



**Spatial Transcriptomics and Cell Lineage Analysis in  
Craniofacial Development**

Jifan Feng

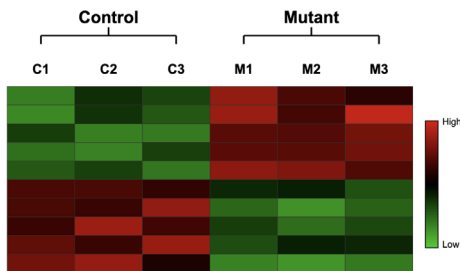
Chai Lab | University of Southern California

# Disclosure

We have no conflicts of interest to disclose.

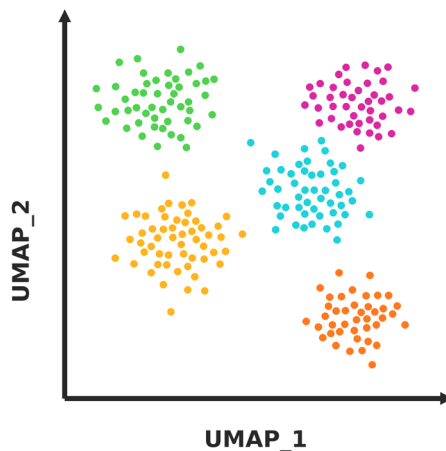
# From bulk to spatial: the evolution of transcriptomics

## Bulk RNA-seq



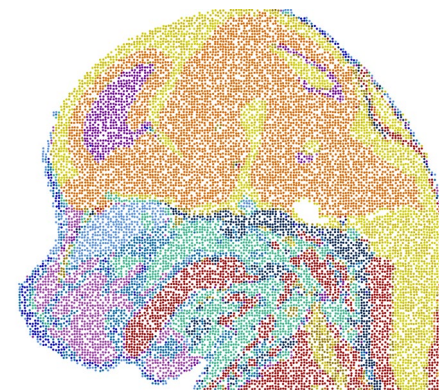
Tissue-level gene expression averaging

## scRNA-seq



Single-cell resolution,  
no spatial context

## Spatial Transcriptomics



Gene expression mapped *in situ*

# Sequencing-based and imaging-based platforms for spatial genomics

## Sequencing-Based

Whole transcriptome | 0.5–55  $\mu\text{m}$  resolution

**Visium** 55  $\mu\text{m}$  | **Visium HD** 2  $\mu\text{m}$  | **Stereo-seq** 0.5  $\mu\text{m}$  | **Slide-seq** 10  $\mu\text{m}$

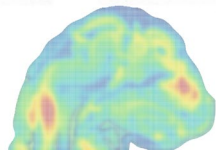
Barcoded spots



Sequencing



Computational reconstruction

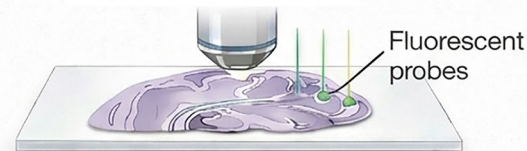


Position from barcode

## Imaging-Based

Targeted gene panel | Subcellular resolution

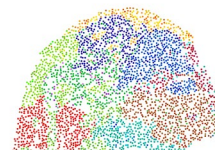
**seqFISH** | **Xenium** | **MERFISH** | **CosMx** — all subcellular resolution



Imaging



Signal decoding



Single-molecule map

Position from microscope

# Spatial genomics in craniofacial development

## MOUSE

Multimodal spatiotemporal transcriptomic resolution of embryonic **palate** osteogenesis

*Nature Communications*  
Piña et al. 2023

Visium

High-resolution spatial transcriptomics and cell lineage analysis reveal spatiotemporal cell fate determination during **craniofacial** development

*Nature Communications*  
Feng et al. 2025

seqFISH

Spatial transcriptomics reveals a role for sensory nerves in preserving **cranial suture** patency through modulation of BMP/TGF- $\beta$  signaling

*PNAS*  
Tower et al. 2021

Visium

Single cell spatial transcriptomics links Wnt signaling disruption to extracellular matrix development in a cleft **palate** model

*Scientific Reports*  
Piña et al. 2025

Visium HD + Xenium

## HUMAN

Integrated multi-omics profiling characterizes the crucial role of human dental epithelium during **tooth** development

*Cell Reports*  
Zhang et al. 2025

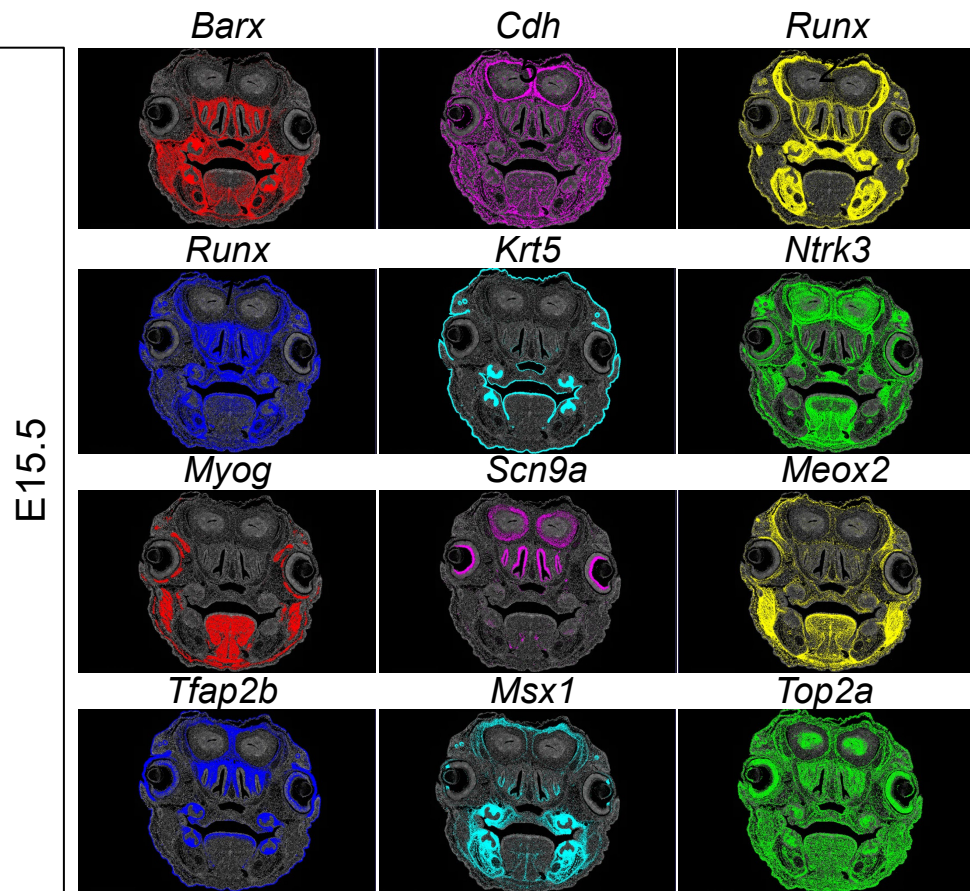
Visium

An atlas of early human mandibular endochondral and osteogenic paracrine signaling regions of **Meckel's cartilage**

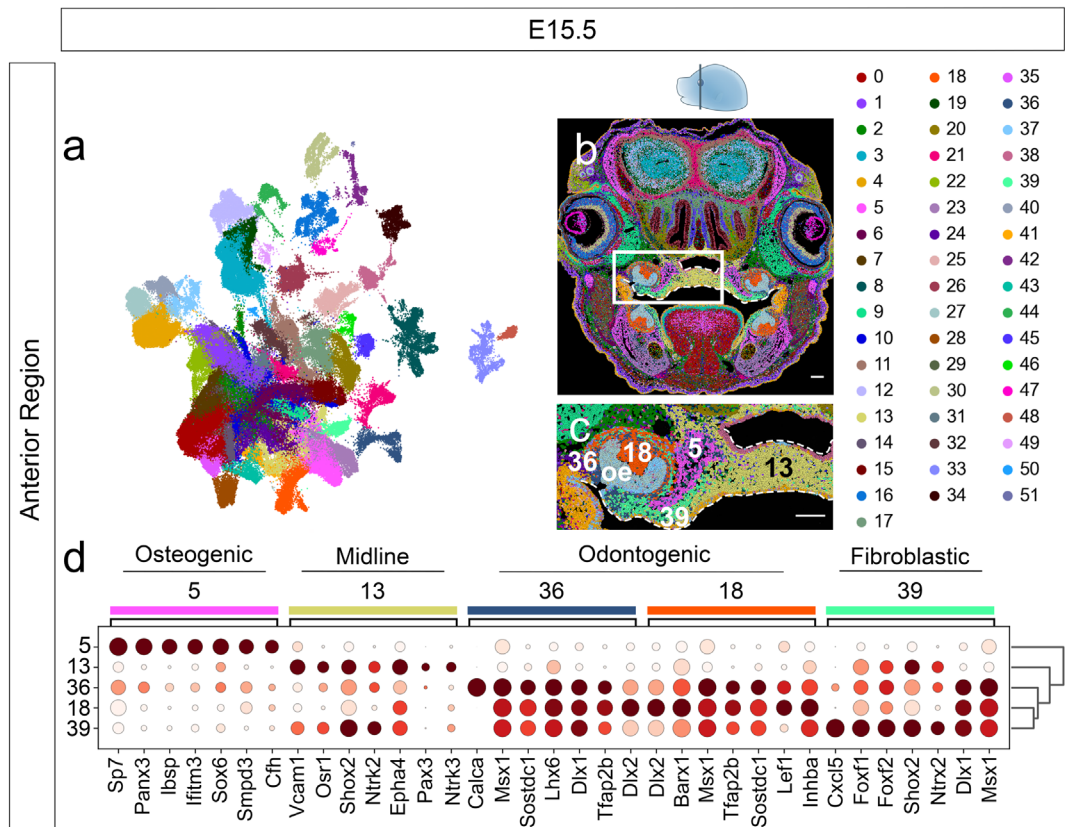
*PNAS*  
Shen et al. 2025

Stereo-seq

# Spatial genomics data as a spatially resolved gene expression atlas of the craniofacial complex



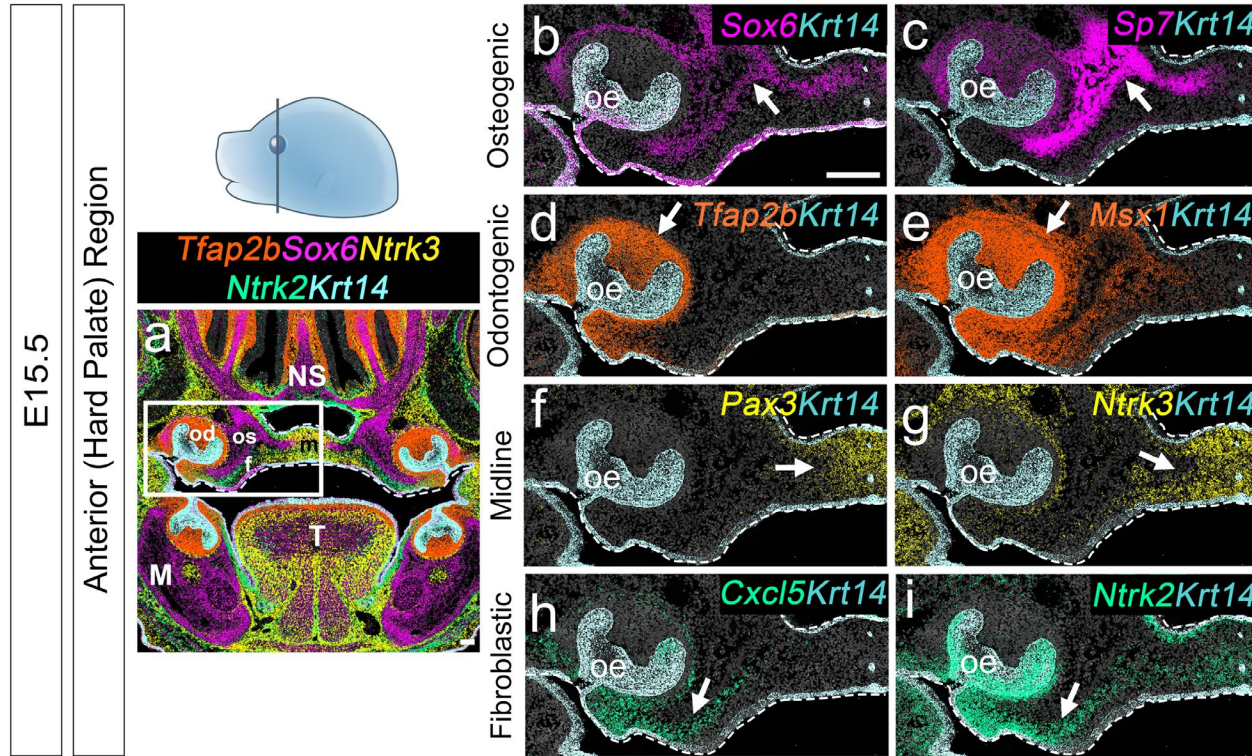
# Spatial mapping of mesenchymal populations in the anterior region of the E15.5 mouse head



Abbreviations: odontogenic epithelium (oe)

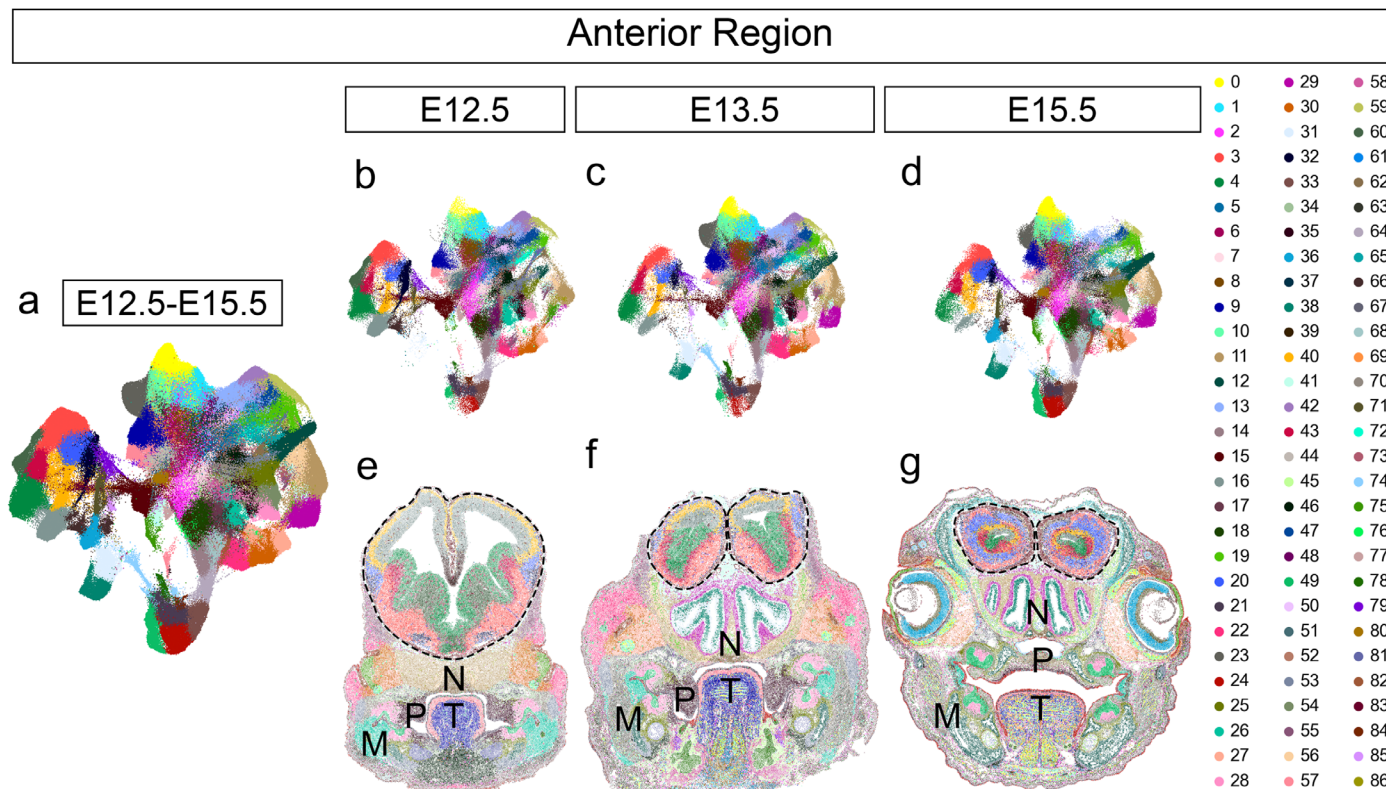
Feng et al., Nat Commun 2025

# Spatially variable gene detection across cell types in craniofacial tissues



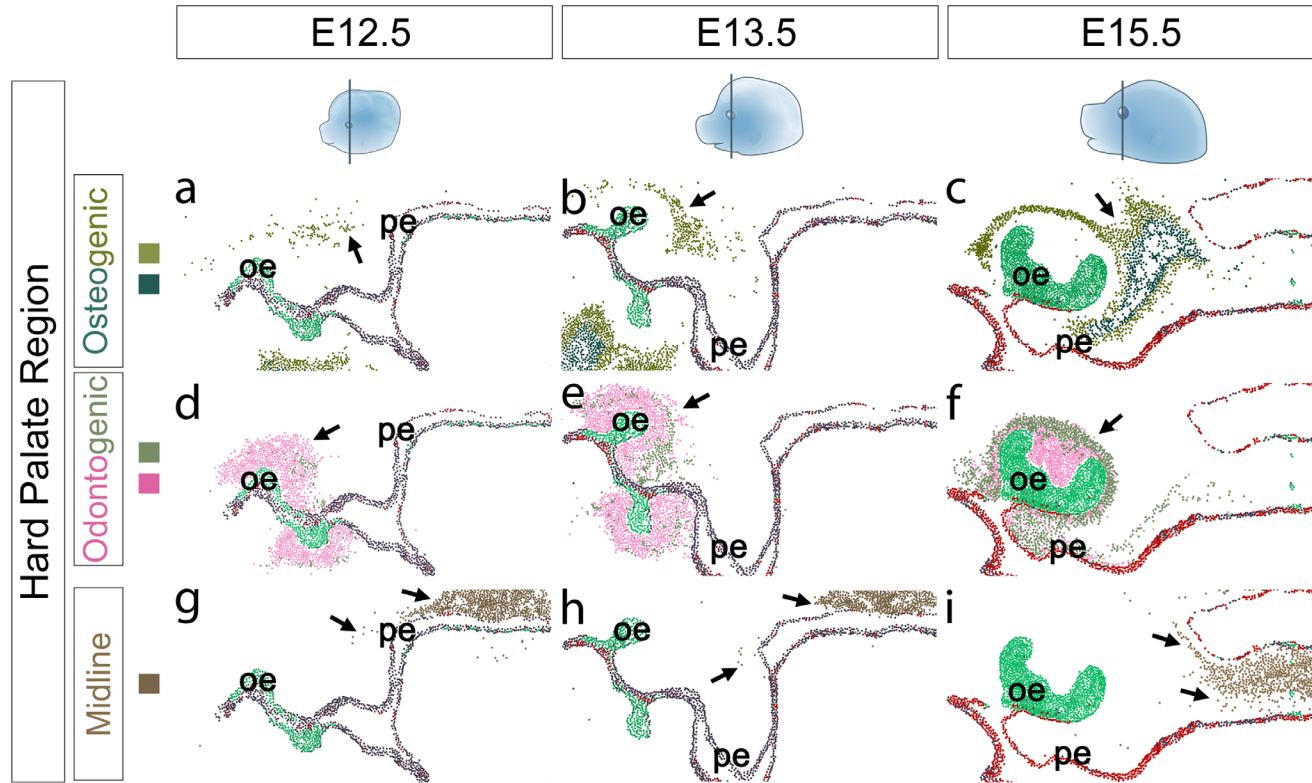
Abbreviations: fibroblasts (f), mandible (M), midline (m), nasal septum (NS), odontogenic region (od), odontogenic epithelium (oe), osteogenic region (os), tongue (T)

# Dynamic spatial and temporal mapping of anterior craniofacial cell populations



Abbreviations: nasal region (N), mandible (M), palate (P), tongue (T)

# Dynamic spatial and temporal mapping of mesenchymal populations associated with the maxillary region

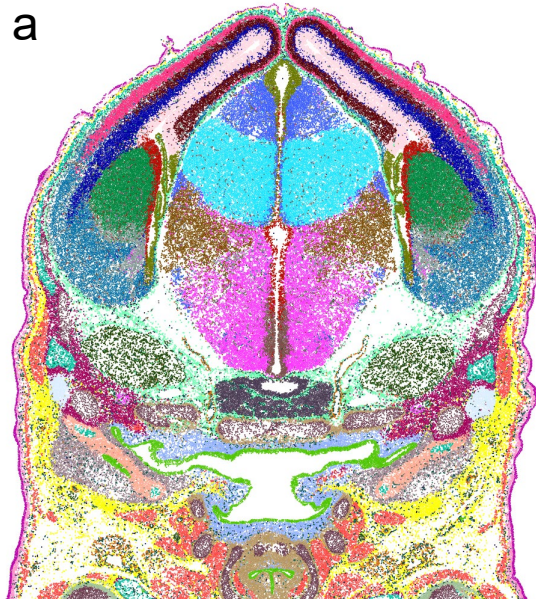


Abbreviations: odontogenic epithelium (oe), palatal epithelium (pe)

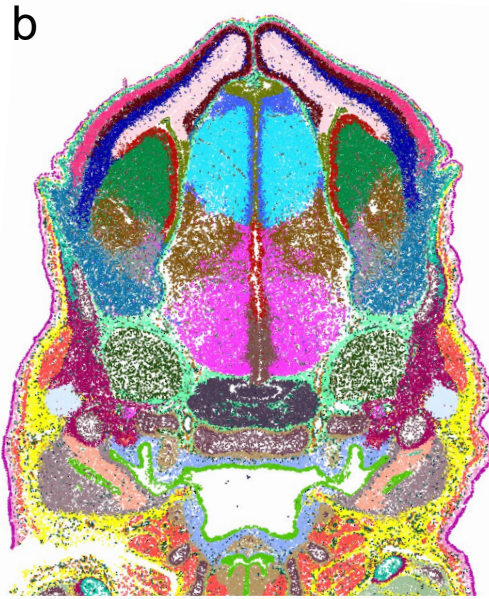
# Spatial analysis identified location-specific cellular differences in control and mutant mice

E14.0

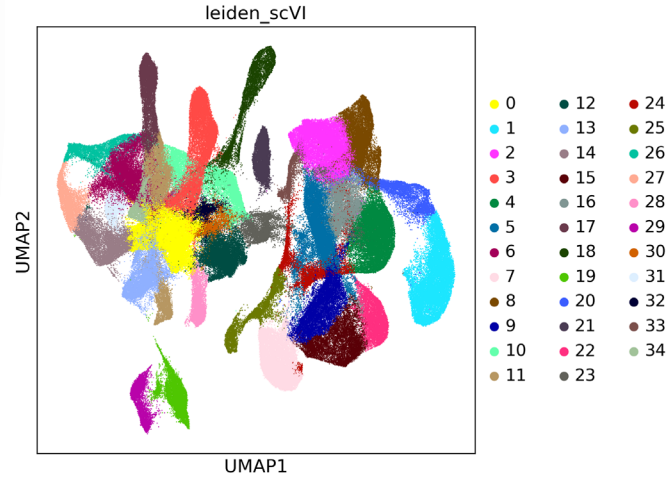
Control



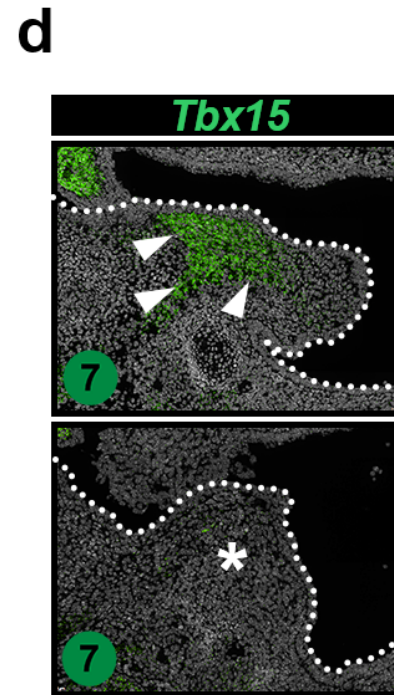
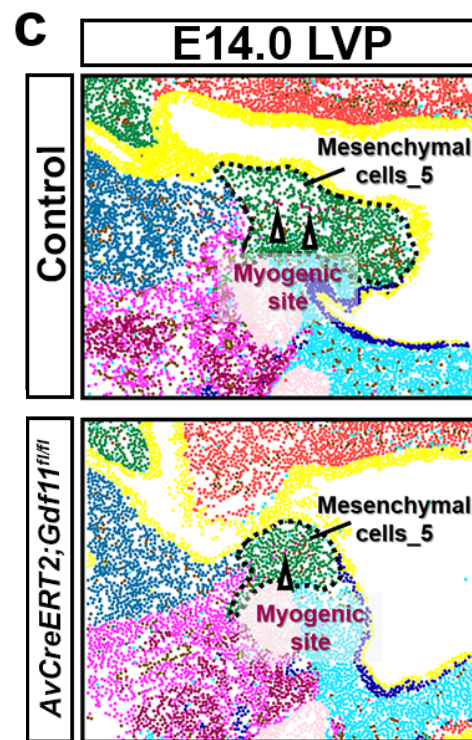
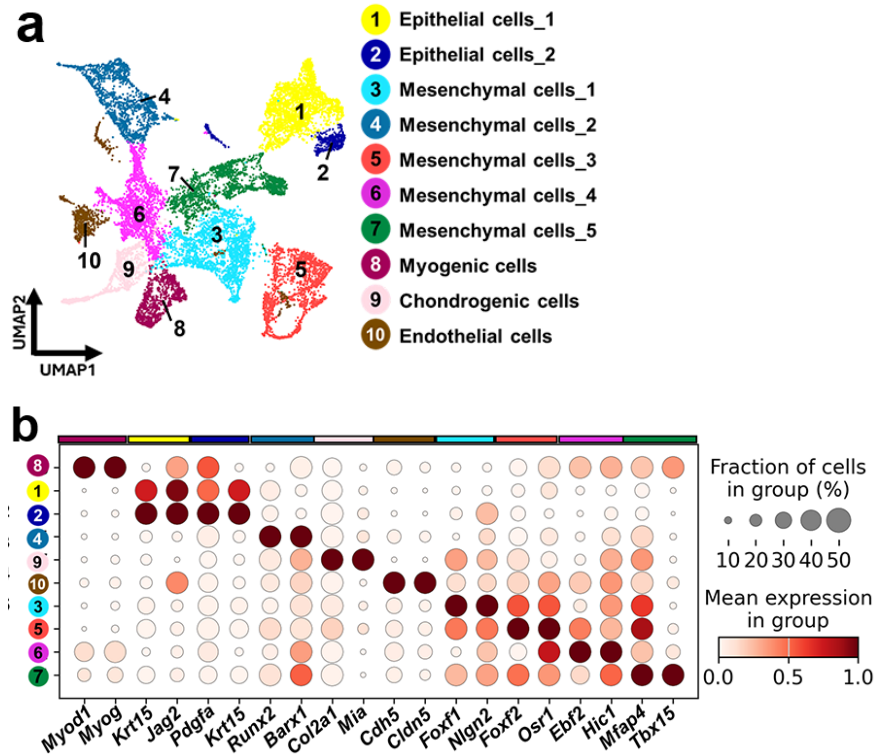
*AvCreERT2;Gdf11<sup>fl/fl</sup>*



c

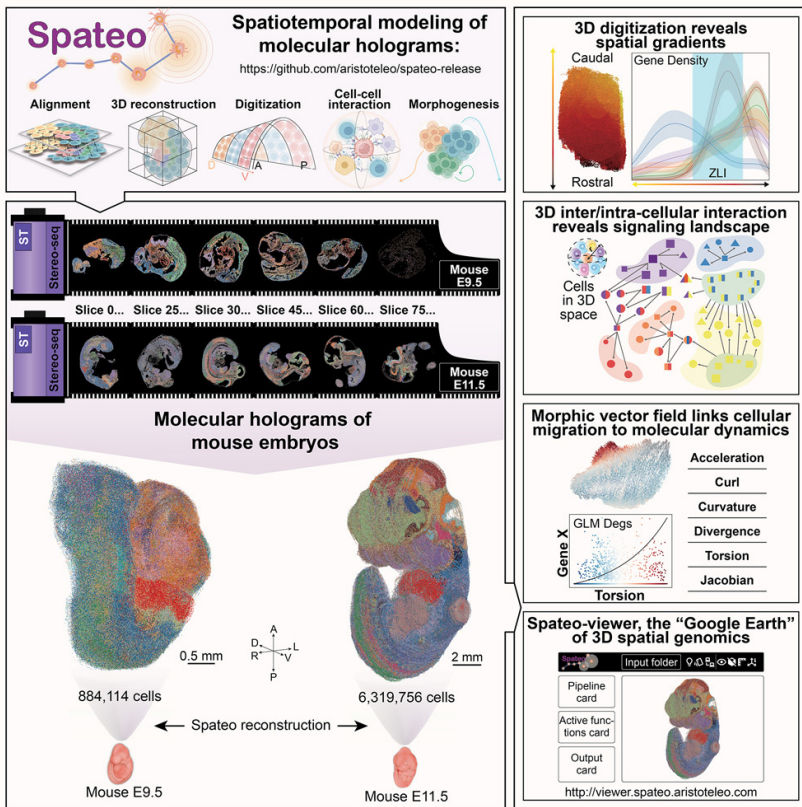


# Spatial analysis identified location-specific molecular differences in control and mutant mice





# Next-generation spatial genomics approaches



Qiu et al., Cell 2024

## Spatial Proteomics

PLATO, iPEX, DBiTplus, etc. enable multiplexed protein localization at single-cell resolution

Hu et al., Cell 2025; Wang et al., Nature 2026; Enniful et al., Nature Methods 2026;

## Spatial Epigenomics

Spatial-ATAC-seq, SPACE-seq, SCA-seq, etc. map chromatin accessibility and enhancer-promoter contacts

Deng et al., Nature 2022; Huang et al., PNAS 2025; Xie et al., eLife 2024,

## Spatial Multi-Omics

DBiT-seq, Slide-tags, Spatial ATAC-RNA-seq, etc. co-profile epigenome, transcriptome, and proteome


Liu et al., Cell 2020; Russell et al., Nature 2024; Li et al., Nature Protocols 2025

# FaceBase hosts multi-modal datasets for dental, oral, craniofacial, and related systems research


**FaceBase**  
A Resource For Craniofacial Researchers

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[Sign Up](#) [Log In](#)

 **FaceBase Community Forum: May 4–5, 2026**  
Registration and Call for Abstracts are now open. Location: Arlington, VA. [Learn more and participate »](#)

## The trusted data resource for craniofacial researchers worldwide


FaceBase is a [collaborative NIDCR-funded project](#) .


Enter keywords to search across datasets (e.g., *mus musculus mandible, Fgfr1*) **SEARCH DATA**


### Image Search


Below are some examples of the types of imaging data available in FaceBase.


[Click here to search through all imaging records.](#)

[MicroCT](#)  


[Fluorescence microscopy](#)  


[Enhancer activity](#)  


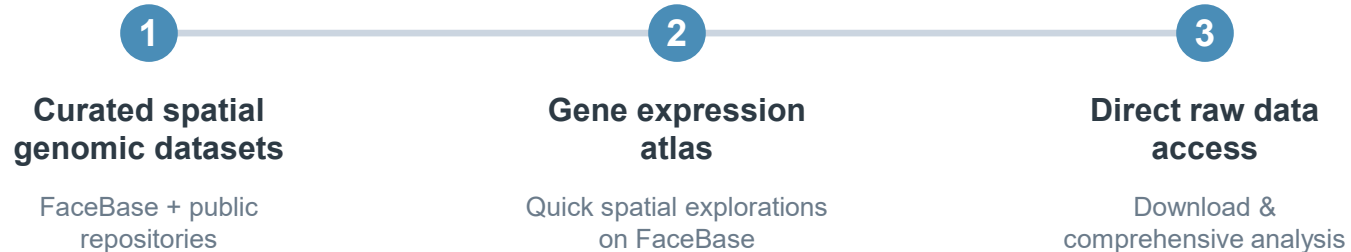
[Microscopy assay](#)  


[Histological staining](#)  


**Bulk RNA-seq • scRNA-seq • snRNA-seq • ChIP-seq • Imaging • Facial scans**  
**Human • Mouse • Zebrafish • Chimp • Chick • Rat**

# FaceBase to serve as a hub for spatial genomics datasets related to the craniofacial region

The screenshot shows the FaceBase website homepage. At the top, there is a navigation bar with the FaceBase logo (A Resource For Craniofacial Researchers) and menu items: DATA, RESOURCES, CONTRIBUTE, POLICIES, COMMUNITY, and HELP. On the right side of the navigation bar are links for Sign Up and Log In. Below the navigation bar is a light blue banner for the FaceBase Community Forum: May 4–5, 2026, with a sub-message: Registration and Call for Abstracts are now open. Location: Arlington, VA. There is a link to Learn more and participate. Below this banner is a white section with the heading "The trusted data resource for craniofacial researchers worldwide" and a sub-text: FaceBase is a collaborative NIDCR-funded project. Below this is a search bar with the placeholder text "Enter keywords to search across datasets (e.g., mus musculus mandible, Fgfr1)" and a blue "SEARCH DATA" button. At the bottom of this section is a blue banner with the text: Bulk RNA-seq • scRNA-seq • snRNA-seq • CHIP-seq • Imaging • Facial scans, followed by species names: Human • Mouse • Zebrafish • Chimp • Chick • Rat.



# FaceBase provides a comprehensive *in vivo* gene expression atlas for craniofacial and related regions

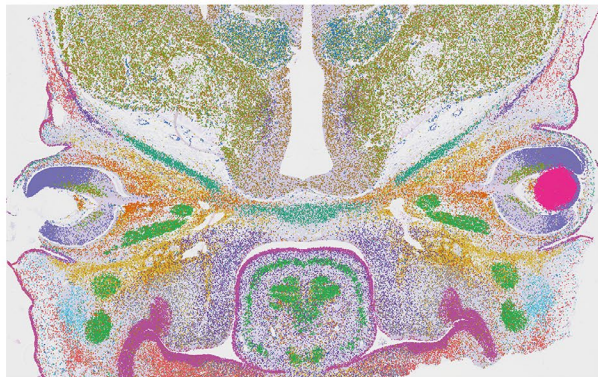
- Coverage of craniofacial and related regions for dental, oral, and craniofacial research and beyond
- Multi-platform spatial transcriptomic datasets (seqFISH, Visium HD, and Stereo-seq)
- Large-scale *in vivo* gene expression profiling (~100–1,000 genes/cell)
- Anatomical structure-specific expression information for development- and disease-associated genes

seqFISH



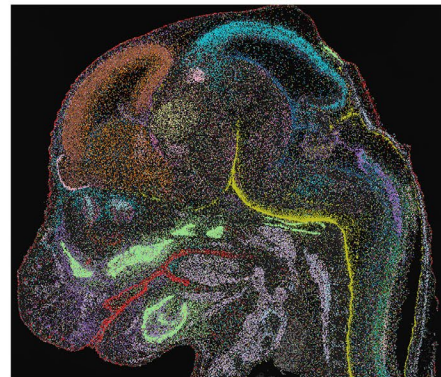
E12.5 · E13.5 · E15.5  
Mouse Head

Visium HD



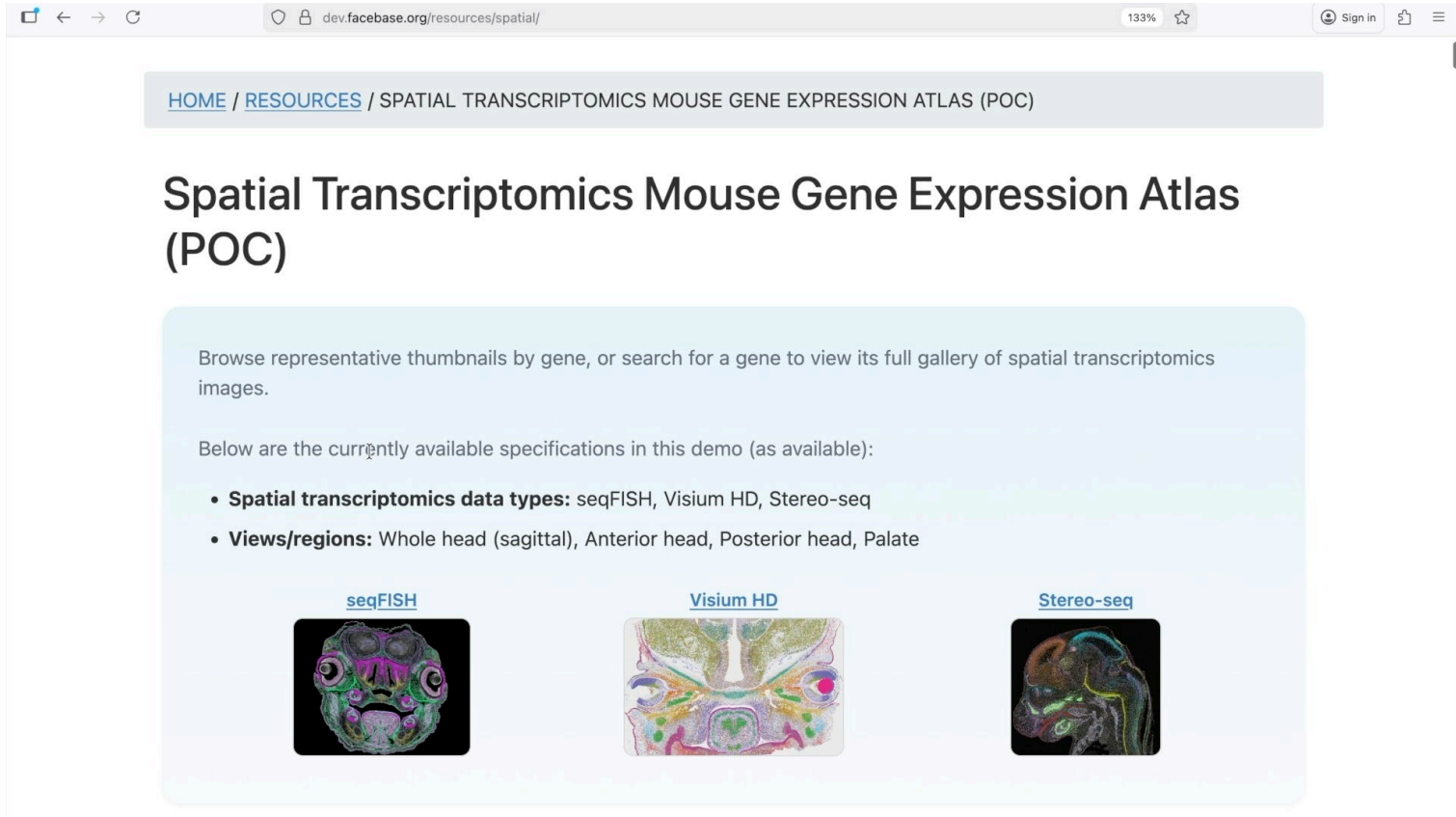
E12.5 · E13.5  
Mouse Palate

Stereo-seq



E12.5 · E14.5 · E16.5  
Mouse Head

# Spatial gene expression atlas with intuitive interface and one-click access



The screenshot shows a web browser window with the URL `dev.facebase.org/resources/spatial/`. The page features a breadcrumb trail: [HOME](#) / [RESOURCES](#) / SPATIAL TRANSCRIPTOMICS MOUSE GENE EXPRESSION ATLAS (POC). The main heading is "Spatial Transcriptomics Mouse Gene Expression Atlas (POC)". Below the heading, a light blue box contains the following text:

Browse representative thumbnails by gene, or search for a gene to view its full gallery of spatial transcriptomics images.

Below are the currently available specifications in this demo (as available):

- **Spatial transcriptomics data types:** seqFISH, Visium HD, Stereo-seq
- **Views/regions:** Whole head (sagittal), Anterior head, Posterior head, Palate

Three representative thumbnails are displayed below the list:

- seqFISH:** A 3D reconstruction of a mouse head showing gene expression patterns in various colors.
- Visium HD:** A 2D spatial transcriptomics image showing gene expression patterns in a mouse head section.
- Stereo-seq:** A 2D spatial transcriptomics image showing gene expression patterns in a mouse head section, with a different color palette.

# Interactive visualization of spatial gene expression patterns associated with anatomical locations


**Dlx2** seqFISH  
E13.5 · Anterior

[Open Interactive Viewer](#)

**Dlx2** seqFISH  
E13.5 · Posterior

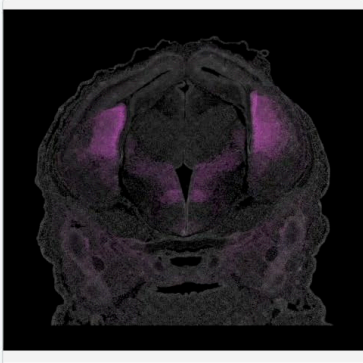
[Open Interactive Viewer](#)

## E15.5



**Dlx2** seqFISH  
E15.5 · Anterior

[Open Interactive Viewer](#)



**Dlx2** seqFISH  
E15.5 · Posterior

[Open Interactive Viewer](#)

# Analyze spatial gene expression levels across cells in the craniofacial region

www.facebase.org/chaise/viewer/#1/imaging:Image/RID=98-N61G?waterMark=FaceBase&meterScaleInPixels=1150787

This repository is under review for potential modification in compliance with Administration directives.

FaceBase  
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Sign Up Log In

## 95-TR5C (Dlx2\_E15.5\_Anterior-s0-z0-c0.ome.tif)

Annotations

Line Thickness 3.47

Search in the list

Found 8 of 8 (8 Displayed)

- eye (UBERON:0000970)
- mandible (UBERON:0001684)
- tongue (UBERON:0001723)
- tooth (EMAPA:32906)
- olfactory bulb (UBERON:0002264)
- nasal septum (UBERON:0001706)
- skull (UBERON:0003129)
- palate (ZFA:0005509)

Hide Annotations Show Channel List Zoom In Zoom Out Reset Zoom Take a Screenshot

1 mm

# Upcoming feature: multi-channel viewer for simultaneous visualization of whole gene panels

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A Resource For Craniofacial Researchers

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Sign Up Log In

## A9-6TD4: seqfish\_expression\_94genes\_DS1\_S1\_2x5x.ome.tiff

Hide Annotations Hide Channel List Zoom In Zoom Out Reset Zoom Take a Screenshot

Annotations

Image Thickness 3.46

Search in the list

Found 7 of 7 (7 Displayed)

- eye (UBERON:0000970)
- mandible (UBERON:0001684)
- tongue (UBERON:0001723)
- tooth bud (UBERON:0008281)
- nasal septum (UBERON:0001706)
- skull (UBERON:0003129)
- Palate (MESH:D010159)

### Channels

- DAPI
  - Intensity range 0 255
  - Gamma 0.875
  - Saturation 0
  - Hue Greyscale
- Barx1
  - Intensity range 0 255
  - Gamma 0.875
  - Saturation 100
  - Hue Greyscale
- Rfxn2
  - Intensity range 0 255
  - Gamma 0.875

DAPI Hic1 Acan

E NS P M T

500 μm

# FaceBase spatial gene expression atlas release at FaceBase Forum, May 4–5

**Arlington, VA**  
*Also available via Zoom*

**ADVANCES IN DATA REUSE,  
INTEGRATION, AND AI-READY  
BIOMEDICAL RESEARCH IN DENTAL,  
ORAL, CRANIOFACIAL, INNER EAR AND  
RELATED RESEARCH.**

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COMMUNITY FORUM**

**INVITED TALKS, PANEL DISCUSSIONS,  
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**Starts: Mon, May 4 at 9 am ET  
Ends: Tues, May 5 at 12 pm ET**

**Learn more and register at:  
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## FaceBase Community Forum

**May 4–5, 2026**

USC/ISI East Office · Arlington, VA

*In person or remote*

 [www.facebase.org](http://www.facebase.org)

 [help@facebase.org](mailto:help@facebase.org)

## Summary

Spatial genomics bridges gene expression to anatomy, uncovering location-specific molecular and cellular changes that are undetectable by conventional methods.

# Acknowledgements



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 **USC** University of  
Southern California



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