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Cortical interneuron specification and diversification in the era of big data

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Abstract

Inhibition in the mammalian cerebral cortex is mediated by a small population of highly diverse GABAergic interneurons. These largely local neurons are interspersed among excitatory projection neurons and exert pivotal regulation on the formation and function of cortical circuits. We are beginning to understand the extent of GABAergic neuron diversity and how this is generated and shaped during brain development in mice and humans. In this review, we summarise recent findings and discuss how new technologies are being used to further advance our knowledge. Understanding how inhibitory neurons are generated in the embryo is an essential pre-requisite of stem cell therapy, an evolving area of research, aimed at correcting human disorders that result in inhibitory dysfunction.

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Introduction

Inhibitory neurons in the cerebral cortex represent around 20–30% of the neuronal population. Their heterogeneity has been extensively studied in an effort to define subtypes and explore their function. Recent transcriptomic and epigenomic studies have provided unprecedented insight into the extent of heterogeneity but have also questioned the definition of cell types. The neuroepithelial origin of cortical inhibitory neurons in the embryo has been studied in mice for years. Recent data from human studies have shown remarkable developmental conservation between the two species but have also re-introduced the idea of additional sources of cortical interneurons in primates. The interneuron population continues to be moulded beyond the initial specification stages through processes such as migration, morphological and functional maturation and cell death. All these processes, from cell birth to cell function, are controlled by transcriptomic, epigenomic and proteomic networks that underlie the emergence of cortical inhibition.

In this review, we discuss how new technologies have provided novel insight into the question of diversity and specification. We report on emerging aspects of cortical interneuron development, focusing on novel transcriptomic epigenetic and post-translational findings, and propose how new technical breakthroughs that combine the many different levels of molecular control can be harnessed to further understand cortical interneuron development and diversification.

Cortical interneuron subtypes: how many are there?

For many years, cortical interneuron classification had relied on their molecular, morphological and electrophysiological characteristics [1–3]. Interneuron populations had been defined on the basis of expression of neurochemical markers, such as Parvalbumin (PV) and Somatostatin (SST), axonal morphology and physiological characteristics [4]. These criteria, as well as the firing times of cortical interneurons during circuit function, led to the identification of 21 interneuron subtypes in the hippocampal CA1 area [1]. For a while, this provided a broad appreciation of interneuron diversity and function and numerous studies were subsequently conducted in several species, including mouse and human, in an effort to identify common and distinct interneuron subtypes.

An explosion in the classification field came recently from large scale single cell transcriptomic studies (Table 1). While previous work had relied on a handful of markers to identify interneuron types, single cell and single nucleus sequencing studies made use of the entire transcriptome of cells to identify and classify them (Figure 1). Based on transcriptomic findings, cell types have been mapped in fine detail and comparisons have

Table 1

Single cell/nuclei sequencing studies (published from 2016 onwards) that characterise cortical interneuron diversity and development.

Reference	Age	Area	Cells sequenced	Approach	Comments/findings
Mouse adult					
Tasic et al., 2016 [66]	8-weeks male	primary visual cortex	761 GABA	sc RNA-seq	A pilot study that identified 23 transcriptomic GABAergic cell types. Combined retrograde labelling with sc RNA seq to examine axonal projections. Combined Cre-labelling to examine electrophysiological features of one population.
Paul et al., 2017 [67]	6-weeks	motor cortex, somatosensory cortex	584 GABA	sc RNA-seq	Used recombinase-based tracing to isolate 6 cardinal interneuron populations for high-resolution transcriptional profiling. Synaptic communication profiles distinguish major classes of cortical interneurons.
Tasic et al., 2018 [6]	P53–P91 males and females	primary visual cortex, anterior lateral motor cortex	10,534 GABA	sc RNA seq	Identified 61 transcriptomic GABAergic cell types in the adult cortex. Embryonic origin (MGE vs CGE) defines the biggest subdivision of cortical interneurons. Identified 31 MGE-derived, 29 CGE-derived with their inferred layer distribution. Combined with retrograde labelling to match transcriptomic identity with projection specificity. GABA cell types shared across the two areas.
Scala et al., 2020 [68]	P75 males and females	primary motor cortex	1,329 patch-seq (all cells) 646 morphologies	Patch-seq morphological reconstruction	Whole-cell patch recording followed by ss RNA-seq and morphological reconstruction. Transcriptomic families and their morpho-electric properties are discrete. Within each family, transcriptomic cell types have overlapping morpho-electric features.
Gouwens et al., 2020 [10]	P45–P70 males and females	visual cortex	4,270 GABA patch-seq 517 morphologies	Patch-seq, layer mapping, morphological reconstruction	Whole cell patch-recording followed by single cell sequencing, mapping of cell soma location onto the Allen Mouse Common Coordinate Framework and reconstruction of the dendritic and axonal morphologies. Identified 28 met-types of cortical interneurons distinguished by their morphological, electrophysiological and transcriptomic properties.
Yao et al., 2021 [69]	P50–P121 males and females	isocortex and hippocampus	>1.3 million (all cells)	sc RNA seq	Compared cortical and hippocampal GABAergic transcriptomic types. Most are shared between the two areas and are found in similar proportions. A cortical subset is missing from the hippocampus and vice versa.
Mouse embryonic					
Chen et al., 2017 [70]	E11.5 E13.5 E15.5 E17.5	MGE MGE MGE MGE	96 48 63 18	sc RNA-seq	Identified VZ/SVZ progenitors and immature MGE neurons of the cortex, the striatum and the globus pallidus. Compared these to ES-derived MGE cells.
Mi et al., 2018 [28]	E12.5/E14.5 E12.5/E14.5 E12.5/E14.5	Dorsal MGE ventral MGE CGE	298/307 363/288 466/281	sc RNA-seq	Identified embryonic emergence of cortical interneuron subtype diversity. Used adult databases to assign developmental identity to adult subtypes.
Mayer et al., 2018 [27]	E13.5 E14.5 E14.5 E18.5, P10	MGE CGE LGE sorted cortical interneurons	5622 7401 8543 8382	sc RNA-seq	Identified developmental trajectories of cortical interneurons. Used adult databases and correlated precursor with adult cell heterogeneity.

Allaway et al., 2021 [37]	E13.5 E18.2, P2, P10, P28	MGE Sorted cells from the cortex		sc RNA-seq sn ATAC-seq	Distal elements are accessible before gene expression. Subclass-specific (SST vs PV) chromatin states discernible only from P2 onwards.
Lee et al. 2022 [26]	E12.5/E14.5	MGE LGE CGE	12,052/8,389 10,316/8,658 9,275/7,171	sc RNA-seq	WT and Nes-dVenus embryos were used to identify and enrich for ventricular zone cells. Temporal changes in gene expression are reported between E12.5 and E14.5 VZ cells.
Human adult					
Lake et al., 2018 [71]	One female aged 51	six brain areas	4,488 (all cells)	sn RNA-seq	Eight inhibitory subtypes identified. Grouped by developmental origin. Subtypes parallel those in the mouse somatosensory cortex.
Boldog et al., 2018 [23]	Two males aged 50, 54	layer 1 middle temporal gyrus	769 NeuN	sn RNA seq	Combined transcriptomics and electrophysiology to study layer 1 neurons – mostly GABAergic. Identified 11 GABAergic clusters in layer 1. Identified a new GABAergic cell type not seen in mouse cortex.
Hodge et al., 2019 [7]	Eight males and females aged 18-68	middle temporal gyrus	4,297 GABA	sn RNA seq	45 transcriptomic GABAergic cell types identified. Hierarchical relationships mirror developmental origins: 'major classes' (excitatory and inhibitory), 'classes' (e.g., MGE and CGE), 'subclasses' (intermediate order nodes) and 'cell types' (clusters). All classes and subclasses are conserved between mouse and human. Homologous cell types show divergence of gene expression between the two species. This divergence is related to connectivity and signalling.
Krienen et al., 2020 [8]	Human, macaque, marmoset, mouse, ferret	across different regions	188,876 GABA	sn RNA seq	Ivy cells of the mouse hippocampus are also found in the neocortex of humans, macaque and marmosets but not mice or ferrets. A new striatal interneuron identified in primates that is absent in mice and ferrets and constitutes ~30% of all striatal interneurons.
Human embryonic					
Yu et al., 2021 [30]	Human GW9-GW12	subpallium	40,572	sc RNA-seq	Used scRNA-seq data for in situ sequencing to identify spatial distributions of cell types. Identified VZ and SVZ genes expressed in the subpallium. Similar to rodents, class-specific transcriptional identity specified in immature neurons before migration into the cortex.
Shi et al., 2021 [29]	Human GW9-GW18	ganglionic eminences (MGE, LGE, CGE)	56,412	sc RNA-seq	Identified expansion of intermediate precursor cells in the human ganglionic eminences. Report conserved mechanisms underlying, not only specification, but also migration and differentiation of interneurons between mouse and human. Using MGE-SST as an example, they identify 11 subtypes in the adult, of which 7 can be detected in the ganglionic eminences before migration. Therefore, cortical interneuron subtype-specific transcriptional identity is specified shortly after neuron birth.
Zhao et al., 2022 [31]	Human GW9 and GW13 Macaque GW7, GW10 and GW12 Human GW9	ganglionic eminences (MGE, LGE, CGE)	13,782 29,269	sc RNA-seq sc RNA-seq sc ATAC-seq	Report strong conservation of cell diversity and lineage between human and macaque.

been made across areas and species [5]. Subclasses such as PV and SST have been split into >15 transcriptomic subtypes each in both mice [6] and humans [7,8]. Altogether, >50 interneuron subtypes have been identified based on transcriptomic content and unbiased statistical classification (see Table 1). At the same time, some of these studies reported unexpected clustering of small populations that was inconsistent with previous knowledge (e.g. *Lamp5;Lhx6;Nkx2-1* interneurons were found to cluster with CGE-derived populations, despite expressing the two classical markers of MGE-derived interneurons [6]). Overall, single cell RNA sequencing findings confirmed much of previous work, in terms of molecular identity of interneuron classes, but raised the important questions what is an interneuron subtype? and just how many subtypes really exist? [9]. Transcriptomic analysis alone will not answer these questions. Some studies are beginning to integrate transcriptomic data with electrophysiological and morphological characteristics (see Table 1) and have already clustered the cortical GABAergic population into 28 met-types (morphology, electrophysiology and transcriptome) in the mouse visual cortex [10] (Figure 1a). This combinatorial approach has narrowed down the transcriptomic diversity into a more tangible classification with functional relevance. The next step should be to expand this work to cover all subtypes and arrive at a generally accepted consensus that includes well-defined criteria that can be applied across laboratories. At the same time, -omic technologies and analysis pipelines need to be streamlined to make them more accessible and affordable.

The spatial embryonic origins of cortical interneurons: a new challenge to the dogma

Genetic fate-mapping in mice has demonstrated that subcortical germinal zones generate distinct populations of cortical GABAergic neurons [11–15]. The medial and caudal ganglionic eminences (MGE and CGE, respectively) are the two major sources, while the preoptic area (POA) is an additional minor source. Further parcellations of these germinal zones have been reported on the basis of combinatorial transcription factor expression [16]. However, to date, there is only little evidence of distinct neuronal fates being generated from these subdomains [12,16].

Classical studies in primates and humans had suggested that unlike the mouse, human and non-human primate cortical interneurons originate, not only in the ganglionic eminences, but also in cortical progenitor regions [17]. Guided by studies in mice and the observations of clear migrations from the MGE and CGE towards the cortex in primate and human embryos *in vitro*, it was later suggested that, like the rodent, the majority of primate neocortical GABAergic interneurons originate from the ganglionic eminences of the ventral telencephalon [18,19]. Novel studies that combine progenitor tagging with high-throughput sequencing in human *in vitro* slices now challenge this view and postulate that some cortical interneurons in humans share their origin with pyramidal neurons [20]. These cortical-derived neurons have transcriptional similarity to both CGE-derived inhibitory and cortical-derived excitatory neurons, indicating that the cortex may form an additional source of cortical interneurons in humans [20]. This additional source, together with observations of expanded ganglionic eminences and protracted neurogenesis periods, may explain how the human brain can generate larger numbers and perhaps new types of interneurons for a bigger cortical volume [21,22]. Transcriptomic studies combined with morpho-electric observations have found evidence of a human-specific GABAergic neuron with rosehip morphology, the origin of which remains unknown [23]. Whether cortical interneuron generation from local progenitors occurs in humans *in vivo* and the role of evolutionarily novel neurons in human cortical circuits and disease remain exciting unexplored avenues for future research.

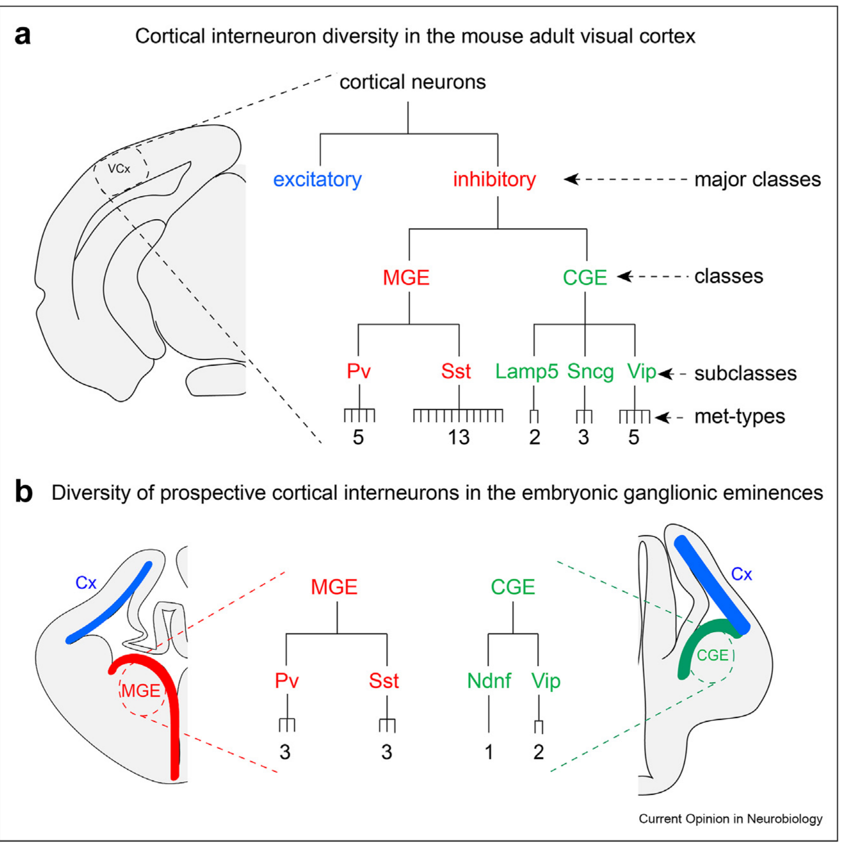
The temporal emergence of cortical interneuron heterogeneity: at the foothills

Developmental studies have been instrumental for the classification of cortical interneuron subtypes in the adult cortex: the embryonic origin of cortical interneurons has been incorporated into all reported transcriptomic-based classification schemes, as it provided a genetic basis for lineage divergence (Figure 1a). ‘Major classes’ (excitatory versus inhibitory) and ‘classes’ (MGE versus CGE) of neurons in the adult cortex have been found to cluster according to their developmental origin, indicating that their neuroepithelial origin defines their transcriptome and their broad identity [7]. Key transcriptional regulators that drive pan-GABAergic and origin-specific identities in cortical interneurons have been defined in mice and humans using mutational analysis and modelling [24,25]. However, neither the embryonic origin, nor the exclusive or combinatorial expression patterns of a handful of key transcription factors are sufficient to explain the diversity of cortical interneurons and the segregation of ‘classes’ into ‘subclasses’ and ‘subtypes’. When does this extensive diversity emerge? Is it present within cycling progenitors in the ganglionic eminences or in emerging young immature neurons? Can diversity be traced to newborn neurons or is diversity imposed when interneurons reach their destination and integrate into networks? Attention turned to single-cell transcriptomic and epigenomic tools in an attempt to tackle these questions.

Transcriptomics

Ground-breaking single-cell RNA sequencing studies in the developing mouse and human brain were undertaken in an effort to reveal the temporal emergence and genetic networks that underlie diversity. Transcriptomic studies focussing on early ventricular zone progenitors report significant shifts in gene expression with

Figure 1



Diversity and development of cortical GABAergic interneurons in the single cell era. **a**. Analysis of single cells from the mouse adult visual cortex has revealed the extent of diverse met-types of inhibitory neurons that can be distinguished on the basis of morphological, electrophysiological and transcriptomic signatures. 'Major classes' and 'classes' of neurons cluster according to their embryonic origins (see B). The cladogram is based on Gouwens et al., 2021 [10] and Hodge et al., 2019 [7].**b**. The embryonic cortical progenitors generate all cortical excitatory neurons found in the adult cortex while the MGE and the CGE are the two major sources of cortical GABAergic interneurons. Single cell RNA sequencing of dissociated embryonic MGE and CGE cells identified numerous prospective interneuron subtypes demonstrating an early divergence of cortical GABAergic interneurons in the ganglionic eminence before migration into the cortex. The cladogram is based on Mi et al., 2018 [28]. VCx, visual cortex; MGE, medial ganglionic eminence; CGE, caudal ganglionic eminence; Cx, cortex.

advancing development and postulate that these may underlie temporal changes in cell fates [26]. Indeed, previous findings had reported temporal biases in the generation of interneuron subtypes from the ganglionic eminences [2]. It seems likely, therefore, that a temporal code of cortical interneuron subtype generation may be a strong contributor to the generation of diversity.

Transcriptomic studies in mouse and human embryos have also revealed a clear diversity among newborn neurons as soon as these cells emerge from the ventricular zone (Figure 1b). Distinct groups of immature neurons with regional identities have been found in the mouse embryonic ganglionic eminences [27,28]. Human studies found similar GABAergic interneuron diversity among newborn neurons and reported conservation of developmental programs between mouse and human [29–31]. Interestingly, single-cell RNA sequencing studies that combined lineage tracing found no evidence of mixed excitatory and inhibitory clones, confirming that mouse cortical precursors do not generate interneurons *in vivo* [32]. Transcriptomic studies have not detected as many postmitotic precursor clusters as there are mature neuronal pools in the adult cortex, pointing to only limited diversity among newborn neurons. This is not surprising given that transcriptomic classification in the adult cortex relies on expression of maturation markers that define these cells and their functional characteristics. Heterogeneity within progenitors or newborn neurons may be too subtle to detect at the level of differential transcript expression. Attention turned to epigenetics, because it provided an exciting possibility that chromatin marks preceding gene expression may reveal early additional heterogeneity within progenitors and newborn neurons.

Epigenomics

Epigenetic mechanisms - molecular processes that impose specific and heritable patterns of gene expression on the progeny of differentiated cells without altering the DNA sequence — include, histone modifications (acetylation, methylation, phosphorylation and ubiquitination) and DNA methylation. Histone methylation or acetylation at distinct lysine (K) residues of histone 3 have been associated with gene activation (H3K4me1/3, H3K9ac, H3K27ac, H4K36ac) and repression (H3K27me3) and chromatin immunoprecipitation with sequencing (ChIP-seq) has been used to interrogate chromatin accessibility. Using bulk epigenomic approaches, several studies had examined the chromatin status of basal forebrain progenitors during the acquisition of GABAergic identity and had linked specific transcription factors to the regulation of the epigenome. NKX2-1 and LHX6, two core regulators of generic MGE identity are involved in the regulation of chromatin state that permits MGE gene expression and represses alternative fates [33]; DLX proteins, transcription factors that act further up the hierarchy to control generic GABAergic fates, are also involved in the regulation of the epigenome by directly interacting with and recruiting chromatin modifiers to gene regulatory elements [34,35]. Additionally, deletion of genes that encode components of chromatin modifying complexes revealed defects in several aspects of cortical interneuron development, including cell proliferation and death [36].

Bulk epigenomic studies gave us a broad picture of the epigenomic state of interneuron precursors and their progeny. By combining high-throughput scRNAseq and single-cell assay for transposase-accessible chromatin with sequencing (scATAC-seq), Allaway et al. explored the epigenetic divergence among embryonic progenitors in the ganglionic eminences at the single cell level. Distinct chromatin landscapes were found to predict and stabilize the mature identity of future interneuron subclasses. However, chromatin accessibility signatures were found to be broader than gene expression profiles, starting earlier and lasting longer and only stabilizing when interneurons settle within the cortical layers [37]. This indicated that the epigenome alone cannot be used to infer identity at embryonic stages. Furthermore, the transcriptome and the epigenome together are not sufficient to explain diversity. Instead, downstream protein interactions and cellular events dictated by temporal and spatial cues may drive lineage divergence within the more 'plastic' or more subtly heterogenous clusters of newborn neurons. This plasticity of embryonic clusters may also confer an evolutionary advantage as minor variations within conserved initial classes of neurons may drive expanded variation of neurons in primates [38].

DNA methylation is another form of epigenetic modification that can impact development. Prenatal stress in mice has been reported to elevate the expression of the DNA methyltransferases DNMT1 and DNMT3A in GABAergic interneurons, while inducing schizophrenia-like phenotypes in their offspring [39]. Although studies to examine the role of DNA methylation in cell fate determination are yet to be reported, DNTM1 has recently been described to regulate cortical interneuron migration and survival of POA-derived interneurons, not through canonical DNA-methylation mechanisms, but through a cross-talk with histone modifiers [40—42]. The full impact of DNA methylation mechanisms in cell fate decisions of cortical interneurons remains unclear. Emerging single cell methylome profiling technologies [43] can be applied to cortical interneurons in order to gain further insight into the mechanisms of developmental diversification.

Beyond transcriptomic and epigenomic signatures

Undoubtedly, lineage specification in neuronal progenitors involves epigenetic and transcriptional regulation. However, the levels of mRNA transcripts and their encoded proteins do not always correlate. Post-transcriptional and post-translational regulation also need to be considered. Regulation of protein synthesis, protein modification and degradation all impact the cellular protein content. Proteomic approaches uncover the protein components and their abundance inside cells. Large-scale proteomic studies in the developing healthy telencephalon have not been performed. One of the first attempts to obtain a brain-wide high-resolution mass spectrometry—based proteome identified proteins in cortical oligodendrocytes, astrocytes, microglia and neurons [44]. However, deeper coverage of protein content awaits further improvements in technology. Uncovering post-translational modifications and cell-type-specific protein isoforms lag even further behind.

At the single cell level proteomics has proved even more difficult as there is no PCR equivalent for protein amplification and detection of low-abundance proteins. In this regard, the field is about to undergo a transformation. Advances in sample preparation and analysis pipelines will soon allow characterisation of proteins in single cells [45,46]. Single cell proteomics with intracellular spatial resolution is another dimension that will undoubtedly appear in the future. Currently, Deep Visual Proteomics, a strategy that uses artificial intelligence-driven image analysis, laser microdissection and ultrasensitive proteomics, can characterise as few as 100 cells with spatial information [47]. Transferring this technology to single cells will be truly transformative.

An integrated approach to understanding the molecular specification and diversification of cortical interneuron subtypes

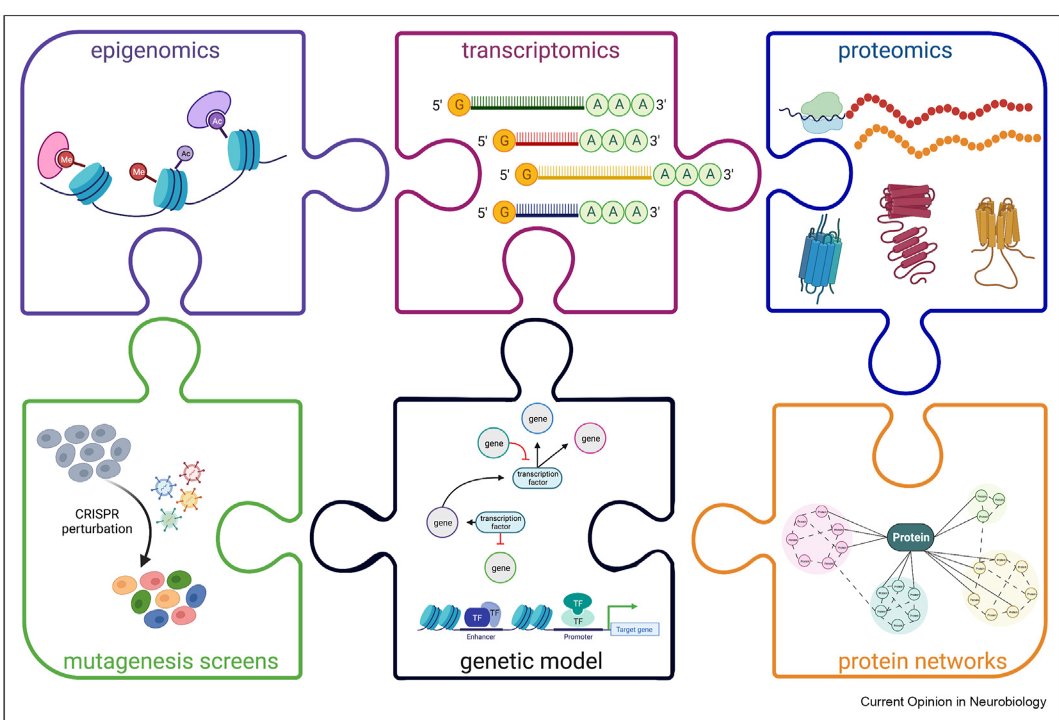
Understanding the genetics of cortical interneuron specification and diversification requires a multi-modal approach (Figure 2). This includes: quantifying (1)

gene expression (transcriptome) and (2) protein expression (proteome) in single cells at different stages of development, (3) identifying key transcription factors and regulators that drive cell fate decisions (e.g. through small- or large-scale CRISPR-based mutagenesis screens [48]), (4) identifying the binding sites for these transcription factors within the genome, (5) probing the accessibility of these binding sites in different cells and at different stages of development (e.g. through epigenomic studies, ChIP-seq, Cut&Run and scATAC-seq) and (6) determining how these different levels of control come together to form cell-type-specific protein networks that mediate cell fate specification of cortical interneuron ontogeny.

The most comprehensively studied core transcriptional regulators of cortical interneuron specification to date are the pan-GABAergic DLX proteins. The impact of mutations in *Dlx* genes [49–51], the putative binding sites of DLX proteins in the genome with their accessibility during development [34,52], as well as some of their interacting partners [35] have been identified. The core MGE regulators NKX2-1 and LHX6 have also been studied in some depth: the consequence of NKX2-1 [53,54] and LHX6 [55] mutations, as well as the binding sites for these two key MGE regulators [33] have been identified.

Until recently, binding partners specific to LHX6, beyond the typical LIM-homeodomain binding protein partners [56,57] have been elusive. However, a recent study from our laboratories demonstrated that LHX6 interacts with a novel transcriptional regulator of cortical interneurons, MTG8, and the two together are essential for the early specification of cortical interneuron subsets that co-express SST and neuropeptide Y (NPY) [58]. When ectopically expressed in developing cortical progenitors, LHX6 and MTG8 are sufficient to activate expression of critical identity factors of the SST-NPY lineage. The mechanism of action of MTG8 within the LHX6-MTG8 complex has not been determined. There is evidence that LHX6 acts in a dose-dependent manner to specify distinct MGE interneuron fates [59]. By binding to LHX6, MTG8 may stabilise LHX6 onto its targets, increasing its effective concentration, a mechanism previously proposed for another member of the MTG family [60]. Alternatively, through its high networking capacity, MTG8 may attract other regulatory

Figure 2



Proposed framework for understanding the genetic networks that underline of cortical GABAergic interneuron specification and diversification. A multi-modal, integrative approach that combines different levels of information provided by advanced single cell –omic approaches is fundamental to puzzling out cortical GABAergic interneuron development and diversification. Key genetic players can be identified by large scale epigenomic, transcriptomic and proteomic studies, complemented by mutagenesis screens. Computational methods that take advantage of emerging advances in deep learning and artificial intelligence can integrate this information to build protein networks and genetic models that can be used to map out the consequence of developmental mutations on the cortical interneuron population.

partners, including histone modifiers, which are known interacting partners of this protein family [61,62]. The interaction of the MGE-specific master-regulator LHX6 with the more widely expressed MTG8 is an example of a core transcription program coming together with a lineage-restricted parallel program to specify cell fate. The finding that a protein partner of LHX6 mediates one of its multiple functions suggests that, beyond transcriptomic, epigenomic and proteomic studies, protein–protein interactions may hold the key to understanding cortical interneuron subtype specification. The early loss of subsets of SST-NPY interneurons following the loss of MTG8 further indicates that, not only 'major classes' and 'classes', but also 'subclasses' and 'subtypes' of cortical interneurons are specified through genetic programs initiated in the ganglionic eminences [58].

Into the future

Bulk and single-cell 'omic' studies continue to generate an enormous amount of complex data that must be harnessed further to provide a better understanding of the genetics of cortical interneuron generation. Emerging analytic techniques that employ deep learning and artificial intelligence will need to be used to mine these data further. For example, deep neural networks that can simulate ChIP-seq can be used to find transcription factor binding sites in the genome [63]. Software that integrates single cell and ATAC sequencing data to generate gene-regulatory-networks and perturb them *in silico* can also be used to predict the impact of gene perturbations on cell lineages [64]. Understanding the genetics of cortical interneuron development is ongoing, alongside stem cell studies using human induced pluripotent stem cells and organoids, which recapitulate the early stages of human cortical development *in vitro* [65]. Ultimately, this huge amount of new knowledge can be integrated to build developmental models that can be used to map disease states, predict the impact of human mutations on cortical interneuron development and develop bespoke stem cell therapies for cortical interneuron disorders.

Conflict of interest statement

Nothing declared.

Data availability

No data was used for the research described in the article.

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