



GENOME EXPLORATION. SIMPLIFIED. AUTOMATED.

microRNA Profiling

BIOMARKER SIGNATURE DEVELOPMENT





miRNA Biomarker Profiles from Blood

MicroRNAs (miRNAs) are endogenous, non-coding RNAs with critical functions across various biological processes. They represent a regulatory mechanism that coordinates gene expression and whose deregulation is inevitably linked to human diseases such as cancer, infectious or inflammatory diseases.

miRNAs are not only differentially expressed in tumor versus normal cells. Moreover, different tumor entities show unique patterns of miRNA expression, related to their tissue of origin, accurately classifying tumors to their developmental lineage and differentiation state.

The role of miRNAs in pathogenesis and the power to associate expression changes with disease states underscores their value as molecular biomarkers: miRNA profiles serve as highly specific markers for diagnosis, prognosis, disease monitoring as well as prediction of therapeutic response.

Early diagnostic detection and assessment of disease progression are essential for successful disease management, especially in tumor patients, where timely therapeutic interventions are extremely critical. Translating these findings into clinical practice, the application of diagnostic biomarkers to cancer and other diseases brings us closer to personalized medicine and thus, improved healthcare management.

Modern patient care requires easily implementable tests. Using the Geniom RT Analyzer, miRNA biomarker profiling can be integrated into a standard, non-invasive blood test.

miRNA BIOMARKER PROFILING ON THE GENIOM RT ANALYZER

- miRNA biomarker signatures from blood and other body fluids, FFPE, fresh or frozen tissue
- No amplification or enrichment required
- Minimal sample amount
- Test automation for reliable and precise measurement
- Full bioinformatics solution for publication-ready results
- Excellent array-to-array reproducibility
- Flexible Geniom miRNA Biochip customization

Requiring minimal sample amounts, this sensitive high-throughput Biochip technology makes it possible to measure marker miRNAs and develop predictive miRNA signatures from limited clinical sample material, such as

- blood or other body fluids
- FFPE samples
- fresh or frozen tissue

Complete automation of Biochip processing and integrated bioinformatics solutions guarantee quick test results and publication-ready data.



BIOCHIPS FACTS

- Microfluidic Biochip with precise fluid control for reproducible hybridization and washing conditions
- Closed compartment eliminates evaporation and enables high temperature hybridization conditions
- 8 separate microchannels each with up to 15,624 features
- 124,992 features per Biochip
- Enables parallel hybridization of 8 different samples

miRNA Biochips for Biomarker Tests

INSTANT ACCESS TO THE NEWEST BIOMARKERS ON GENIOM BIOCHIPS

The heart of the Geniom Technology is the microfluidic Geniom Biochip. Catalog Geniom miRNA Biochips are available with validated and optimized probes for reliable test results. Probe design is always based on the latest Sanger miRBase update, thus

guaranteeing that the newest miRNA biomarkers are included in your signature assessment. Optionally, probe content can easily be customized to include proprietary, predicted or mutated miRNA sequences.

GENIOM miRNA BIOCHIPS ARE USEABLE WITH FEBIT'S GENOMIC SERVICES OR ON YOUR GENIOM RT ANALYZER

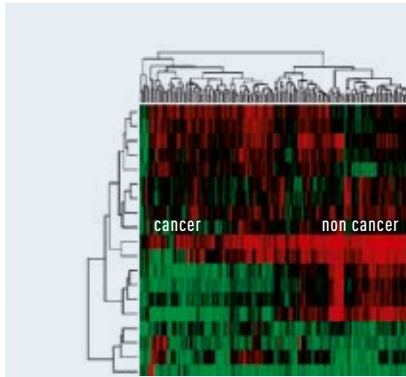
Full miRNA profiling service provided by febit

- From any sample to publication-ready data
- Project consulting
- Sample quality control
- Sample labeling
- Microarray hybridization and read out
- Full bioinformatics solution for publication-ready results
- Flexible biochip customization service

Profiling with Geniom RT Analyzer in your lab

- Fully automated microarray processing for your fast and easy analysis
- Intuitive software and short hands-on time
- Flexible biochip design
- Bioinformatics solution

miRNA BIOMARKER SIGNATURE DEVELOPMENT



CLUSTER ANALYSIS
Clustering of 20 most variable miRNAs from different tumor and normal tissues.

On-Chip Labeling for Simplified Sample Testing

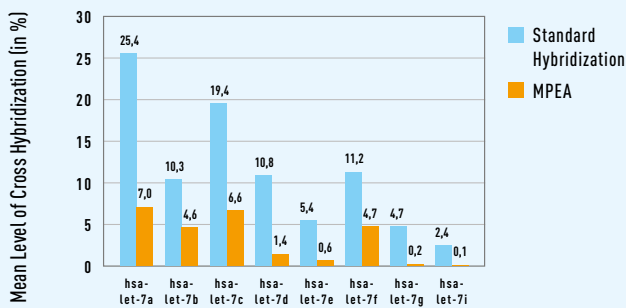
MPEA BENEFITS

- Minimal sample amounts
- Unbeatable sensitivity and specificity
- Discrimination power
- Test requires no prior enrichment, amplification or labeling
- Easy to use protocol for Geniom RT Analyzer

MPEA MINIMIZES SAMPLE REQUIREMENTS

In addition to the standard hybridization of pre-labeled RNA, the microfluidic Geniom Biochip enables a highly sensitive on-chip labeling protocol. No prior sample treatment is necessary, thus greatly simplifying the biomarker test. The unique Microfluidic Primer Extension Assay (MPEA) uses unlabeled RNA samples for hybridization. In a second step, the specific enzymatic elongation of the bound miRNAs takes place. This method reduces the required sample amount to a minimum, taking into account that clinical samples are typically limited.

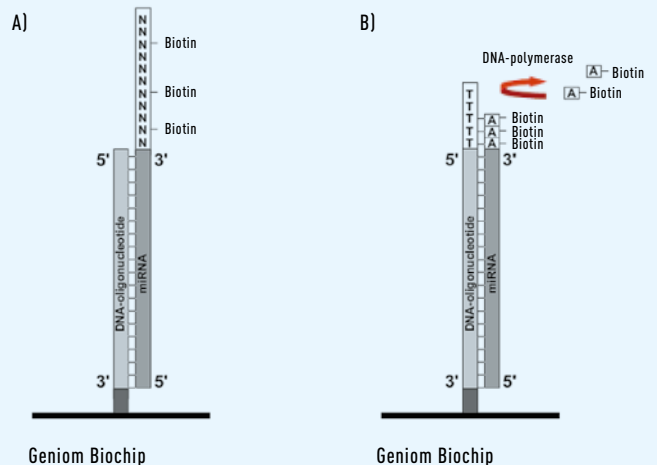
MPEA FOR RELIABLE miRNA FAMILY MEMBER ANALYSIS



U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	A	U	A	C	U	U	hsa-let-7a		
U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	G	U	G	U	C	U	U	hsa-let-7b
U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	A	U	C	U	U	U	U	hsa-let-7c
A	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	C	A	U	A	C	U	U	hsa-let-7d
U	C	A	C	G	U	A	C	G	U	A	C	G	U	U	C	U	U	A	U	A	C	U	U	hsa-let-7e
U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	A	U	A	C	U	U	U	hsa-let-7f
U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	A	U	A	C	U	U	U	hsa-let-7g
U	C	A	C	G	U	A	C	U	A	C	G	U	U	C	U	U	G	C	U	U	U	U	U	hsa-let-7i

Analysis of the hsa-let-7 miRNA family illustrates the significant reduction of cross hybridization, highlighting the reliable detection of even single nucleotide mismatches with MPEA labeling of miRNA samples.

MICROARRAY-BASED ASSAYS FOR miRNA PROFILING



A) Conventional hybridization assay: miRNAs are labeled first and hybridized afterwards to the microarray containing reverse complementary oligonucleotides.

B) Principle of MPEA: The hybridized, unlabeled miRNA functions as primer for an enzymatic elongation in which biotinylated nucleotides are incorporated.

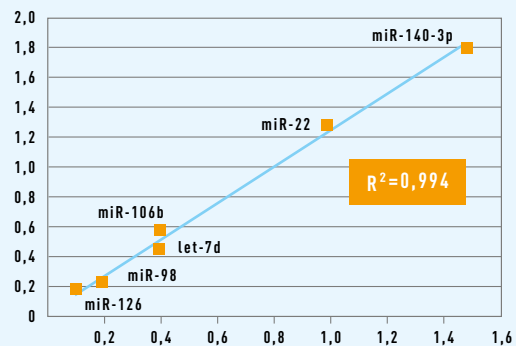


miRNA Footprints in Blood

BLOOD-BASED miRNA BIOMARKERS FOR NON-INVASIVE CANCER DIAGNOSIS

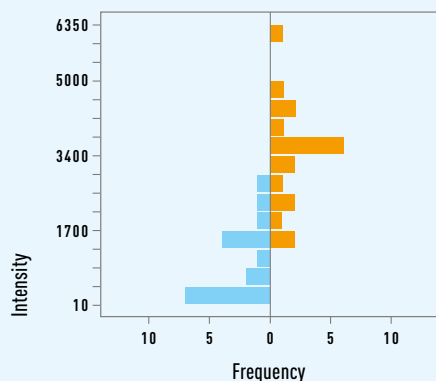
It has been shown that deregulated miRNAs are not only found in tumor tissue but also in peripheral blood of tumor patients. miRNA biomarkers exhibit a remarkable stability in blood and their measurement represents a diagnostic tool with great potential.

Performing analyses of complex miRNA expression patterns in blood of cancer patients compared to blood of healthy donors allows for distinct classification of the samples. The Geniom RT Analyzer and Geniom miRNA Biochips ensure highly reproducible test results.

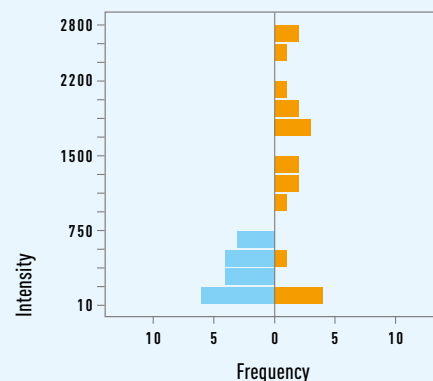


Validation of blood-based biomarker test. miRNA expression results were verified using quantitative RT-PCR. Scatterplot of fold quotients of qRT-PCR (x-axis) and Geniom RT Analyzer microarray experiments (y-axis).

miR-126



miR-98



Blood-based biomarker test reveals deregulated expression of microRNAs in lung carcinoma patients vs. healthy controls. Back to back histograms of two example microRNAs. Blue bars correspond to lung cancer blood samples, red bars to control blood samples.

febit's microRNA Profiling Service

YOUR BENEFITS	SAMPLE ANALYSIS REQUIRES MINIMAL ...	FEBIT'S FULL SERVICE INCLUDES	BIOINFORMATICS DATA SERVICE
<ul style="list-style-type: none"> - Fast service from sample to ready-to-publish data - Up-to-date miRNA arrays based on the latest miRBase version (http://microrna.sanger.ac.uk/) - Flexible and fast biochip design for custom biochips - Comprehensive analysis report of your results 	<ul style="list-style-type: none"> - TIME from sample submission to data results report in 2-3 weeks - EFFORT total RNA as starting material - SAMPLE AMOUNT only 130 ng total RNA needed 	<ul style="list-style-type: none"> - Project consulting - Sample quality control - Sample labeling - Microarray hybridization and read out - Comprehensive data analysis and easy-to-understand bio-informatics report 	<ul style="list-style-type: none"> - Customized design and data analysis - Detailed data interpretation and an easy-to-understand analysis report - Personal support by febit's experienced in-house experts - Validation and development of biomarkers

Catalog Order Numbers

GENIOM® RT ANALYZER - Instrument, software package, PC, screen, installation, training, service package	P001
STANDARD miRNA SCREENING	S001
CUSTOM miRNA SCREENING	S004
CUSTOM GENIOM® BIOCHIP DESIGN SERVICE - Design Service (From RNA sequences to Geniom® Biochip design; up to 5 MBases) - Please inquire for genomes or target sequences exceeding 5 MBases	S005
CUSTOM GENIOM® BIOCHIP SYNTHESIS SERVICE - Synthesis Service 30nt (30nt-Probe design and Geniom® Biochip-Synthesis) - Synthesis Service 60nt (Probe synthesis 30-60 nt according to your specifications)	S006 S0061
GENIOM® DATA BIOINFORMATICS SERVICE - Bioinformatics Service Geniom® Data (From raw data to analysis and bioinformatics report within 2-4 weeks)	S0070

Please refer to febit's Product Catalog to see the complete list of catalog Biochips.

For research use only.

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