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空间多组学临床转化医学创新研究策略

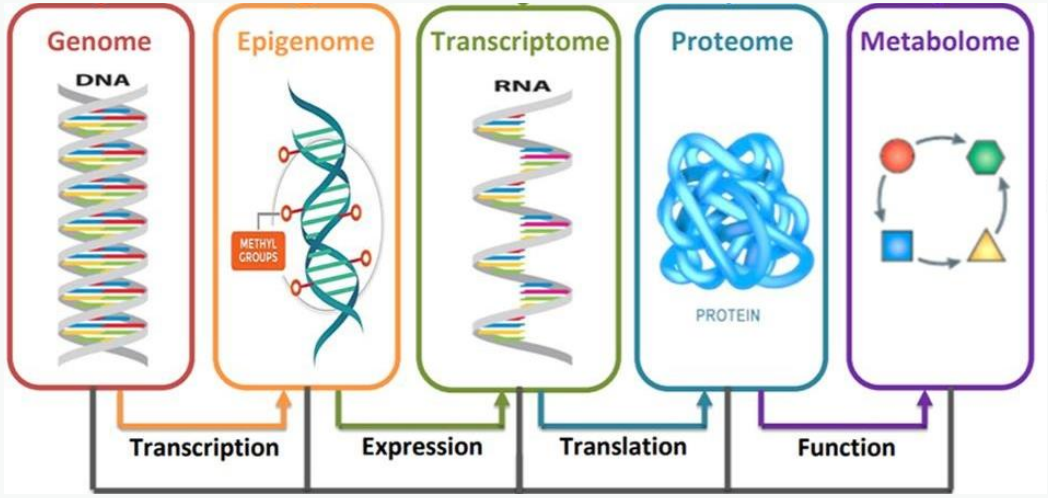
李振亚　博士

非因生物科技（山东）有限公司
Fynn Biotechnologies Ltd.

Mills 癌症个体化诊疗研究中心
Mills Institute for Personalized Cancer Care

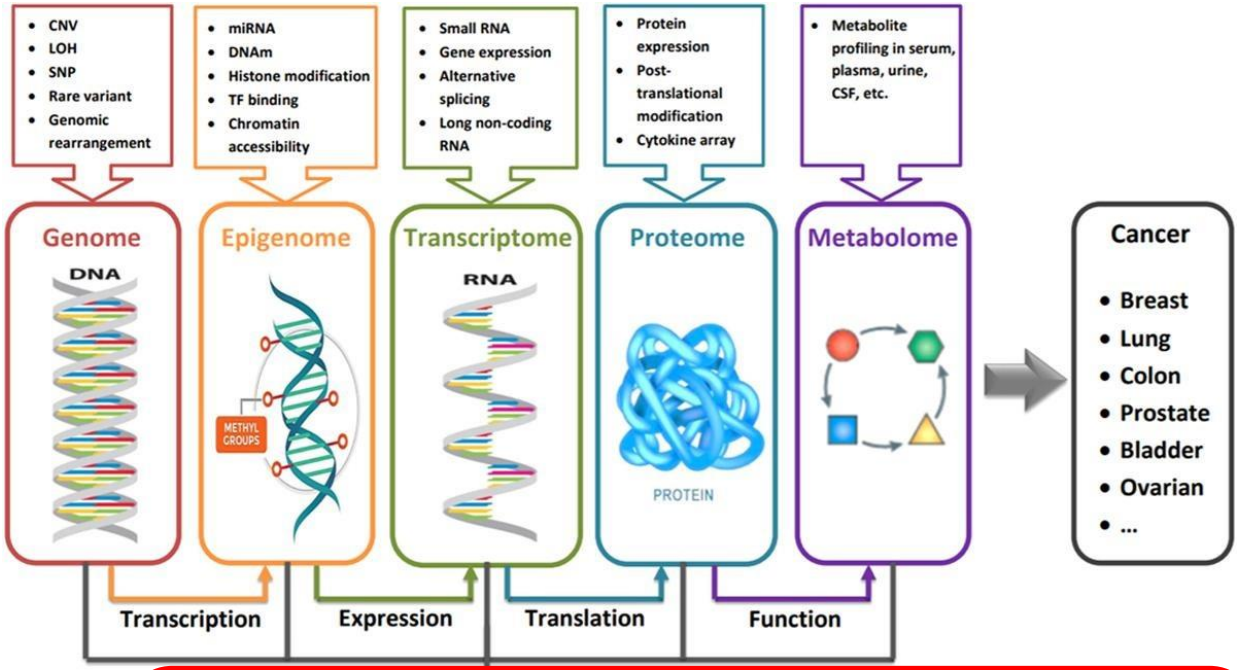
经典的多组学研究策略

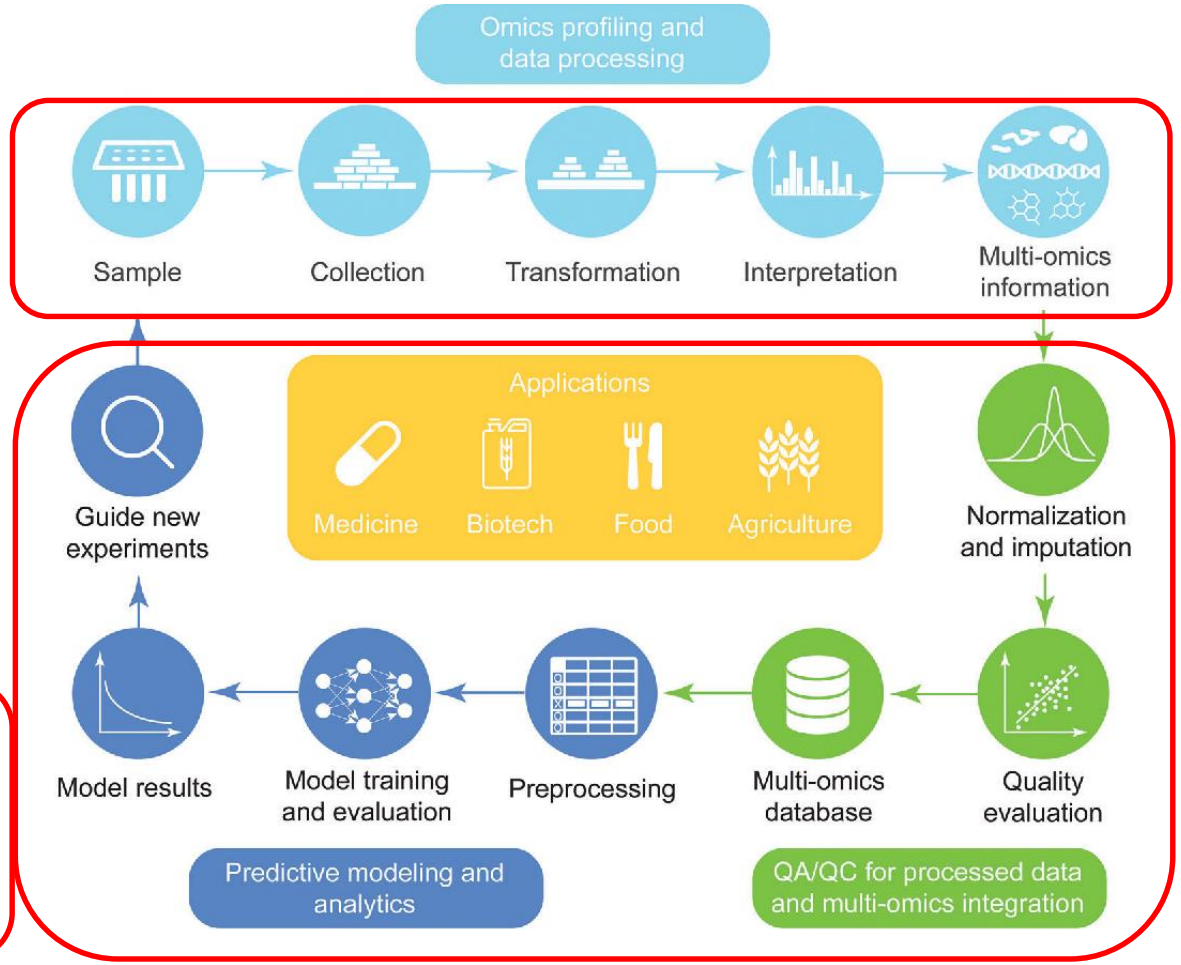
- 病人组织样本
- 外周血
- 外泌体
- 细胞模型
- 动物模型



整合型多组学分析

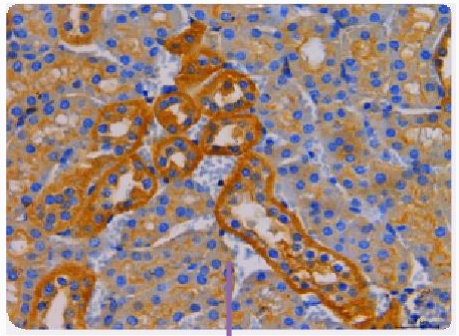
多组学交互研究


CNV
LOH
SNP
Rare variant
Genomic rearrangement
miRNA
DNAm
Histone modification
TF binding
Chromatin accessibility
Small RNA
Gene expression
Alternative splicing
Long non-coding RNA
Protein expression
Post-translational modification
Cytokine array
Metabolite profiling in serum, plasma, urine, CSF, etc.
Genome
DNA
Epigenome
METHYL GROUPS
Transcriptome
RNA
Proteome
PROTEIN
Metabolome
Transcription
Expression
Translation
Function
Cancer
Breast
Lung
Colon
Prostate
Bladder
Ovarian
...
Multi-Omics
Single-Omics
Challenge
Feature Selection
Challenge
Data Integration


Omics profiling and data processing
Sample
Collection
Transformation
Interpretation
Multi-omics information
Guide new experiments
Applications
Medicine
Biotech
Food
Agriculture
Normalization and imputation
Model results
Model training and evaluation
Preprocessing
Multi-omics database
Quality evaluation
Predictive modeling and analytics
QA/QC for processed data and multi-omics integration

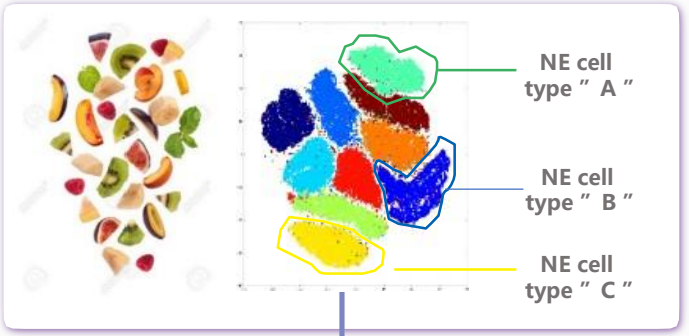
空间生物学的革命正在发生

探究微环境中组织结构、细胞亚型分布、特殊基因表达的重要性



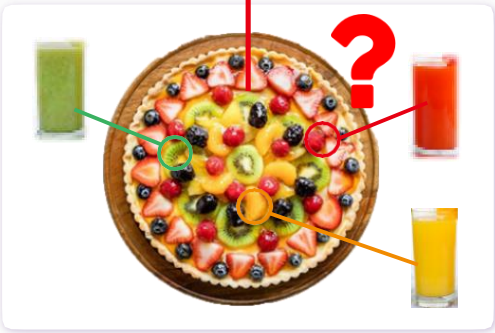
组织形态及功能
传统方式

TCGA和bulk组织
NGS分析
2006 年至今



单细胞测序，细胞分群
2012 年至今

组学结果如何与组织原位空间信息对应起来进行验证?



数字化空间分析(DSP)技术的出现

nature biotechnology

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Letter | Published: 11 May 2020

Multiplex digital spatial profiling of proteins and RNA in fixed tissue

Christopher R. Merritt, Giang T. Ong, Sarah E. Church, Kristi Barker, Patrick Danaher, Gary Geiss, Margaret Hoang, Jaemyeong Jung, Yan Liang, Jill McKay-Fleisch, Karen Nguyen, Zach Norgaard, Kristina Sorg, Isaac Sprague, Charles Warren, Sarah Warren, Philippa J. Webster, Zoey Zhou, Daniel R. Zollinger, Dwayne L. Dunaway, Gordon B. Mills & Joseph M. Beechem

Nature Biotechnology **38**, 586–599 (2020) | Cite this article

20k Accesses | **119** Citations | **133** Altmetric | Metrics

Abstract

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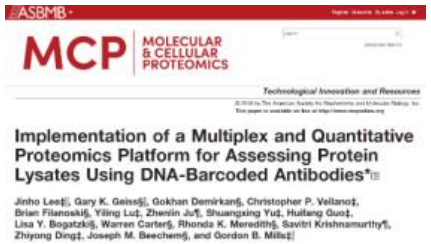
高维度分析与空间表达信息的解决方案

Gordon B. Mills

Dr. Joseph Beechem

Digital Spatial Profiler (DSP) 是一个全新的技术平台，Dr. Mills 是该项技术的共同发明人之一。它将传统的免疫荧光技术与数字可视化编码技术相结合，因此不仅能获得清晰的空间信 息，而且可以做到多重蛋白/RNA靶标的检测。目前在单个样本中的检测上限能够达到 150 种蛋白 / 18000 种 RNA，很好的将空间信息及其他多组学数据结合起来，极大的帮助科研工作者来解读 肿瘤异质性及其复杂的微环境。

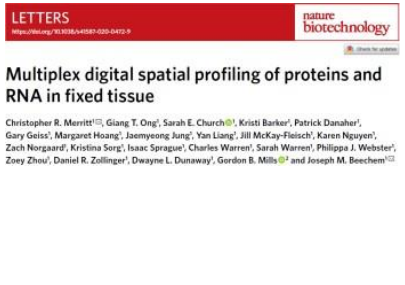

ASBMB

MCP MOLECULAR & CELLULAR PROTEOMICS

Technological Innovation and Resources

Implementation of a Multiplex and Quantitative Proteomics Platform for Assessing Protein Lysates Using DNA-Barcoded Antibodies*

Jinho Lee‖, Gary K. Geiss‖, Gokhan Demirkan§, Christopher P. Vellano‡, Brian Filanoski‖, Yiling Lu‡, Zhenin Ju¶, Shuangxing Yu‡, Huifang Guo‖, Lisa Y. Bogatzki‖, Warren Carter§, Rhonda K. Meredith§, Savitri Krishnamurthy¶, Zhiyong Ding‡, Joseph M. Beechem§, and Gordon B. Mills‖‡


LETTERS

nature biotechnology

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nanoString

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

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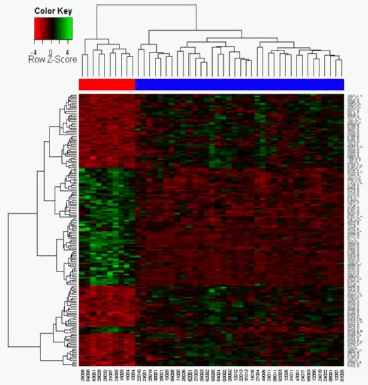
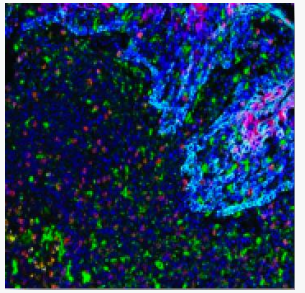
解决现有技术存在问题，可进行RNA-蛋白共分析

高维度表达谱分析	OR	低维度图像分析





高维度 ⟷ 空间性 ⟷ 定量性 ⟷ 准确性

GEP:
Multi-plex PCR (bulk),
RNAseq (bulk),
Single-cell RNAseq,
PEP:
Flow Cytometry,
Mass cytometry,
DSP

IHC,
Immunofluorescence,
FISH

- 相对荧光强度定义的表达量，各个荧光基团的激发强弱差异
- 定量存在偏倚
- 自荧光
- 荧光信号交叠
- 多重靶标检测能力限制在30-40重（实操）

高维度分析与空间表达信息的解决方案

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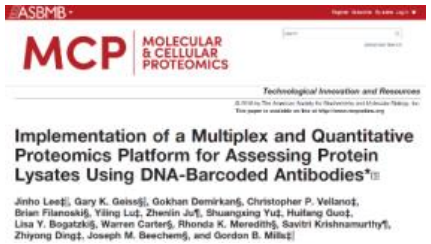
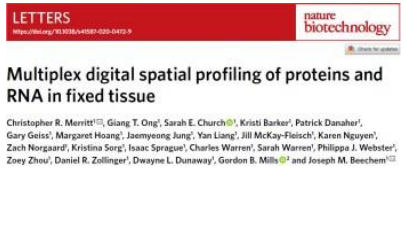




nanoString

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

- 适用于FFPE样本和新鲜样本
- 样本制备简便容易
- 兼顾形态学与原位信息对应关系
- 适用于大样本空间组分析（TMA）
- 样本覆盖区域大，不同组织区域或结构异质性信息更为全面丰富
- 可同时分析蛋白和RNA，可实现原位全转录组高通量分析

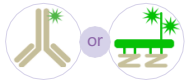
蛋白组和空间组为核心的多组学研究策略

DSP技术原理及流程

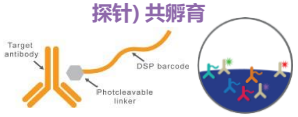
- 石蜡样本/冰冻切片/穿刺样本等多样本、珍贵样本策略
- 前处理简单，无需优化，视野区域广阔，无需盲选
- 靶向检测，对中低表达靶点友好
- 自动化程度高，结果可重复性强

特定标记荧光抗体(或探针)与所选待测指标共孵育

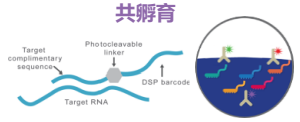
形态学标记荧光抗体或RNA探针



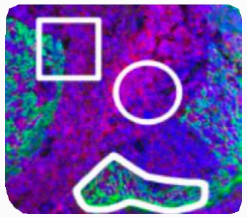
蛋白检测
待测靶点抗体+特定标记荧光抗体(或探针) 共孵育

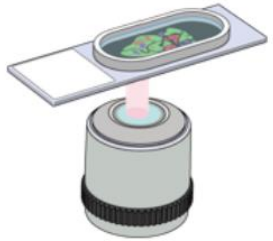


RNA检测
探针孵育+特定标记荧光抗体(或探针)共孵育

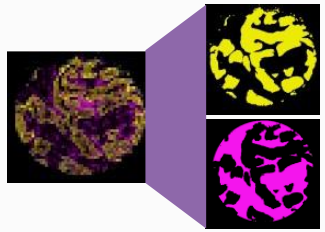


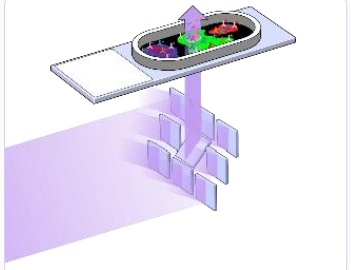
形态学标记荧光成像 ROI（感兴趣区域）圈选





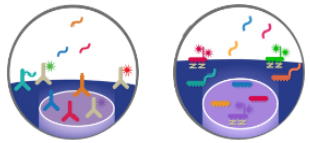
区域划分（Segment, 可选）紫外光解 DSP barcode



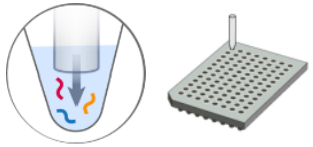


逐个 ROI 收集 DSP barcode 到 96 孔收集板

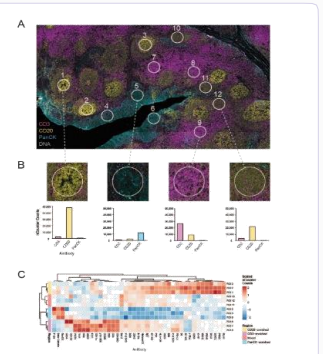
紫外光照射，linker断裂，DSP barcode解离至上层缓冲液



毛细管将解离的DSP barcode收集至96孔板



计数、测序和数据分析

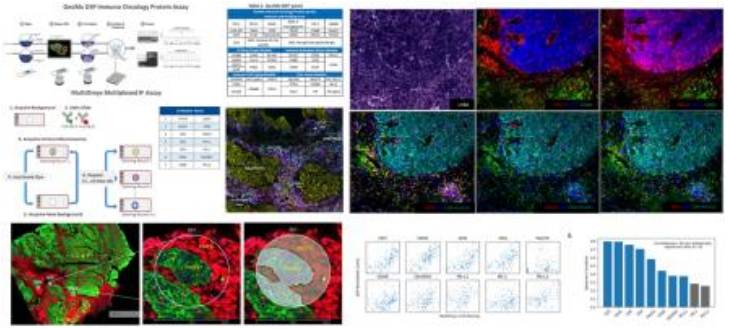


DSP技术的应用场景

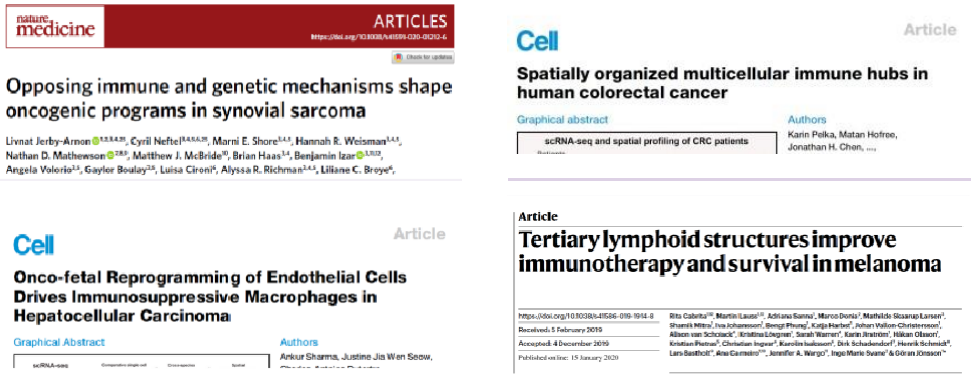
运用 DSP 作为探索性工具

运用 DSP 与高通量多组学数据进行整合

DSP 与单细胞空间组联合分析



运用 DSP 与单细胞测序交叉验证



高维度分析与空间表达信息的解决方案

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Letter | Published: 11 May 2020

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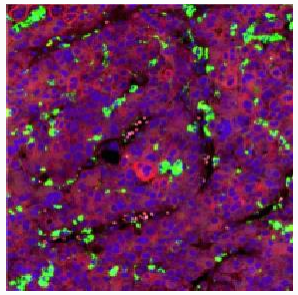
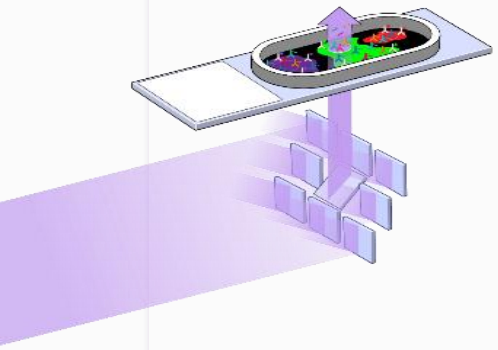
特殊光学技术助力灵活的ROI 选择和Masking 覆盖

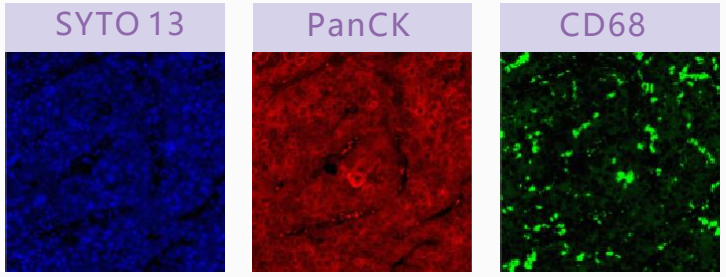
细胞亚群纯化策略

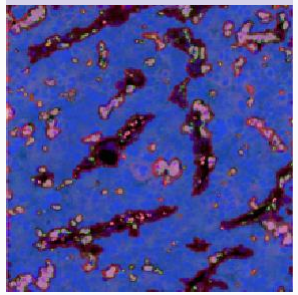
Full Channel Overlay





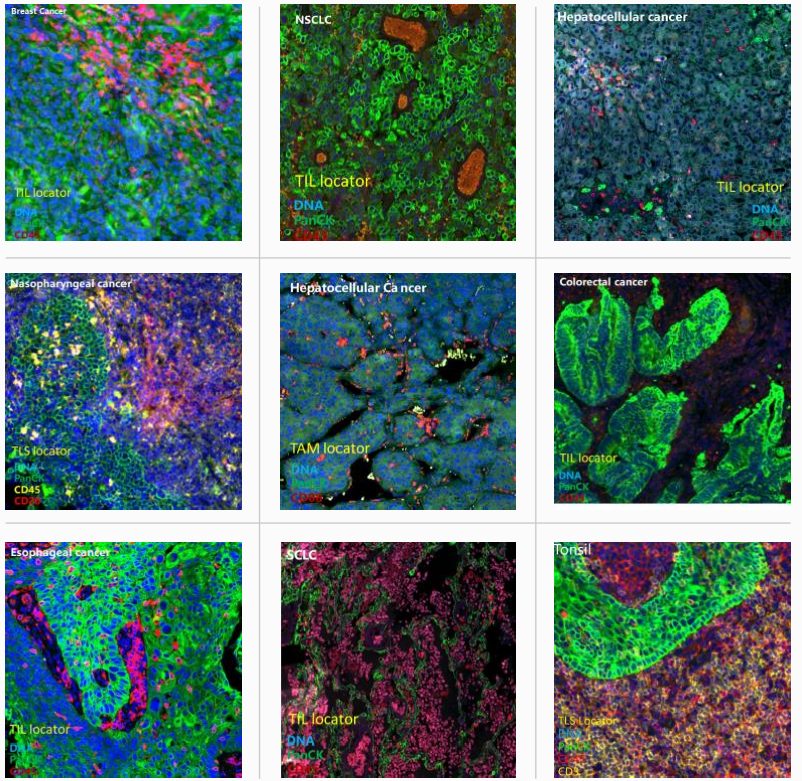
Single Channel（Mask）





细胞亚群及特殊组织结构定位

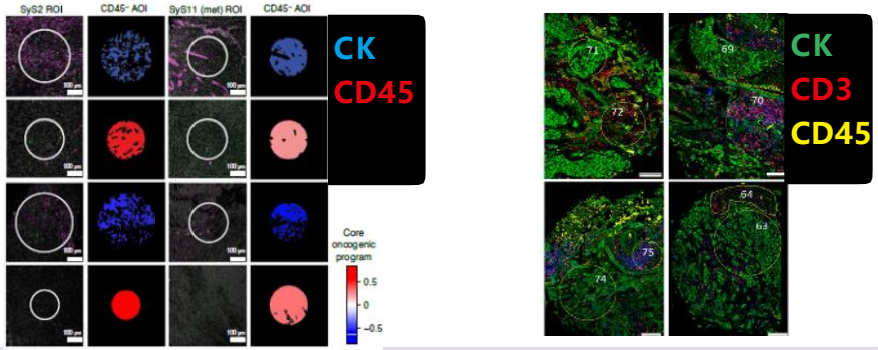
(TLS/TIL/TAM)



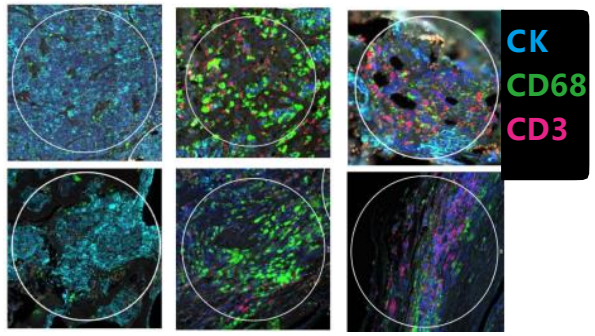
DSP染色解决方案

- 合适的亚组织结构或细胞群标志物，有助于ROI的选择和后续分析。

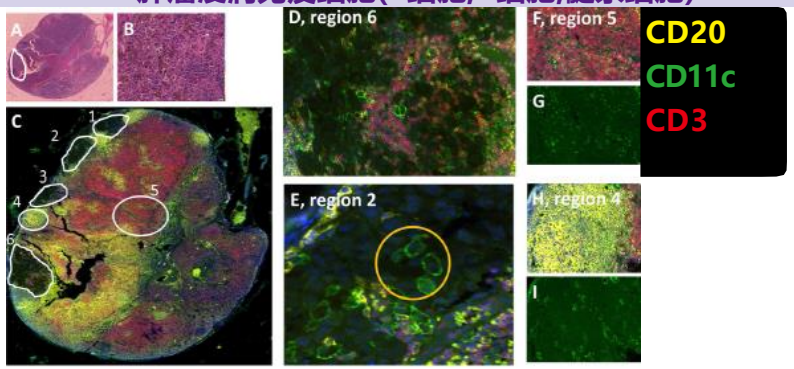
肿瘤及肿瘤浸润免疫细胞(白细胞，T细胞)



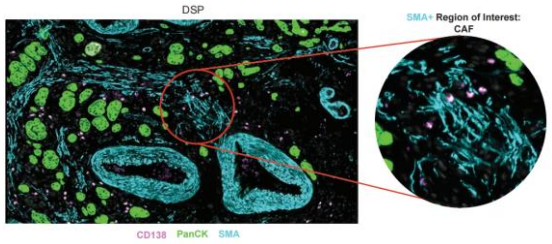
肿瘤及肿瘤浸润免疫细胞(T细胞,巨噬细胞)



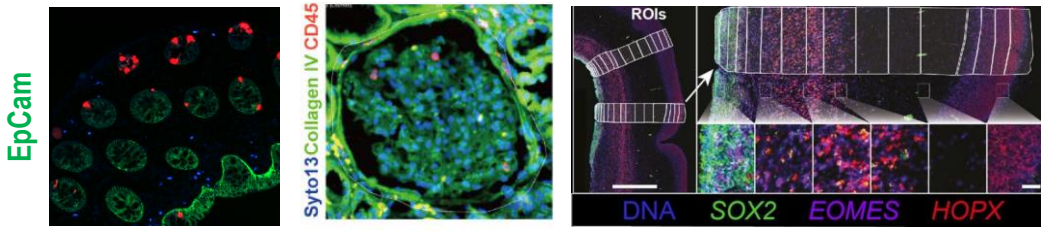
肿瘤浸润免疫细胞(T细胞,B细胞,髓系细胞)



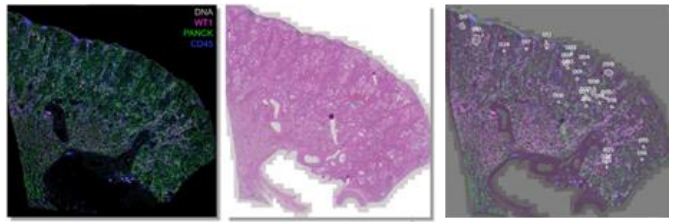
肿瘤相关基质细胞(成纤维类)



其他特殊标志物染色



通过HE确定待分析结构



DSP检测panel 设置（蛋白+RNA）

Neural Cell Profiling Panel
- Alzheimer's Pathology Panel
- Alzheimer's Pathology Extended Panel
- Alzheimer's Pathology Extended Panel
- Autophagy Panel
- Glial Cell Subtyping Panel

75 targets

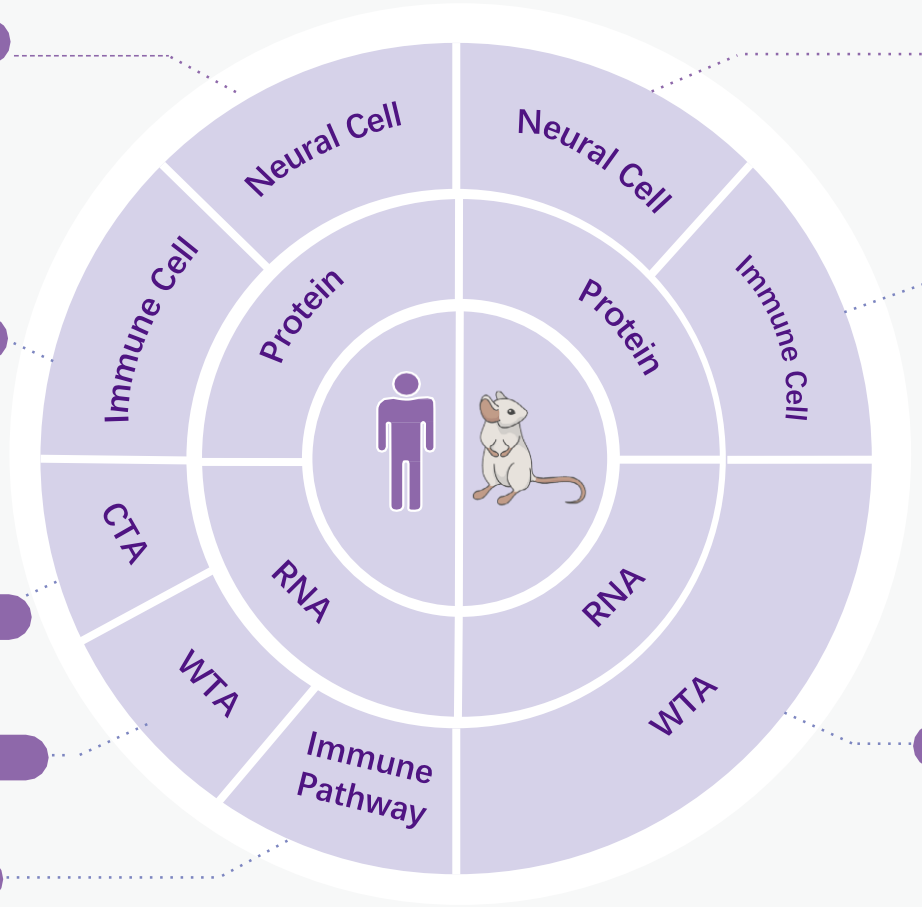
Immune Cell Profiling Panel
- IO Drug Target Panel
- Immune Activation Status Panel
- Immune Cell Typing Panel
- Pan-Tumor Panel
- MAPK Signaling Panel
- PI3K/AKT Signaling Panel
- Cell Death Panel

140 targets

1,800 targets

18000 targets

84 targets



Neural Cell Profiling Panel
- Alzheimer's Pathology Panel
- Alzheimer's Pathology Extended Panel
- Parkinson's Pathology Panel
- Autophagy Panel
- Glial Cell Subtyping Panel

Immune Cell Profiling Panel
- IO Drug Target Panel
- Immune Activation Status Panel
- Immune Cell Typing Panel
- Pan-Tumor Panel

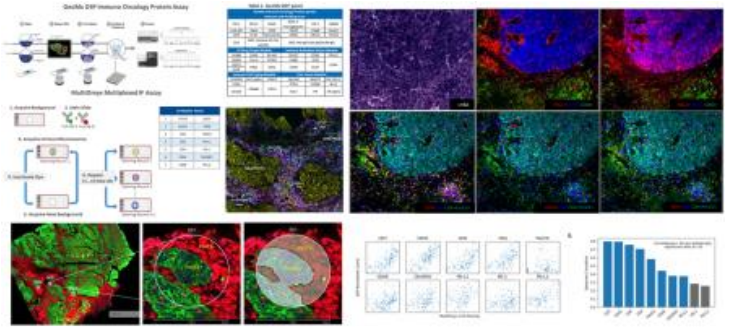
21000 targets

DSP在肿瘤微环境相关研究中的切入点

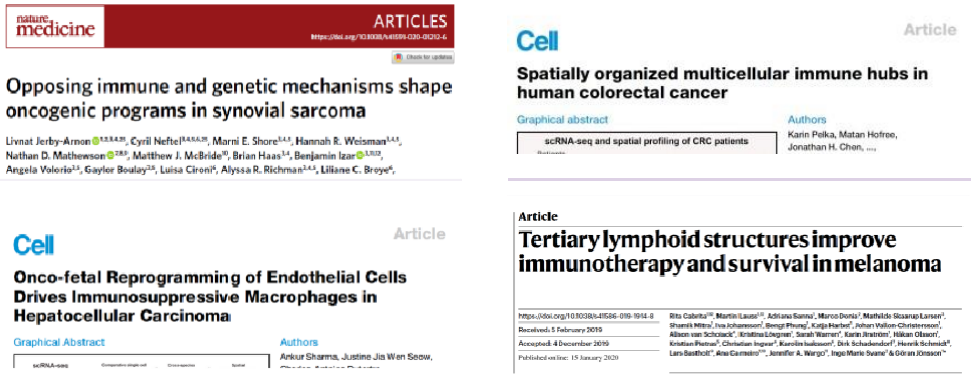
运用 DSP 作为探索性工具

运用 DSP 与高通量多组学数据进行整合

DSP 与单细胞空间组联合分析



运用 DSP 与单细胞测序交叉验证



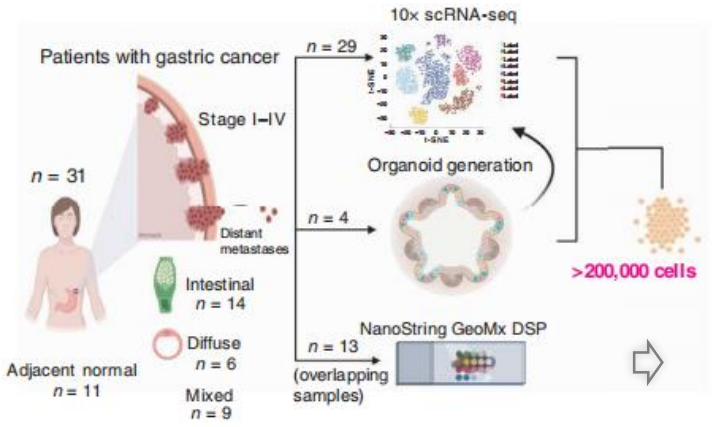
本次系列讲座探讨的核心内容

- 如何合理设计研究方案并最大化利用样本，开展空间多组学研究?
- 如何对多组学技术平台获得的数据进行集成分析，并有效进行验证?

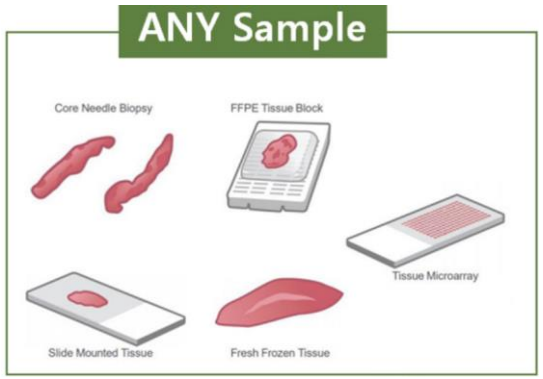
DSP空间组学的样本规划

研究样本

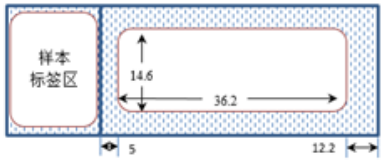
- 新鲜组织样本 → RNA-seq，sc-RNAseq，蛋白组分析、DSP分析等
- 体外模型(细胞、动物、类器官) → 各类体外实验
- FFPE组织切片或组织芯片 → 病理学分析/DSP分析/mIHC



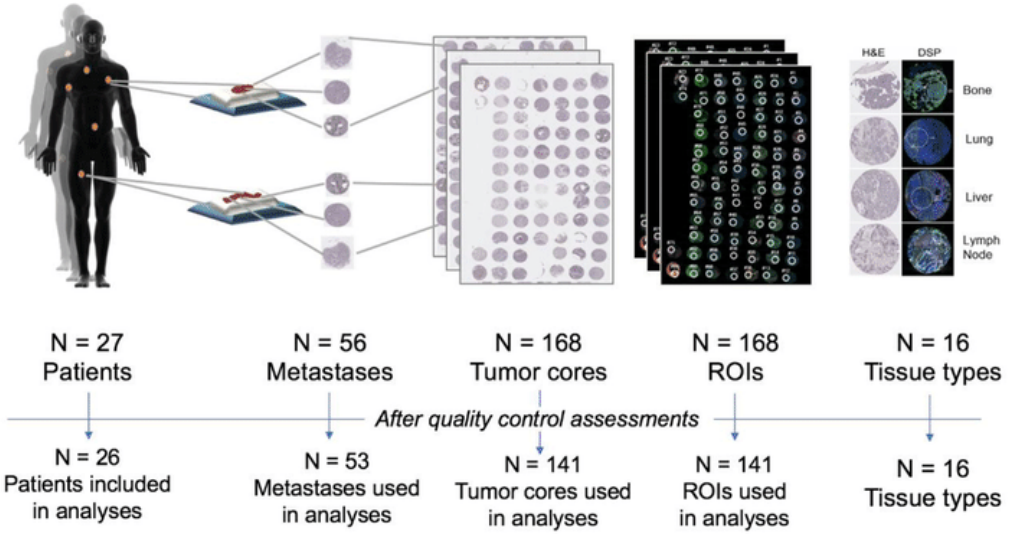
满足DSP分析的样品类型



普通组织切片



组织芯片(TMA)



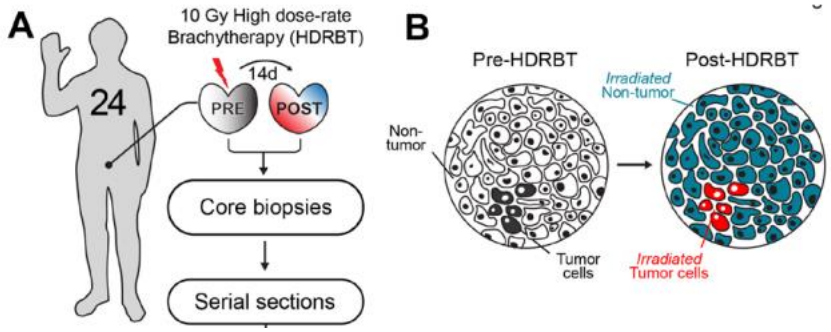
DSP空间组学的样本规划

样本收集（穿刺/手术）	
瘤内异质性	Clinical Cancer Res 2020 (软骨肉瘤)
原发转移灶异质性	Journal of Immunotherapy of Cancer 2022 (肉瘤)
外周基质微环境	Journal of Immunotherapy of Cancer 2020 (前列腺癌骨转移)
特定细胞亚群	Cancer Cell 2021 (胰腺癌)
特定病理学形态学结构	Nature 2019 (黑素瘤相关三级淋巴结构)

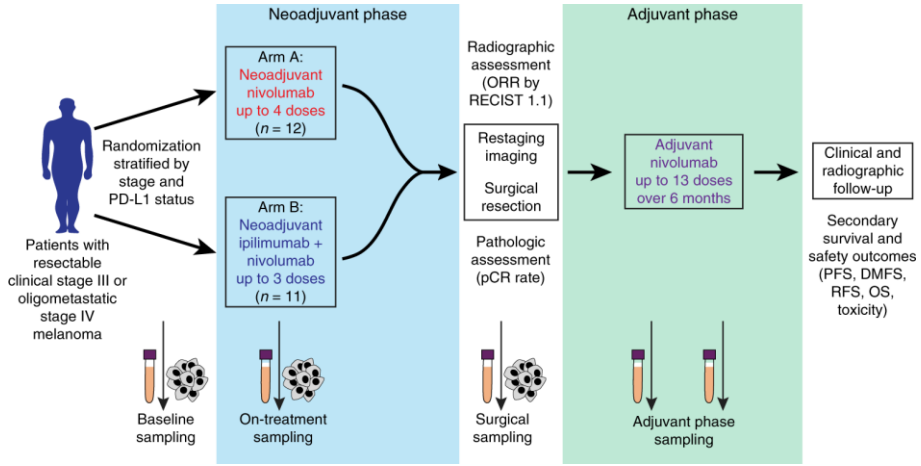
样本收集(组织芯片)	
肿瘤核心/病灶异质性	Nat Comm 2020 (前列腺癌---常规转录组/基因组联用)
肿瘤免疫微环境	Clinical Cancer Res 2020 (肺癌生物标志物挖掘)
外周基质微环境	Cell Rep 2021 (神经母细胞瘤相关基质微环境)
特定细胞亚群	Clinical Cancer Res 2019 (黑素瘤-巨噬细胞/免疫基质)
特定病理学特征/形态学结构	Nature 2019 (黑素瘤相关三级淋巴结构)

DSP空间组学的样本分组

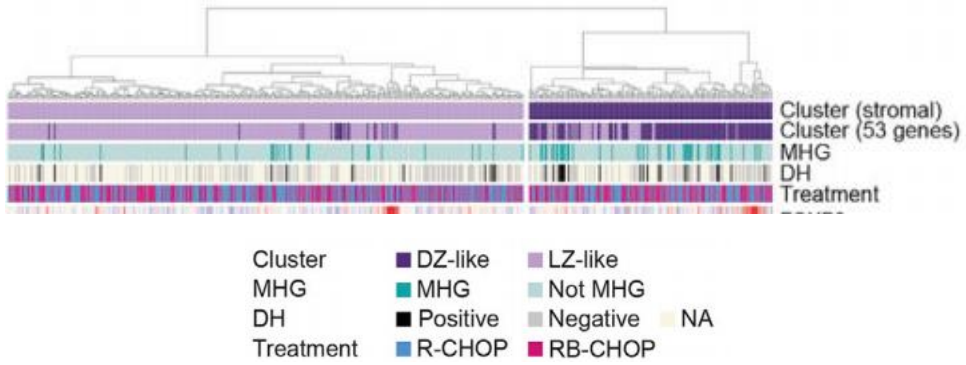
样本分组(治疗前与治疗后)



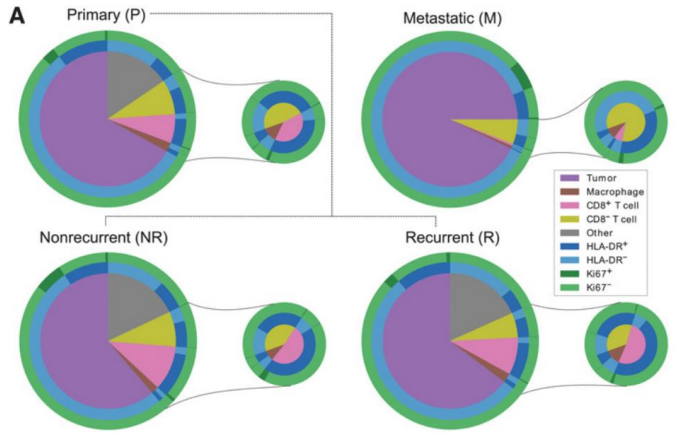
样本分组(治疗进程取样)



样本分组(疾病亚型与治疗分组)



样本分组(疾病发展过程)



DSP空间组学的样本分组

样本分组(病理分型和分子分型)

Table 1 Summary of patient and tumor characteristics

Patient	Tissue	Diagnosis	ER(%)/ PR(%)/ HER2(+)	PAM50 Subtype	TIS Status	Treatment at the time of sample collection
1	Breast	IDC, DCIS	2/0/3	Luminal A	High	Gemcitabine and trastuzumab
1	Breast	Tumor emboli	N/A	Luminal A	High	Nab-paclitaxel and trastuzumab
1	Lung	Metastatic	0/0/3	HER2 enriched	High	Nab-paclitaxel and trastuzumab
2	Breast	ICD, DCIS	0/0/3	HER2 enriched	Low	None. Initial diagnosis
2	Breast	Residual IDC	0/0/N/A	HER2 enriched	High	TDM1, pertuzumab, doxorubicin and cyclophosphamide*
2	Soft tissue	Local recurrence	0/0/3	HER2 enriched	Low	Trastuzumab and pertuzumab
3	Brain	Metastatic	15/0/3	HER2 enriched	Low	None. Discontinued due to toxicities
4	Breast	IDC	0/0/3	Basal like	High	None. Initial diagnosis
4	Breast	Local recurrence	N/A	Luminal A	High	Doxorubicin, cyclophosphamide, paclitaxel and trastuzumab
5	Brain	Metastatic	0/0/3	Basal like	Low	TDM1 and anastrozole
6	Breast	IDC, DCIS	80/70/2**	Luminal A	High	None. Initial diagnosis
7	Breast	IDC, DCIS	0/0/3	HER2 enriched	High	None. Initial diagnosis
7	Breast	Local recurrence	N/A	Basal like	High	None. Completed neoadjuvant and adjuvant therapy
8	Breast	IDC, DCIS	10/15/1	Luminal A	Low	None. Initial diagnosis
8	Soft tissue	Local recurrence	0/0/3	Basal like	Low	Nab-paclitaxel and atezolizumab (previously had triple negative disease)

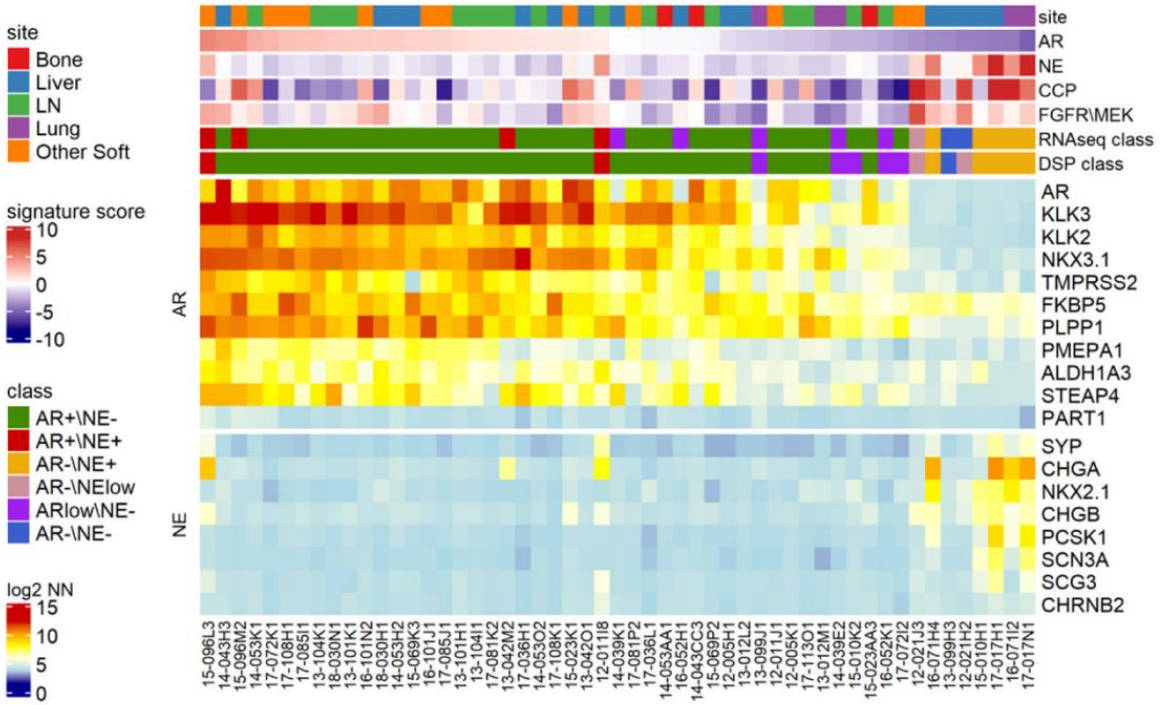
DCIS: ductal carcinoma in situ; DCIS: ductal carcinoma in situ; ER: estrogen receptor; HER2: human epidermal growth factor 2; IDC: invasive ductal carcinoma; IDC: invasive ductal carcinoma; PR: progesterone receptor; TDM1: ado-trastuzumab emtansine; TIS: tumor inflammation score

* Neoadjuvant therapy in the ISPY2 clinical trial

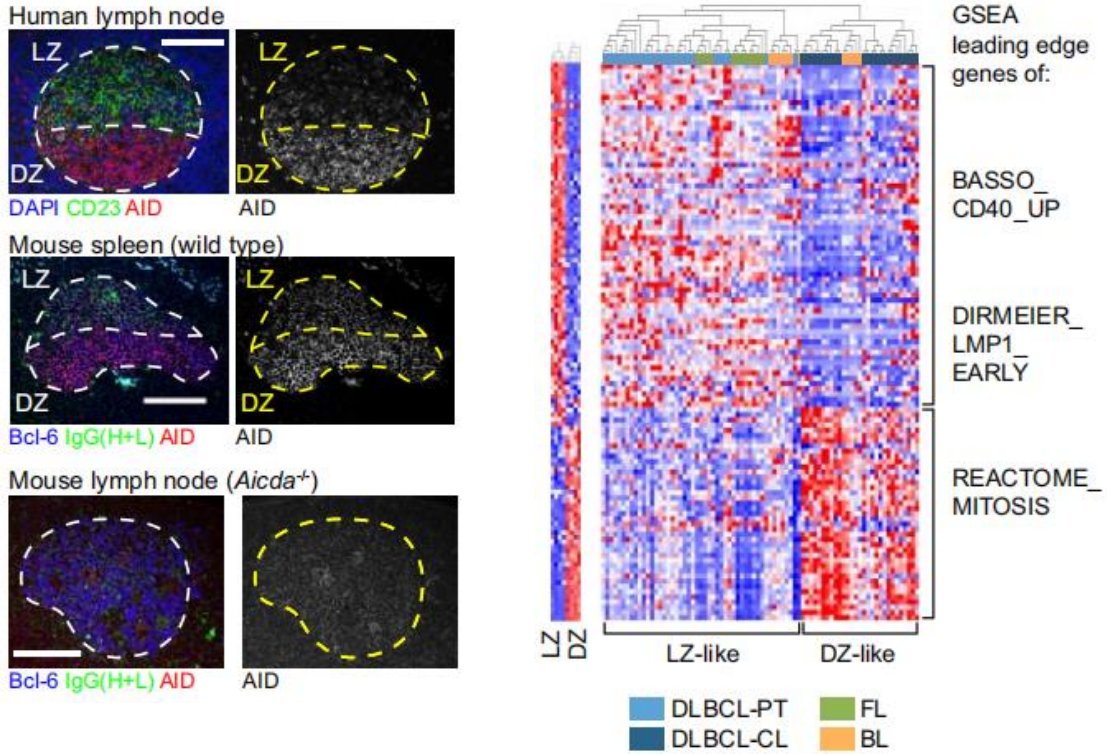
** HER2/CEP17 ratio: 2.13 (amplified by FISH)

DSP空间组学的样本分组

样本分组(特征基因集分型)

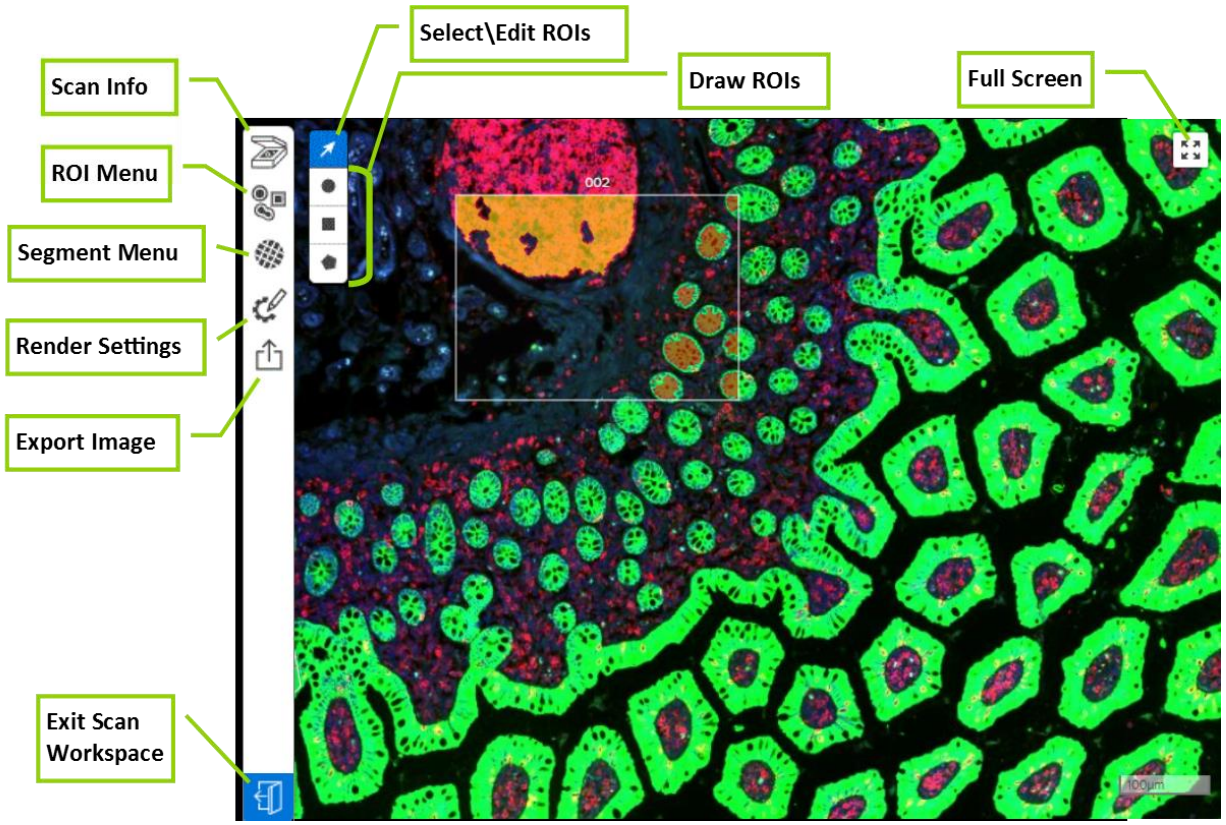


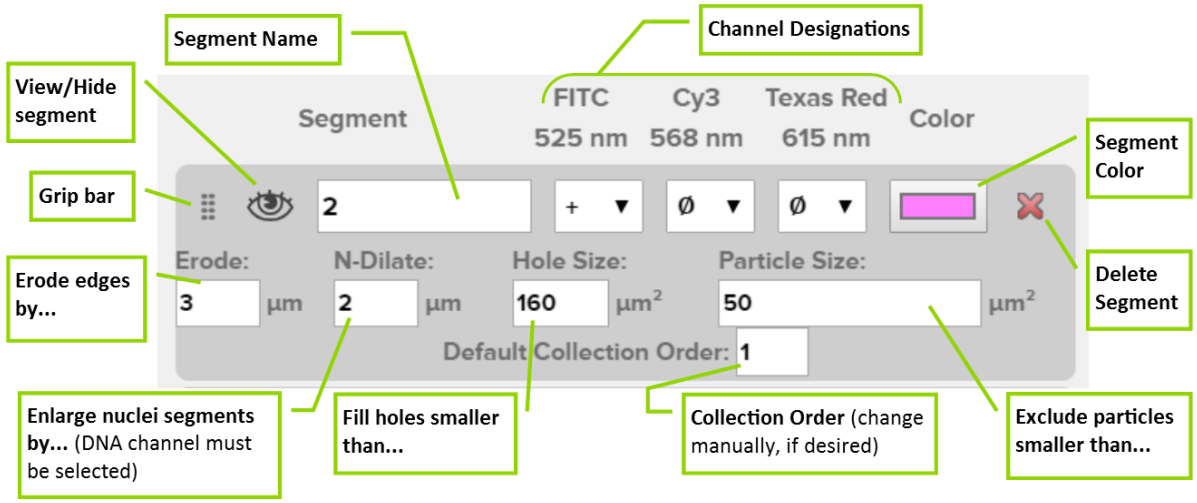
样本分组(病理组织结构结合特征基因集分型)



DSP空间组学的兴趣区域(ROI)选择

ROI的选择是DSP技术最大化应用的核心环节

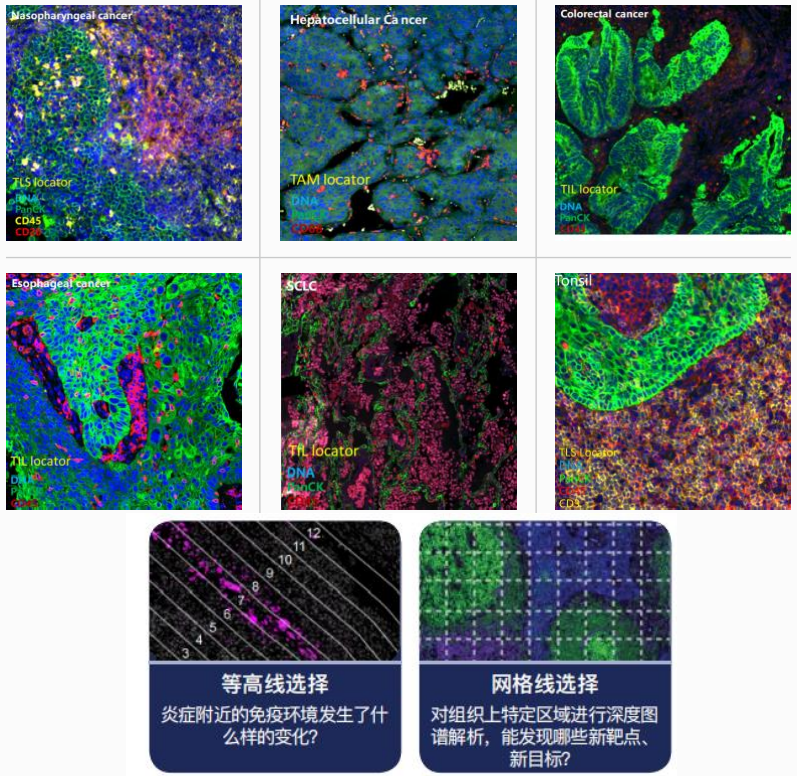




DSP空间组学的兴趣区域(ROI)选择

ROI的选择是DSP技术最大化应用的核心环节

特定组织结构区域选取策略



等高线选择

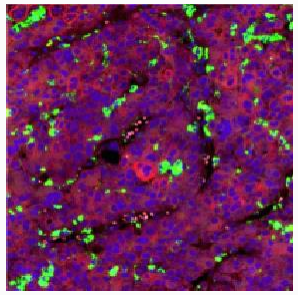
炎症附近的免疫环境发生了什么样的变化?

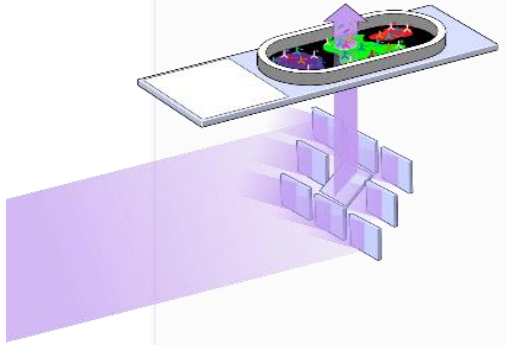
网格线选择

对组织上特定区域进行深度图谱解析，能发现哪些新靶点、新目标?

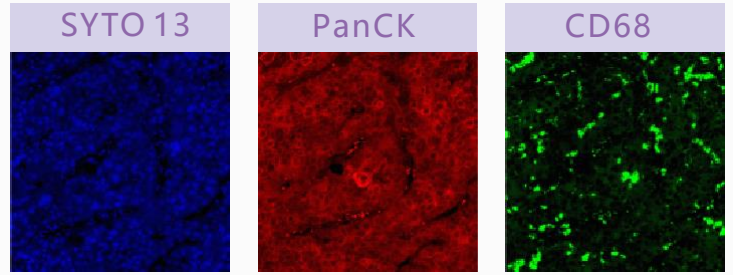
特定细胞群选取策略

Full Channel Overlay

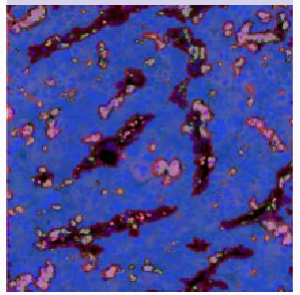




Single Channel（Mask）

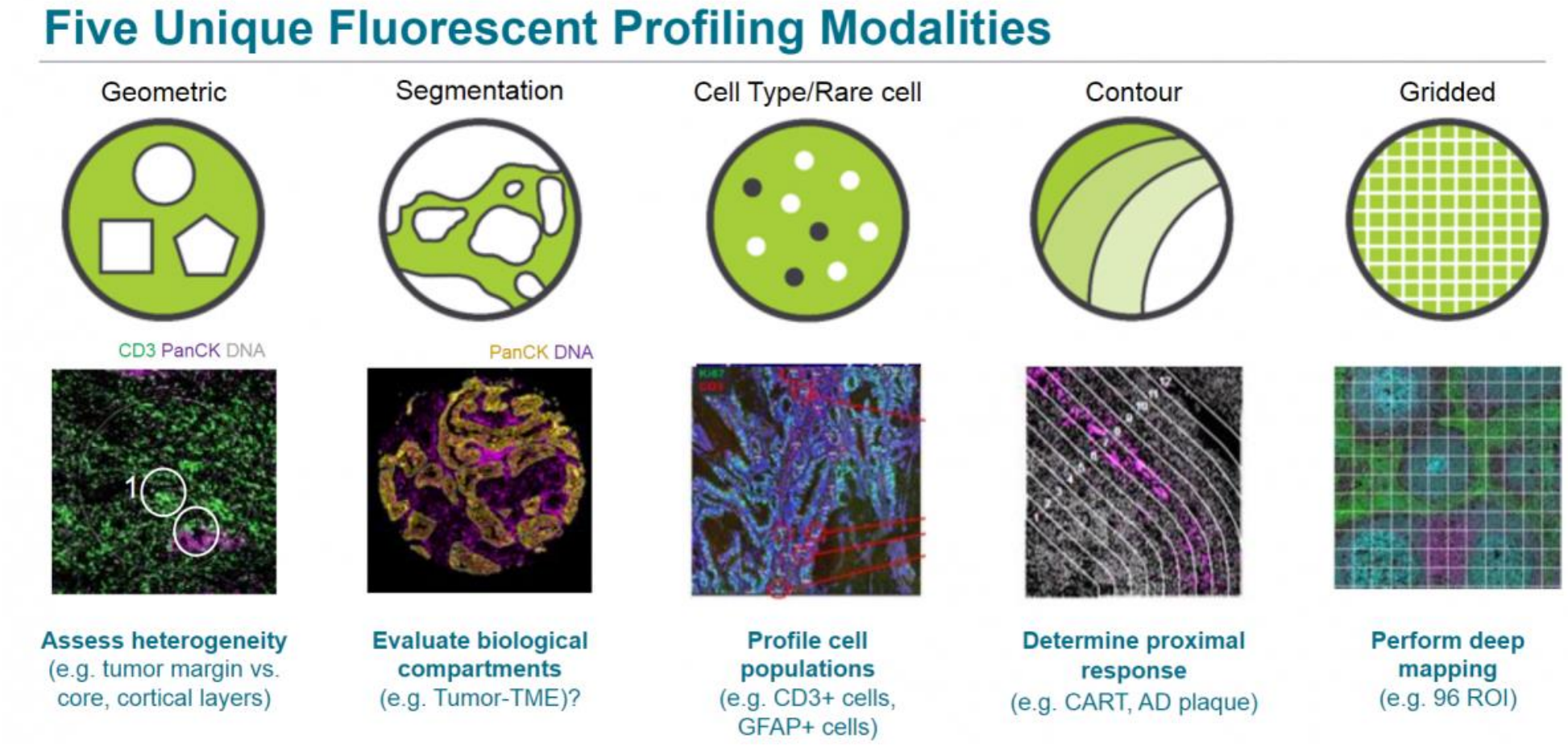


Segmentation

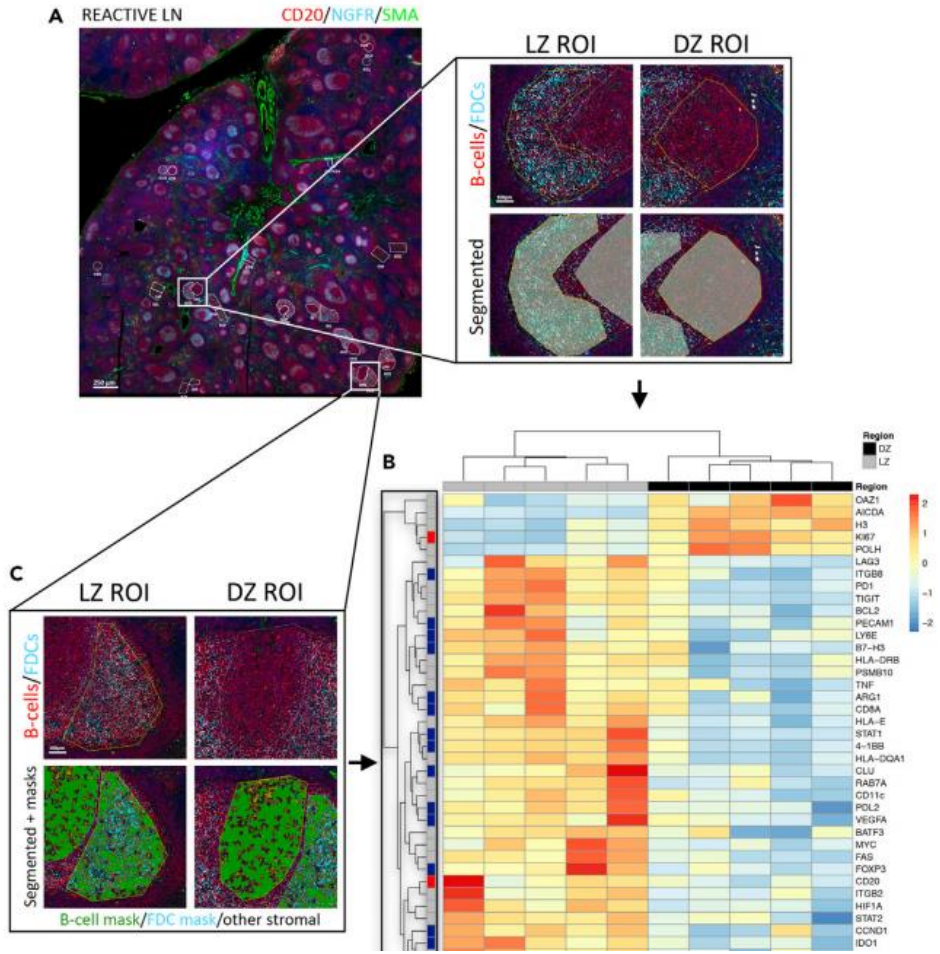


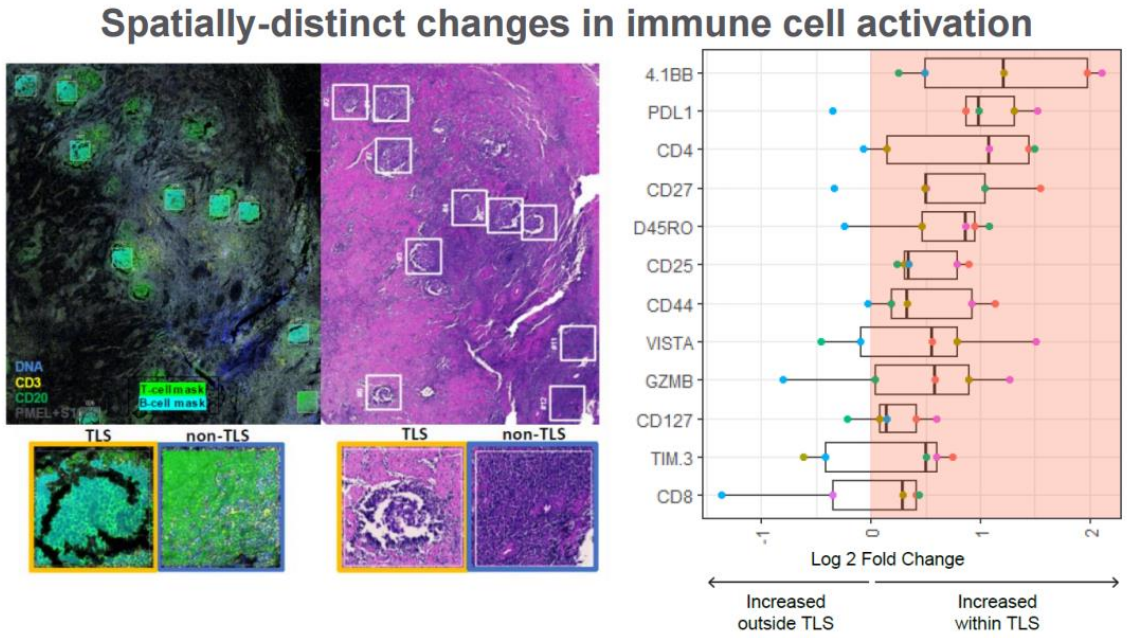
DSP空间组学的兴趣区域(ROI)选择

ROI的选择是DSP技术最大化应用的核心环节

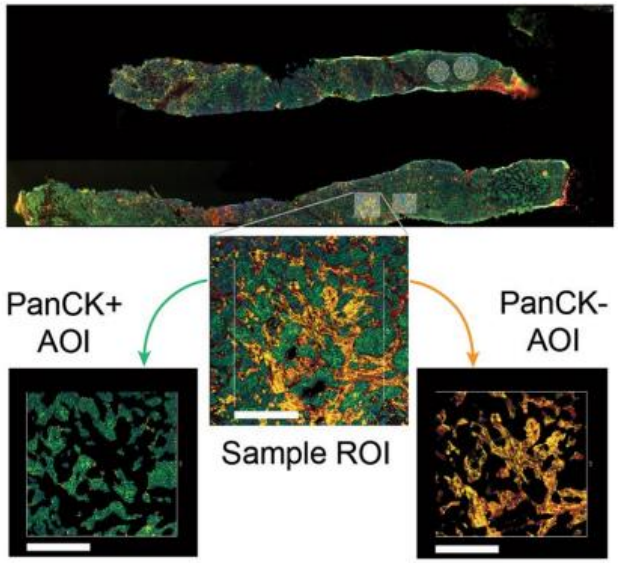


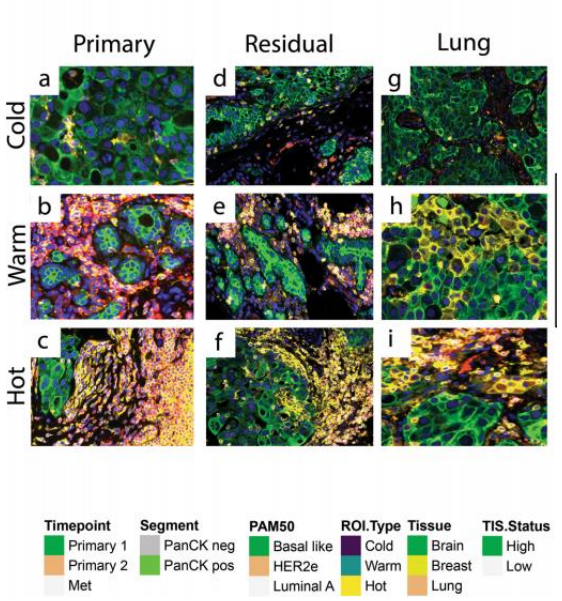
DSP空间组学的兴趣区域(ROI)选择

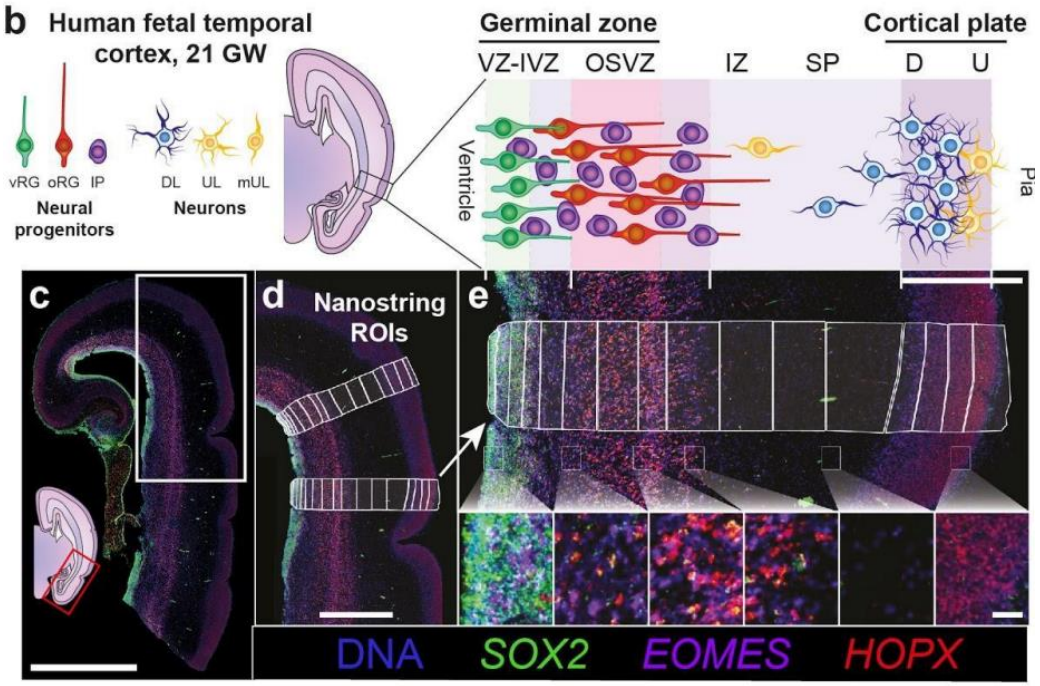


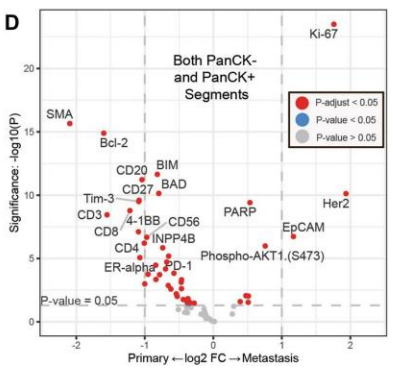


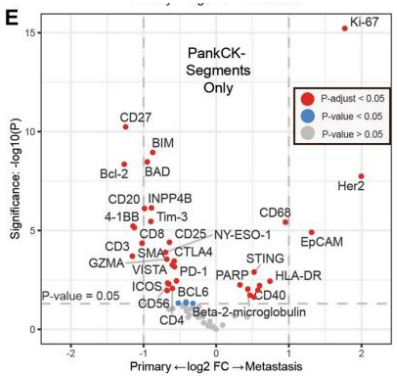
DSP空间组学的兴趣区域(ROI)选择

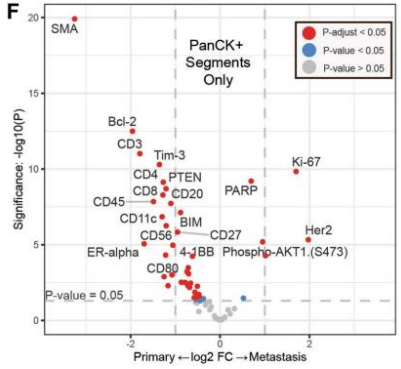






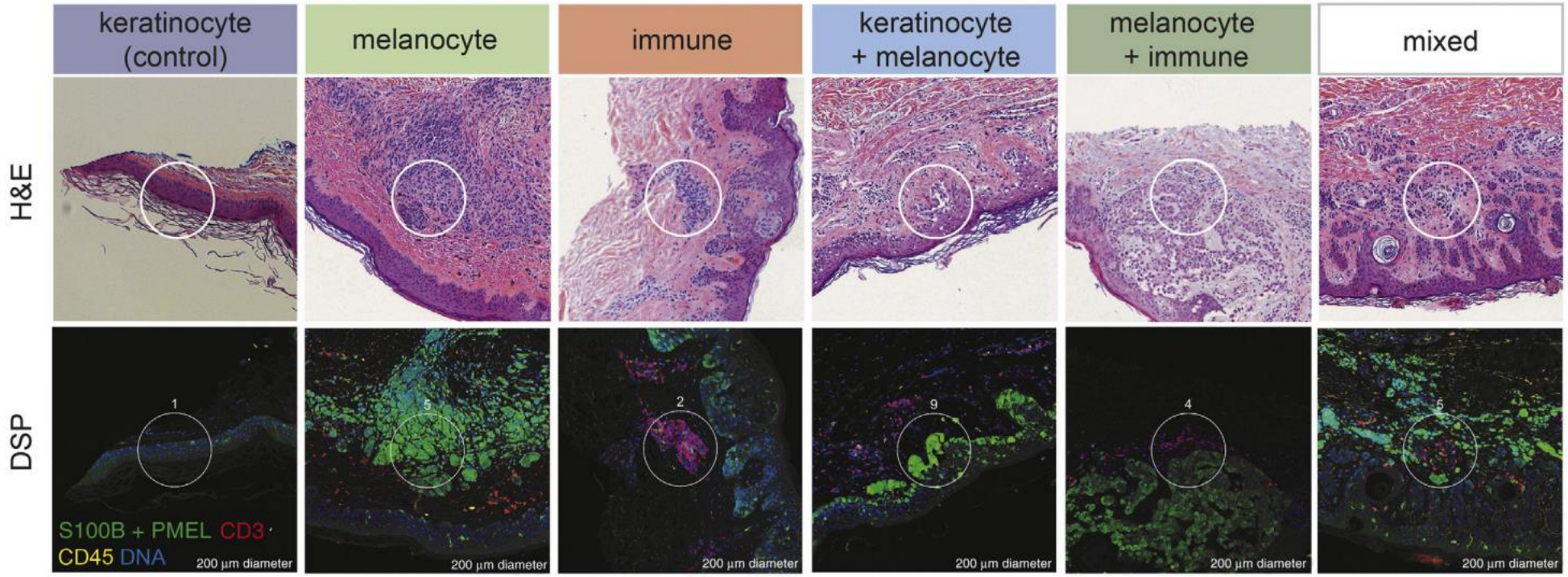






DSP空间组学的兴趣区域(ROI)选择

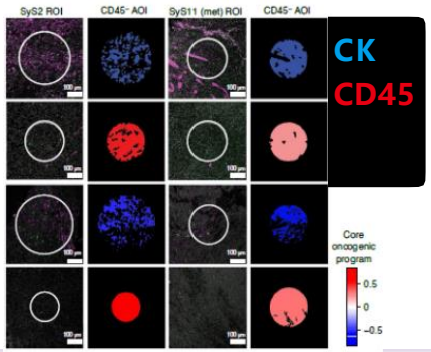
圈选ROI时，HE/IHC图片与DSP扫描的荧光图像互为参考，所选区域会更加准确。

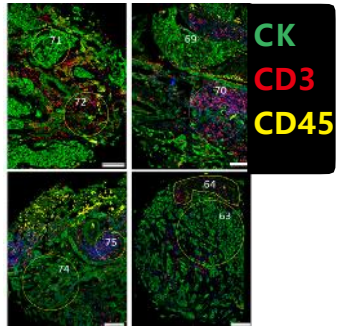


DSP空间组学分析相关细胞标志物选择

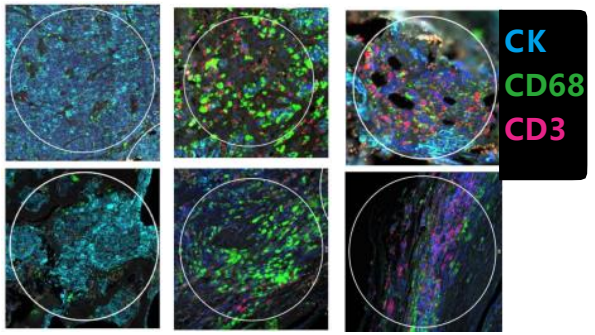
合适的组织结构或细胞群标志物，有助于ROI的选择和后续分析。

肿瘤及肿瘤浸润免疫细胞(白细胞，T细胞)

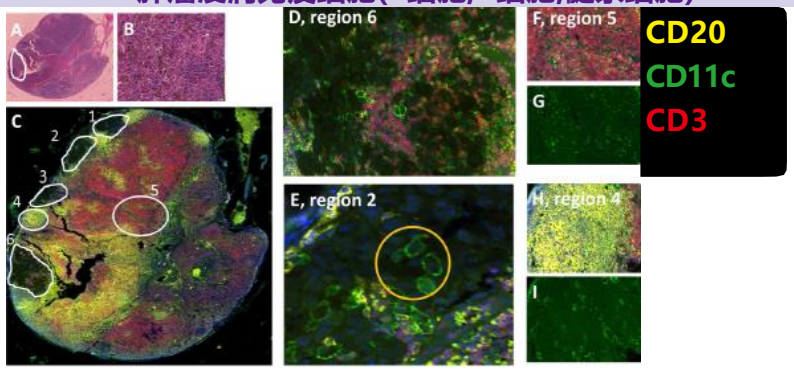




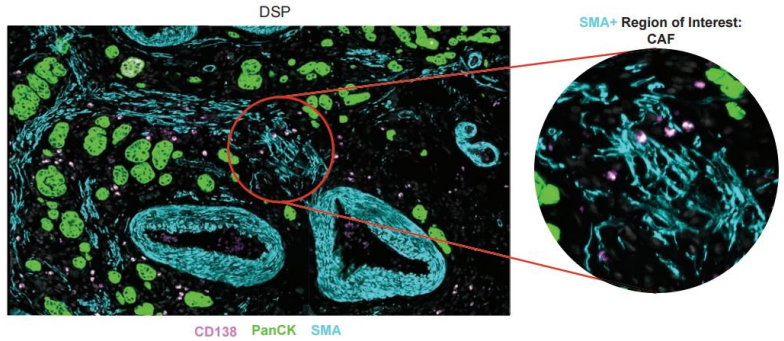
肿瘤及肿瘤浸润免疫细胞(T细胞,巨噬细胞)



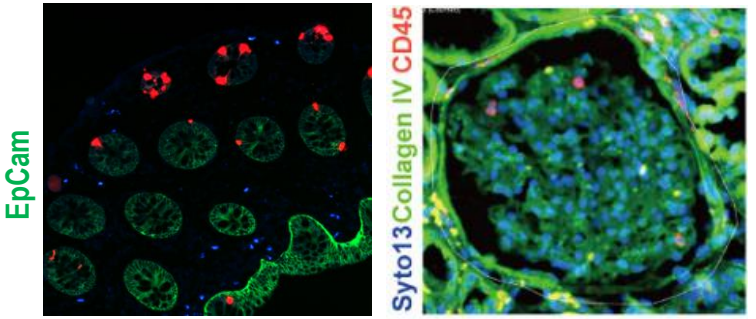
肿瘤浸润免疫细胞(T细胞,B细胞,髓系细胞)

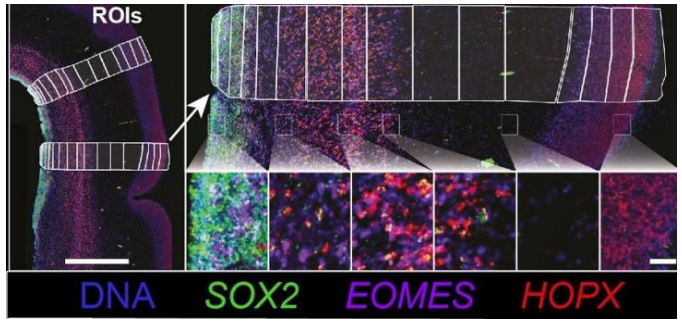


肿瘤相关基质细胞(成纤维类)



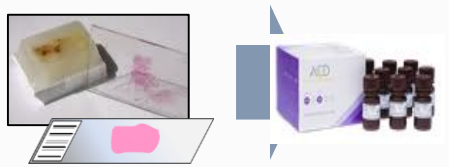
其他特殊标志物染色



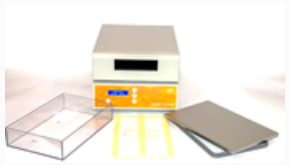


结合RNA原位杂交的DSP空间分析策略

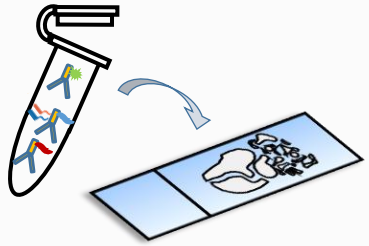
1. Samples pretreatment



2. RNA Scope Probe Hybridization

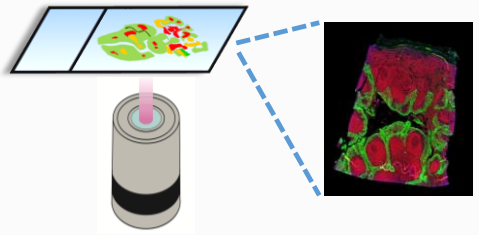


3. Incubation with protein target or RNA probe mix and morphology makers



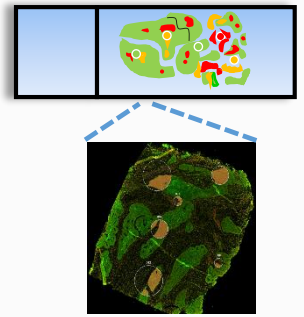
非常适合于病毒感染类疾病及神经科学研究

4. Scan and imaging

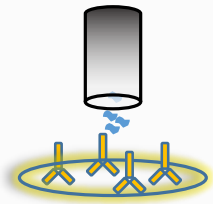


Combined DSP Workflow with RNA Scope Workflow

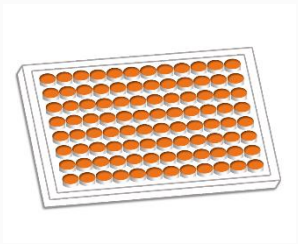
5. ROI selection



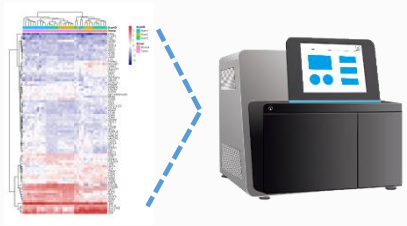
6. Oligo release by UV light and collection via microcapillary



7.Set up indexing PCR

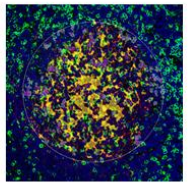


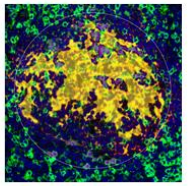
8. Sequence library & data analysis

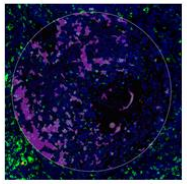


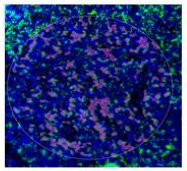
结合RNA原位杂交的DSP空间分析策略

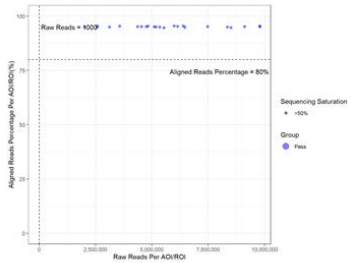
RNAScope

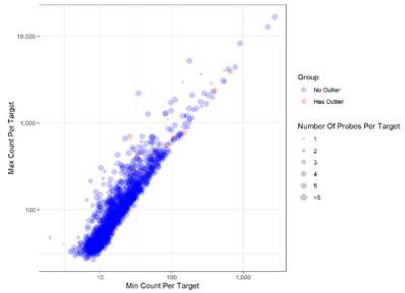


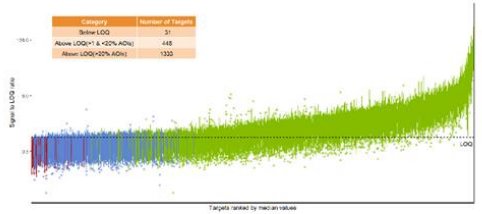






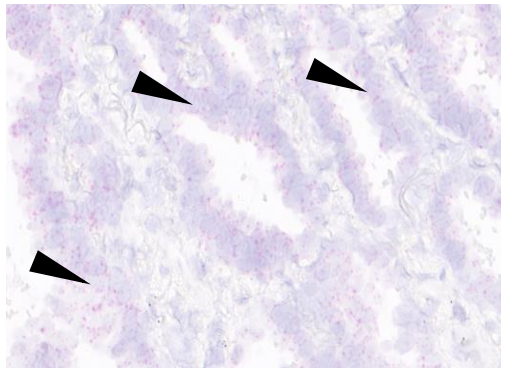


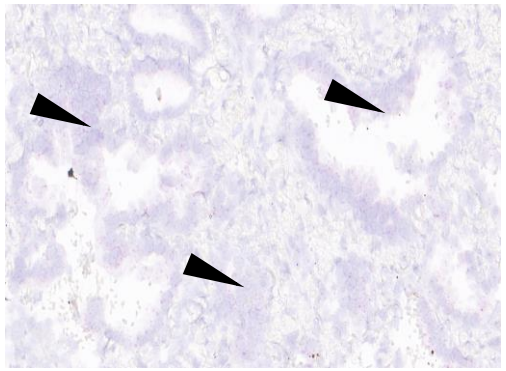




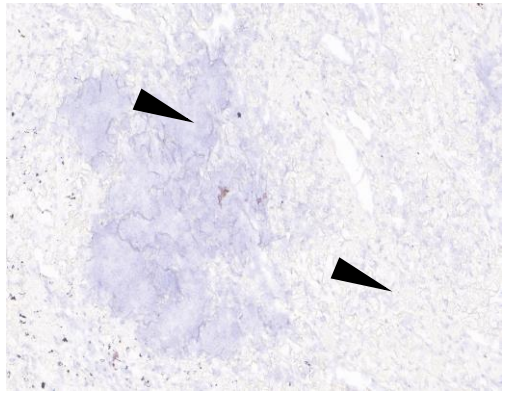
Base Scope

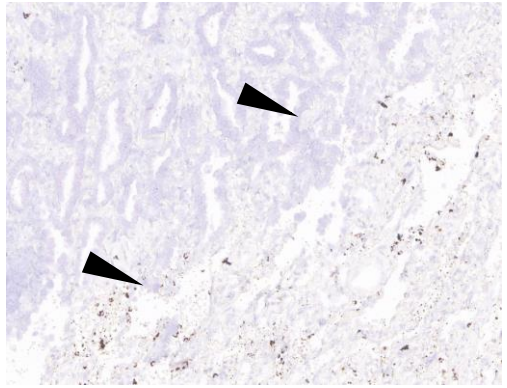
Amplified HER2





Non-Amplified regions





基于临床病理切片的常见空间分析策略组合

基于数字化空间分析技术(DSP)的深度分析策略

其他验证性空间分析策略

临床分组病理切片

特定组织区域或细胞亚群的空间多组学分析策略

基于病理组织切片的细胞类型相关基因或蛋白表达谱原位分析

基于病理组织切片的细胞类型、构成比例、功能状态原位分析

基于病理组织切片的细胞相互作用、免疫调节网络的深度分析

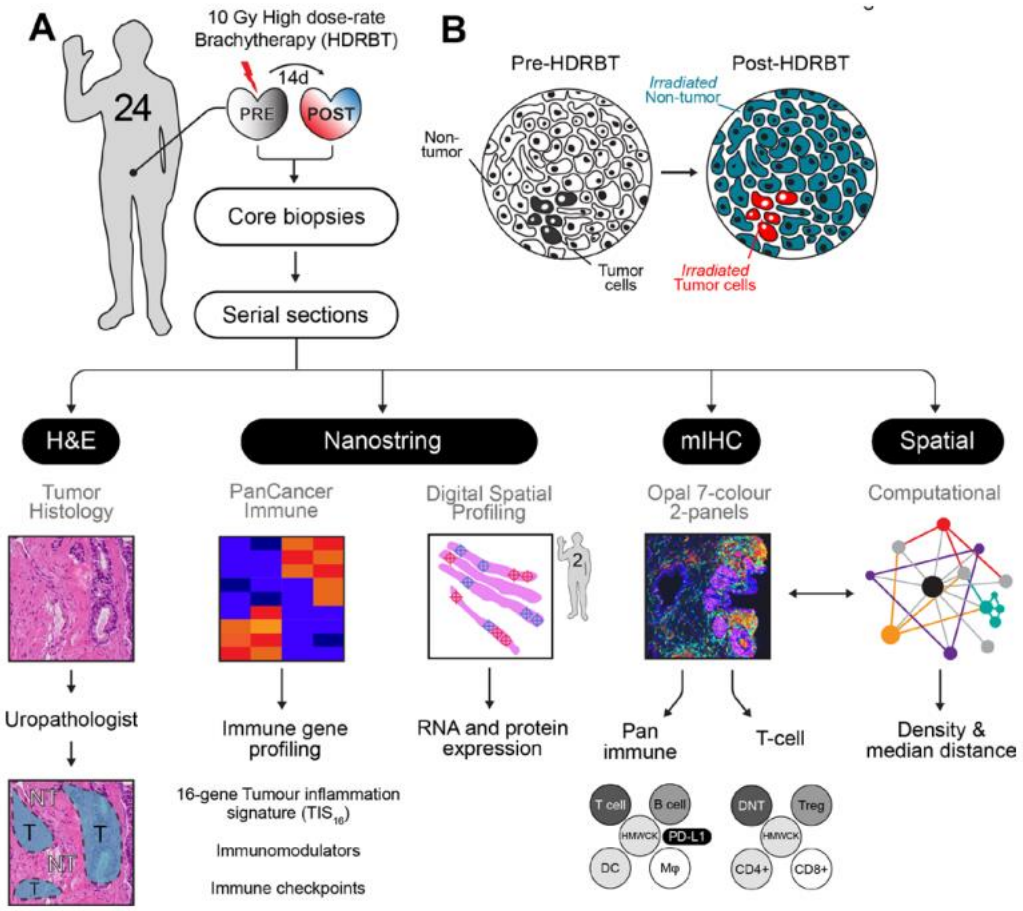
基于流式细胞术的分离鉴定分析策略

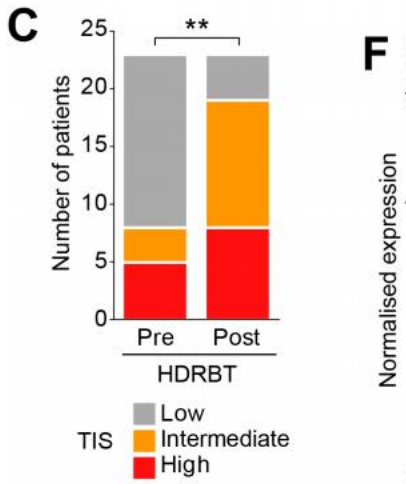
基于多重免疫荧光(mIF)的标志物验证分析策略

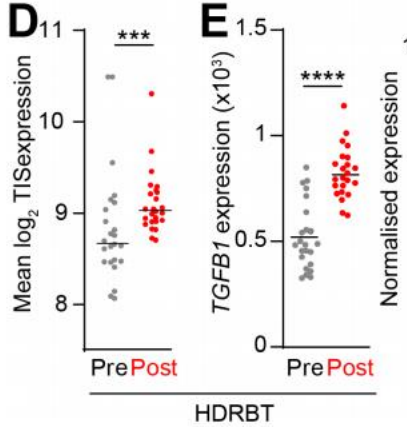
基于多重免疫组化(mIHC)的细胞类型构成及空间分析策略

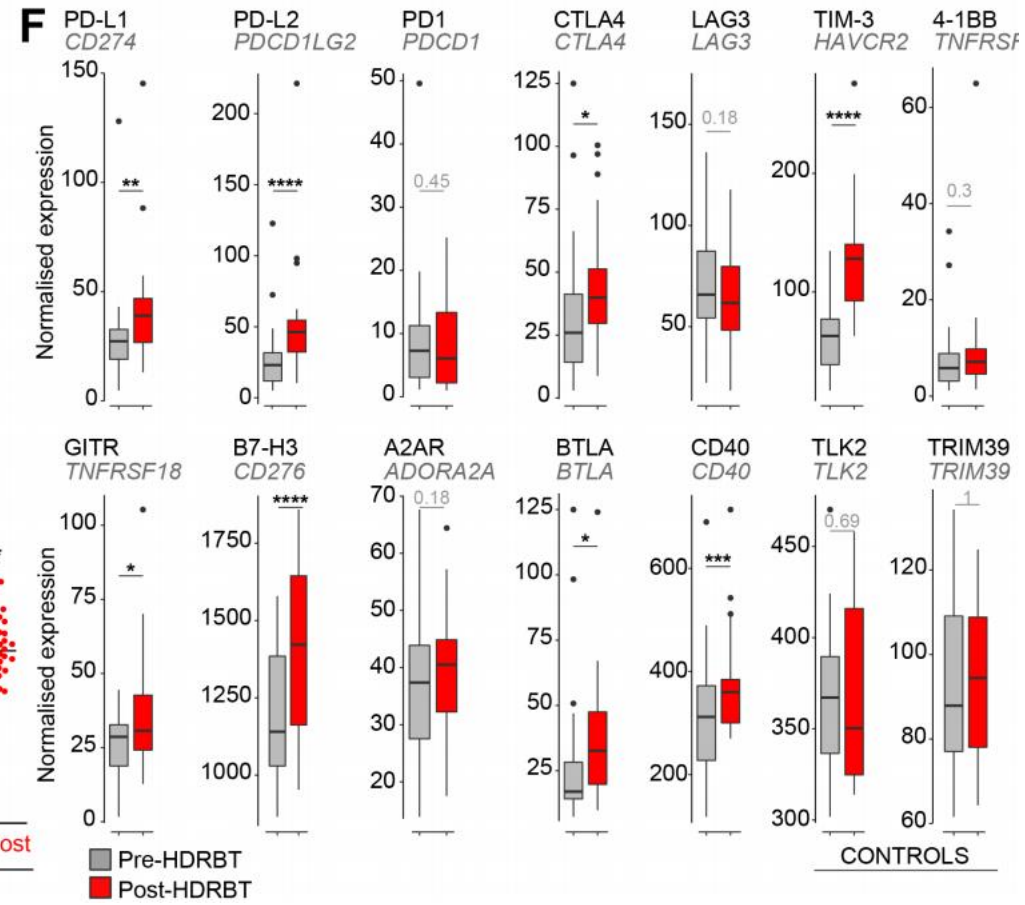
基于临床病理切片的常见空间分析策略组合

通过DSP技术对自定义的肿瘤免疫特征基因或蛋白集群进行聚类和分型



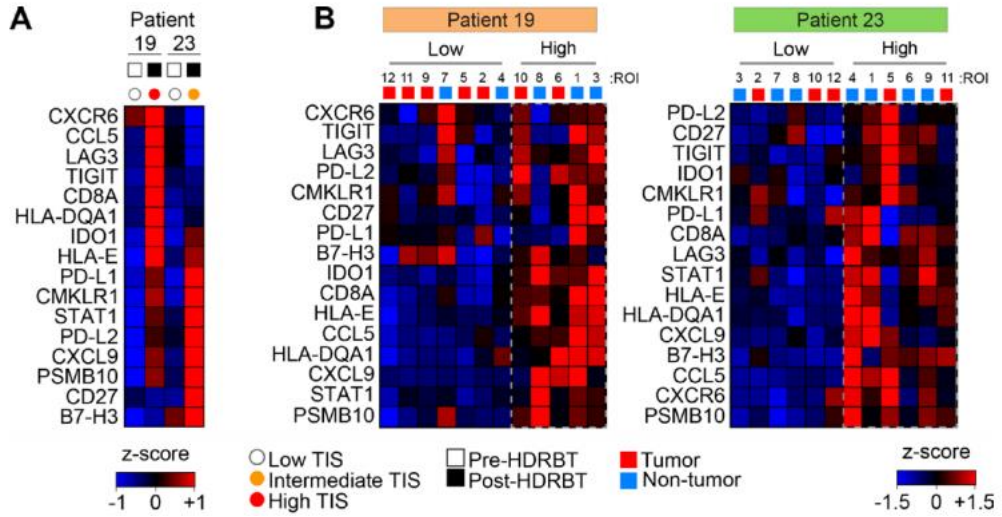


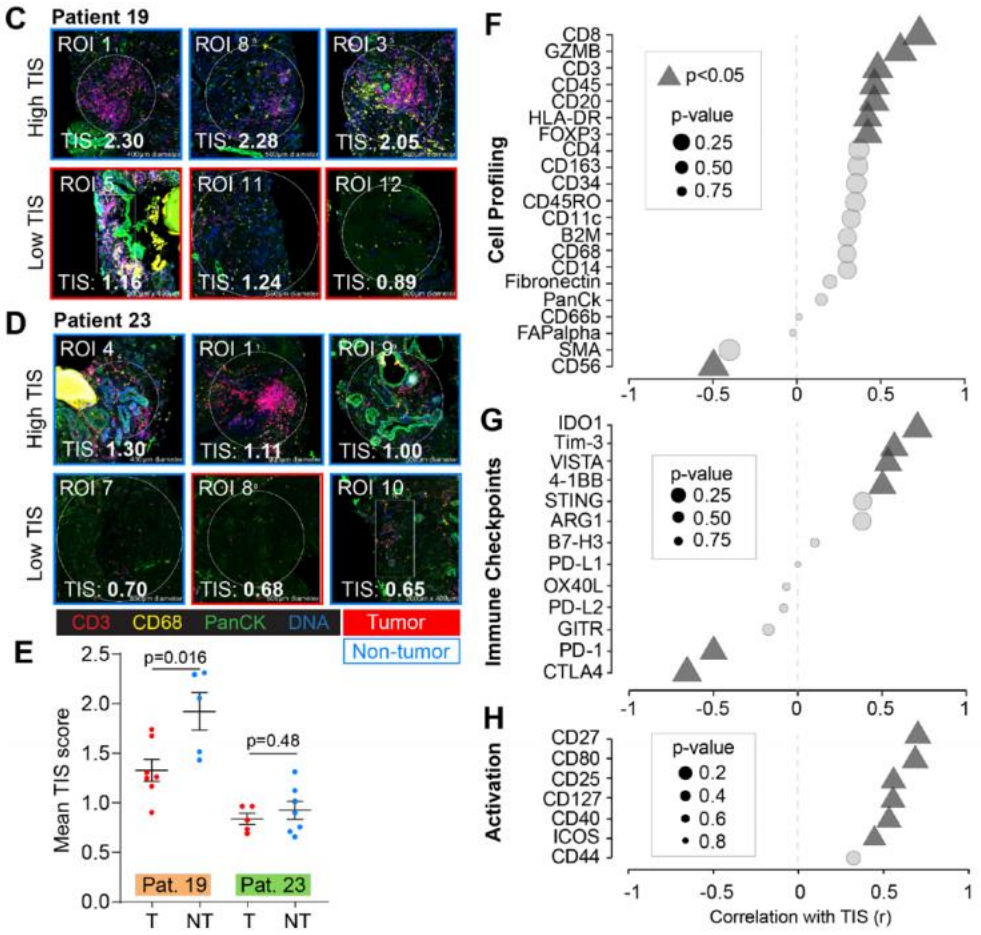




基于临床病理切片的常见空间分析策略组合

通过DSP技术对不同患者的不同ROI区域的肿瘤免疫特征基因或蛋白集群进行聚类和分型





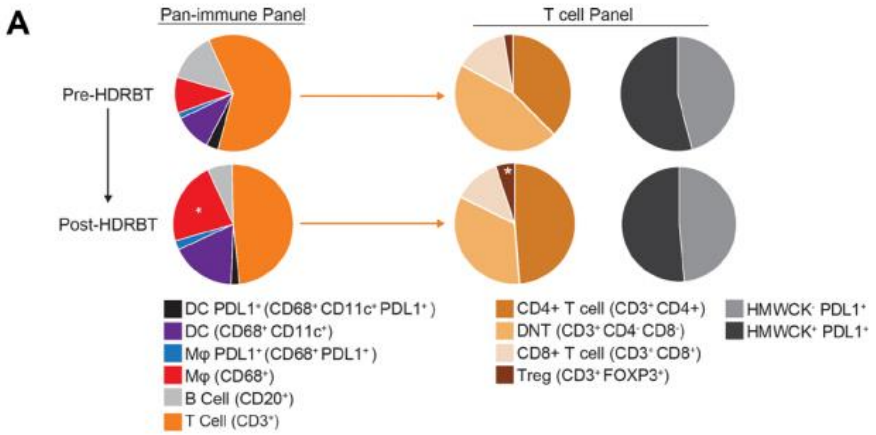
基于临床病理切片的常见空间分析策略组合

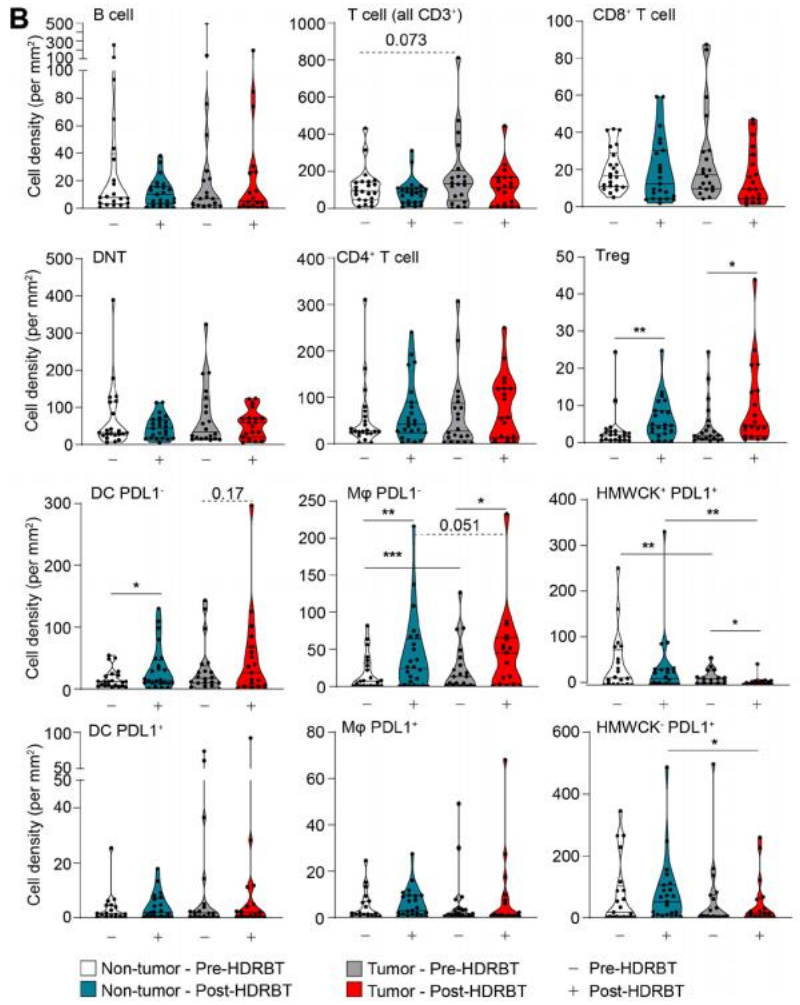
通过mIHC技术对治疗前后的各类免疫细胞类型分布、密度进行分析

Table 2 Immune subsets assessed by multiplex IHC

Marker expression	Panel	Cell subset	Abbreviation
$CD3^+CD4^+CD8^-$	T cell	T-helper	T-helper
$CD3^+CD8^+CD4^-$	T cell	$CD8^+$ T cells	$CD8^+$ T cells
$CD3^+CD4^+FOXP3^+$	T cell	Regulatory T cell	Treg
$CD3^+CD4^-CD8^-$	T cell	Double negative T cell	DNT
$CD3^+$	Pan immune	Pan T cell	T cell
$CD20^+$	Pan immune	B cell	B cell
$CD68^+$	Pan immune	Macrophage	ϕ
$CD68^+CD11c^+$	Pan immune	Dendritic cell	DC
$CD68^+PDL1^+$	Pan immune	$PDL1^+$ macrophage	ϕ^{PDL1+}
$CD68^+CD11c^+PDL1^+$	Pan immune	$PDL1^+$ dendritic cell	DC^{PDL1+}
$HMWCK^+PDL1^+$	Pan immune	$PDL1^+$ basal cells	$HMWCK^+PDL1^+$
$HMWCK^-PDL1^+$	Pan immune	$PDL1^+$ nonbasal cells	$HMWCK^-PDL1^+$

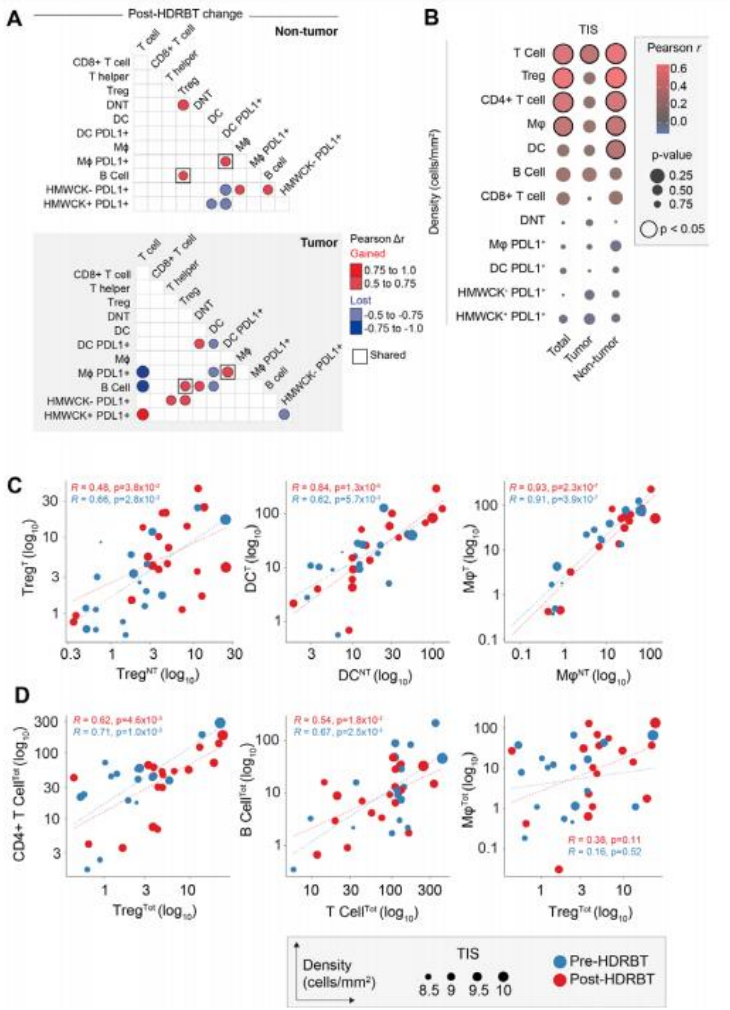
IHC, immunohistochemistry.

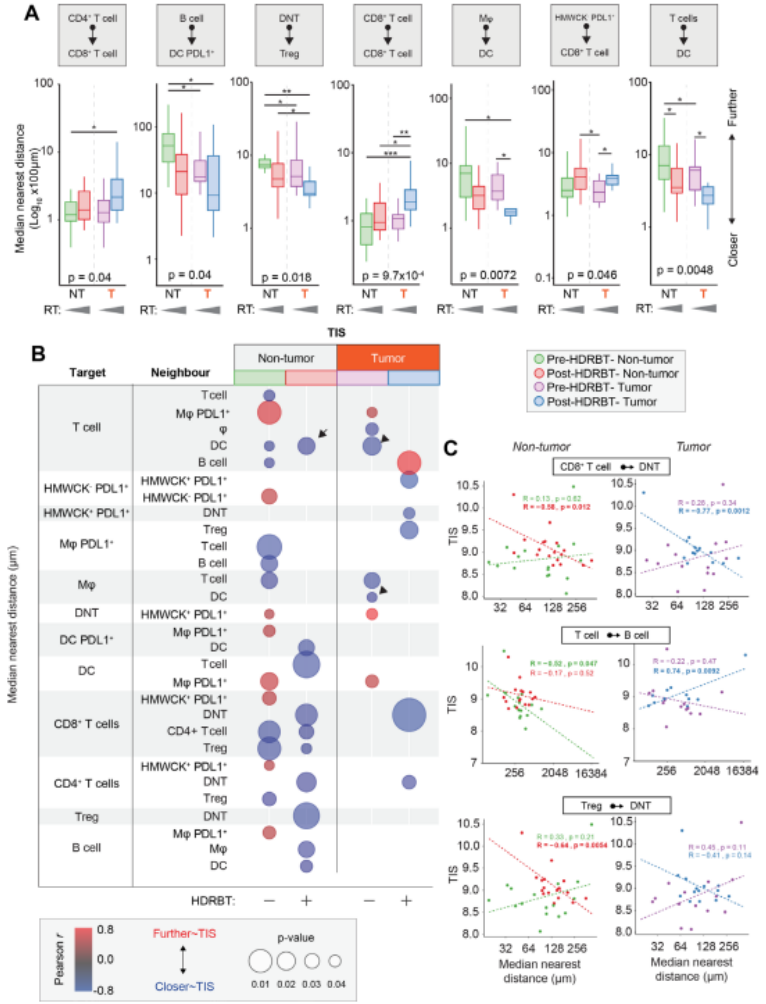




基于临床病理切片的常见空间分析策略组合

通过DSP技术分析获得肿瘤免疫特征基因信息与mIHC技术分析获得的细胞密度与空间分布信息，可以进行交互分析，获得两者与疾病治疗有关的相关性数据





非因生物多组学研究策略助力转化医学研究

药物筛选平台	空间多组学平台	靶向蛋白组平台	单细胞转录组平台	靶向转录组平台
• 肿瘤细胞系(80+) • PDC平台 • 分子克隆平台 • 基因敲除平台	• DSP空间组技术 • 空间单细胞技术	• RPPA靶向蛋白组技术（400+药物靶点） • TargetScan信号通路分析平台	• GexScope技术	• nCounter技术 • PCR-Array技术

非因生物多组学研究策略

整合型多组学分析

- **普通基因组转录组**：结合二代SNP、CNV、TMA与三代结构变异，串联重复，融合基因的相互优势
- **nCounter多基因分析**：肿瘤组织FFPE样本转录组分析金标准，目前最为精准的高通量定量方式
- **单细胞转录组**：sc-RNAseq，肿瘤异　质性解决方案的新标 准
- **QuantiNova LNA PCR Array集成式基因表达谱分析系统**：针对信号转导、生物过程或疾病研究通路设计

→ 专业生信团队
制式报告
深度分析模块
多组学联合分析

质粒载体构建
慢病毒包装
基因敲除
基因突变
细胞原代培养（PDC）

→ **细胞与动物模型**

→ **蛋白组学分析平台（RPPA+质谱）**：基于临床样本的功能蛋白组与系统生物学研究利器

→ 多种蛋白水平的验证性实验

⇄ **空间多组学**：还原空间异质性的真实面貌，生物标志物挖掘的新策略

- **空间转录组**：84 RNA / 1833RNA / 全转录组
- **空间蛋白组**：Panel 设置
- **单细胞空间蛋白组**：Panel 设置
- **HE/IHC/IF**

非因生物简介——致力于转化医学

转化医学研究综合解决方案

基础研究

- **RPPA 蛋白组学**
  国内唯一技术服务商；
  350+ 经严格验证的抗体资源库；
  1700+ 学术论文，8+ 平均影响因子
- **DSP空间多组学**
  DSP技术合作开发方；
  国内首个官方认证技术服务商；
  80+项目，800+样本；
  100+学术论文，10+平均影响因子
- **单细胞空间蛋白组学**
  国内领先的空间单细胞蛋白组学服务商；
  350+经严格验证的抗体资源库；
  40+学术论文，5+平均影响因子

转化医学

- **RPPA蛋白组学**
  临床蛋白生物标志转化的完美解决方案；
  高样本通量（单次上样多达1000+）；
  多标志物平行分析（同时分析10-500个潜在生物标志物）；
  高度可定制化（靶点根据需求开发）；
  高准确度（基于高度定量的免疫学反应原理）；
  广泛适用于组织和体液来源的样本
- **空间多组学**
  基于微环境的生物标志物转化解决方案

临床应用

- **RPPA蛋白组学**
  作为新型的LDT药物伴随诊断技术，已经在2021年开始实现临床应用；

  临床适应症开发涵盖乳腺癌，结直肠癌，肺癌，胰腺癌等领域；

  非因生物致力打造以DSP技术为核心竞争力的临床伴随诊断产品。

非因生物搭建的符合国际标准的精准医疗研究中心

Mills癌症个体化诊疗研究中心

RPPA蛋白组学平台

细胞学平台

分子生物学平台

nCounter及空间生物学平台

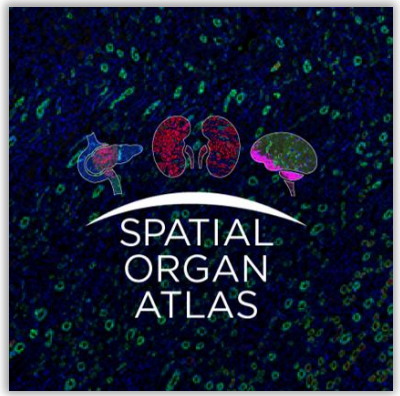
空间单细胞表型平台

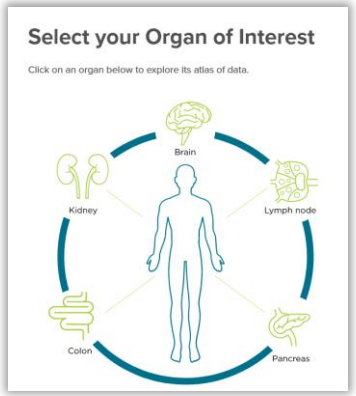
病理学平台

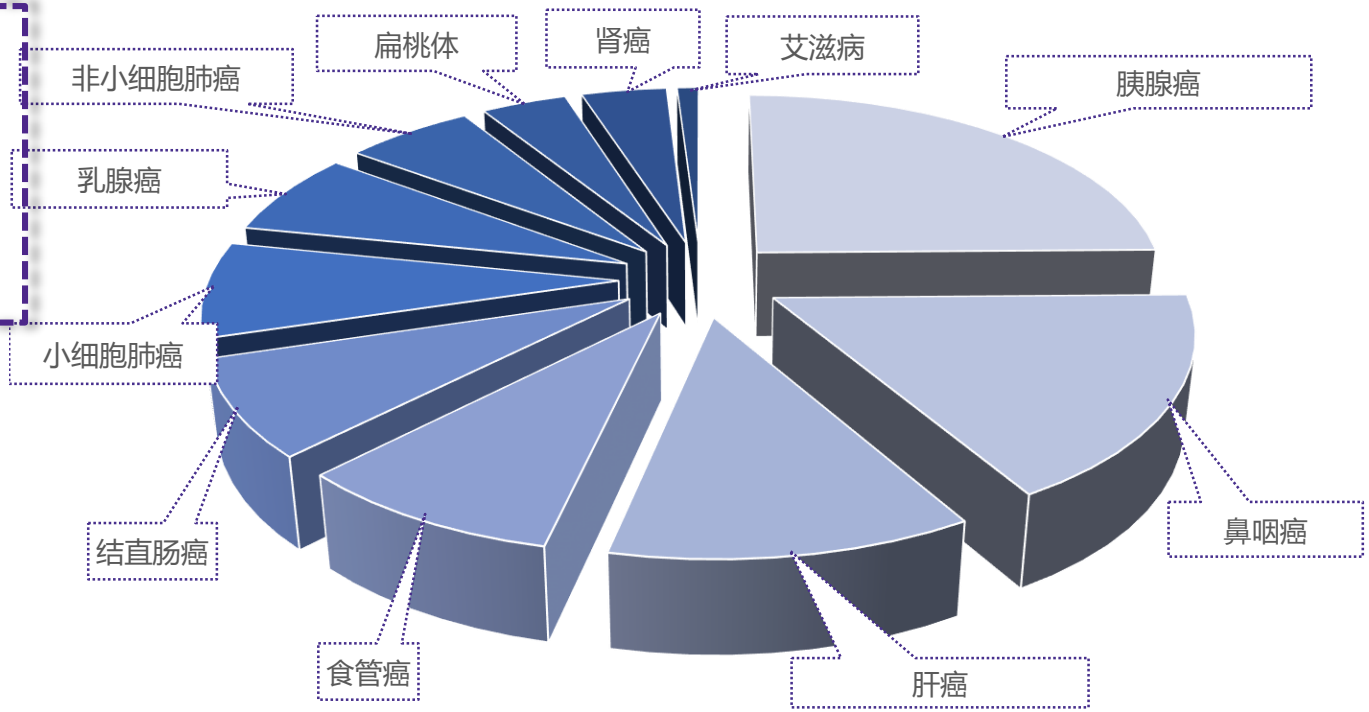
单细胞转录组平台

非因生物建设的国内最大的空间组学研究平台

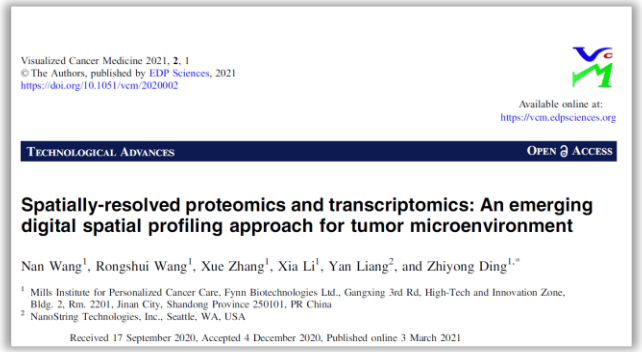
- ✓ nanoString全球8大DSP空间组Premier access site
- ✓ 全球第一批5家获得nanoString官方认证DSP空间组学服务商之一(国内唯一)
- ✓ Organbook空间组学国际研究合作方







非因生物助力创新科学研究



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https://vcm.edpsciences.org

TECHNOLOGICAL ADVANCES — OPEN ACCESS

Spatially-resolved proteomics and transcriptomics: An emerging digital spatial profiling approach for tumor microenvironment

Nan Wang[1], Rongshui Wang[1], Xue Zhang[1], Xia Li[1], Yan Liang[2], and Zhiyong Ding[1,*]

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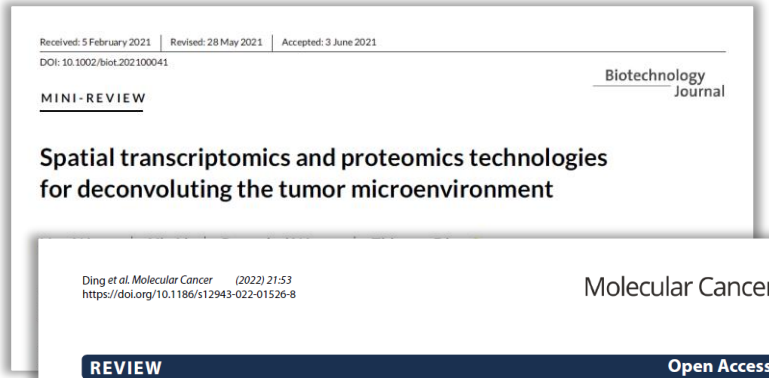

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DOI: 10.1002/biot.202100041

Biotechnology Journal

MINI-REVIEW

Spatial transcriptomics and proteomics technologies for deconvoluting the tumor microenvironment

Ding *et al. Molecular Cancer* (2022) 21:53
https://doi.org/10.1186/s12943-022-01526-8

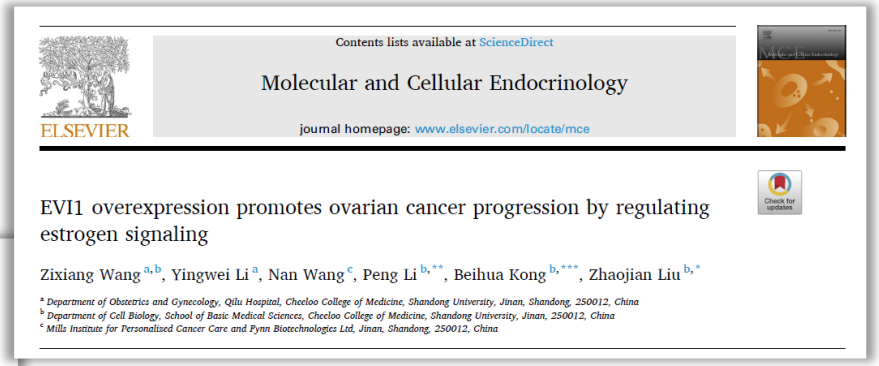
Molecular Cancer

REVIEW — Open Access

Proteomics technologies for cancer liquid biopsies

Zhiyong Ding[1*], Nan Wang[1], Ning Ji[2,3] and Zhe-Sheng Chen[2*]

Abstract



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ELSEVIER

EVI1 overexpression promotes ovarian cancer progression by regulating estrogen signaling

Zixiang Wang[a,b], Yingwei Li[a], Nan Wang[c], Peng Li[b,**], Beihua Kong[b,***], Zhaojian Liu[b,*]

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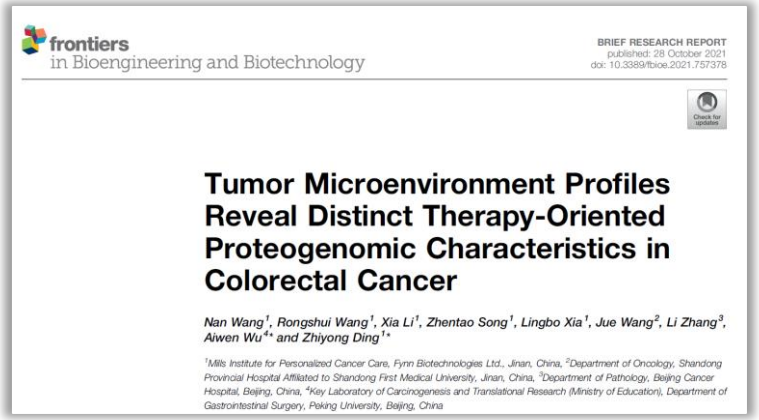
[c] Mills Institute for Personalised Cancer Care and Fynn Biotechnologies Ltd, Jinan, Shandong, 250012, China



frontiers in Bioengineering and Biotechnology

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Tumor Microenvironment Profiles Reveal Distinct Therapy-Oriented Proteogenomic Characteristics in Colorectal Cancer

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Ameliorative effect of *Gastrodia elata* Blume extracts on depression in zebrafish and cellular models through modulating reticulon 4 receptors and apoptosis

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Recent progress on targeting leukemia stem cells

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