

# 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, WBGS, LncRNA-Seq, single cell sequencing, microbiome sequencing, Nanostring 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

- 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.



**Thermo KingFisher Flex**  
**QIAGEN QIASymphony SP**  
Fully Automated Workflow  
Reproducible Results




**MGI MGISEQ-2000**  
Medium-Throughput  
Flexible  
Low Cost



**Illumina Novaseq 6000**  
Illumina's Most Powerful  
Production-Scale Sequencer



**PacBio Sequel II**  
Third-Generation Sequencing with  
Highly Accurate Long Reads



**Bionano Saphyr® II**  
Next-Generation Cytogenetics with  
Optical Genome Mapping

### Standard Genomics Services

- Sample preparation:
  - DNA/RNA extraction
  - mRNA purification
  - microRNA extraction
  - NGS library preparation
- Conventional assays:
  - Target gene expression assay
  - Virus copy number assay
  - Gene copy number variation analysis
  - Gene mutation validation
  - Gene fusion validation

### Advanced Genomics and NGS Services

- RNA-Seq
- WES
- WGS
- WBGS
- LncRNA-Seq
- Single cell sequencing
- PacBio: Long read sequencing
- Bionano: Structural variation (SV) detection
- Microbiome sequencing
  - Full length 16S sequencing
  - Metagenomics sequencing
  - Metatranscriptomics sequencing
- Nanostring services

### Our Unique NGS services

- Mouse I/O RNA-Seq panel
- Cell line authentication with deep sequencing

### 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

#### The first commercial 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

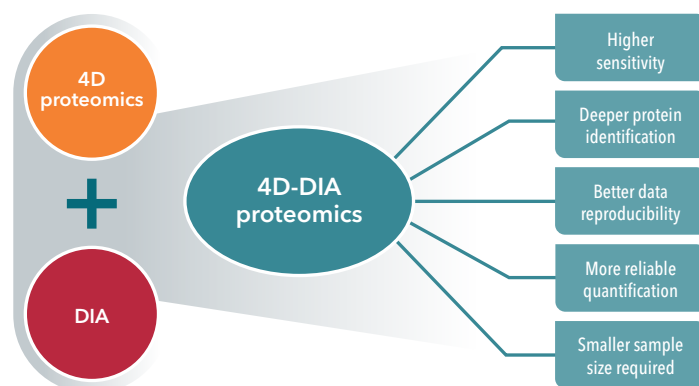
#### Rapid, Deep and Accurate Phosphoproteome Analysis

- 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



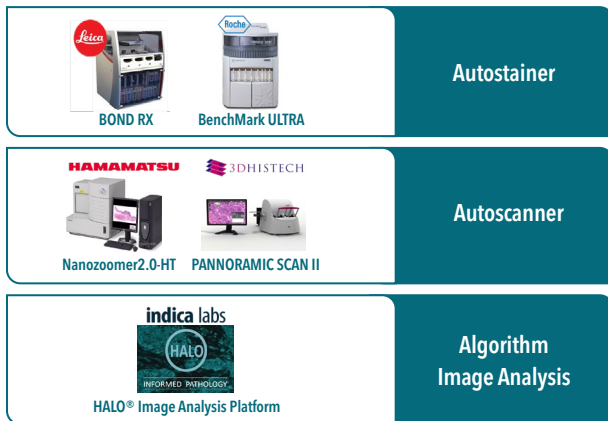
# Spatial Biology and Digital Pathology

## Digital Pathology Platform

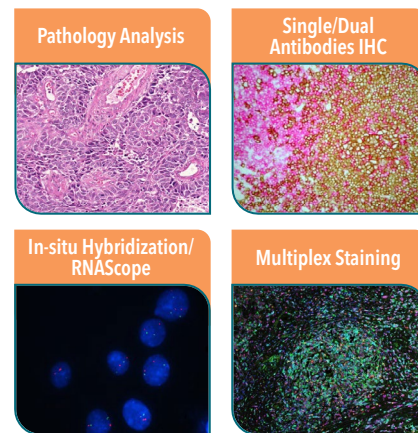
- Efficiently progress your research by taking advantage of our collection of over 400 IHC validated markers
- Save time with our automated multiplex IHC, IF, RNAscope/FISH and H&E staining platform, utilizing industry standard Leica BOND RX, BenchMark ULTRA IHC/ISH System by Roche Diagnostics, and Sakura Tissue Tek Prisma® Plus Automated Slide Stainer

- Rapidly review slide image files through high-throughput automated scanning and data sharing, utilizing industry standard NanoZoomer 2.0-HT and 3DHISTECH Panoramic Scan
- 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

### Automated Workflow AI-Driven Image Analysis



### Comprehensive Assays



## 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.

### Rare Cell Analysis Applications

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

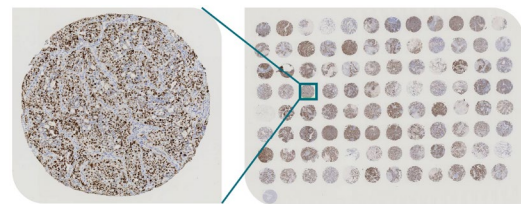
### Rare Cell Picker Downstream Applications

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

## Tumor Tissue 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

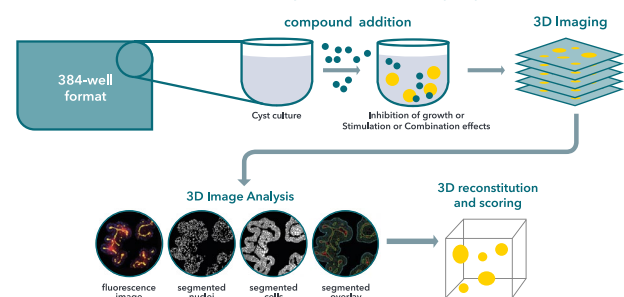
### Tumor Tissue Microarray



## 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

### 3D In vitro High Content Imaging



# Immune Monitoring

We offer a wide collection of immune monitoring assays, including some unique services. Rely on our immunological expertise, broad capabilities, flexibility to customize assays to your special needs, quick turnaround, and cost-efficient services to accelerate your drug development:

- **Mouse I/O RNA-Seq Panel:** Comprehensive profiling of 1080 gene transcripts associated with tumor immunity
- **Flow cytometry:** Immune cell activation assay, immuno-phenotyping, T cell proliferation assay, receptor occupancy, cytotoxicity, cellular immune response, and immunogenicity study
- **Cytokine and chemokine profiling**
- **ELISA and multiplex immunoassays:** Cellular immune response, humoral immune response (T cell dependent antibody response, TDAR), and immunogenicity
- Antibody-dependent cell-mediated cytotoxicity (ADCC) assays, functional assays and more. Please see our *in vivo* services

## Flow Cytometry Platform

Gain new insights into your molecule’s mechanism of action and PD through robust and in-depth immunophenotyping. Maximize immunotherapeutic benefit, limit unwanted toxicities, and increase your chances of preclinical/clinical success through comprehensively characterizing cells of interest.

Use our high quality flow cytometry data to better understand:

- The immune make-up of relevant organs such as tumor, blood, spleen, and lymph nodes
- Therapeutic effect on the frequencies and functionality of cell subsets
- Individual specimen variations and heterogeneity of response

### Industry-leading Flow Cytometry Platform



**GentleMACS™ Dissociators**  
 > 20 tumor dissociation protocols



**BD LSRFortessa™ Flow Cytometers**  
 Up to 17 colors



**Global Data Processing Center**  
 Consistent statistical analysis from global sites

### Most Requested Marker Examples

#### for Murine Markers

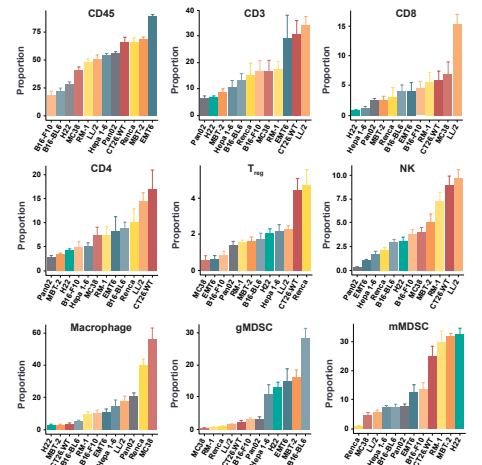
- CD45
- CD3
- CD4
- CD8
- ^CD44/CD62L
- ^CD69/CD44OX40/CD25 etc
- CD4+CD25+FoxP3+
- CD11b+IA/IE<sup>low</sup>/Ly6c/Ly6g
- CD11b+F4/80
- TCR γδ
- IA/IE/CD11c/CD206
- CD3-CD335+
- CD3+CD335+
- CD19
- ^TNF-α/IFN-γ/IL-7/IL-3 etc
- ^PD-1/PD-L1/CTLA4/TIM-3 etc
- ^Granzym B etc
- KI67/Brd U/PNCA etc
- Live/Dead (fixable)

#### for Human Markers

- CD45
- CD3
- CD4
- CD8
- CD127low/Foxp3+
- CD197/CD45RA
- CD19+/HLA-DR+: Total B
- CD16/CD56
- NKp46-/CD14-/HLA-DR+
- CD33+CD11b+CD15+
- CD15+CD33+CD11b-CD16
- CD11b+CD14+
- CD11b+CD33+CD16+
- CD11b+CD33+

### Baseline Profiling Data Available for In-House Models

#### Baseline Syngeneic Tumor Immune Profiling



## Cytokine and Chemokine Profiling

Use our cytokine and chemokine profiling platform through ELISA, MSD and Luminex® to fully understand:

- *In vitro* therapeutic effect on the amount of cytokines and chemokines produced
- Immunogenicity induced by your agent *in vivo*
- How cytokines in the tumor microenvironment regulate immune responses and their relationships
- Candidate biomarkers for predicting response and/or toxicity

# 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)

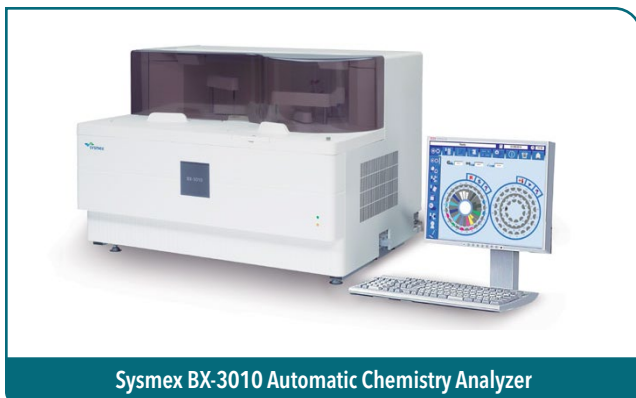
#### Platform:

- 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

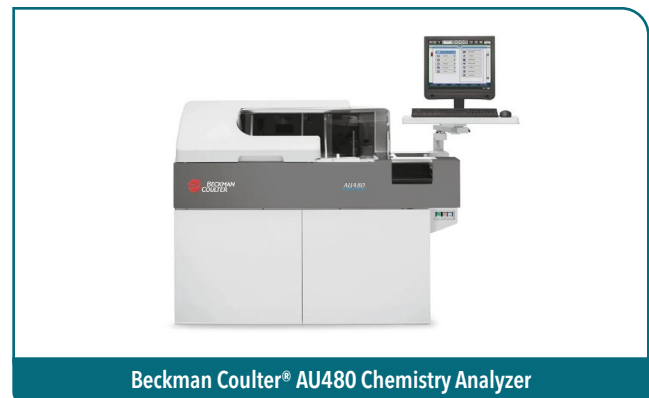
### Blood and Urine Chemistry Testing



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



## Bioinformatics

### 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

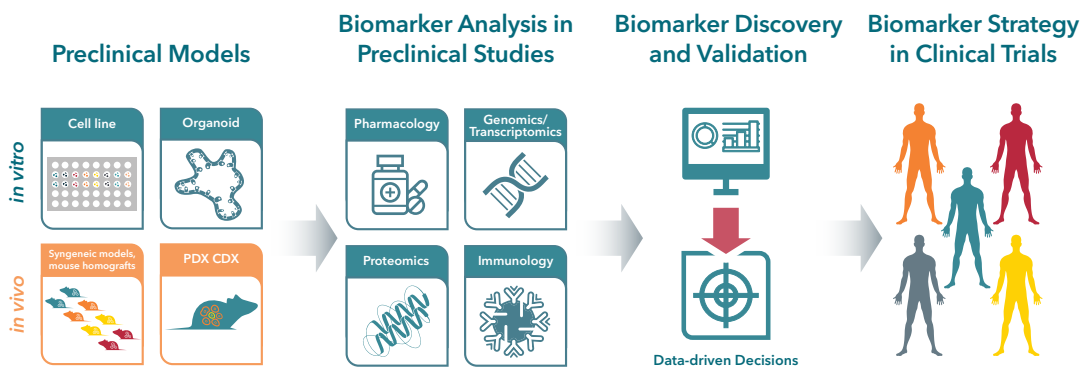
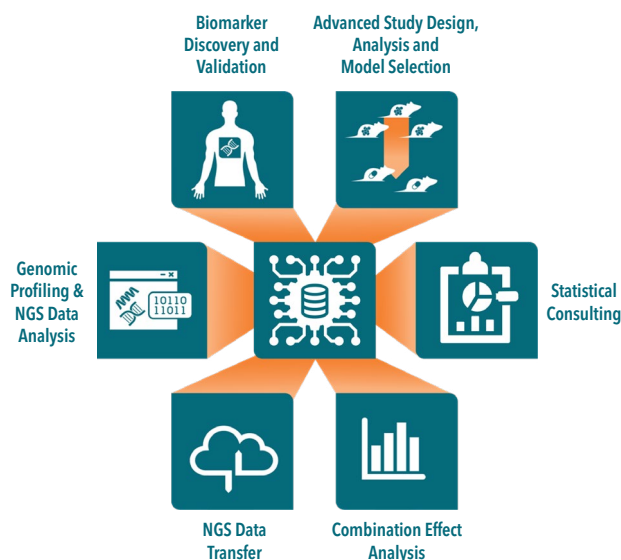
#### Advanced Study Design, Analysis, and Model Selection

- 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

#### 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

## Get in touch



Sales

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