

# Biomarker, Bioanalysis and Bioinformatics Services

Discover data-driven solutions and in-depth biological insights to maximize the success of your drug development pipeline with laboratory services and data science



## Overview

Searching for consolidated laboratory services to help expedite your next drug development project? Looking for deeper understanding into your drug mechanism of action, and meaningful translational biomarkers to improve patient stratification? Partner with us for fast, reliable, accurate, and cost-effective studies to improve your data-driven decision-making.

With biomarker and bioanalysis laboratories across North America, APAC, and Europe, and a team of over 150 dedicated laboratory scientists, we can customize our laboratory services to meet your specific research and drug development needs.

Our team provides flexible and comprehensive multi-omics methodologies, cutting-edge technologies, well-established and validated workflows, and ready-to-use markers. With our cloud-based customer portal, **CrownLink™**, you can track your data anywhere, anytime. Paired with our bioinformatics services team, and their experience in handling multi-omics big data, we can ensure you maximize the value of your data.

Our laboratory services are available as stand-alone services or can be integrated into our preclinical and/or translational studies. Let our expertise help you achieve your research goals.



**Comprehensive capabilities**



**Flexibility**



**Expertise**



**Speed**



**Cost Efficient**



### Genomics and Transcriptomics

- Standard Genomics: Sample preparation, PCR, qPCR, Sanger Sequencing
- Advanced Genomics and Next Generation Sequencing (NGS): WGS, WES, RNA-Seq, WGBS, LncRNA-Seq, single cell sequencing, microbiome sequencing, Nanostring nCounter services, etc.
- Mouse I/O RNA-Seq Panel
- Cell line authentication with deep sequencing



### Proteomics

- Immunoassays: ELISA, MSD, Luminex®, Western Blot, 2D gel, and ELISpot
- Mass spectrometry-based proteomics: 4D-DIA quantitative proteomics, 4D phosphoproteomics and post-translational modification analysis
- Sample preparation and protein separation



### Spatial Biology and Digital Pathology

- Spatial omics services with NanoString GeoMx® DSP and 10x Genomics Visium
- Digital pathology, IHC, IF, *in-situ* hybridization/RNAScope
- Tumor tissue microarray
- Rare cell analysis
- High content imaging



### Immune Monitoring

- Mouse I/O RNA-Seq Panel
- Flow cytometry
- Cytokine and chemokine profiling
- ELISA and multiplex immunoassays



### Bioanalysis

- DMPK
- ELISA, MSD, HPLC, LC-MS/MS based bioanalysis
- Biofluid test
- Flow cytometry
- Cytokine and chemokine profiling

# Genomics and Transcriptomics

## Genomics and High-Throughput Sequencing Platform

Besides the conventional genomics assays, Crown Bioscience has introduced industry-leading high-throughput technological platforms, including second- and third-generation sequencing, an optical genome mapping platform, single-cell sequencing, and NanoString platforms to provide our customers with the most cutting-edge and comprehensive solutions for genomics analysis.

Our dedicated bioinformatics team can help with data analysis, to achieve a deeper understanding of your drug mechanism of action, and discover meaningful biomarkers, so you can realize the full potential of your molecules.

 <p><b>MGI MGISEQ-2000</b> Medium-Throughput Flexible Low Cost</p>	 <p><b>Illumina Novaseq 6000</b> Illumina's Most Powerful Production-Scale Sequencer</p>	 <p><b>PacBio Sequel II</b> Third-Generation Sequencing with Highly Accurate Long Reads</p>	 <p><b>Bionano Saphyr® II</b> Next-Generation Cytogenetics with Optical Genome Mapping</p>	 <p><b>10x Genomics Chromium</b> Industry Standard Single Cell Sequencing</p>
---	---	--	--	--

Standard Genomics Services	Advanced Genomics and NGS Services	Our Unique NGS services
<ul style="list-style-type: none"><li>• Sample preparation:<ul style="list-style-type: none"><li>▪ DNA/RNA extraction</li><li>▪ mRNA purification</li><li>▪ microRNA extraction</li><li>▪ NGS library preparation</li></ul></li><li>• Conventional assays:<ul style="list-style-type: none"><li>▪ Target gene expression assay</li><li>▪ Virus copy number assay</li><li>▪ Gene copy number variation analysis</li><li>▪ Gene mutation validation</li><li>▪ Gene fusion validation</li></ul></li></ul>	<ul style="list-style-type: none"><li>• RNA-Seq</li><li>• WES</li><li>• WGS</li><li>• WGBS</li><li>• LncRNA-Seq</li><li>• Single cell sequencing</li><li>• PacBio: Long read sequencing</li><li>• Bionano: Structural variation (SV) detection</li><li>• Microbiome sequencing<ul style="list-style-type: none"><li>▪ Full length 16S sequencing</li><li>▪ Metagenomics sequencing</li><li>▪ Metatranscriptomics sequencing</li></ul></li><li>• Nanostring nCounter services</li></ul>	<ul style="list-style-type: none"><li>• Mouse I/O RNA-Seq panel</li><li>• Cell line authentication with deep sequencing</li></ul>

### Mouse I/O RNA-Seq Panel

- Comprehensive profiling of 1080 genes associated with tumor immunity from a single sample
- Rapid transcriptomic insights into key immune cell populations and I/O pathways and process in the tumor microenvironment (TME)
- Compared to array-based I/O profiling relying on hybridization with DNA probes, this NGS panel has higher sensitivity and accuracy, especially on low expressing genes

### Cell Line Authentication (CLA) with Deep Sequencing

#### Patented deep sequencing-based CLA service

Targeted NGS panel covering 600+ SNPs and chromosome segments to accurately characterize mouse and human samples. Compared to conventional PCR-based STR assay for CLA, which targets only 9 to 24 gene sites (vendor dependent), our CLA service significantly overperforms with increased accuracy, sensitivity, throughout, and provides more extensive information. Virus infection and mycoplasma contamination checks are available.

## Proteomics

### Immunoassays

Immunoassays are powerful tools for detecting and quantifying a wide range of molecules, including proteins, hormones, and drugs in biological samples.

#### Technical Platforms

- ELISA
- Meso Scale Discovery (MSD)
- Luminex® multiplex assay
- ELISpot
- Western blot and 2D gel

#### Applications

- Singleplex and multiplex cytokine and chemokine profiling
- Intracellular signaling pathway analysis
- Therapeutic protein assays
  - PK/PD
  - Toxicity
  - Immunogenicity

### Mass-Spectrometry-Based Proteomics

#### Services Offered

- 4D-DIA quantitative proteomics
- 4D phosphoproteomics
- Post-translational modification (PTM) analysis

#### Applications

- Global proteomics profiling of cells or tissues, with/without treatment
- Proteomics biomarker discovery and validation
- Drug mechanism of action and toxicity studies
- Disease mechanism studies
- Target identification and validation
- Complementary analysis and correlation approaches for other omics analysis

### Key Advantages of our MS-based Proteomics Services

- **Cost-effective and fast turnaround time, with no compromise on quality**
- **Enhanced sensitivity:** Ion mobility can improve the sensitivity of MS by reducing the background signal and increasing the signal-to-noise ratio. This is particularly useful for identifying and quantifying low-abundance proteins
- **Superior data quality and reproducibility:** Data independent acquisition (DIA) provides a more comprehensive analysis of all ions in the sample, rather than just a select few in data dependent acquisition (DDA)
- **Improved PTM identification:** Ion mobility mass spectrometry can separate isobaric species and provide improved resolution of PTMs, to facilitate the identification and characterization of PTMs in proteins
- **Proteomics-based biomarker discovery capability:** Customized bioinformatic analysis available for large cohort studies

### 4D-DIA Quantitative Proteomics

#### Rapid, Unbiased and Deep Proteome Profiling

A new generation technology combines 4D proteomics, which added ion mobility as the fourth separation dimension to traditional LC-MS/MS (retention time, mass-to charge ratio [m/z] and MS/MS fingerprint), with DIA strategy, which avoids data imbalance caused by randomness by realizing “lossless acquisition” of all possible data.

### 4D Phosphoproteomics

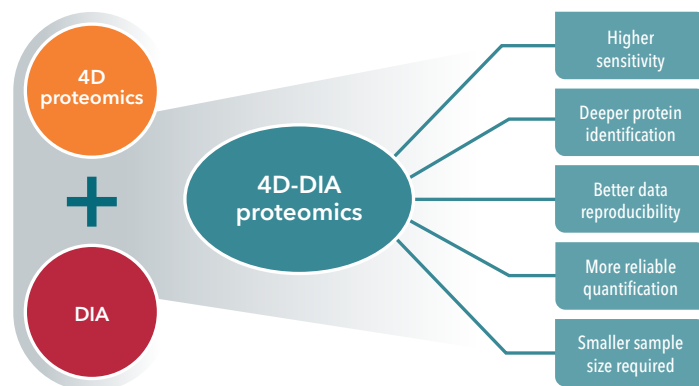
#### Rapid, Deep and Accurate Phosphoproteome Analysis

- Immobilized metal affinity chromatography (IMAC) strategy: Using proprietary targeted antibodies to enrich phosphopeptides, to reduce sample complexity
- Additional ion mobility separation: Resolve the issue of isomerization in PTMs and enables more reliable and deeper coverage for phosphorylation
- Strict dual quality control to remove low confidence data
- Upgraded bioinformatic analysis available

### Mass Spectrometry Facility



### Advantages of 4D-DIA Proteomics



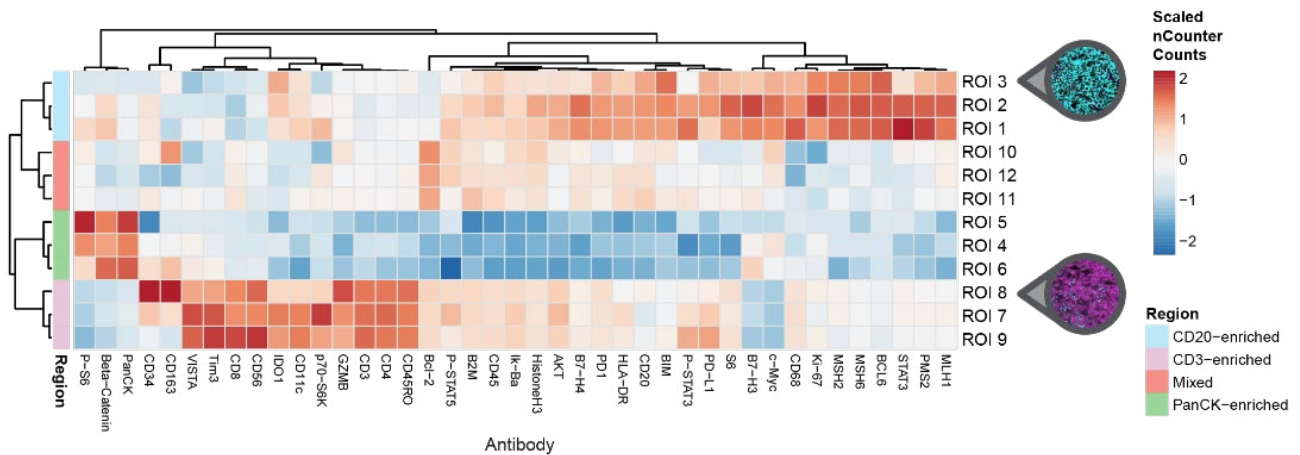
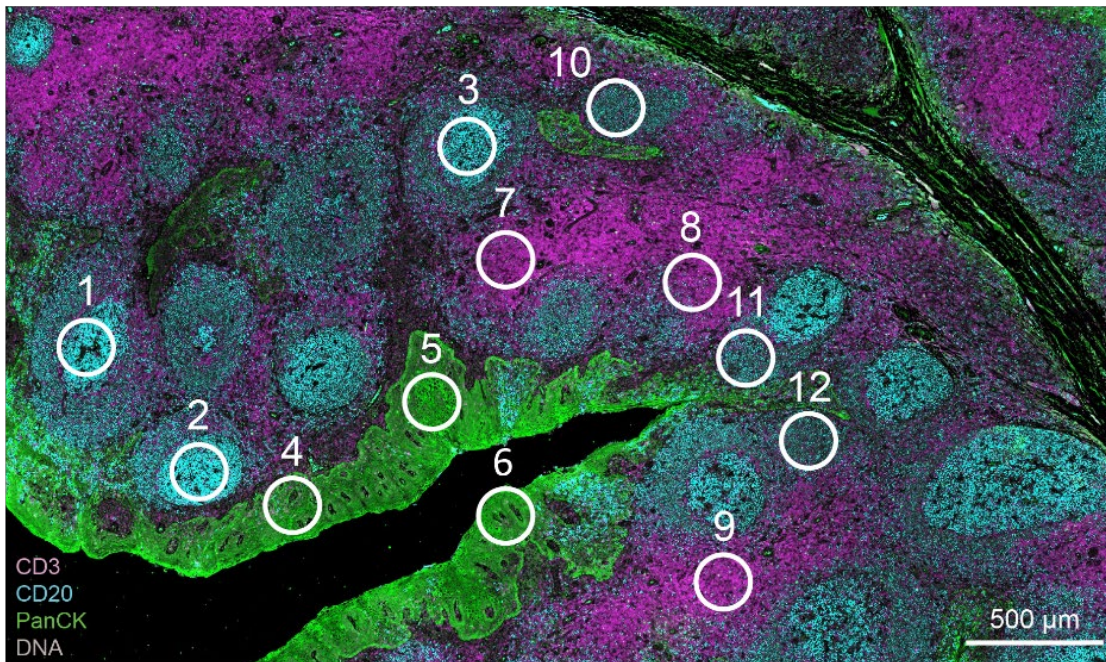
# Spatial Biology and Digital Pathology

## Spatial Omics Services

Crown Bioscience is an authorized service provider for both the NanoString GeoMx® DSP and 10x Genomics Visium platforms (Indivumed Services, a Crown Bioscience company). If you're seeking guidance on aligning the right platform with your research needs, contact us.

## Spatial Transcriptomics and Proteomics with NanoString GeoMx DSP

Our approach employs morphologically guided gene expression, utilizing NanoString's expertly crafted panels. The process is streamlined for our clients: simply provide your tissue samples, select the desired NanoString panel and readout method, and let our professionals manage everything else. Experience the next level of tissue profiling with ease!

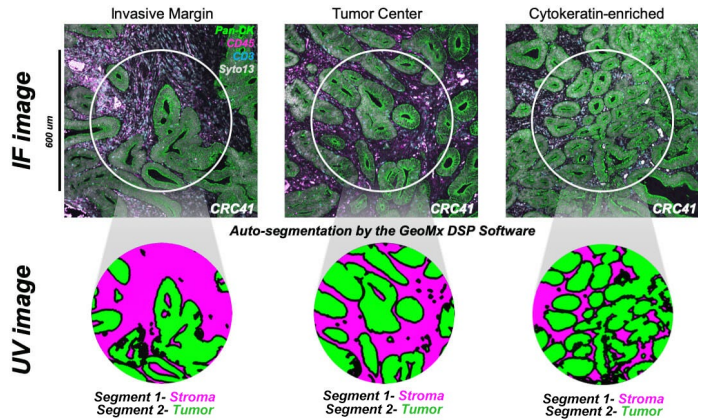


## Profile the Whole Transcriptome and 570+ Proteins from Intact Tissue

Explore the complete transcriptome and over 570 protein targets individually or in tandem, utilizing a range of sample inputs, including whole tissue sections (fresh frozen or FFPE), tissue microarrays (TMAs), or organoids.

### You Decide Where to Draw the Line with Biology-Driven Profiling

Decide where to draw the line and let the tissue be your guide with biology-driven profiling that empowers you to choose the tissue microenvironments and cell types that matter most to you. Choose which regions to profile and segment each region into different compartments using fluorescent staining patterns as a mask to profile expression in certain tissue types or cell populations.



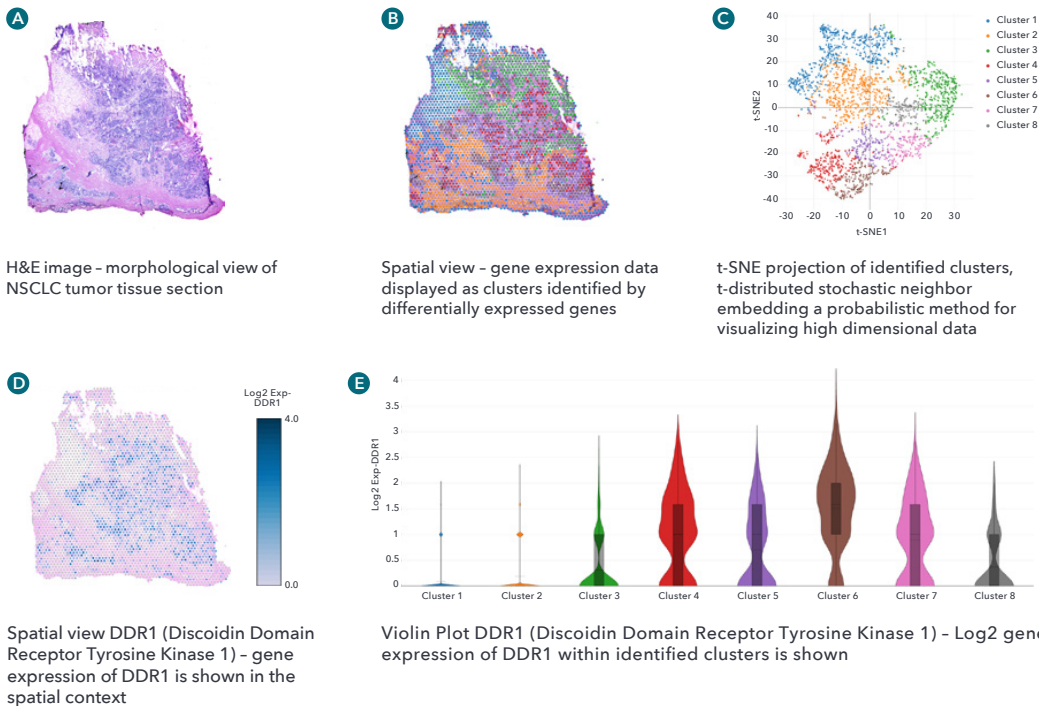
## Spatial Transcriptomics Services with 10x Genomics Visium

Indivumed Services, a Crown Bioscience company, implements the "Visium Spatial Gene Expression" Solution from 10x Genomics offering:

- Analysis of the total transcriptome in the morphological context with just one tissue section (fresh frozen or FFPE)
- High-resolution view of gene expression variability in the tissue of interest
- Combination with our high-quality, low-ischemia time tissue samples from our clinical network



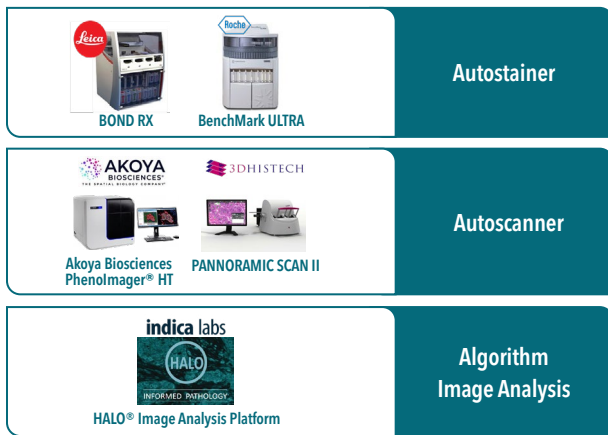
### From morphological view to spatially-resolved cluster analysis and target gene expression



## Digital Pathology Platform

- Efficiently progress your research by taking advantage of our collection of over 400 IHC validated markers
- Save time with our automated multiplex IHC, IF, RNAscope/FISH and H&E staining platform, utilizing industry standard Leica BOND RX, BenchMark ULTRA IHC/ISH System by Roche Diagnostics, and Sakura Tissue Tek Prisma® Plus Automated Slide Stainer
- Akoya OPAL TSA system multiplex IHC staining, and image scanning 7-color scanner Akoya Biosciences Phenolmager® HT, NanoZoomer S60 and 3D HISTECH Pannoramic SCAN

### Automated Workflow AI-Driven Image Analysis



## Rare Cell Analysis

Utilize our rare cell analyzer and picker to improve rare cell detection sensitivity and recovery. Rare cells from different sample types can be quantified and visualized with a sensitivity as low as two cells and a recovery rate of up to 90%. This enables you to better understand drug mechanisms of action, monitor disease progression, and maximize overall therapeutic effect.

## Tumor Tissue Microarrays (TMA Tumor)

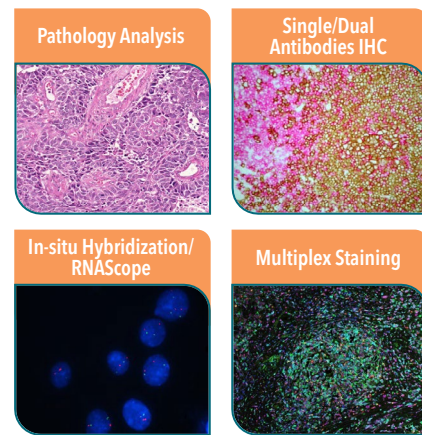
- Screen hundreds of tumor samples at a time for biomarkers of interest
- PDX TMAs: Cancer types: bladder, breast, cervical, colorectal, esophageal, gastric, head & neck, kidney, leukemia, lymphoma, liver, lung, melanoma, ovarian, pancreatic and sarcoma
- Cell Line Derived Xenograft TMAs
- Syngeneic Model TMAs
- Tumor Homograft TMAs

## 3D In Vitro High Content Imaging Service

- Capture and store 300+ image-based data points
- Revisit data as drug candidate moves through the pipeline
- Layer and score drug effects with image mediated screens
- Identify and validate morphological and phenotypic changes

- Characterize tissue morphology in depth with highplex FL and multiplex IHC
- Classify tissues, and analyze spatial distribution and proximity utilizing industry gold standard HALO® image analysis platform
- Ensure accurate and consistent results with our stringent validation and QC process
- Tissue bank from syngeneic/CDX/PDX/PDXO models

## Comprehensive Assays



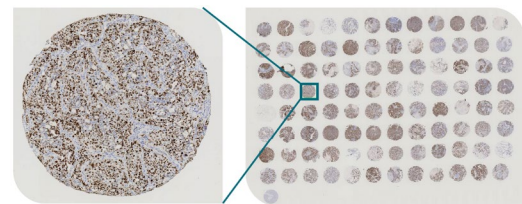
## Rare Cell Analysis Applications

- CTCs
  - From cancer patient samples
  - From *in vivo* models
- Cell therapy
  - CAR-T, TCR-T and CAR-NK
- Cell picker

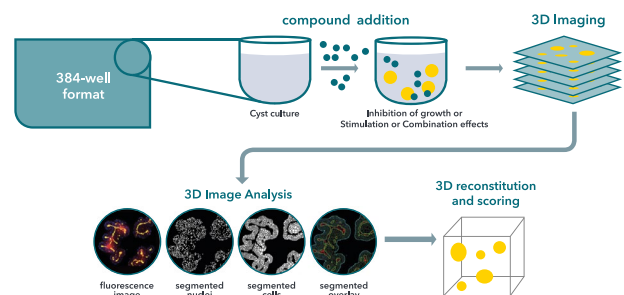
## Rare Cell Picker Downstream Applications

- Single cell sequencing
- qRT-PCR
- Differential gene expression analysis (RNA-Seq)
- Proteomics analysis (ICC, FISH)
- Cell culture

## Tumor Tissue Microarray



## 3D In vitro High Content Imaging







# Bioanalytical Services

## DMPK and Bioanalytical Services

### In vivo PK of Small and Large Molecules

- Samples for various species (mouse, rat, rabbit, dog, NHP, pig, human)
- Various administration routes (i.v., p.o., i.p., s.c., i.m.)
- In vivo PK study design
- Single, multiple, and cassette dosing PK
- In vivo crossover studies for bioavailability (F)
- Pathology expertise and sample preparation
- Serial blood collection over 24 hours
- PK issue distribution and mass balance
- Excretion assays
- Maximum tolerated dose (MTD)

### LC-MS/MS

- For small molecules
- Assay protocol design
- Method development
- Pre-dose formulation test
- Data analysis (Phoenix™ WinNonlin 8.2)
- Reporting

### ELISA

- Monoclonal antibodies
- Antibody-drug conjugates (ADCs)
- Bispecific antibodies
- Immunogenicity

### MSD

- Therapeutic antibodies/proteins
- High sensitivity and large dynamic range

### HPLC-UV

- Agilent 1200 and Waters UPLC

### Bioanalysis

- Method development and validation
- Quantitation analysis (parent compound, metabolites)
- Dosing solution analysis
- Various biological sample analysis (blood, plasma, bile, urine, feces, tumor tissue)



Waters Q-ToF



SCIEX Triple Quad 6500+



SCIEX API 4000



SCIEX API 4000

## Biofluid Testing

### Complete Blood Count (CBC)

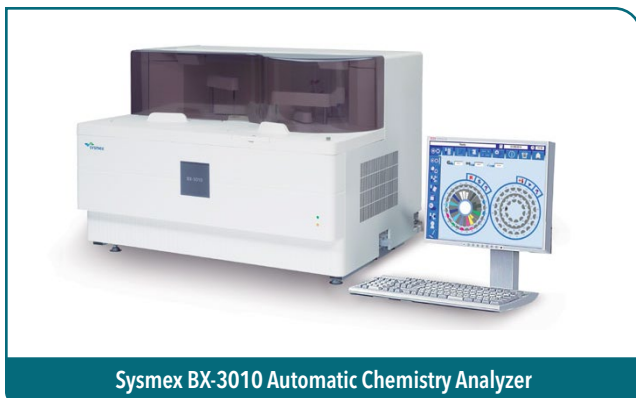
#### Platform:

- Element HT5 Veterinary Hematology Analyzer
- VETSCAN® HM5 Hematology Analyzer

#### CBC 22 Parameters:

WBC, LYM, MON, NEU, WBC%, LYM%, MON%, NEU%, RBC, HCT, MCV, RDWc, RDWs, HGB, MCH, MCHC, PLT, MPV, PCT, PDWc, PDWs

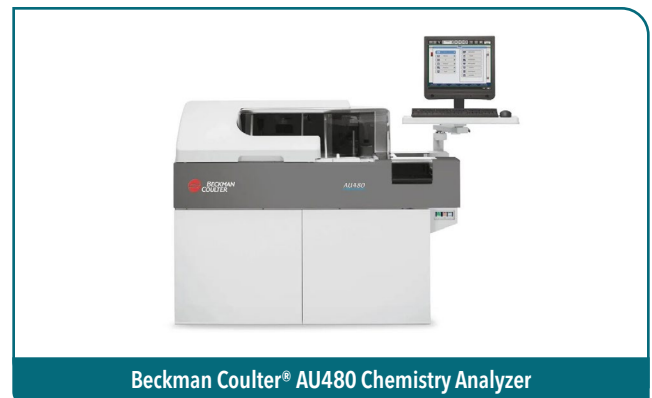
### Blood and Urine Chemistry Testing



Sysmex BX-3010 Automatic Chemistry Analyzer

#### 24-parameters:

AST, ALT, ALP, ALB, TP, CHE, BUN, CREA, UREA, UA, CK, LDH, Ca, IP, AMY, GLU, TCHO, TG, HDL-C, LDL-C, CRP, GGT, TBIL, DBIL



Beckman Coulter® AU480 Chemistry Analyzer

#### Parameters:

**Blood panel:** Alb, ALP, ALT, Amy, AST, CO2, BUN, Ca, CHOL, CK, Cr, DBIL, GGT, Glu, HDL, LDH, LDL, Lip, Mg, Phos, TBIL, TP, TRIG, UA, VLDL, Na, K, Cl, B2M, BHOB, CRP, Cys C, Fe, Hcy, NEFA, Hb, HbA1c, Ferr, UIBC

**Urine panel:** Alb, BUN, Cr, Glu, TP, NH3, and MALB

## Data Science and Bioinformatics Services

### Unlocking Potential: Data-driven Insights for Informed Decision-making

In the realm of preclinical drug discovery, bioinformatics stands as a vital catalyst. Leveraging computational analysis and data-driven insights, it accelerates target identification, disease and drug mechanism of action (MoA) discovery, and biomarker discovery, reducing costs and late-stage risks. Crown Bioscience's in-house bioinformatics team excels in harnessing 'omics' big data, unlocking innovation-driven insights. By leveraging bioinformatics, we maximize data value, enabling informed decisions, including biomarker-driven clinical trial design, derisking drug development, and offering cost savings. Our commitment to innovation drives us to bring promising drugs to the clinical stage, advancing healthcare and improving outcomes.

#### Our Advantages:



##### **In-house Expertise with Proven Publication History:**

Our dedicated in-house bioinformatics team has a proven history of contributing to peer-reviewed publications, bringing specialized knowledge to your projects.



##### **Vast 'OMICS' Data Expertise:**

With deep expertise in handling and interpreting 'omics' big data, we harness its full potential to drive meaningful insights.



##### **Customized Solutions:**

Our services are tailored to meet your unique research needs, offering flexibility and adaptability.



##### **Collaborative Partnership:**

We work closely with you, enhancing the success of your research endeavors.



##### **Rapid Response:**

Known for our prompt communication and efficient project management, we deliver timely results.



##### **Cost-effective Solutions:**

We optimize study design and resource usage to provide cost-effective solutions.

#### Our Bioinformatics Services at a Glance

- **Preclinical Biomarker Discovery:**  
Uncover insights for cell line, organoid, and mouse screening studies.
- **OMICS Data Analysis:**  
Harness extensive 'OMICS' datasets, including Genomics, Transcriptomics, and Proteomics.
- **Unique NGS Services:**  
Innovative NGS offerings, such as Mouse Immunology RNA-Seq and Patented Cell Line and Biosample Authentication with Deep Sequencing.
- **Drug Combination Analysis:**  
Enhance *in vitro* and *in vivo* combination studies.
- **General Bioinformatics and Statistical Consulting:**  
Tailored support for your research and development needs, including expert statistical guidance.
- **NGS Data Purchase/Transfer:**  
Secure and ethical data procurement is facilitated through Material Transfer Agreements (MTAs).

## Bioinformatics (continue)

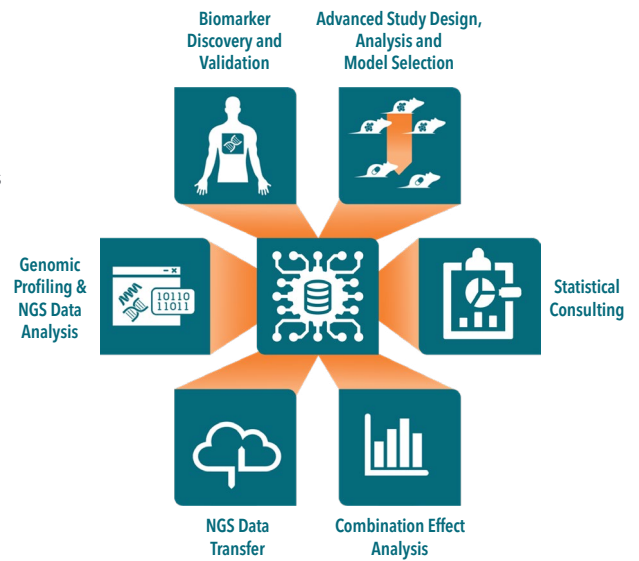
### Integrated *In Silico* Modeling To Accelerate Drug Discovery

Apply the most appropriate *in silico* framework to your pharmacology data or historical datasets to:

- Improve your chances of clinical success through early identification of candidate biomarkers
- Elevate study design and analysis by selecting the most appropriate models, moving beyond target gene expression or t-test/ANOVA analyses
- Understand combination treatment benefits by determining synergistic, antagonistic, and additive effects

#### Advanced Study Design, Analysis, and Model Selection

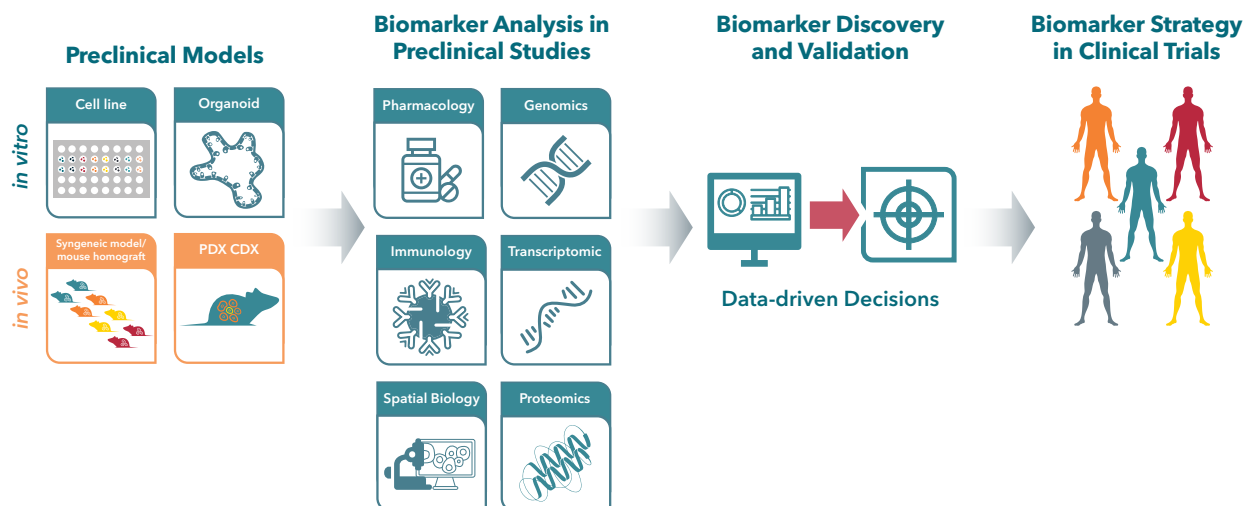
- Study design, sample size calculation, power determination
- Correlate all canonical pathway activities to target gene and protein expression
- Associate target gene expression to patient clinical information and public databases
- Optimize MCT study design through statistical framework
- Empirical analysis of historical data and advanced statistics



#### Biomarker Discovery and Validation

Preclinical biomarker discovery strategies help to identify potential therapeutic targets, assess the safety and effectiveness of new compounds, identify subgroups of patients who are likely to respond to a particular therapy and inform the design of clinical trials. If introduced early in preclinical studies, they can play a key role in reducing the cost and time required for drug development. Utilize our services to make informed decisions:

- Large-collection of *in vivo* and *in vitro* preclinical models and screening services
- Comprehensive multiomics biomarker analysis
- Complementary databases covering baseline profiling data and historical data of our in-house models
- Experimental design aids
- Powerful bioinformatics data processing capabilities to maximize the value of your data



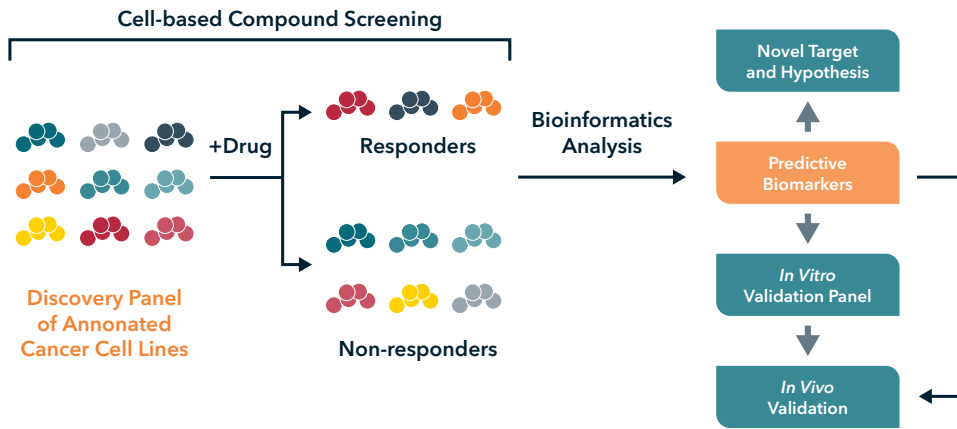
#### Biomarker Discovery via *in vitro* studies

- Cell line-based studies, such as high throughput cell line screens (**OmniScreen™**)
- Organoid-based studies
- **OrganoidXplore**, a large-scale organoid panel drug screening

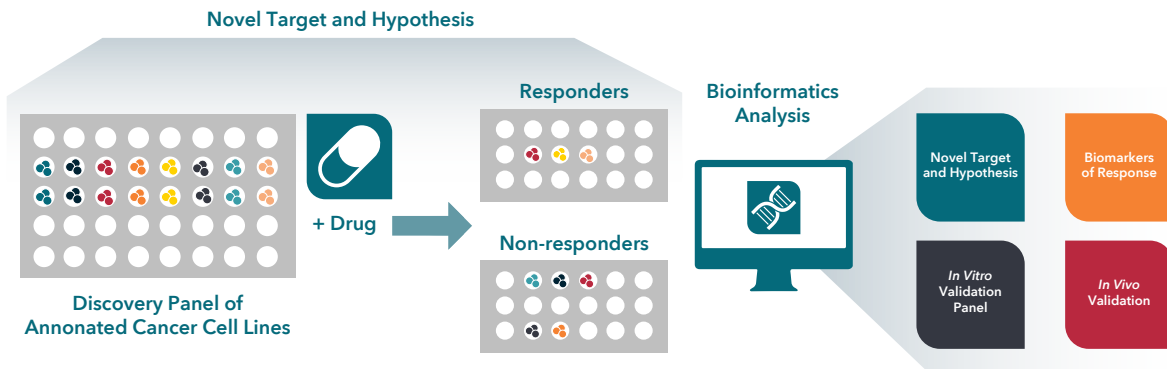
#### Biomarker Discovery via *in vivo* studies

- High throughput *in vivo* screens (such as **MuScreen™** for immunotherapies)
- Mouse clinical trials: Preclinical population studies to help stratify patients for clinical trials

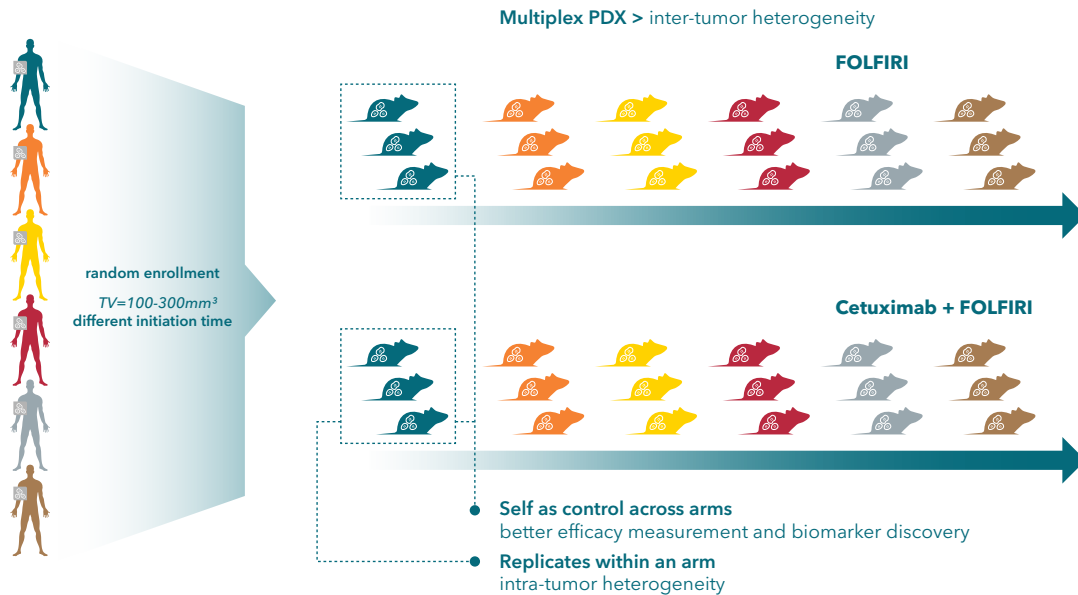
**Biomarker discovery can be conducted using data from cell line and organoid screens.**



**OmniScreen™ Cell based screening service.**  
 Well-validated *in vitro* screening program for rapid and cost-effective screening of over 500 cell lines.



**Mouse clinical trials. Design and advantages with inter-tumor heterogeneity.**



**Get in touch**



**Sales**

US: +1 858 622 2900  
 UK: +44 870 242 2900

busdev@crownbio.com  
 www.crownbio.com



**Science**

consultation@crownbio.com

