Nucleic Acids Research, 2026, **54**, D1301–D1308
https://doi.org/10.1093/nar/gkaf1103
Advance access publication date: 17 November 2025
Database issue

Spatial GWAS Atlas: a knowledgebase for decoding the genetic architecture of complex traits in spatial resolution

Hongen Kang[1], **Xiaoxi Jing**[1], **Jiecong Lin**[1], **Siyu Pan**[2], **Jiaxiang Zhang**[1], **Junpeng Zhao**[1], **Yajie Zhao**[1,*]

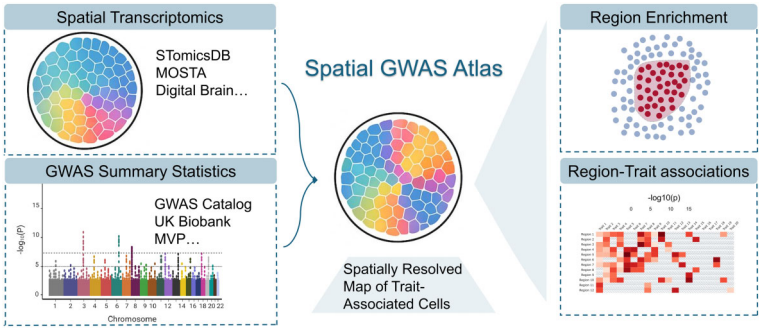
[1]Changping Laboratory, Beijing 102206, China
[2]Renal Electrolyte and Hypertension Division, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, United States

*To whom correspondence should be addressed. Email: yajiezhao@cpl.ac.cn

Abstract

Genome-wide association studies (GWAS) have identified a large number of variants linked to complex traits and diseases, most of which lie in noncoding regions and act in a tissue- and cell type-specific manner. However, how these genetic effects are distributed within the spatial architecture of tissues remains poorly understood. Spatial transcriptomics (ST) profiles gene expression while preserving spatial coordinates, offering a powerful way to localize genetic effects within tissue architecture. Here, we present the Spatial GWAS Atlas (https://zhaolab.cpl.ac.cn/spatialgwas), the first comprehensive resource systematically integrating GWAS summary statistics with ST data to map trait-associated cells at single-cell resolution with spatial context. By leveraging 3854 curated GWAS datasets spanning diverse traits and 635 ST datasets across multiple species, tissues, and platforms, we identified extensive trait–region and trait–spot associations. The database provides keyword search, multicriteria browsing, interactive visualization, and bulk download capabilities. By linking genetic association signals to spatially resolved transcriptomics, the Spatial GWAS Atlas enables high-resolution dissection of the cellular and spatial basis of complex traits, facilitating mechanistic studies, therapeutic target discovery, and precision medicine applications.

Graphical abstract



Introduction

Genome-wide association studies (GWAS) have identified a large number of genetic variants associated with complex traits and diseases, greatly advancing our understanding of disease etiology and revealing potential therapeutic targets [1–3]. Most GWAS-identified variants reside in noncoding regions and exert regulatory effects that are often tissue- and cell type-specific [4]. Linking genetic signals to their relevant cell types and anatomical contexts is therefore a critical step toward uncovering the molecular and cellular basis of complex traits and diseases [5, 6]. Recent methodological advances, such as scDRS [7], sc-linker [8], and scGWAS [9], have enabled the integration of single-cell transcriptomic data with GWAS summary statistics to identify trait-associated cell populations at single-cell resolution. Building on these efforts, the development of sc2GWAS has provided a comprehensive database documenting large-scale GWAS trait–cell regulatory associations at single-cell resolution [10]. Collectively, these approaches and resources have yielded important insights into the cell-type and even single-cell specificity of genetic effects.

The development of spatial transcriptomics (ST) technology has enabled high-throughput, transcriptome-wide profiling of gene expression while preserving the precise spatial coordinates of individual cells [11, 12]. By utilizing this capability, numerous studies have explored the diversity and spatial organization of cells across diverse tissues [13–16]. Disruption

Received: August 15, 2025. **Revised:** September 21, 2025. **Accepted:** October 4, 2025

of spatial organization and spatially resolved gene expression patterns has been implicated in the onset and progression of various complex diseases, including cancers [17], neurodegenerative disorders [18], and aging [16]. Despite its significance, the spatial context of genetic variant effects within tissue architecture remains largely unexplored. Recently, the genetically informed spatial mapping (gsMap) framework was developed to integrate ST data with GWAS summary statistics, enabling spatially resolved mapping of cells to complex traits and diseases [19]. This approach provides an unprecedented opportunity to investigate the interplay between genetic variation and spatial cellular organization, allowing researchers to localize genetic effects *in situ* and uncover microenvironmental patterns associated with disease.

However, there is currently no comprehensive resource that systematically integrates GWAS summary statistics with ST data across multiple traits and tissues. Existing tools and databases typically focus on either single-cell resolution without spatial context or spatial data without genetic association mapping, limiting their ability to provide a holistic view of trait-associated cells in tissue architecture.

To address this gap, we developed the Spatial GWAS Atlas (https://zhaolab.cpl.ac.cn/spatialgwas), a genetically informed atlas systematically mapping GWAS signals to trait-associated cells at single-cell resolution with spatial context. By integrating a wide range of ST datasets spanning diverse platforms, species, and tissue types, together with GWAS results covering a broad spectrum of traits and diseases, we systematically inferred the spatial distribution of trait-associated cells using the gsMap framework. The current release comprises 635 ST datasets and 3854 GWAS datasets, yielding 1 753 303 candidate trait–region pairs as well as a large number of candidate trait–spot pairs. This represents the most comprehensive atlas of spatial spot–trait associations for human complex traits to date, enabling high-resolution localization of genetic risk within ST data. The platform provides advanced capabilities for data exploration, interactive visualization, region-level enrichment analysis, and trait–spot association mapping. By bridging the gap between genetic associations and spatially resolved cell biology, the Spatial GWAS Atlas provides a unique resource to explore the cellular basis of complex traits and diseases, facilitating mechanistic insights, accelerating drug target discovery, and supporting translational applications in precision medicine.

Materials and methods

Spatial transcriptomics dataset collection and processing

We retrieved ST datasets from five primary sources: the Spatial TranscriptOmics DataBase (STOmicsDB) [20], the Macaque Spatial Transcriptomics Atlas [15, 21], the Mouse Organogenesis Spatiotemporal Transcriptomics Atlas (MOSTA) [22], and the Mouse Spatial Transcriptomics Atlas [23], as well as various other published studies and projects. When raw count matrices were available, they were used directly; otherwise, normalized expression matrices were retrieved. For each dataset, we collected and curated spot-level cell type and anatomical region annotations, when available. Datasets with too few spots to support analysis were excluded. Quality-control thresholds embedded in the gsMap pipeline were applied, including exclusion of genes not expressed in any spot and filtering out cell types represented by fewer than 30 spots.

In total, 635 ST datasets spanning three species—human, macaque, and mouse—were assembled, covering a broad array of tissues including brain, heart, liver, lung, lymphoid tissues, spleen, testis, spinal cord, intestine, and embryo. These datasets were generated using diverse ST platforms, such as Stereo-seq, 10x Visium, and MERFISH, comprising a total of 68 322 222 spots and an average of 18 119 detected genes per spot. Each dataset was formatted as an AnnData object containing the expression count matrix, cell annotations, and spatial coordinates, and saved in H5AD format. A detailed summary of all ST datasets is provided in Supplementary Table S1.

GWAS summary statistics collection and curation

GWAS summary statistics for complex traits and diseases were obtained from publicly available databases and literature sources. For the UK Biobank (UKBB), we used the GWAS summary statistics calculated from two robust methods: fastGWA [24] and fastGWA-GLMM [25], which effectively control for confounding effects such as population stratification and relatedness. For the FinnGen, we used the released R9 results [26], covering hundreds of disease endpoints and quantitative traits. For the Million Veteran Program (MVP), we used publicly available GWAS summary statistics from the genetically inferred ancestry version, obtained from the recently published study and the dbGaP database [27]. Moreover, we obtained GWAS summary statistics from online repositories including GWAS Catalog [28], COLOCdb [29], PharmGWAS [30], and Brain Catalog [31]. Finally, we collected the GWAS results from some large-scale GWAS consortia and projects, including the Psychiatric Genomics Consortium [32], Complex Trait Genetics (https://ctg.cncr.nl), Complex Trait Genomics (https://cnsgenomics.com/content/data), GWAS & Sequencing Consortium of Alcohol and Nicotine Use [33], the International Multiple Sclerosis Genetics Consortium [34], and the Sleep Disorder Knowledge Portal [35], among others.

Redundant datasets across sources were removed. Binary phenotype studies with a case proportion below 1% were excluded to minimize low-powered results. After removing molecular-level traits, we curated a total of 3854 GWAS datasets from European (EUR) populations, encompassing thousands of complex traits across anthropometric, metabolic, cardiovascular, neurological, immune-related, and behavioral domains, with sample sizes ranging from thousands to over 1 million individuals. All datasets were harmonized to the dbSNP 151 build. Header formats were standardized, and missing statistics were imputed based on relationships among available summary statistics. Specifically, if both β- and *P*-values were reported, *Z*-scores were computed as $z = \text{sign}(\beta) \times \Phi^{-1}(1 - p/2)$, where Φ^{-1} is the standard normal quantile function. Metadata including sample size, ancestry, and release year were obtained from GWAS Catalog or manually extracted from the original publications. A summary of GWAS datasets is shown in Supplementary Table S2.

Identification of GWAS trait–cell relationships in spatial and single-cell resolution

First, ST datasets and GWAS summary statistics were processed following the gsMap pipeline documentation. For ST datasets, the spot-level gene expression matrices, spatial coor-

dinates, and cell type or anatomical region annotations were compiled into an AnnData object and saved in H5AD format. Gene identifiers, including both gene IDs and Ensembl IDs, were converted to official gene symbols. Moreover, the input GWAS dataset was required to be a plain text file with five required columns: SNP (rsID), A1 (effect allele), A2 (non-effect allele), *Z* (Z-statistic), and *N* (sample size).

Second, since currently available ST datasets cover only a limited set of tissue types, we implemented a semiautomated ontology-driven strategy to assign each GWAS trait to its most relevant tissue. Each trait was queried against the Ontology Lookup Service to retrieve the top three Experimental Factor Ontology (EFO) terms. String similarity between the trait name and candidate EFO terms was calculated using the stringdist R package (Levenshtein distance), and the highest-scoring EFO term was selected. Tissue information was then assigned by mapping the chosen EFO term to Uber-anatomy ontology (Uberon) term. The confidence score was defined as the similarity score, set to 0 if no Uberon mapping was found. Traits without an automatic mapping were manually assigned to the most biologically relevant tissue, and if no suitable match was available, defaulted to embryo. This hybrid strategy balances automation with expert curation, improving reproducibility while minimizing bias. Consequently, embryonic datasets were analyzed across all traits, while tissue-specific ST datasets were restricted to traits relevant to those tissues. This manual annotation ensured biologically meaningful and interpretable tissue-specific analyses.

Finally, we employed the *Quick Mode* of gsMap to calculate the association scores between each spatial spot and each trait. This mode optimizes runtime and configuration complexity by utilizing precalculated weights derived from the 1000 Genomes Project European (EUR) reference panel and protein-coding genes defined in the GENCODE v46 GTF file. The gsMap framework is flexible and supports alternative LD reference panels from other populations as well as different GTF annotation file, including those with noncoding genes, depending on study design. According to the recommendations of gsMap documentation, we set the parameter *num_neighbour* to 21 and the parameter *num_neighbour_spatial* to 101 for ST data generated from the 10X Visium platform. For Stereo-seq data and imputed MERFISH ST data [13], these parameters were set to 51 and 201, respectively. When normalized gene expression matrices were provided, the data_layer parameter was set to "SCT" to skip gsMap's preprocessing step. Additionally, we used the Cauchy combination test to aggregate *P*-values from individual spots within specific spatial regions or cell type annotations to quantify the significance of trait–region or trait–cell type associations.

Database implementation

The Spatial GWAS Atlas is deployed on an Alibaba Cloud ECS (Elastic Compute Service) instance running the Ubuntu 22.04 LTS (Long Term Support) operating system. Nginx v1.18.0 (https://nginx.org/en/) is configured as both an HTTP server and a reverse proxy. MySQL v8.0.42 (https://www.mysql.com) is used as the database engine. The backend RESTful web service is implemented using the Java Spring Boot framework (https://spring.io/projects/spring-boot). The frontend interface is developed with React (https://reactjs.org) and structured using the UMI framework (https://umijs.org). For the user interface components, we adopt Ant Design (https://ant.design), which provides a set of high-quality, extensible components for building rich and interactive web interfaces. Interactive data visualizations are rendered using a combination of libraries, including Plotly.js (https://plotly.com/javascript) and ECharts (https://echarts.apache.org).

Database content and usage

Overview of Spatial GWAS Atlas

Spatial GWAS Atlas aims to establish the most comprehensive spatially resolved map of trait-associated cells to date. It currently incorporates 3854 curated GWAS datasets from the UKBB [36], FinnGen [26], MVP [27], the GWAS Catalog [28], and multiple large-scale research consortia. In addition, it encompasses 635 ST datasets spanning 3 species, 10 tissue types, and 3 experimental platforms. We implemented the standard pipeline of gsMap to calculate the association scores between spatial spots and traits by linking the high-resolution ST data with GWAS results. The outline of Spatial GWAS Atlas is illustrated in Fig. 1. At present, the database contains a total of 1 753 303 genetically informed trait–region/cell type pairs. Among all results, brain-related ST data account for ∼56% and embryo-related ST data ∼41%. On the results browsing pages, entries are by default sorted in descending order of statistical significance (*P*-values). To our knowledge, the Spatial GWAS Atlas represents the first systematic and comprehensive resource for decoding the genetic architecture of complex traits within the spatial context.

User interface and functions

Spatial GWAS Atlas provides a user-friendly interface designed for intuitive exploration, visualization, and data download (Fig. 2). A keyword-based search function on the homepage supports rapid queries across multiple item types, including disease names, tissue types, and so on (Fig. 2A). Users can also navigate the entire database through three main modules: Browse, Search, and Visualization. All processed data in Spatial GWAS Atlas are freely accessible.

The Browse module comprises four pages facilitating exploration of ST datasets, GWAS datasets, and associated results. It integrates extended interactive features, such as multicriteria search and bulk download, to help users quickly locate data of interest (Fig. 2B). The "Spatial Dataset" browse page provides extensive meta-information, including species, tissue, platform, number of spots, number of genes, PMID, title, publication year, and download links. Similarly, the "GWAS Dataset" browse page contains key metadata such as trait type, trait name, trait description, GWAS sample size, number of cases and controls, PMID, title, publication year, and data sources. Clicking a "Dataset ID" directs users to a detailed page for the selected ST or GWAS dataset. This page displays the study's metadata, an overview heatmap of the top 1000 significant trait–region/cell type pairs derived from the dataset, and a comprehensive results table (Fig. 2D). Users can filter these results by entering keywords such as trait, tissue, cell type annotation, or region annotation. Table columns can be sorted by clicking their headers. Selecting an "Association ID" opens a dedicated visualization page featuring detailed statistics and interactive charts for that specific association (Fig. 2D).

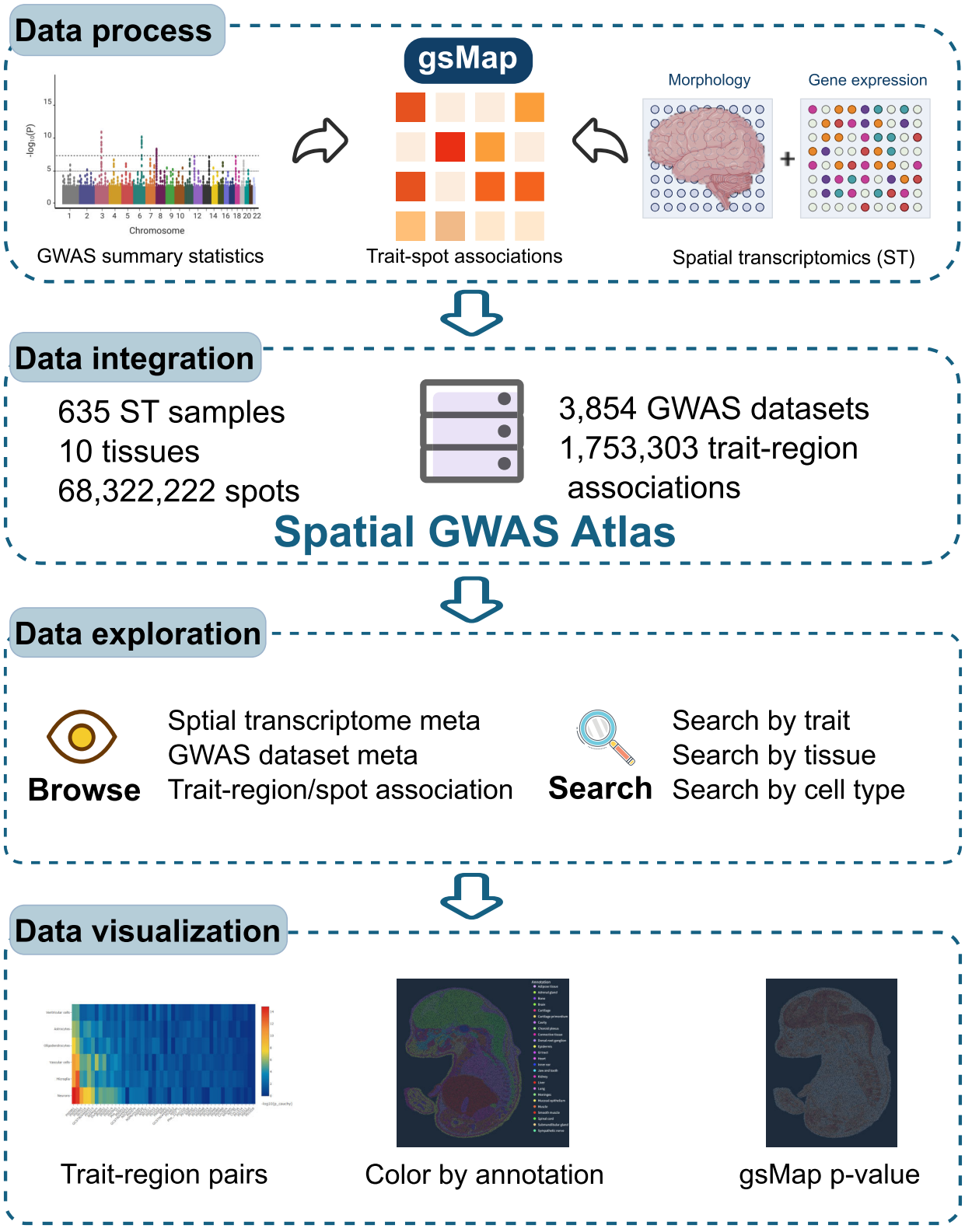


Figure 1. The overview of the Spatial GWAS Atlas. The pipeline and contents of the Spatial GWAS Atlas are organized into four sections: data processing, data integration, data exploration, and data visualization.

Figure 2. Screenshots of the major web interfaces for Spatial GWAS Atlas. (**A**) Homepage search function supporting rapid queries across multiple item types, including ST datasets and GWAS datasets. (**B**) Browse module with multicriteria search and filtering options to refine datasets of interest. (**C**) Search module providing three primary query functions for ST datasets, GWAS datasets, and trait–region/cell type associations. (**D**) Detailed browse page for an individual ST or GWAS dataset, displaying metadata, summary statistics, and heatmap of top association results. (**E**) Visualization page for a selected ST–GWAS pair, featuring interactive plots and customizable display options.

The Search module provides three primary functions: querying ST datasets, GWAS datasets, and all trait–region/cell type pairs across all datasets (Fig. 2C). Users can select a search category, enter a keyword, and retrieve the corresponding results. The trait–region/cell type association search supports multiple filtering criteria, enabling refined queries. From the browse pages, users can access detailed information for a specific trait–region/cell type pair by clicking on its "Association ID." In addition, all processed results are freely available for download.

The Visualization module consists of three sections: two panels display the metadata of the paired ST and GWAS datasets, and the third panel presents an interactive scatter plot (Fig. 2E). This plot can be colored using three alternative schemes: cell type annotation, region annotation (when available), and $-\log_{10}$ *P*-values representing the statistical significance of trait–spot associations. Users can switch between different paired ST–GWAS results and toggle color schemes using the drop-down menus located above the chart.

Case study: identification of schizophrenia-associated cell distribution in the whole mouse brain

We conducted a case study using the recently published whole-brain mouse ST dataset from Han *et al.* to demonstrate the application of the Spatial GWAS Atlas. This dataset provides a spatial transcriptomic atlas of the entire mouse brain at single-cell resolution and includes 195 samples, 123 from one brain and 72 from another [23]. We selected section T311, which contains the largest number of spots, as the showcase example. As show in Fig. 2D, the top five trait–region/cell type associations involved two traits: schizophrenia and bipolar disorder. We focused on schizophrenia, using GWAS summary statistics from Pardinas *et al.* [37] as the target dataset. First, we examined the distribution of schizophrenia-associated cells in embryonic ST data from MOSTA, confirming their overall enrichment in brain tissue (Supplementary Fig. S1) (Cauchy P-value = 8.64e−12). However, these embryonic data lacked the resolution to resolve subregional and cell-type specificity within the brain. By leveraging the high-resolution cell type and anatomical annotations in the Han *et al.* dataset, we identified significant enrichment of schizophrenia-associated cells in neurons (Cauchy *P*-value = 1.44e−15). Spatially, these cells were concentrated in the cerebral cortex, hippocampus, and thalamus (Fig. 2E). Previous large-scale GWAS–magnetic resonance imaging integration study have revealed that schizophrenia shares substantial genetic architecture with cortical structure across most regions [38]. In addition, reduced hippocampal subfield volumes are strongly associated with cognitive impairment in schizophrenia [39], and diminished thalamocortical functional connectivity, particularly within key cognitive networks, has been linked to cognitive deficits even at prodromal stages [40]. In summary, these regions have been consistently implicated in schizophrenia by prior studies, and our results provide spatially resolved, single-cell-level evidence that further substantiates these established associations.

Discussion and future directions

In this study, we present Spatial GWAS Atlas, a comprehensive spatially resolved map of trait-associated cells by leveraging the gsMap framework that integrates GWAS data with ST profiles. This database fills an important gap between genetic association studies and spatially resolved cell biology. It is particularly timely, as genetic variant effects are increasingly recognized to be context specific [41, 42], and the spatial architecture of tissues can profoundly influence cellular phenotypes, signaling networks, and disease processes [43]. Our work extends previous large-scale efforts such as sc2GWAS [10], which maps GWAS signals to single-cell populations. While single-cell atlases can reveal cell-type specificity, they typically lack the anatomical context necessary to capture microenvironmental influences and regional variation within tissues. Conversely, existing ST resources generally do not incorporate genetic association information [20, 44], limiting their ability to link spatial gene expression patterns to disease risk loci. By overcoming the limitations of existing approaches, the Spatial GWAS Atlas enables researchers to precisely localize genetic effects within tissue architecture and elucidate how neighboring cell types and the local microenvironment modulate these effects.

The breadth of our curated datasets supports both trait-centric and tissue-centric explorations. In particular, the inclusion of embryonic datasets for traits without a clear tissue of origin allows exploratory mapping of genetic signals in a developmental context, potentially providing insight into early-life origins of complex diseases. Our platform also supports multitrait and cross-tissue comparisons, enabling users to identify convergent spatial signatures across biologically related traits.

Despite these advances, several limitations remain. First, the current coverage of ST datasets is uneven across tissues, species, and experimental platforms, reflecting the field's early stage. While brain is relatively well represented, many human tissues have limited or no high-resolution ST data, constraining the scope of trait mapping in those contexts. Second, tissue assignment for GWAS traits, although supported by a semi-automated ontology-driven strategy and manual curation, remains approximate for traits with systemic or pleiotropic effects. As more multitissue ST data become available, it will be possible to perform cross-tissue integration without relying on preassigned tissue relevance. Third, the spatial resolution of current ST platforms remains lower than true single-cell resolution for many current ST platforms, meaning that spot-level associations may reflect composite signals from heterogeneous cell populations. Advances in high-resolution and multiplexed spatial profiling will mitigate this limitation in future releases.

Looking ahead, we anticipate two directions for expansion. First, the integration of spatial multi-omics data [45, 46], such as epigenomics, proteomics, and metabolomics, could further refine mechanistic links between genetic variants and spatially resolved molecular phenotypes. Second, because all GWAS summary statistics in the current database are derived from European populations, generalizability across ancestries remains limited. Future updates will incorporate data from diverse populations to improve cross-ancestry applicability and equity, thereby addressing the Eurocentric bias of current GWAS resources.

In summary, the Spatial GWAS Atlas provides a unique and valuable resource for exploring the spatial context of genetic risk in complex traits and diseases. By systematically integrating GWAS findings with ST data across diverse tissues and species, it sheds light on the interplay between genetic variation, cellular identity, and tissue architecture, thereby laying

a foundation for both mechanistic understanding and translational applications. We anticipate that the Spatial GWAS Atlas will serve as an important resource for the genetics and translational research communities, with substantial potential to advance drug discovery and precision medicine.

Acknowledgements

We thank Prof. Jian Yang and Liyang Song for their valuable suggestions on gsMap implementation. We thank Xiaoyu Zhang for providing support in database deployment. We are grateful to all members of the Zhao lab of Changping Laboratory for their valuable comments.

Author contributions: Hongen Kang (Conceptualization [equal], Data curation [equal], Formal analysis [equal], Visualization [equal], Writing—original draft [equal], Writing—review & editing [equal]), Xiaoxi Jing (Data curation [equal], Validation [equal]), Jiecong Lin (Validation [equal], Visualization [equal]), Siyu Pan (Resources [equal]), Jiaxiang Zhang (Investigation [equal]), Junpeng Zhao (Software [equal]), and Yajie Zhao (Conceptualization [equal], Funding acquisition [equal], Methodology [equal], Project administration [equal], Resources [equal], Supervision [equal], Writing—review & editing [equal])

Supplementary data

Supplementary data is available at NAR online.

Conflict of interest

None declared.

Funding

This work was supported by Changping Laboratory. Funding to pay the open access publication charges for the article was provided by Changping Laboratory.

Data availability

Spatial GWAS Atlas is available at https://zhaolab.cpl.ac.cn/spatialgwas. Users can freely access all processed data and results through the web service.

References

1. Lappalainen T, Li YI, Ramachandran S *et al.* Genetic and molecular architecture of complex traits. *Cell* 2024;187:1059–75. https://doi.org/10.1016/j.cell.2024.01.023
2. Abdellaoui A, Yengo L, Verweij KJH *et al.* 15 years of GWAS discovery: realizing the promise. *Am J Hum Genet* 2023;110:179–94. https://doi.org/10.1016/j.ajhg.2022.12.011
3. Minikel EV, Painter JL, Dong CC *et al.* Refining the impact of genetic evidence on clinical success. *Nature* 2024;629:624–9. https://doi.org/10.1038/s41586-024-07316-0
4. Hekselman I, Yeger-Lotem E. Mechanisms of tissue and cell-type specificity in heritable traits and diseases. *Nat Rev Genet* 2020;21:137–50. https://doi.org/10.1038/s41576-019-0200-9
5. Sumida TS, Hafler DA. Population genetics meets single-cell sequencing. *Science* 2022;376:134–5. https://doi.org/10.1126/science.abq0426
6. Perez RK, Gordon MG, Subramaniam M *et al.* Single-cell RNA-seq reveals cell type-specific molecular and genetic associations to lupus. *Science* 2022;376:eabf1970. https://doi.org/10.1126/science.abf1970
7. Zhang MJ, Hou K, Dey KK *et al.* Polygenic enrichment distinguishes disease associations of individual cells in single-cell RNA-seq data. *Nat Genet* 2022;54:1572–80. https://doi.org/10.1038/s41588-022-01167-z
8. Jagadeesh KA, Dey KK, Montoro DT *et al.* Identifying disease-critical cell types and cellular processes by integrating single-cell RNA-sequencing and human genetics. *Nat Genet* 2022;54:1479–92. https://doi.org/10.1038/s41588-022-01187-9
9. Jia P, Hu R, Yan F *et al.* scGWAS: landscape of trait–cell type associations by integrating single-cell transcriptomics-wide and genome-wide association studies. *Genome Biol* 2022;23:220. https://doi.org/10.1186/s13059-022-02785-w
10. Yin M, Feng C, Yu Z *et al.* sc2GWAS: a comprehensive platform linking single cell and GWAS traits of human. *Nucleic Acids Res* 2025;53:D1151–61. https://doi.org/10.1093/nar/gkae1008
11. Rao A, Barkley D, Franca GS *et al.* Exploring tissue architecture using spatial transcriptomics. *Nature* 2021;596:211–20. https://doi.org/10.1038/s41586-021-03634-9
12. Moses L, Pachter L. Museum of spatial transcriptomics. *Nat Methods* 2022;19:534–46. https://doi.org/10.1038/s41592-022-01409-2
13. Zhang M, Pan X, Jung W *et al.* Molecularly defined and spatially resolved cell atlas of the whole mouse brain. *Nature* 2023;624:343–54. https://doi.org/10.1038/s41586-023-06808-9
14. Huuki-Myers LA, Spangler A, Eagles NJ *et al.* A data-driven single-cell and spatial transcriptomic map of the human prefrontal cortex. *Science* 2024;384:eadh1938. https://doi.org/10.1126/science.adh1938
15. Lei Y, Liu Y, Wang M *et al.* Single-cell spatial transcriptome atlas and whole-brain connectivity of the macaque claustrum. *Cell* 2025;188:3863–81.e25. https://doi.org/10.1016/j.cell.2025.02.037
16. Ma S, Ji Z, Zhang B *et al.* Spatial transcriptomic landscape unveils immunoglobin-associated senescence as a hallmark of aging. *Cell* 2024;187:7025–44.e34. https://doi.org/10.1016/j.cell.2024.10.019
17. Tagore S, Caprio L, Amin AD *et al.* Single-cell and spatial genomic landscape of non-small cell lung cancer brain metastases. *Nat Med* 2025;31:1351–63. https://doi.org/10.1038/s41591-025-03530-z
18. Gong Y, Haeri M, Zhang X *et al.* Stereo-seq of the prefrontal cortex in aging and Alzheimer's disease. *Nat Commun* 2025;16:482. https://doi.org/10.1038/s41467-024-54715-y
19. Song L, Chen W, Hou J *et al.* Spatially resolved mapping of cells associated with human complex traits. *Nature* 2025;641:932–41. https://doi.org/10.1038/s41586-025-08757-x
20. Xu Z, Wang W, Yang T *et al.* STOmicsDB: a comprehensive database for spatial transcriptomics data sharing, analysis and visualization. *Nucleic Acids Res* 2024;52:D1053–61. https://doi.org/10.1093/nar/gkad933
21. Chen A, Sun Y, Lei Y *et al.* Single-cell spatial transcriptome reveals cell-type organization in the macaque cortex. *Cell* 2023;186:3726–43.e24. https://doi.org/10.1016/j.cell.2023.06.009
22. Chen A, Liao S, Cheng M *et al.* Spatiotemporal transcriptomic atlas of mouse organogenesis using DNA nanoball-patterned arrays. *Cell* 2022;185:1777–92.e21. https://doi.org/10.1016/j.cell.2022.04.003
23. Han L, Liu Z, Jing Z *et al.* Single-cell spatial transcriptomic atlas of the whole mouse brain. *Neuron* 2025;113:2141–60.e9. https://doi.org/10.1016/j.neuron.2025.02.015
24. Jiang L, Zheng Z, Qi T *et al.* A resource-efficient tool for mixed model association analysis of large-scale data. *Nat Genet* 2019;51:1749–55. https://doi.org/10.1038/s41588-019-0530-8
25. Jiang L, Zheng Z, Fang H *et al.* A generalized linear mixed model association tool for biobank-scale data. *Nat Genet* 2021;53:1616–21. https://doi.org/10.1038/s41588-021-00954-4

26. Kurki MI, Karjalainen J, Palta P *et al.* FinnGen provides genetic insights from a well-phenotyped isolated population. *Nature* 2023;613:508–18. https://doi.org/10.1038/s41586-022-05473-8
27. Verma A, Huffman JE, Rodriguez A *et al.* Diversity and scale: genetic architecture of 2068 traits in the VA Million Veteran Program. *Science* 2024;385:eadj1182. https://doi.org/10.1126/science.adj1182
28. Sollis E, Mosaku A, Abid A *et al.* The NHGRI-EBI GWAS Catalog: knowledgebase and deposition resource. *Nucleic Acids Res* 2023;51:D977–85. https://doi.org/10.1093/nar/gkac1010
29. Pan S, Kang H, Liu X *et al.* COLOCdb: a comprehensive resource for multi-model colocalization of complex traits. *Nucleic Acids Res* 2024;52:D871–81. https://doi.org/10.1093/nar/gkad939
30. Kang H, Pan S, Lin S *et al.* PharmGWAS: a GWAS-based knowledgebase for drug repurposing. *Nucleic Acids Res* 2024;52:D972–9. https://doi.org/10.1093/nar/gkad832
31. Pan S, Kang H, Liu X *et al.* Brain catalog: a comprehensive resource for the genetic landscape of brain-related traits. *Nucleic Acids Res* 2023;51:D835–44. https://doi.org/10.1093/nar/gkac895
32. Mullins N, Forstner AJ, O'Connell KS *et al.* Genome-wide association study of more than 40,000 bipolar disorder cases provides new insights into the underlying biology. *Nat Genet* 2021;53:817–29. https://doi.org/10.1038/s41588-021-00857-4
33. Liu M, Jiang Y, Wedow R *et al.* Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. *Nat Genet* 2019;51:237–44. https://doi.org/10.1038/s41588-018-0307-5
34. International Multiple Sclerosis Genetics Consortium. Multiple sclerosis genomic map implicates peripheral immune cells and microglia in susceptibility. *Science* 2019;365:eaav7188.
35. Cade BE, Lee J, Sofer T *et al.* Whole-genome association analyses of sleep-disordered breathing phenotypes in the NHLBI TOPMed program. *Genome Med* 2021;13:136. https://doi.org/10.1186/s13073-021-00917-8
36. Consortium UKBW.-G.S. Whole-genome sequencing of 490,640 UK Biobank participants. *Nature* 2025;645:692–701.
37. Pardinas AF, Holmans P, Pocklington AJ *et al.* Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nat Genet* 2018;50:381–9. https://doi.org/10.1038/s41588-018-0059-2
38. Stauffer EM, Bethlehem RAI, Dorfschmidt L *et al.* The genetic relationships between brain structure and schizophrenia. *Nat Commun* 2023;14:7820. https://doi.org/10.1038/s41467-023-43567-7
39. Yasuda K, Yamada S, Uenishi S *et al.* Hippocampal subfield volumes and cognitive function in schizophrenia and mood disorders. *Neuropsychobiology* 2022;81:204–14. https://doi.org/10.1159/000521102
40. Wang Y, Ouyang L, Fan L *et al.* Functional and structural abnormalities of thalamus in individuals at early stage of schizophrenia. *Schizophr Res* 2024;271:292–9. https://doi.org/10.1016/j.schres.2024.07.045
41. Fang L. Context-specific regulatory variants in precision medicine and agriculture. *Nat Rev Genet* 2025;26:81. https://doi.org/10.1038/s41576-024-00798-8
42. Lappalainen T, MacArthur DG. From variant to function in human disease genetics. *Science* 2021;373:1464–8. https://doi.org/10.1126/science.abi8207
43. Song L. Mapping trait-associated cells with spatial transcriptomics. *Nat Rev Genet* 2025;26:739. https://doi.org/10.1038/s41576-025-00877-4
44. Wang G, Wu S, Xiong Z *et al.* CROST: a comprehensive repository of spatial transcriptomics. *Nucleic Acids Res* 2024;52:D882–90.https://doi.org/10.1093/nar/gkad782
45. Vandereyken K, Sifrim A, Thienpont B *et al.* Methods and applications for single-cell and spatial multi-omics. *Nat Rev Genet* 2023;24:494–515. https://doi.org/10.1038/s41576-023-00580-2
46. Guo P, Mao L, Chen Y *et al.* Multiplexed spatial mapping of chromatin features, transcriptome and proteins in tissues. *Nat Methods* 2025;22:520–9. https://doi.org/10.1038/s41592-024-02576-0

Received: August 15, 2025. **Revised:** September 21, 2025. **Accepted:** October 4, 2025