16-19) has been achieved using multiplex PCR (20). However, the brain-wide data are difficult to interpret because the information is not available for the localization of individual transcripts at the cellular level (21, 22), whereas the single-cell methods have issues of increased false negatives and reduced reproducibility (23, 24). Given these difficulties, understanding of gene expression at the cellular level mainly comes from pooled cells obtained by several techniques such as laser-capture microdissection (LCM) (25-27), fluorescence-activated cell sorting (FACS) (28-32), immunopanning (PAN) (32-34), and translating ribosome affinity purification (TRAP) (35-38).

In this article, we will first provide an overview of common cell types in mammalian brains and of experimental techniques for cell purification and identification. Then, we will review recent microarray- and NGS-based studies on transcriptomics of specific neural cell type. The future prospects of cell type-specific studies are also discussed.

3. IDENTIFICATION AND ISOLATION OF CELL-TYPE SPECIFIC POPULATIONS IN A MAMMALIAN BRAIN

3.1. Common neural cell types

A mammalian brain is made up of a large number of cell types that are vital to proper functioning of the central nervous system (CNS). Foremost among them is neuron, a primary vehicle for long-distance electrical communication and computation among cells in mammals (39). Neurons are interconnected cells, each possessing a large cell body (soma), as well as cell projections called dendrites and an axon. The dendrites are thin, branched projections that receive neurotransmitters from other neurons, while the axon is a long projection sending electrical signals to the next neuron. Neurons send signals among themselves by changing electrical potentials, which can spread along the axon of a neuron. The bulb-like end of the axon, termed axon terminal, is separated from the dendrites of the next neuron by a narrow space (synapse). When electrical signals travel to the axon terminal, neurotransmitters are released across synapse and bind post-synaptic receptors, stimulating receiving neurons to modulate electrical potentials and continue nerve impulse. Neurons are arguably the most important cell type in the body, enabling computations required for vital behaviors such as balance, communication, and the ability to learn and make decisions. Changes in the gene expression of neurons can lead to an over- or under-expression of important genes, which can radically change the overall topology of the CNS and lead to severe disorders. For example, the Parkinson’s disease is characterized by an accumulation of alpha-synuclein and a subsequent deficiency of dopamine in the brain as the dopamine-producing cells die (40). The Huntington’s disease is caused by the production and accumulation of mutant Huntingtin (Htt) proteins (41).

Glia cells are non-neuronal cells, including astrocytes, oligodendrocytes, and microglia, which are smaller in size (compared with neurons) and vary in structure (42). Astrocytes are star-shaped cells with great structural complexity (43-45). Traditionally, astrocytes are considered to be ancillary, satellite cells that provide a physical support network to neurons, and regulate the environment so that neurons can function properly. As such, astrocytes maintain extracellular ion balance and pH homeostasis (46). They hold important stores of glycogen, providing surrounding cells with glucose as needed (47). Moreover, astrocytes interact with the synapses of neurons, and work to both produce and remove neurotransmitters and other compounds from the intercellular space (48). Recent studies have revealed new roles of astrocytes (49-52). First, astrocytes establish separate territories that define functional domains of a brain (49). Second, astrocytes can release neuroactive agents such as glutamate to modulate synaptic transmission (50). Third, astrocytes interact with neurons and endothelial cells to form higher-order gliovascular units, bridging neuronal and vascular structure to match local neural activity and blood flow (51). Currently, astrocytes are seen as an important communication element of the brain, and their dysfunction may lead to aberrations of neuronal circuitry that underlies several neurodevelopmental disorders such as the Rett syndrome (53) and the fragile X mental retardation (54) (reviewed in ref. 55, 56).

Besides astrocytes, oligodendrocytes and microglia are two types of glial cells. The main function of oligodendrocytes is to produce and maintain myelin sheath which wraps around axons. Myelin helps to support and insulate axons in the CNS. Oligodendrocyte progenitor cells (OPCs) are precursors to oligodendrocytes and can also differentiate into neurons and astrocytes. Microglial cells are resident macrophages that provide the first line of immune defense in the CNS. Oligodendrocytes and microglial cells account for 75.6% and 6.5% of the cerebral cortex glia, respectively (57).

3.2. Experimental techniques to isolate and purify specific neural cell types

Cell type-specific transcriptomics require completion of several steps (Figure 1). First, brain tissues need to be isolated as fixed/frozen sections or live samples. Second, cells of interest need to be identified and collected. Third, RNA from the collected cells needs to be extracted and, if necessary, amplified. Fourth, relative mRNA expression levels need to be measured...
Transcriptomic profiling of mammalian neural cells

Figure 1. Typical workflow of cell type-specific transcriptome profiling experiments. Cell-specific transcriptome profiling requires completing several steps such as brain sample collection, cell purification, RNA extraction, and RNA abundance measurement by microarray or RNA sequencing. At the last step, genes that are differentially expressed are identified by bioinformatic tools. If the protein products of these genes are directed to the surface of target cells, they can be used as cell markers. The cells presenting these proteins on the surface can be identified and purified by FACS and PAN. This process can undergo multiple iterations to differentiate a neural cell type into many subclasses.

by microarray or RNA-seq. Finally, downstream analyses need to be performed using bioinformatics tools. In this section, we focus on the first two steps because tissue heterogeneity of a mammalian brain has been a major obstacle (Figure 1). A pure collection of neural cells is the key to profiling cell-type specific transcriptomes. It is worth noting that the problem of neural cell identification has been discussed (58, 59). Cell type-specific markers and Cre-driver mouse lines are available to identify specific neural cell types (see online resources in ref. 60).

Technically, specific neural cell types can be harvested by four methods: (1) laser-capture microdissection (LCM) or laser-directed microdissection (LDM) (25-27); (2) fluorescence-activated cell sorting (FACS) (28-32); (3) immunopanning (PAN) (32-34); and (4) translating ribosome affinity purification (TRAP) (35-38). A quantitative analysis on cell type-specific microarray data has revealed that LCM and TRAP samples show significantly higher levels of contamination than FACS and PAN samples (60). Below, we provide a brief overview of these four methods.

3.2.1. LCM/LDM

LCM and LDM use a laser to isolate specific cell populations under a microscope from mounted thin-tissue sections that are either fixed or frozen. In LCM, a laser excises a small region (~7.5. μm) of a plastic membrane on the surface of tissue sections. Cells underneath adhere to the membrane upon cooling and are collected after the membrane is removed. One limitation of this method is that it does not allow users to extract a given cell by tracing its particular morphology. To overcome this limitation, LDM uses a much narrower ultraviolet laser
Transcriptomic profiling of mammalian neural cells

(~0.5. µm), which allows users to make precise cuttings along the outline of target cells.

3.2.2. FACS

FACS requires that target cells are labelled by fluorophores. The fluorophores are typically attached to antibodies that recognize a target feature on the cells. Based on the specific light scattering and fluorescent characteristics of each cell, FACS can sort a heterogeneous mixture of a cell population into subgroups that may belong to specific cell types. In FACS, the live, acutely-dissected brain tissue is digested in a protease solution with artificial CSF (ACSF), which keeps dissociated cells in a healthy condition. One main advantage of the FACS method is that it can sort a large number of cells in a high-throughput manner.

3.2.3. PAN

PAN relies on antibodies against specific proteins on the surface of target cells, not fluorescent signals. Panning plates are first coated with antibodies, and dissociated cells are then placed in the plates for 30 minutes to 1 hour, allowing target cells to bind the antibodies. The plates are then washed to collect the cells of interest. Multiple iterations of plating and antibody interactions may be required, which may be more time-consuming than other techniques.

3.2.4. TRAP

TRAP uses special transgenic mice with restricted cell populations in the CNS. TRAP harvests RNA on labelled polysomes directly from tissue homogenates. Only ribosome-associated mRNA rather than the full population of transcribed RNA is detected. As a result, the noncoding RNAs that play an important role in gene regulation are discarded. Since tissue homogenates are used for analysis, TRAP samples often have contamination, as shown by previous studies (61).

4. CELL TYPE-SPECIFIC TRANSCRIPTOME PROFILING

4.1. Expression profiling of acutely-isolated cells

Microarrays have been used to analyze the functional genomics of different cell types acutely purified from the brain (Table 1). One of the first examples came from Dugas et al. (62) who compared gene expression in the oligodendrocytes (OLs) generated from cultured oligodendrocyte progenitor cells (OPCs) in vitro and the OLs isolated acutely from animal brains. The OLs and OPCs were purified by PAN. Dugas et al. (62) found that OL differentiation occurs in at least two sequential stages, the early stage and the late stage, which are characterized by different expression patterns of transcription factors and myelin genes. Genes encoding cytoskeletal proteins are up-regulated during the OL differentiation. These findings were confirmed later by Cahoy et al. (32) who found that multiple signaling pathways including actin cytoskeleton signaling are enriched in the OLs. A separate study showed that a miRNA species, miR-9, is important for the OL differentiation and its expression inversely correlates with the expression of peripheral myelin protein PMP22 (64). This finding highlights the importance of miRNAs in neuronal cell specification (75).

Transcriptomic analyses of pooled neurons have shown that neurons have an elevated expression of genes involved in glycolysis and oxidative metabolism (63). The enzymes in the tricarboxylic acid (TCA) cycle are expressed at low levels. Several pathways involved in calcium signaling, axonal guidance signaling, glutamate receptor signaling, and GABA receptor signaling are enriched in neurons (32). Further studies on transcriptomes of rostral and caudal serotonin neurons provide evidence for the complexity of gene regulatory networks in different types of neurons (66). In particular, hundreds of transcripts are differentially expressed in rostral and caudal serotonin neurons, in which a homeodomain code seems to play a key role in differentiating these two types of neurons. Finally, gene expression profiling of neural stem cells (NSCs) has revealed that the growth factor insulin-like growth factor 2 (IGF2) is expressed at high levels, which suggests that IGF2 plays an important role in adult neurogenesis (68).

Expression profiling on isolated astrocytes has uncovered that the enzymes in the tricarboxylic acid (TCA) cycle are expressed at higher levels than in neurons (61). Not surprisingly, the TCA cycle is found to be one of the metabolic pathways enriched in astrocytes (32). Moreover, the Notch signaling pathway is one of the top pathways enriched in astrocytes. Although Notch signaling has been suggested to play a role in differentiating neural progenitor cells into astrocytes, these findings indicate that Notch signaling may be required for maintaining astrocyte fate, preventing them from reverting to undifferentiated states (76). Note that gene expression patterns in astrocytes vary as a function of age: young astrocytes have high expression levels of genes involved in neuronal differentiation and hemoglobin synthesis, whereas aged astrocytes are characterized by increased inflammatory phenotypes and zinc ion binding (70).

Transcriptomic analyses of purified microglia reveal distinct gene expression patterns for young and aged microglia. Young microglia cells are characterized with increased transcript levels of chemokines such as CCL2 and CCL7 (70). These chemokines have been linked to differentiation and maturation of neurons (77). By contrast, genes within the tumor necrosis factor-ligand family, such as TNFSF12 and TNFSF13b, are up-regulated in aged microglia (70, 78, 79). Microarray analyses on acutely-isolated brain endothelial cells (65) and Purkinje cells (67) have also provided cell type-specific gene signatures.
Transcriptomic profiling of mammalian neural cells

Table 1. Cell type-specific transcriptomic studies in mammalian brain

<table>
<thead>
<tr>
<th>Cell preparation</th>
<th>Purification</th>
<th>Cell type</th>
<th>Exp. method</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acutely purified</td>
<td>PAN</td>
<td>Oligodendrocyte</td>
<td>Microarray</td>
<td>62</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>LDM</td>
<td>Neuron</td>
<td>Microarray</td>
<td>26</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Astrocyte</td>
<td>Microarray</td>
<td>63</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>TRAP</td>
<td>24 Cell types</td>
<td>Microarray</td>
<td>32</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS, PAN</td>
<td>Astrocyte, neuron, oligodendrocyte</td>
<td>Microarray</td>
<td>64</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Oligodendrocyte</td>
<td>Microarray</td>
<td>65</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Endothelial cell</td>
<td>Microarray</td>
<td>66</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>5HT neuron</td>
<td>Microarray</td>
<td>67</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>LCM</td>
<td>Purkinje cell</td>
<td>Microarray</td>
<td>68</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Neural stem cell</td>
<td>Microarray</td>
<td>69</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Microglia</td>
<td>Microarray</td>
<td>70</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Astrocyte, microglia</td>
<td>Microarray</td>
<td>71</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS</td>
<td>Microglia</td>
<td>Microarray</td>
<td>72</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>LCM</td>
<td>Neuron</td>
<td>RNA-seq</td>
<td>73</td>
</tr>
<tr>
<td>Acutely purified</td>
<td>FACS, PAN</td>
<td>Astrocyte, neuron, oligodendrocyte, endothelial cell, microglia, pericyte</td>
<td>RNA-seq</td>
<td>74</td>
</tr>
<tr>
<td>Cultured</td>
<td></td>
<td>Oligodendrocyte</td>
<td>Microarray</td>
<td>62</td>
</tr>
<tr>
<td>Cultured</td>
<td></td>
<td>Astroglia</td>
<td>Microarray</td>
<td>32</td>
</tr>
<tr>
<td>Cultured</td>
<td></td>
<td>Microglia</td>
<td>Microarray</td>
<td>69</td>
</tr>
<tr>
<td>Cultured</td>
<td></td>
<td>Neuron</td>
<td>RNA-seq</td>
<td>74</td>
</tr>
<tr>
<td>Cultured</td>
<td></td>
<td>Astrocyte, neuron, oligodendrocyte progenitor cell</td>
<td>RNA-seq</td>
<td>92</td>
</tr>
</tbody>
</table>

The aforementioned gene expression profiling experiments are performed by microarrays. While microarray-based methods have been used for many years, these methods have numerous limitations. For example, microarrays can have cross-hybridization artifacts, detection difficulties due to the dye, and can be very limited in terms of alternative splicing (80). In recent years, next-generation sequencing (NGS) has become a popular tool for accurate, reproducible measurements of transcriptomics. This technique can provide sequences of all RNA molecules present within a cell, allowing for an accurate counting of different RNA species. RNA samples can be prepared from pooled cells, brain regions, or even individual cells (81).

Due to its unique ability to uncover details on both the expression level and isoform diversity, RNA sequencing (RNA-seq) has been used to identify gene expression signatures and gene splicing in acutely-isolated neurons (72) and microglia (71). Recently, Zhang et al. (73) used RNA-seq to generate transcriptome databases for eight cell types including neurons, astrocytes, oligodendrocyte precursor cells, newly formed oligodendrocytes, myelinating oligodendrocytes, microglia, endothelial cells, and pericytes from the mouse cerebral cortex. Remarkably, they found that the majority (~92%) of differentially expressed genes identified by microarray (32) are found by RNA-seq. As expected, the authors uncovered well-known cell type-specific markers, e.g., Aqp4 and Aldh111 for astrocytes, and Dlx1 and Stmn2 for neurons (32, 62, 65, 69, 71). Moreover, they have detected a large number of new genes with previously unknown cell type-specific distributions, highlighting the improved sensitivity of RNA-seq over microarrays. For example, the autism and schizophrenia-associated gene Tspan7 is enriched in astrocytes, whereas a gene encoding a novel transmembrane protein Tmem59l is enriched in neurons. These data have provided a set of cell type-specific transcription factors that are important for cell fate determination and differentiation. These databases also allow the detection of alternative splicing events in glia, neurons, and vascular cells of the brain. One important finding is that PKM2, the gene encoding the glycolytic enzyme pyruvate kinase, has unique splicing forms in neurons and astrocytes. This may explain how neurons and astrocytes differ in their ability to regulate the glycolytic flux and lactate generation (82-86).

4.2. Expression profiling of cultured cells

Before the development of technologies like LCM/LDM, FACS, PAN, and TRAP, primary cultures of neural cells such as astroglia (87) had served as
Transcriptomic profiling of mammalian neural cells

an *in vitro* proxy for studying *in vivo* astrocytes. These cultured astrocytes have phenotypic characteristics that are significantly different from their *in situ* counterparts. For instance, astrocytes *in situ* are highly polarized, with distinct sets of processes that project to either synapses or vascular walls (88, 89). Cultured astrocytes, however, appear non-polarized with an epithelioid-like shape in the cultures. Several studies have found that genes that are induced in the cultured astrocytes are not necessarily expressed *in vivo*, suggesting that cultured astroglia do not represent the same cell type as *in vivo* astrocytes (32, 90). This is not true however for oligodendrocytes and retinal ganglion cells (see below), suggesting that at least for certain neural cell types, cells cultured *in vitro* mimic those *in vivo*. Understanding the differences in gene expression between cells grown *in vitro* and those acutely purified from animal brains is critical for making the right decision on what cells can be used under which situation.

Dugas et al. have compared the transcriptomic profiles between cultured OLs and acutely-purified OLs, and found a remarkable similarity in gene expression between the two groups (62). This result indicates that normal OL differentiation can take place in the absence of heterologous cell-cell interactions. This similarity between cultured and acutely-isolated cells is also observed for retinal ganglion cells (91), but not for astrocytes (32) and microglia (69).

Recently, we conducted a comprehensive analysis of transcriptomes in cultured neurons, astrocytes and OPCs through RNA-seq, and identified cell-specific marker genes and characteristic pathways that are known for these cell types (92). We compared our RNA-seq data with those from Zhang et al. (73) and found a number of genes are differentially expressed in cultured cells compared to acutely isolated cells. We conclude that the findings obtained from cells cultured *in vitro* should not be extrapolated to cells *in vivo*, especially when targeting genes or pathways associated with neurological diseases.

5. CONCLUSIONS AND FUTURE PROSPECTS

During the past decade, various types of neural cells have been identified and isolated by experimental techniques such as LCM, FACS, PAN, and TRAP. Most of these techniques depend on antibodies recognizing a small number of cell type-specific surface markers. Transcriptomic studies on the isolated cells of interest (Table 1) have identified numerous cell type-specific genes and pathways. Some of these genes can be used as molecular signatures to identify subclasses of neural cells. That is, if the protein products of these genes are directed to cell surface, they can be recognized by antibodies. A subclass of cells with these surface proteins can be isolated by FACS or PAN. This gene expression-based method allows us to identify many subtypes of a given neural population. This information may be very useful if we intend to link a neurological disease with a particular class of neurons. This gene expression-based classification of neural cells is a promising approach for cell type-specific research in the future.

Most cell type-specific studies so far are focused on transcriptomics, aiming to elucidate gene expression patterns of a given cell type. Few studies are dedicated to epigenomics. Analyses of genome-wide chromatin organization, including histone modification and DNA methylation, may shed new light on: (1) novel cell type-specific markers, (2) chromatin accessibility during differentiation, and (3) mechanisms underlying differential gene expression observed.

Finally, most studies to date have used cells from normal subjects. It would be more valuable to extend cell type-specific research to disease models. Understanding gene regulatory networks in the cell types responsible for a neurological disease would help to uncover the genetic and metabolic basis of this disease, which in turn, could open up new ways to diagnosis and new treatments of the disease. It would be an invaluable contribution to the BRAIN Initiative from which millions of people would benefit.

6. ACKNOWLEDGEMENT

This work was supported by the Start-Up fund of the Rochester Institute of Technology and the National Institute of General Medical Sciences under Award Number R15GM116102 (F.C)

7. REFERENCES


4. Anna Devor, Peter Bandettini, David Boas, James Bower, Richard Buxton, Lawrence Cohen, Anders Dale, Gaute Einevoll, Peter Fox, Maria Franceschini, Karl Friston, James
Transcriptomic profiling of mammalian neural cells


8. Sydney Brenner, Maria Johnson, John Bridgham, George Golda, David Lloyd, Daiva Johnson, Shujun Luo, Sarah McCurdy, Michael Foy, Mark Ewan, Rithy Roth, Dave George, Sam Eletr, Glenn Albrecht, Eric Vermaas, Steven Williams, Keith Moon, Timothy Burcham, Michael Pallas, Robert DuBridge, James Kirchner, Karen Fearon, Jen Mao, Kevin Corcoran: Gene expression analysis by massively parallel signature sequencing (MPSS) on microbead arrays. *Nat Biotechnol* 18, 630-634 (2000) DOI: 10.1038/76469


15. Michael Hawrylycz, Ed Lein, Angela Guillozet-Bongaarts, Elain Shen, Lydia Ng, Jeremy Miller, Louie van de Lagemaat, Kimberly Smith, Amanda Ebbert, Zackery Riley, Chris Abajian, Christian Beckmann, Amy Bernard, Darren Bertagnolli, Andrew Boe, Preston Cartagena, Mallar Chakravarty, Mike Chapin, Jimmy Chong, Rachel Dalley, Barry Daly, Chinh Dang, Suvro Datta, Nick Dee, Tim Dolbeare, Vance Faber, David Feng, David Fowler, Jeff Goldy, Benjamin Gregor, Zeb Haradon, David Haynor, John Hohmann,
Transcriptomic profiling of mammalian neural cells


Transcriptomic profiling of mammalian neural cells

DOI: 10.1038/nn1654

DOI: 10.1002/dneu.20602

DOI: 10.1523/JNEUROSCI.6108-08.2009

DOI: 10.1523/JNEUROSCI.4178-07.2008

DOI: 10.1016/0896-6273(88)90127-4

DOI: 10.1016/0092-8674(92)90531-G

DOI: 10.1016/j.cell.2008.10.029

DOI: 10.1016/j.cell.2008.10.028

DOI: 10.1073/pnas.0907143106

DOI: 10.1093/nar/gkq130

DOI: 10.3389/fncom.2014.00086

DOI: 10.1146/annurev-pathol-011110-130242

DOI: 10.1016/S0140-6736(07)60111-1

DOI: 10.1038/286736a0

No DOI Found

44. Voon Yong, Fiona Yong, Andre Olivier, Yves Robitaille, Jack AnTel: Morphologic heterogeneity of human adult astrocytes in culture: correlation with HLA-DR expression. J Neurosci Res 27, 678-688 (1990)
DOI: 10.1002/jnr.490270428

45. Mary Bailey, Michael Shipley: Astrocyte subtypes in the rat olfactory bulb:


77. Linda Edman, Helena Mira, Ernest Arenas: The beta-chemokines CCL2 and CCL7 are
Transcriptomic profiling of mammalian neural cells


87. Ken McCarthy, Jean de Vellis: Preparation of separate astroglial and oligodendroglial cell cultures from rat cerebral tissue. *J Cell Biol* 85, 890-902 (1980) DOI: 10.1083/jcb.85.3.890


89. Andrea Volterra, Jacopo Meldolesi: Astrocytes, from brain glue to communication elements: the revolution continues. *Nat Rev Neurosci* 6, 626-640 (2005) DOI: 10.1038/nrn1722


Abbreviations: LCM: laser-capture microdissection; LDM: laser-directed microdissection; FACS: fluorescence-activated cell sorting; PAN: immunopanning; TRAP: translating ribosome affinity purification; NGS: next-generation sequencing
Transcriptomic profiling of mammalian neural cells

**Key Words:** Cell Type-Specific, Transcriptomics, Microarray, Next-Generation Sequencing (NGS), Mammalian, Brain, Review

**Send correspondence to:** Feng Cui, Thomas H. Gosnell School of Life Sciences, Rochester Institute of Technology, One Lomb Memorial Dr., Rochester, NY 14623, Tel: 585-475-4115, Fax: 585-475-5866, E-mail: fxcsbi@rit.edu