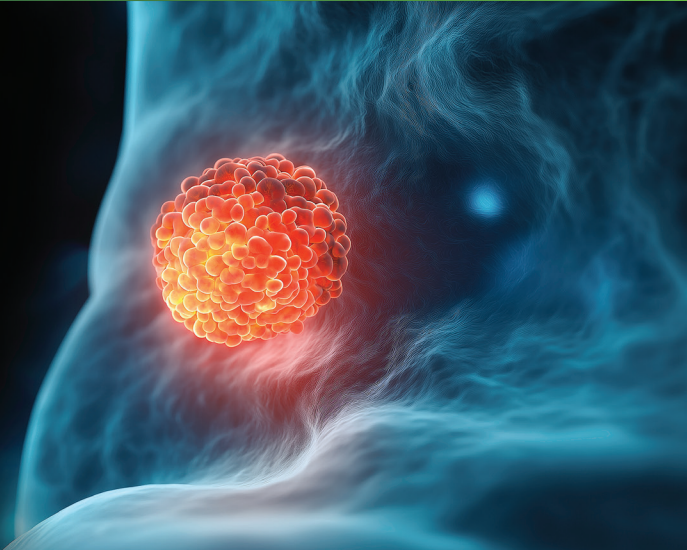


Characterizing solid tumor heterogeneity with multiomic approaches from Signios Bio



Solid tumors present immense complexity, characterized by significant intra-tumoral heterogeneity (ITH) arising from genetic, epigenetic, and transcriptional diversity. Understanding this heterogeneity, including the distinct cell states, their plasticity, and interactions within the tumor microenvironment (TME), is paramount for developing effective targeted therapies and overcoming treatment resistance. Signios Bio offers an integrated suite of advanced genomic, transcriptomic, and epigenomic profiling services designed to help oncology researchers dissect the complexities of solid tumors.

The Challenge: Navigating solid tumor heterogeneity

Solid tumors are not monolithic entities but rather complex ecosystems of diverse cancer cell populations interacting with immune and stromal cells. This heterogeneity is driven by ongoing genetic evolution, epigenetic reprogramming, and dynamic transcriptional states influenced by the TME. Cancer cell plasticity, the ability of cells to switch between states, further complicates the landscape and contributes significantly to therapy resistance. Effectively characterizing solid tumors requires multi-layered approaches capable of resolving this complexity at various levels, from bulk tissue analysis to single-cell and spatial resolution.

Signios Bio solid tumor profiling solutions

Signios Bio offers a comprehensive suite of oncology-optimized workflows to interrogate the molecular complexity of solid tumors. Our platform integrates cutting-edge sequencing technologies (including Illumina NovaSeq X Plus, PacBio Revio, and 10x Genomics Chromium/Visium) with robust bioinformatics, optimized for challenging samples like FFPE and low-yield inputs.

Genome profiling: Characterize the genetic landscape of tumors, including subclonal architecture and alterations linked to therapy resistance with whole genome, whole exome, or targeted assays.

	TSO 500 NGS assay	Whole genome sequencing	Whole exome sequencing
Application	Simultaneously analyze DNA and RNA or ctDNA to detect mutations in 523 specific solid tumor genes	Comprehensive, unbiased detection of mutations across the whole genome	Cost-effective profiling of protein-coding regions
Insights gleaned	SNVs, indels, CNVs, fusions, TMB, and MSI status	SNVs, SVs, CNVs, and non-coding variants	SNVs, SVs, CNVs in protein coding regions

RNA sequencing: Characterize transcriptional states and identify gene expression signatures across tumor cell populations in bulk mRNA/total RNA or at the single-cell level.

	Bulk RNA	Single-cell RNA
Application	Analyze overall gene expression patterns	Resolve heterogeneity at the single-cell level to identify distinct tumor subpopulations and rare cell types
Library preps available	• Kapa or Illumina stranded mRNA • Takara SMART-Seq mRNA for low input • Illumina TruSeq stranded total RNA • Collecta for FFPE samples • PacBio Kinnex full-length RNA	• 10x Genomics 3' GEM or GEM-X • 10x Genomics FLEX for fixed samples • PacBio Kinnex full-length scRNA
Insights gleaned	Differential gene expression	Differential gene expression of identified cell clusters and annotated cell types

Spatial transcriptomics (10x Visium): Localize gene expression patterns within the tissue architecture, enabling analysis of tumor-immune interactions and microenvironmental signals *in situ*.

	High-resolution spatial transcriptomics	Single-cell resolution spatial transcriptomics
Assay(s)	• Visium 6.5 mm x 6.5 mm capture area with 5,000 spots per capture area • Visium 11 mm x 11 mm capture area with 11,000 spots per capture area	Visium HD 6.5 mm x 6.5 mm capture area with a gapless lawn of oligonucleotides for single-cell resolution
Insights gleaned	Spatial gene expression patterns, cell type annotation, and cell-cell interactome	

Epigenomic Profiling: Investigate epigenetic regulation driving tumor phenotypes.

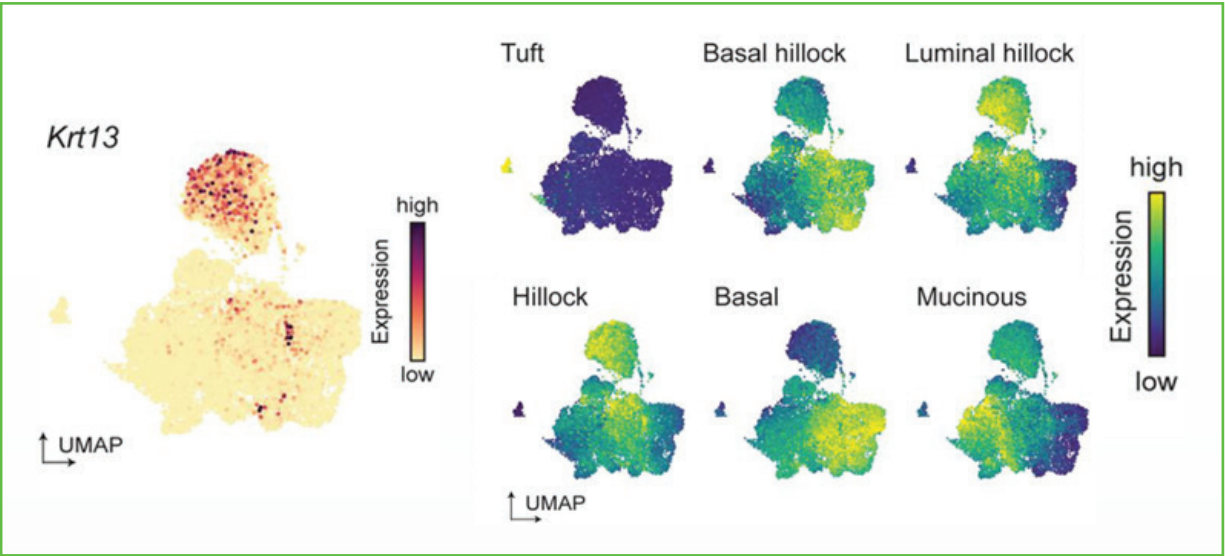
	Methylation profiling	Chromatin structure & interactions
Assay(s)	Characterize DNA methylation patterns across the genome or in targeted regions	Map protein-DNA interactions and chromatin organization to understand gene regulation
Library preps available	- WGS Methyl using NEB EM Seq - Whole genome bisulfite sequencing	- HiC - CUT&RUN - CUT&Tag - ChIP-Seq - ATAC-Seq
Insights gleaned	Single base methylation status, genome wide methylation maps, differentially methylated regions	Chromatin interaction frequency maps, protein binding sites, histone modification locations, protein-DNA interaction sites, accessible chromatin regions

Case study highlight: Dissecting Cellular Heterogeneity in Lung Squamous Cell Carcinoma (LUSC)

A recent study investigated intra-tumoral heterogeneity in LUSC, focusing on understanding the diverse cell fates within these tumors. Signios Bio (formerly MedGenome) contributed critical services for this research, including single-cell RNA sequencing (scRNA-seq) of tumor organoids and bulk RNA sequencing of engineered cell lines.

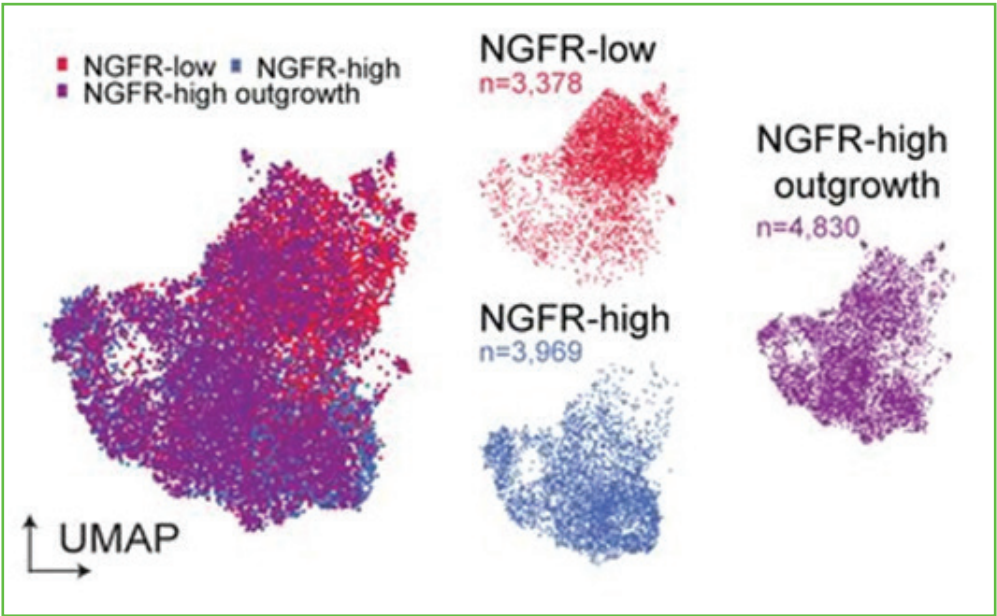
This study leveraged these powerful transcriptomic tools to:

Identify novel cell states: scRNA-seq analysis of mouse LUSC models and patient-derived organoids revealed a previously uncharacterized KRT13-positive tumor cell population resembling normal lung "hillock" cells. This state was distinct from the known basal-like tumor-propagating cells (TPCs).



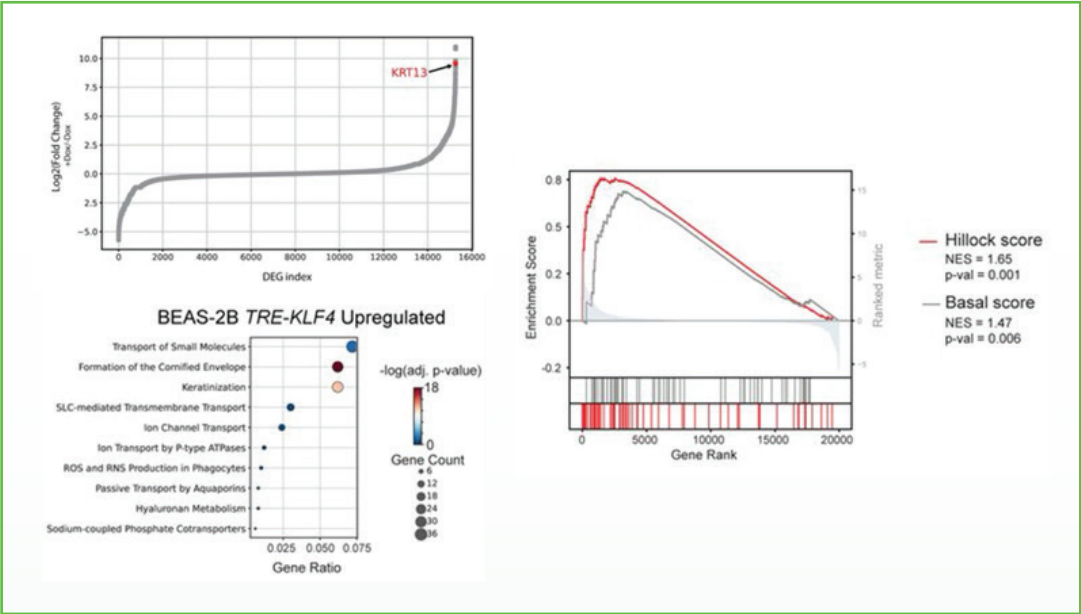
scRNA-seq expression of Krt13 projected on UMAP space (left) and gene scores applied to SNL tumor cells projected onto UMAP space (right). (Izzo, Luke, T. et al. bioRxiv (2025) Figure 2D and Figure 3G.)

Uncover cell state plasticity: By performing scRNA-seq on sorted TPC-like (NGFR-high) cells and their subsequent organoid outgrowths, the researchers demonstrated that basal-like TPCs could differentiate and give rise to the KRT13+ hillock-like state in vitro, highlighting the plasticity between these populations.



scRNA-seq of SNL tumor organoids at time of NGFR sorting (NGFR-high and NGFR-low) and NGFR-high cells after four weeks of growth in organoid conditions ("NGFR-high outgrowth") (Izzo, Luke, T. et al. bioRxiv (2025) Figure 5)

Elucidate transcriptional regulation: Bulk RNA-seq was used on human basal cell lines engineered to overexpress or knock out the transcription factor KLF4. This confirmed KLF4's role as necessary and sufficient to induce KRT13 expression and promote the hillock-like transcriptional program, linking a specific regulator to the observed cell state heterogeneity.



Waterfall plot of differentially expressed genes from RNA-sequencing of TRE-KLF4 BEAS-2B cells treated +/- Dox (top left), GSEA for the general hillock score and basal score derived from RNA-sequencing of TRE-KLF4 BEAS-2B cells treated +/- Dox (right), Gene set enrichment analysis of the top 100 upregulated genes by TRE-KLF4 in BEAS-2B cells treated +/- Dox (bottom left). (Izzo, Luke, T. et al. bioRxiv (2025) Figure 8)

This research underscores how high-quality RNA sequencing services (both bulk and single-cell) are instrumental in resolving tumor heterogeneity, defining distinct cancer cell states, uncovering mechanisms of plasticity, and identifying key transcriptional regulators driving these processes in solid tumors.

The Signios Bio advantage

Choosing Signios Bio provides access to:

Deep expertise



Leverage our team of PhD-level scientists and bioinformaticians for expert consultation throughout your project.

End-to-end solutions



From sample extraction and QC to library preparation, sequencing, and advanced bioinformatics analysis.

Actionable insights



Robust bioinformatics pipelines for comprehensive analysis and publication-ready figures.

Quality & speed



Highly automated workflows ensure reliable, fast, and cost-effective results.

Proven track record



Trusted by leading pharma, biotech, and academic institutions, with over 200 publications in top-tier journals.

Conclusions

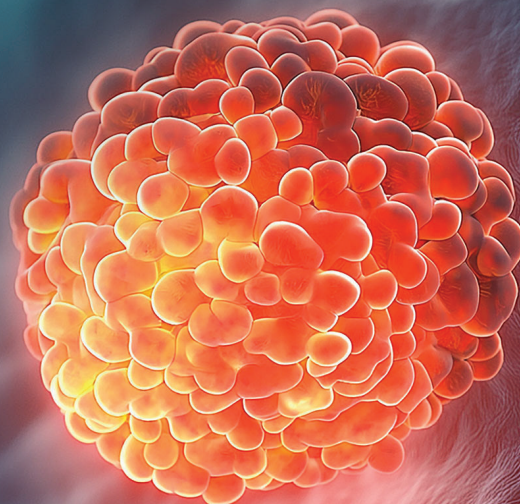
Deciphering the complexity of solid tumors requires a multi-faceted approach. Signios Bio offers a powerful combination of genomic, transcriptomic, epigenomic, single-cell, and spatial technologies, coupled with expert support, to provide a comprehensive understanding of tumor biology. By characterizing genetic alterations, transcriptional programs, epigenetic states, and cellular heterogeneity, Signios Bio empowers you to identify novel therapeutic targets, develop predictive biomarkers, and ultimately improve outcomes for cancer patients.

Let's discuss your research needs

Contact Signios Bio today to learn how our immunoprofiling and multiomics solutions can advance your oncology research.

References

1. Izzo, L.T., *et al.* 2025. KLF4 promotes a KRT13+ hillock-like state in squamous lung cancer. *bioRxiv* doi:10.1101/2025.03.10.641898. (Preprint posted March 13, 2025)



The science of signals, the promise of cures

A MULTIOMICS RESEARCH PARTNER

Spatial transcriptomics | Single-cell | Epigenomics | WGS/WES

Contact

Lab Location

Signios Biosciences
348 Hatch Drive Foster City, CA 94404, USA
info@signiosbio.com
(888) 440-0954

Registered office & Headquarters

Signios Biosciences
108 West 13th Street Wilmington Delaware 19801,
Country of New Castle, USA