COMPLETE SOLUTION FOR BIOMARKER DISCOVERY AND VALIDATION

Dedicated high throughput biomarker discovery services for clinician scientists and researchers

EFFECTIVE BIOMARKERS FOR UNMET CLINICAL NEEDS

The medical industry is entering a new paradigm of predictive, preventive and patient-centric clinical care. However, unmet clinical needs in patient management remain, such as in the areas of risk assessment, prevention, diagnosis, therapy and treatment response monitoring. Biomarker discovery efforts seek to address these gaps across various diseases, including cancer, metabolic, infectious and neurodegenerative diseases.

Limited sensitivity and specificity

Common methodologies for cancer screening such as the mammography for breast cancer have high false-positive rates[1]. Endoscopies to screen for and diagnose gastric and colorectal cancers are invasive and may cause infections or other adverse effects[2]. Liquid biopsies hold promise as non-invasive methods that can be employed for regular screening. Proteins such as prostate-specific antigen (PSA), cancer antigen 125 (CA-125) and carcinoembryonic antigen (CEA) are widely used liquid biopsy biomarkers for cancer diagnosis. They provide some level of discrimination between cancers at first suspicion and guide further investigations. Assessing the levels of these markers in diagnosed patients enables treatment monitoring or the detection of relapse. Though widely incorporated in routine clinical practice, protein biomarkers have significant limitations in both sensitivity and specificity[3].

Limited early disease detection ability

Providing a higher degree of cancer specificity are nucleic acid biomarkers such as circulating tumor DNA (ctDNA). ctDNA released by tumors can be differentiated from normal cell-derived DNA by the presence of specific genetic alterations involved in cancer pathogenesis and by differences in molecular size. These differences form the basis of early cancer detection. Thus far, the ability of ctDNA to detect stage 1 disease is limited - a sensitivity of 43% with CancerSEEK[4], and 39% with GRAIL[5]. Given considerable evidence from studies showing that early diagnosis results in improved outcomes for several cancer types[6], developing effective early detection biomarkers continues to be of great interest.

microRNA - A PROMISING BIOMARKER

More recent biomarker studies demonstrate the potential of microRNAs (miRNAs) biomarkers in meeting various clinical unmet needs[7]. miRNA expression is closely associated with many diseases, highly specific to tissue types and varies in tandem with disease progression. They exist stably and are easily accessible from both tissues and biofluids, making them attractive liquid biopsy biomarkers. Notably, they demonstrate potential as multimarker models for diagnosis, treatment selection and monitoring. The multimarker approach has particular utility in heterogeneous diseases. For instance, a five-miRNA serum test has the ability to can detect early stage non-small cell lung cancer (NSCLC)[8] and a six-miRNA multimarker panel can discriminate between malignant and benign breast lesions among women with abnormal mammograms[9]. Interestingly, a combination of a multi-miRNA panel and NT-proBNP, a protein marker, allow higher discrimination and improved specificity and accuracy in identifying nonacute heart failure[10].

THE NEED FOR STANDARDIZED METHODS FOR BIOMARKER STUDIES

Many biomarker studies fail to control pre- and post-analytical variables, resulting in data irreproducibility that impedes the translation of biomarkers into clinical tools[11]. The development of and adherence to standardized methodologies spanning sample collection, transport, storage, experimental protocols and data normalization and analyses are critical to resolving the reproducibility issue.

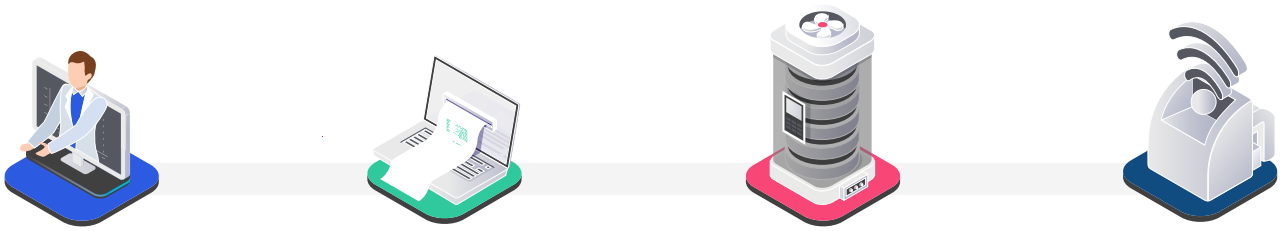
ACCELERATE AND TRANSLATE YOUR BIOMARKER STUDIES

MiRXES provides a one-stop, comprehensive miRNA profiling service in our dedicated high-throughput biomarker discovery laboratory. Our tested and proven biomarker discovery and validation workflow has generated high impact papers and one of the world's earliest miRNA IVD assays for early gastric cancer detection. Our workflow employs extensive pre-analytics and quality control measures that ensure data quality and reliability. We adhere to standardized methodologies published in our national standard to design, develop and validate miRNA-based diagnostics[12].

Speed to Delivery

Leverage our services to focus on your core business.

We deliver data as quickly as four weeks after receiving your samples*.



Technical Consultation

Tell us about your research project. Our specialist will provide advice on the technical feasibility of engaging our services.

Sample Shipment

Fill in the sample manifest form with your sample details. Our specialist will work with you to initiate sample shipment.

Experimental Execution

We take care of the process from start to end - sample isolation, library preparation and QC, sequencing or profiling, bioinformatics and data analysis.

Data Delivery

Softcopy results will be sent and our specialist will arrange for a results review session with you.

**ID3EAL PanoramiR Profiling Service*

Clinically Translatable and Publishable Insights

Discoveries made with our platform have been published in high impact literature.

GASTRIC CANCER

Gut, 2020

Profiling and analysis of 578 miRNA candidates to develop a cost-effective 12-miRNA serum biomarker assay for gastric cancer.

Reference: www.gut.bmj.com/content/70/5/829

LUNG CANCER

PNAS, 2020

Discovery, profiling and analysis of 35 miRNA candidates to develop a minimally invasive 5-miRNA serum biomarker test for detection of early stage non-small cell lung cancer.

Reference: www.pnas.org/content/117/40/25036

CARDIO-VASCULAR DISEASE

J Am Coll Cardiol, 2019

Combining an 8-microRNA panel with NT-proBNP to improve detection of non-acute heart failure.

Reference: www.pubmed.ncbi.nlm.nih.gov/30898206/

METABOLIC DISEASE

Front Physiol, 2019

Integrated analysis on plasma proteins and microRNAs leading to nomination of protein markers and microRNA post-translational regulatory sites.

Reference: www.ncbi.nlm.nih.gov/pmc/articles/PMC6460474/

With the same approach, we have developed and launched **GASTROClear** – one of the world's earliest miRNA IVD assays for early gastric cancer detection. The risk score generated by a 12-miRNA panel can guide reflex testing. GASTROClear is CE-IVD marked in the EU[5].

MiRXES
TO KNOW IS TO ACT

Reliable and Reproducible Findings

Our biomarker discovery workflow has been tested and proven to generate highly reliable and reproducible findings.

- **Extensive Experience**

  We have profiled over 50,000 clinical samples of various types in multiple disease areas and applications for our clients and collaborators globally, including biopharmaceutical companies, academic institutions, and government agencies.

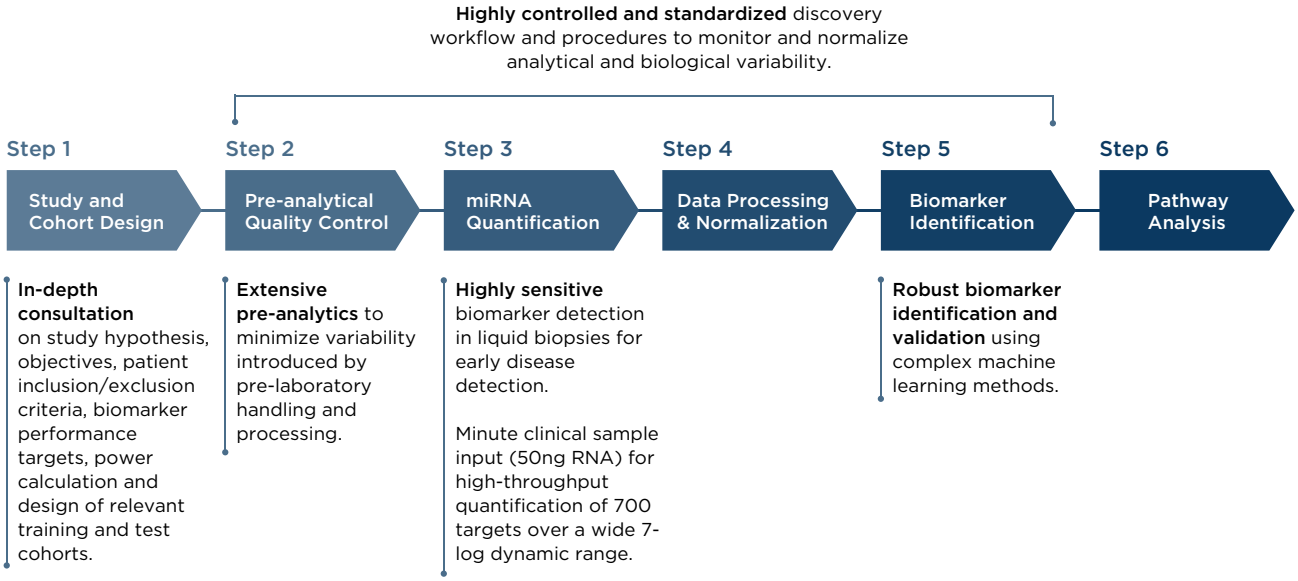
- **Standardized and Optimized Protocols**

  We drafted the national standard for the design, development and validation of miRNA-based diagnostics[6]. To ensure reproducible data and reliable biomarker assays, we adhere to standardized methodologies for:

  - Biomarker discovery and verification
  - Assay design and development
  - Pre-analytical, analytical variations and control measures
  - Pre-clinical and clinical validation

- **Highly Controlled Workflow**

  Our standardized discovery workflow controls and minimizes sources of variability to uncover actual observations. Data from a 2021 cross-platform evaluation study showed that our platform measured miRNAs with the highest precision[7].



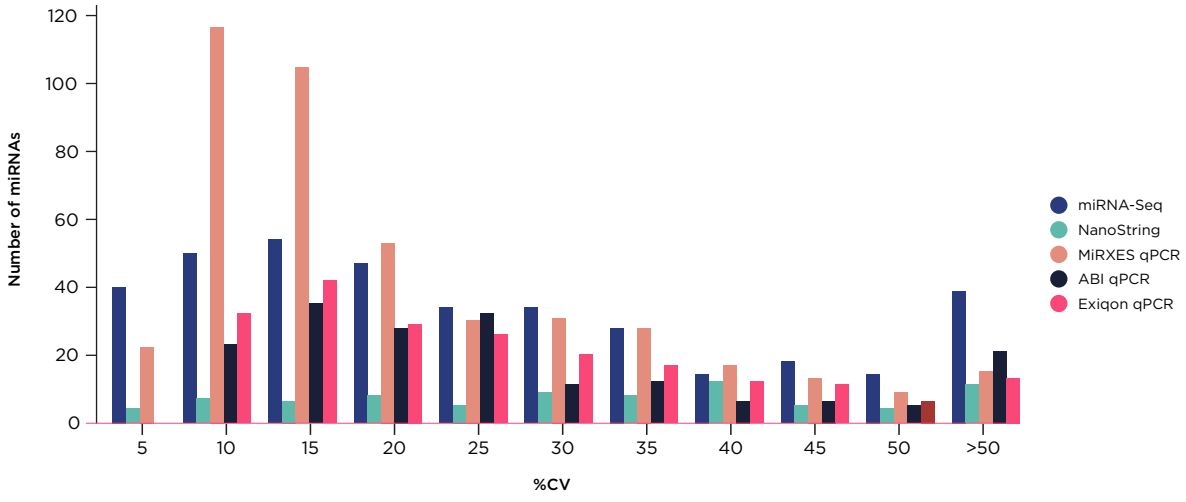


Figure 1

Figure 1: In a 2021 cross-platform evaluation study conducted in collaboration with Merck Sharp and Dohme (MSD), our technology measured miRNA expression levels with the lowest variation[13].

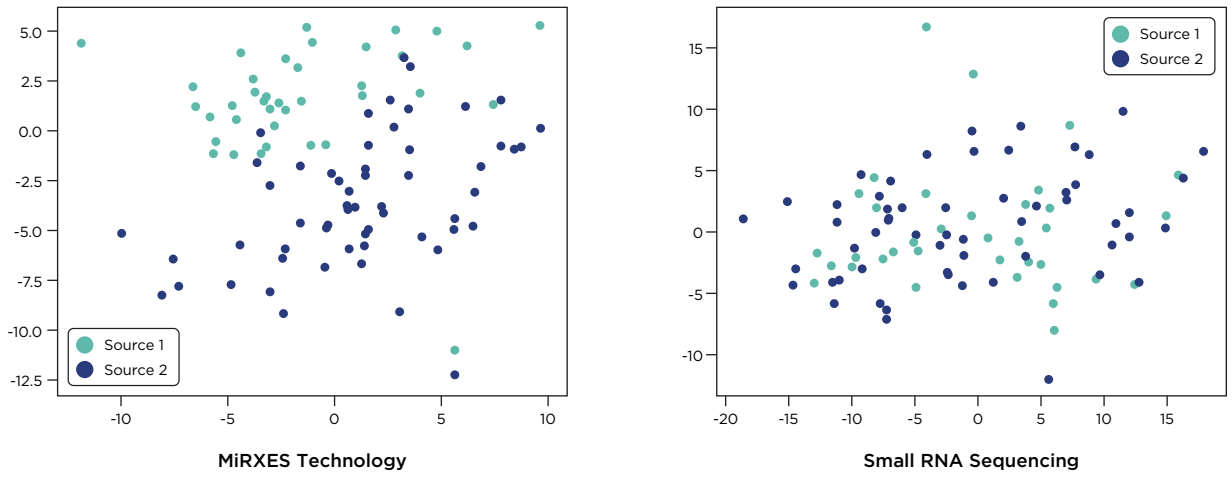


Figure 2

Figure 2: Potential sources of variability could arise from sample collection site bias and non-standardization of sample collection protocols, sample processing protocols, sample shipping and storage conditions. As MiRXES technology produces data with minimal technical variability, pre-analytical variability can be detected and considered during data analysis to ensure the selection of good biomarkers. (Source 1 and Source 2 represent different hospitals from which clinical samples were collected. Dots represent clinical samples.)

- **High Diagnostic Power, Minimal Sample Input**

  Many miRNAs that are lowly expressed (in the range of 100-10,000 copies) have excellent diagnostic power. In a 2021 cross-platform evaluation study conducted in collaboration with Merck Sharp and Dohme (MSD), our technology detected the highest number of miRNAs above the lowest limit of quantification[8]. The study was done with minimal sample input of only 100-200ul of serum/plasma or 50-100ng RNA.

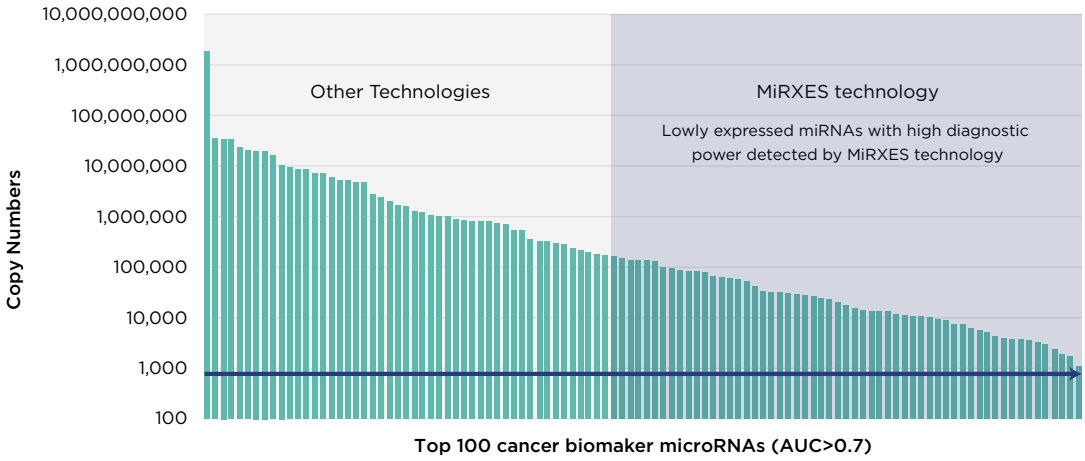
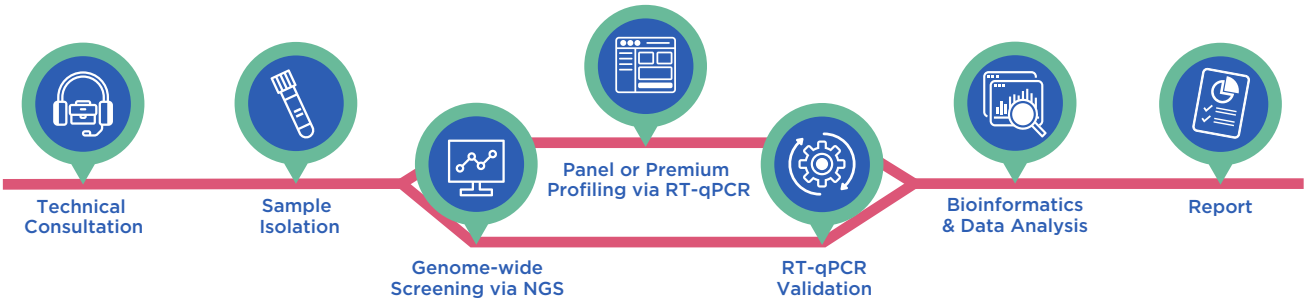


Figure 3

Figure 3: An in-house cross-platform experiment was performed on 200ul serum samples. Our technology detected more cancer biomarkers with higher diagnostic power, particularly those that exist in low copy numbers in serum, emphasizing the importance of assay sensitivity.

Comprehensive Services

We provide end-to-end services - from sample isolation to bioinformatics, from discovery to validation - designed to achieve the objective of assay development or high impact journal publishing. Customized solutions may be tailored to your project goals.



Objective	Discovery			Validation
Service	Small RNA Sequencing	ID3EAL Panel Profiling	ID3EAL Premium 700	Customized panels
Advantages	High coverage	High sensitivity	Highly controlled High sensitivity	High sensitivity
Technology	NGS	RT-qPCR	RT-qPCR	RT-qPCR
No. of Targets	Genome-wide	376	700	As requested
Quantification	Absolute (by read counts)	Relative	Absolute (by reference standards)	As requested
RNA Input Requirement	≥ 3 µg (≥ 20 µL, ≥ 50 ng/µL)	100 ng (≥ 50 ng/µL)	50 ng (≥ 50 ng/µL)	100 ng (≥ 50 ng/µL)

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