

# Biomarker Technologies (BMKGENE)



Introducing the sequencing services of Biomarker Technologies (BMKGENE) -- at EPS course "Single Cell Transcriptomics" 2023

Jie Xu (Jay)  
Business Development Manager



## Biomarker Technologies

A leading sequencing service provider, founded in 2009 in Beijing China, with EU Headquarter located in Münster, Germany.

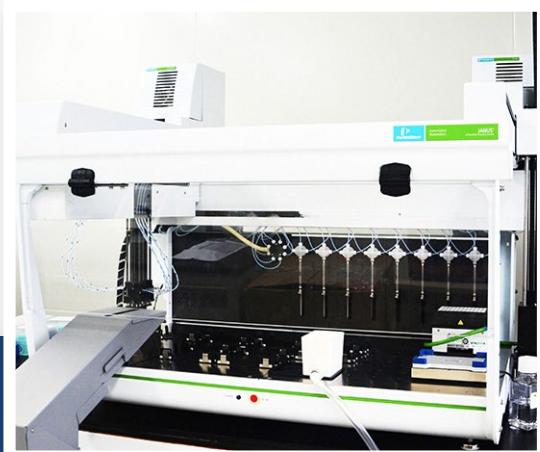


# Biomolecular Laboratory

Professional, Standard, Automatic Molecular Laboratory



- Over 20,000 square meters space.
- Standard procedures from sample extraction to sequencing under strict SOPs.
- Various sequencing platforms and flexible experimental designs fulfilling diverse research goals.
- **Brilliant Laboratory 1000**, a fully automated intelligent sequencing central control system, jointly developed with PerkinElmer.



**BMK Muenster Bio-lab**  
In function in 2022

# Platforms

## Leading, Multi-level High-throughput Sequencing Platforms

**Nanopore (ONT):** (MinION, GridION X5, PromethION P48)

**PacBio:** (RSII, PacBio Sequel, PacBio Sequel II)

Joint laboratory with Pacific Biosciences of California, inc.

**Illumina:** (Illumina NovaSeq 6000)

**MGI:** (DNBSEQ-G400, DNBSEQ-T7)

**10X Genomics :** (Chromium, 10X Visium)

**BMKMANU:** S1000 sub-cellular level Spatial Transcriptomics



PromethION 48



Nanopore GridION X5



Sequel II

Sequel



# Long-read Sequencing Platforms in BMK

2015.12 BMK's First PacBio RSII was set up



2016.12 Joint lab BMK-PacBio-Gene company established

2017.5 First Nanopore R&D project set up

2017.8 MinION experimental platform was set up

2018.8 PromethION beta was set up in BMK

2018.8 Nanopore Single cell yield exceeded 100 Gb.

**2018.9 Certified to provide Nanopore DNA/RNA sequencing on GridION and PromethION**



2018.9 Nanopore-based full-length transcriptome sequencing service was launched

2018.10 PromethION platform produced more than 5,000 Gb data for BMK

2018.11 ONT full-length RNA-seq analysis APP released on BMKCloud

2019.1 ONT-based epigenomics service was launched

2019.1 Nanopore single cell yield reached 164 Gb/cell

2019.6 PacBio Sequel II arrived in Biomarker Technologies

2019.10 World's first PromethION P48 was set up in BMKGNE

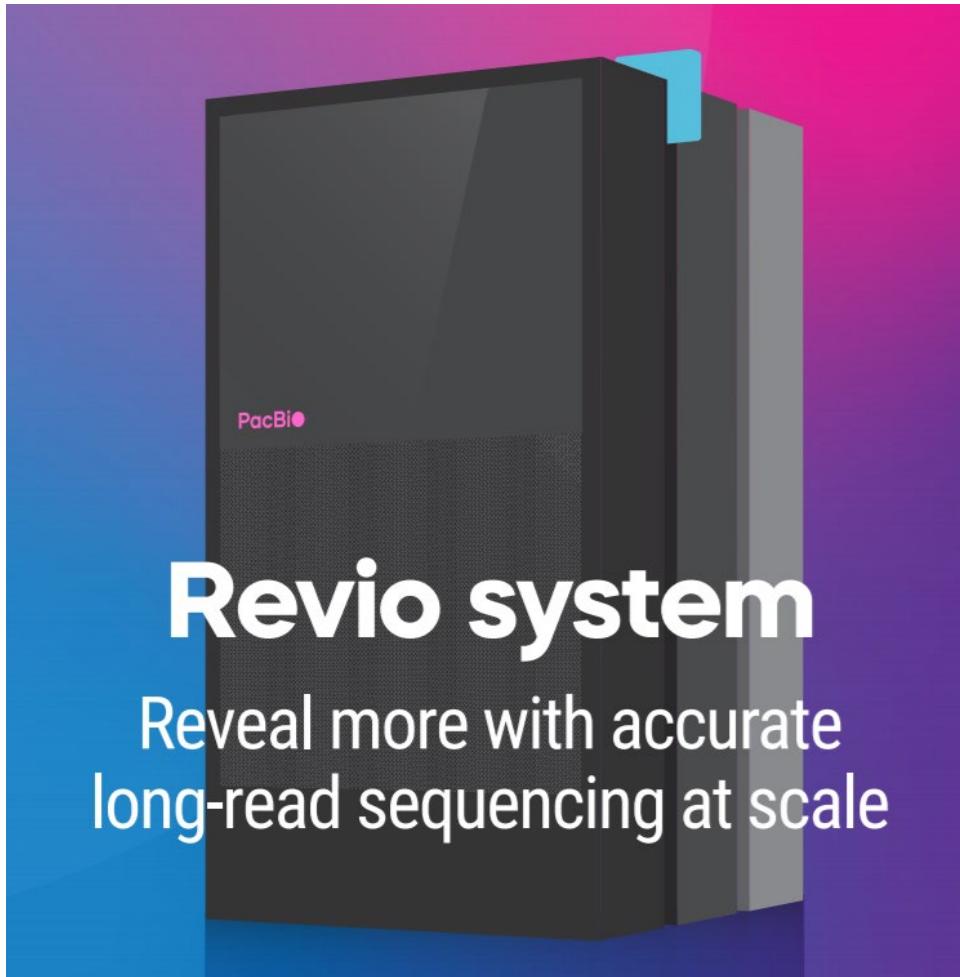
**2019.11 Full-length amplicon Seq service was launched**

2020.12 PromethION P48 flowcell upgraded

2021.5 Over 200 Tb data produced by PromethION

2021.5 60,000+ samples sequenced on PacBio Sequel II

Joining Soon!



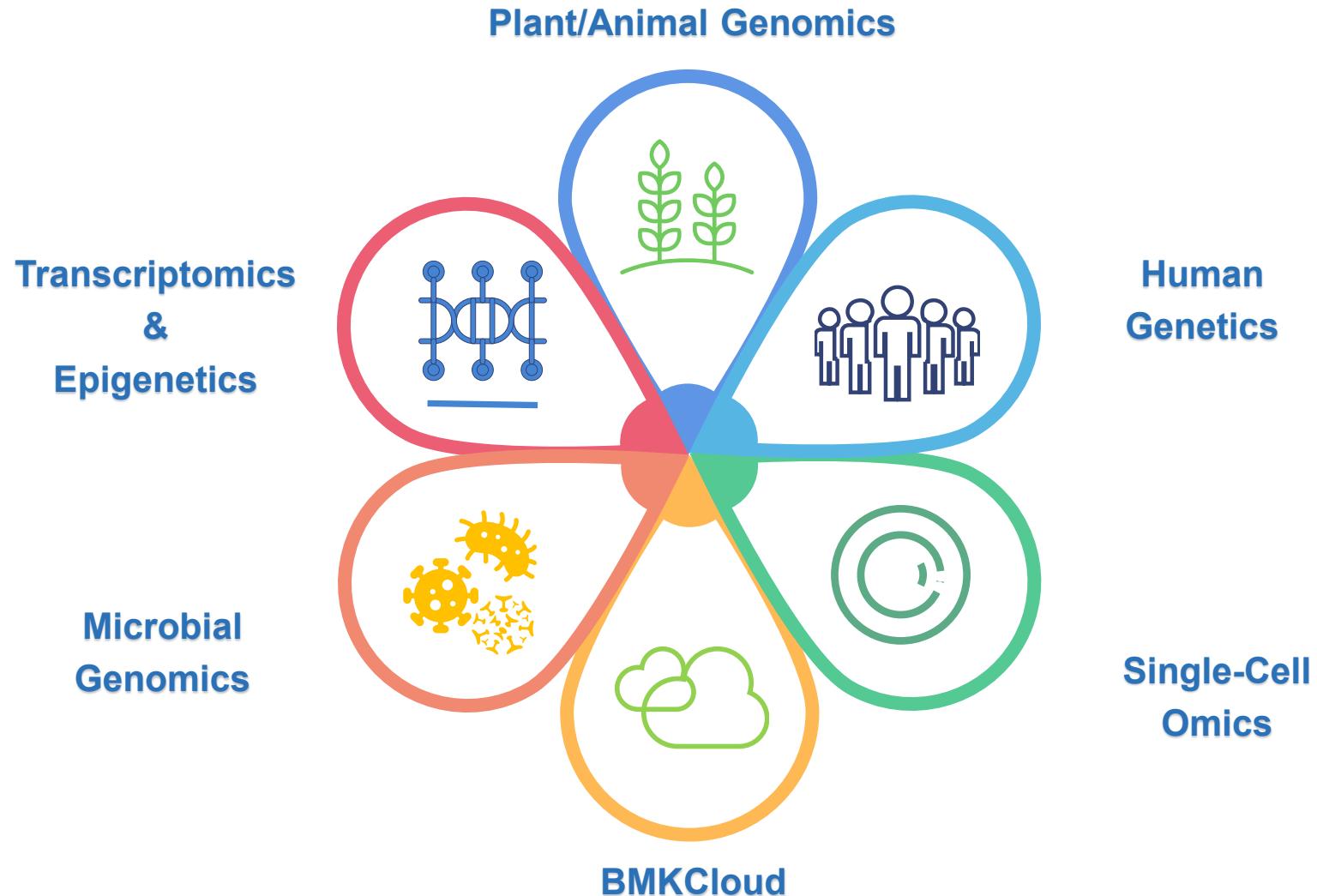
## Revio system

Reveal more with accurate  
long-read sequencing at scale

## Illumina NovaSeq X

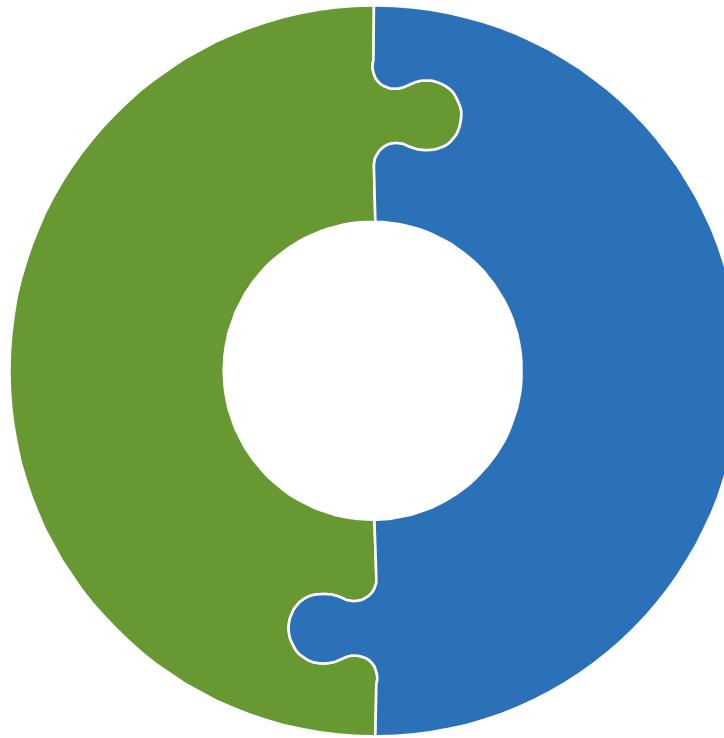


# BMKGENE-Service Scope



## *De novo* Genome Solutions

- ✓ PacBio CCS Sequencing
- ✓ Nanopore Sequencing
- ✓ Genome Survey
- ✓ *De novo* Genome Assembly
- ✓ Hi-C based Genome Sequencing
- ✓ Genome Annotation
- ✓ Comparative Genomics
- ✓ Pan-Genome Construction



## Population Genetics

- ✓ Whole Genome Sequencing (WGS)
- ✓ **SLAF-Sequencing**
- ✓ GWAS
- ✓ Evolutionary Genetics

# BMKGENE *De novo* Genome Sequencing

## One-Stop *De novo* Genome Solutions

01

Genome Survey

Illumina PE150 50 X

02

PB Sequencing

PacBio-CCS 30X Hifi reads

03

*De novo* Assembly

Multiple Strategies

04

Hi-C Sequencing

Illumina PE150 100 X

05

Genome Annotation

Full-length mRNA based  
annotation available

06

Assembly Validation

Comprehensive assembly  
quality assessments



BMKGENE witnessed **168 *de novo* genome research** successfully published in high-impact journals with total impact factors over 1674. **12 of the articles were published in Nature Genetics.**

# BMKGENE Transcriptomics Solutions

## NGS-mRNA

- NGS-based mRNA Sequencing (with ref)
- NGS-based mRNA Sequencing (Directional)
- NGS-based *de novo* mRNA Sequencing



## Full-length mRNA

- Nanopore-based full-length mRNA Sequencing
- PacBio-based full-length mRNA Sequencing (2+3 Solution)

## Non-coding RNAs

- lncRNA Sequencing
- small RNA Sequencing
- circRNA Sequencing
- Whole Transcriptome Sequencing

## Epigenetics

- Hi-C based Chromatin Interaction
- ATAC-Sequencing
- WGBS
- CCS-based methylation profiling
- Chip-Seq
- Cut&Tag and Cut&Run

## Metabarcoding

- NGS-based 16S v3+v4
- NGS-based ITS1
- Full-length 16S/18S/ITS (PacBio)
- Customized amplicons



## Bacterial Genome

- Whole genome resequencing
- Bacterial draft genome
- 0-Gap complete bacterial genome

## Metagenomics

- Shotgun metagenomic sequencing
- Nanopore-based metagenomics sequencing

## Fungal Genome

- Whole Genome Resequencing
- Fungal draft genome
- Fungal genome survey
- Fungal fine genome (PacBio or Nanopore)
- Fungal Hi-C based genome assembly

# Platforms-BMKCloud BI Center

Reliable, Ease-to-use On-line Bioinformatic Analysis Platform



**Self-developed BMKCloud platform**

**CPUs with 41,104 memory and 3 PB total storage**

**4,260 computing cores with peak computing power over 121,708.8 Gflop per second.**

# BMKCloud Automated BI Platform



[en.biocloud.net](http://en.biocloud.net)

## Advanced Analysis

- Advanced data mining tools;
- Multiple group settings being analyzed in parallel;
- Personalized parameter setting available;
- Re-shape the analysis as many times as you want.

## Bioinformatic Tools

**Figure Generator:** Heatmap; Histogram; Circos; Manhattan plot, etc.

**Sequence Analysis:** BLAST; Gene annotation; SNP primer design, etc.

**Data Processor:** FASTA to sqn; Adapter removal; FASTA toolkit, etc.

## Basic Data Analysis

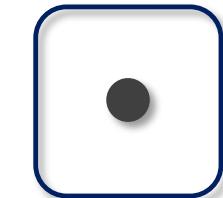
**RNA-Seq:** mRNA-seq; lncRNA-Seq; small RNA-Seq, etc.

**Population Genetics:** GWAS; BSA; Evolutionary genetics, etc.

**Third-Generation Sequencing:** Full length transcriptome, WGS, etc.

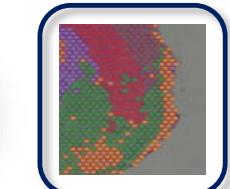
**Microbial genomics:** 16S/18S/ITS-Seq, Metagenomics, etc.

# Spatial Transcriptomics



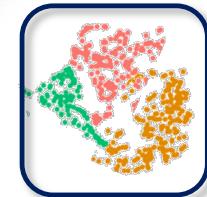
## Bulk mRNA

✓ Average gene expression



## ST-mRNA

✓ Spatially resolved



## SC-mRNA

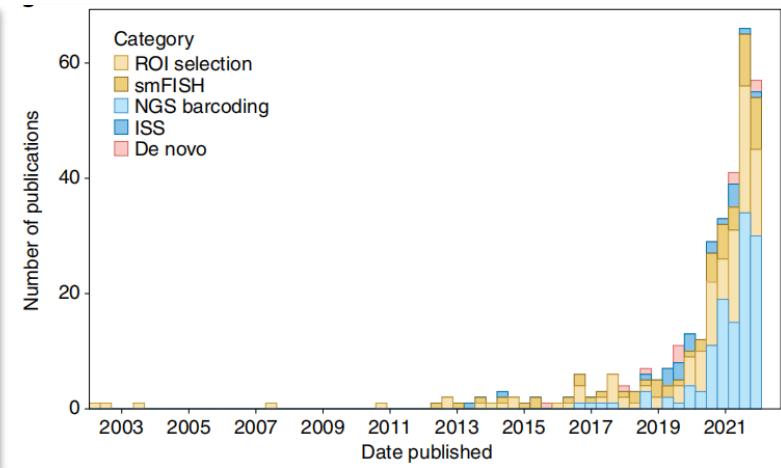
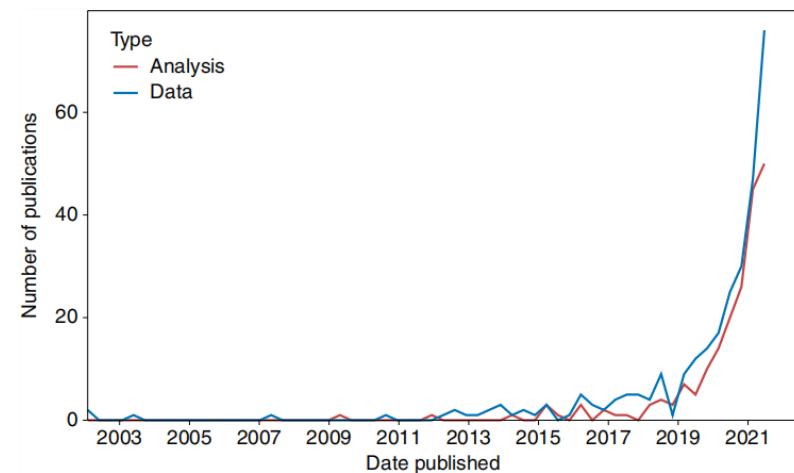
✓ Cell heterogeneity

**A** ROI: LCM

**B** smFISH

**C** In situ Sequencing (ISS)

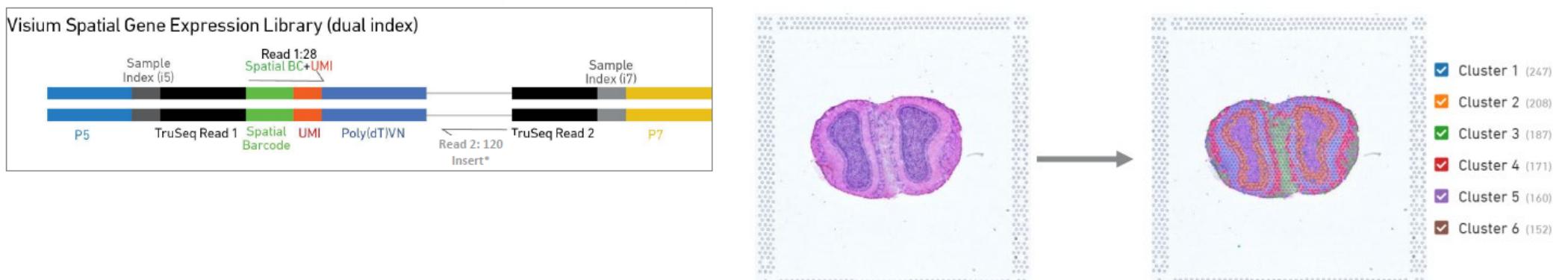
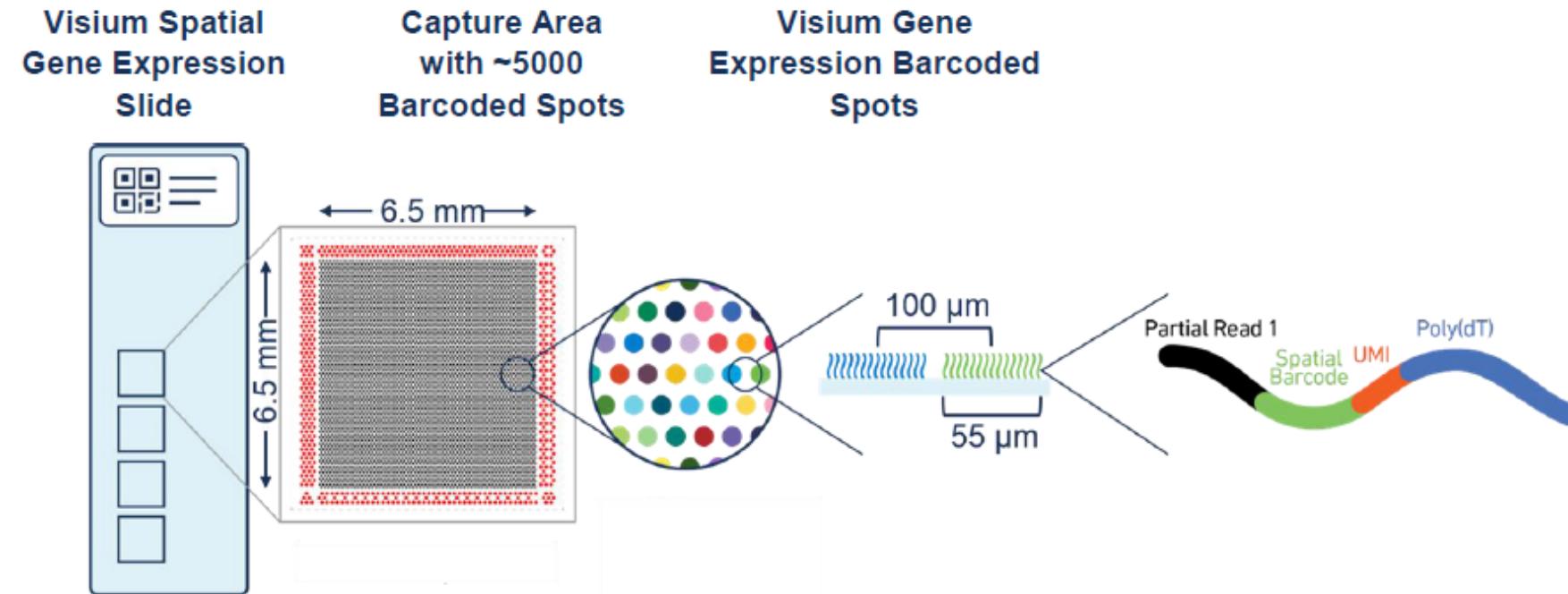
**D** Spatial Barcoding

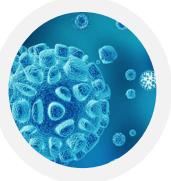


(Lambda Moses and Lior Pachter, 2022)



# 10X Visium Spatial Transcriptomics



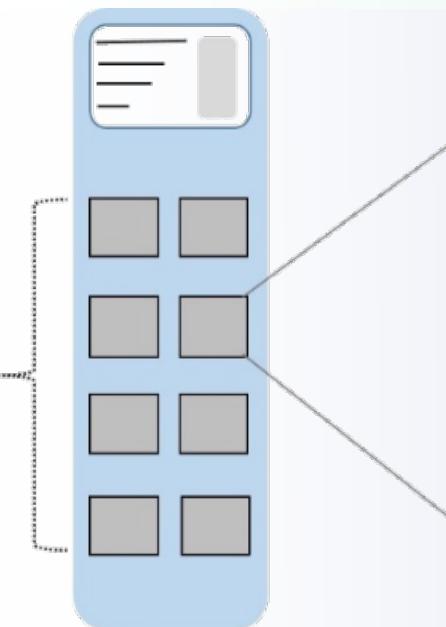


# Biomarker Technologies (Beijing) Launched S1000 Sub-cellular Level Spatial Omics Chip on Apr. 19th. 2022



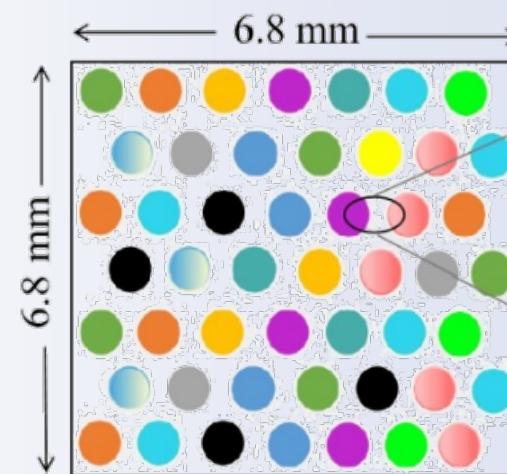
**BMKMANU  
S1000 Chip**

**Flexible Chip design with 1 - 8 capturing area**



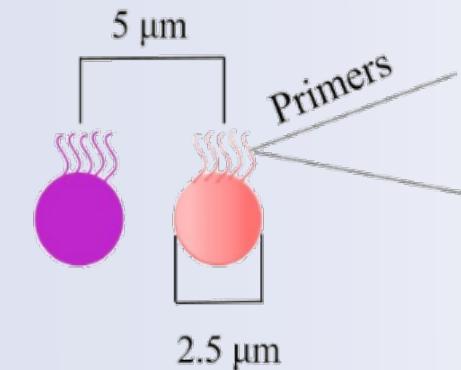
**Capture area**

**> 200 Million spots**



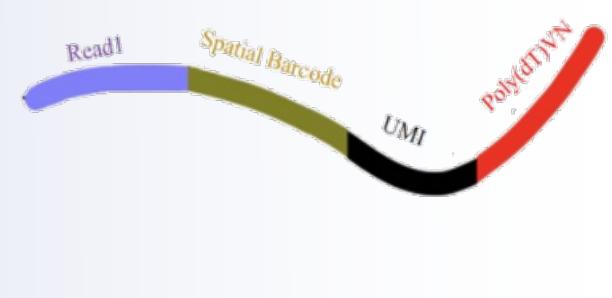
**Resolution: 5  $\mu$ m**

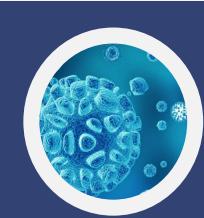
**Subcellular- Resolution**



**Capture probes**

**70 bp spatial barcode**

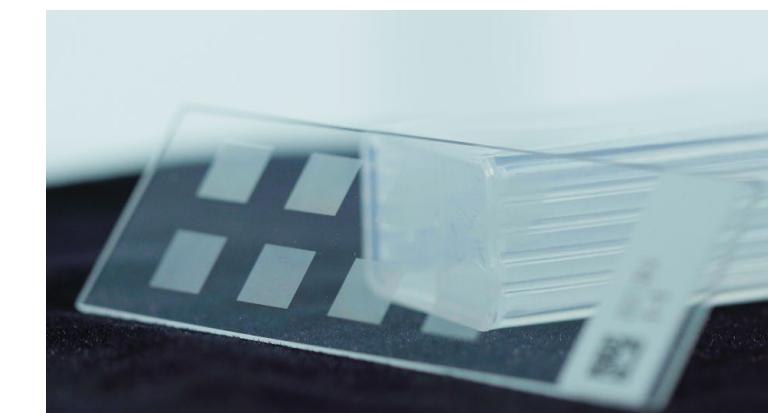
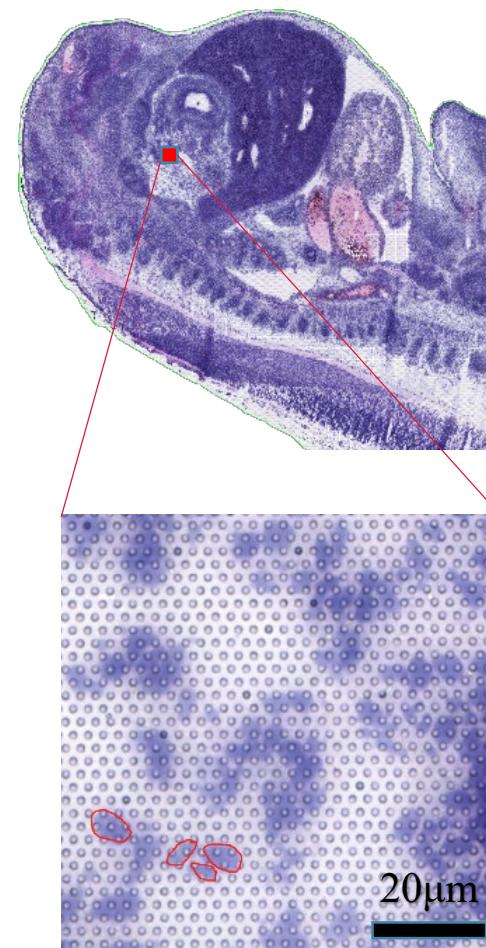
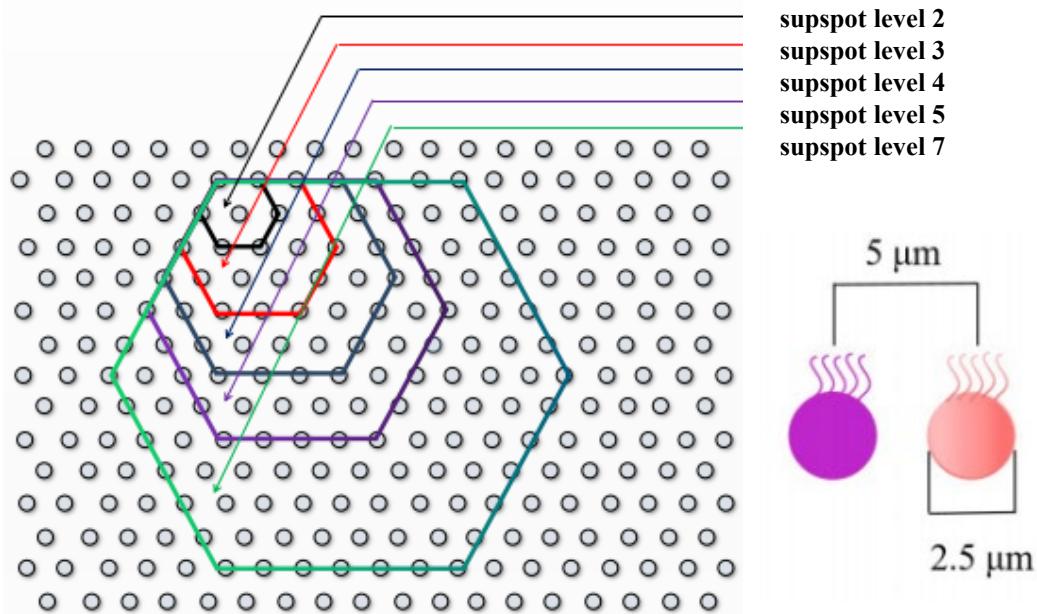




# Biomarker Technologies (Beijing) Launched S1000 Sub-cellular Level Spatial Omics Chip on Apr. 19th. 2022

Customized resolution setting as high as 5  $\mu\text{m}$  fulfilling different tissue type and research goal

From Level 1 (5  $\mu\text{m}$ ) to Level 13 (100  $\mu\text{m}$ )



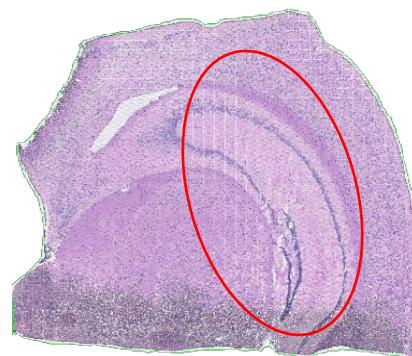
# Sub-cellular Resolution Spatial Transcriptomics



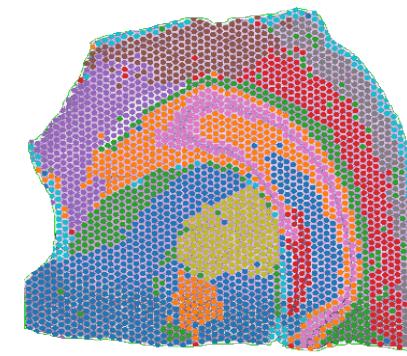
Customized resolution setting fulfilling different tissue type and research goal

## Tissue Structure

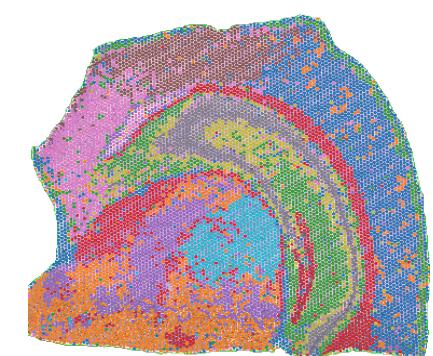
From Level 1 (5  $\mu\text{m}$ ) to Level 13 (100  $\mu\text{m}$ )



H&E Staining

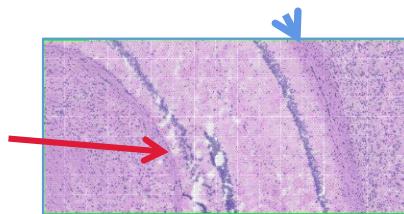


100 $\mu\text{m}$

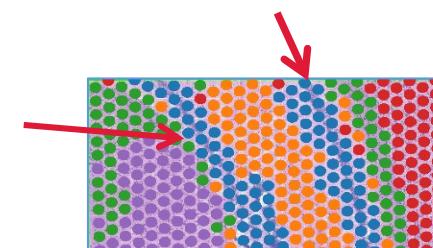


50 $\mu\text{m}$

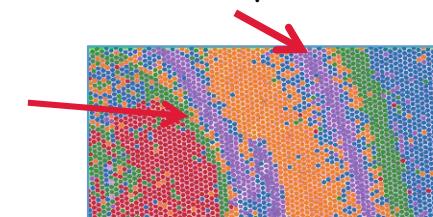
Hippocampus



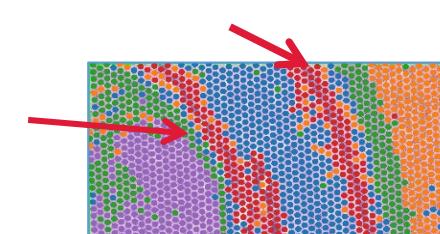
H&E Staining



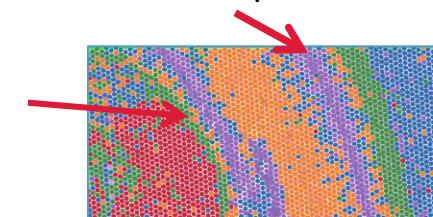
100 $\mu\text{m}$



35 $\mu\text{m}$



50 $\mu\text{m}$



20 $\mu\text{m}$

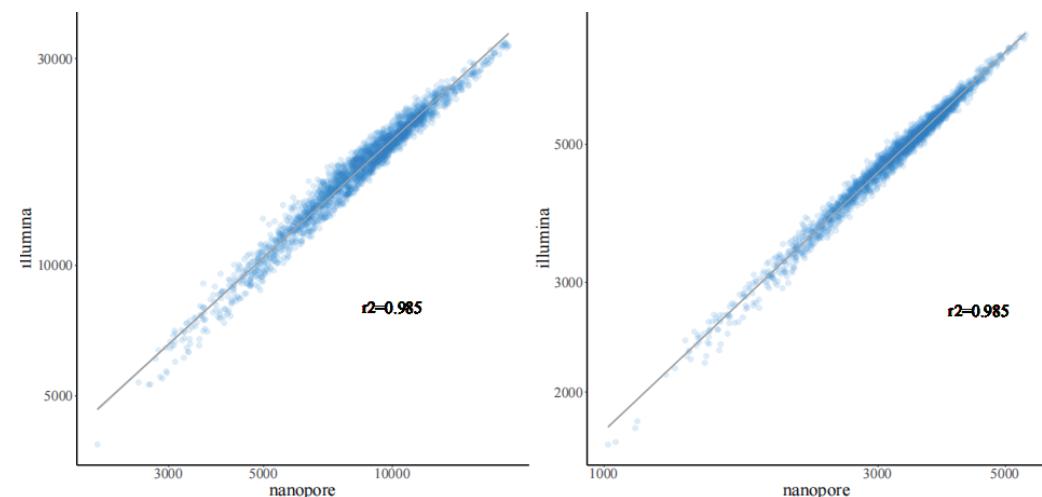
# R&D results on Full-length Spatial Transcriptomics

## Barcode identification and Mapping

Number of Reads	Number of Base	Reads with Valid Barcode	Bases with Valid Barcodes	N50	Bases Mapped to Transcriptome	Bases Mapped to Transcriptome And with Valid Barcode
105,553,898	70,516,281,320	73.85% (88.85%)	73.42%	740	66.44%	49.55%

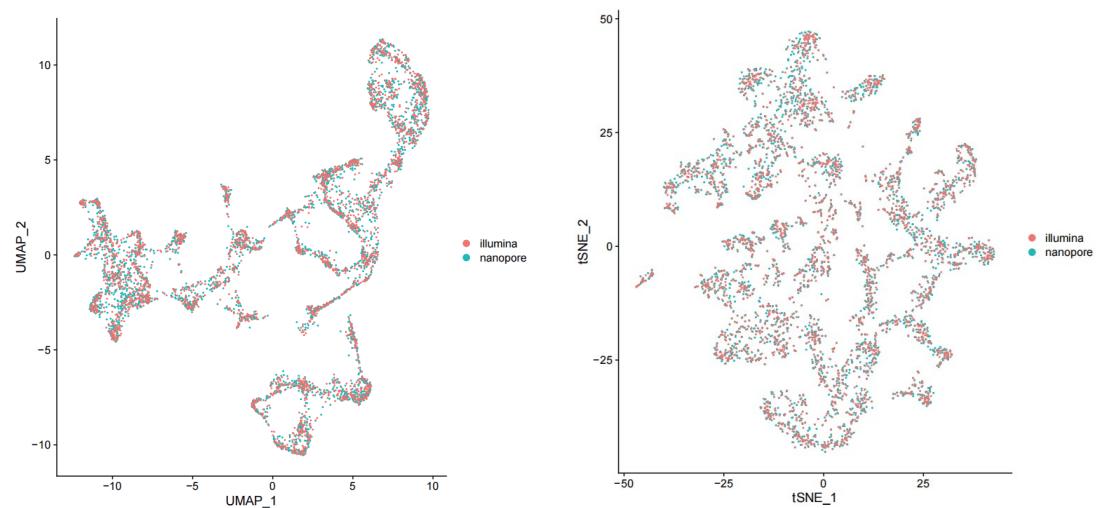
## Correlation on number of UMI and nGene per spot

Illumina vs. Nanopore



## Correlation on spot clustering

Illumina vs. Nanopore

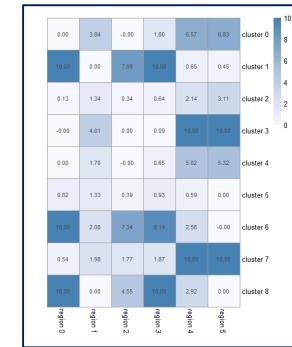
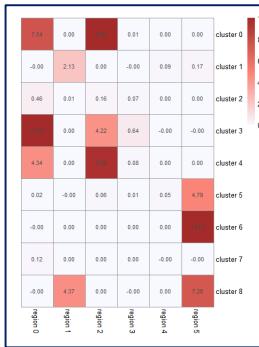
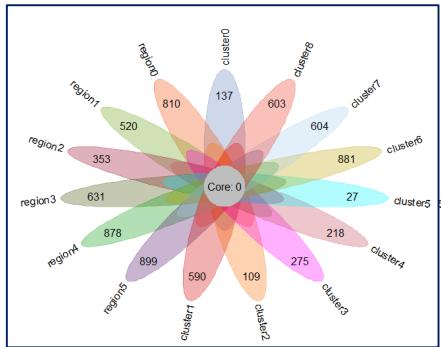


# Joint analysis with single-cell RNA data

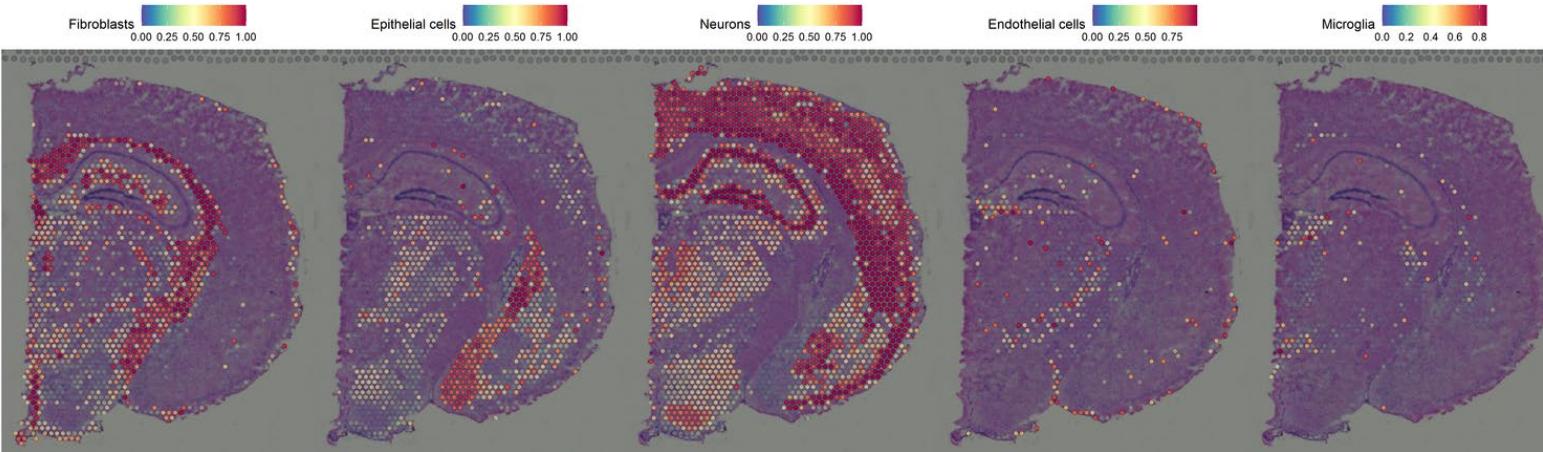
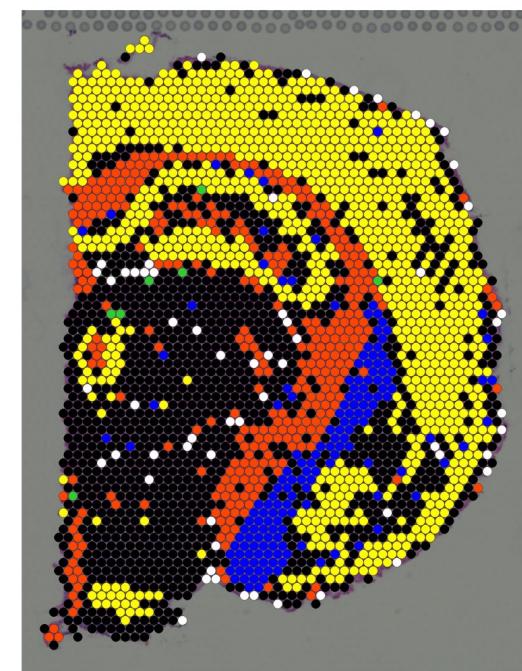
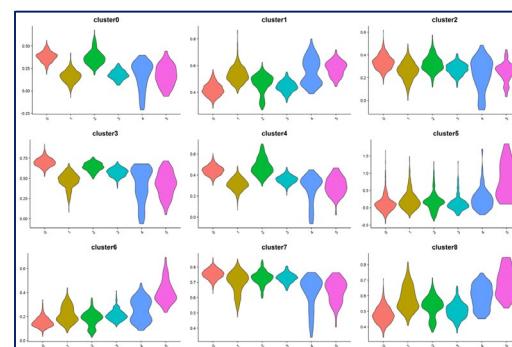


Single-cell RNA sequencing + Spatial transcriptome sequencing Joint Analysis

## Cell annotation



## Cell localization





# CONTACT

Biomarker Technologies (BMK) GmbH

Web: [www.bmkgene.com](http://www.bmkgene.com)

E-mail: [tech@bmkcloud.com](mailto:tech@bmkcloud.com)

 : Biomarker-technologies-overseas

Address: Technologiepark Münster,  
Johann-Krane-Weg 42, 48149,  
Münster, Germany

