The First True High-Density Next Generation Real-Time PCR System

DISCOVER THE NANOSCALE PLATFORM OF CHOICE FOR GENOMIC ANALYSIS

WAFERGEN

Advancing the science of tomorrow today.

Gene Expression Discovery and Validation in a Single Platform

PERFORM > 5,000 REAL-TIME PCR ASSAYS IN A SINGLE RUN

SINGLE PLATFORM VERSATILITY. Enables biomarker discovery and gene signature validation.

PREVALIDATED. Optimized disease-focused or pathway-based gene panels are available.

CUSTOMIZABLE. Gene sets from tens to thousands; chose from prevalidated or custom gene sets in custom layouts.

THROUGHPUT EFFICIENCY. With > 5,000 individual wells, one SmartChip run is equivalent to > thirteen 384-well plates.

COST EFFECTIVE. Reaction volumes of 100 nl per well, providing significant cost savings compared to microliter volume real-time PCR.

SAMPLE SAVINGS. Requires only 100 pg/well of total RNA per experiment.

Over 5,000 real-time PCR reactions in your hand.

THE SMARTCHIP SYSTEM is the first gene expression platform that combines the high-throughput nature of microarrays with the sensitivity, precision, and dynamic range of real-time PCR. With the ability to perform > 5,000 assays in a single run, validation of thousands of genes is now possible in a single experiment. Expression profiles of multiple pathways, disease-related genes, or noncoding RNAs can be analyzed on a single run in less than a day using proven real-time PCR techniques in a novel high-density format.

The SmartChip System can be utilized for, but is not limited to, the following applications:

- Identifying disease signatures and guiding targeted therapy toward personalized medicine.
- Completing discovery-to-clinical therapeutic biomarker development.
- Serving as a molecular diagnostic research guide for patient stratification or a potential theranostic research tool.

The SmartChip System provides a highly flexible platform with predesigned, validated SmartChip Panels consisting of ~1,000 genes per chip in quadruplicate. Users also have the ability to design SmartChip Custom Panels that may vary from tens to thousands of genes and can be used to test tens to hundreds of samples per chip. Additionally, WaferGen Biosystems provides access to the SmartChip technology through SmartChip Services. SmartChip Services can perform a simple evaluation or a complete complex biomarker validation project.

Freedom To Expand Your Experimental Design

CONDUCT A SPECTRUM OF ADVANCED GENE EXPRESSION EXPERIMENTS

With > 5,000 reactions available per SmartChip run, researchers are completely free to use real-time PCR in ways not possible with other platforms.

**Hypothesis-free expression profiling:**
Use the gold standard method of quantitative real-time PCR to validate genes identified from next generation sequencing or microarray expression profiling. The SmartChip System enables the validation of larger numbers of informative biomarkers with real-time PCR in a cost-effective manner.

Hypothesis-based expression profiling:
Discover informative biomarkers at a pathway and disease-focused level in hypothesis-based studies. Current technologies can limit your throughput to 96 or 384 genes per experiment. The SmartChip System can profile > 1,000 genes per run in quadruplicate, effectively analyzing larger sets of genes in a single experiment.

Signature validation:
Use the same technology to validate informative sets of tens to hundreds of genes with multiple samples with SmartChip Custom Panels. Complete your validation studies in a fraction of the time with the throughput capabilities of a 5,184-well plate real-time PCR system.
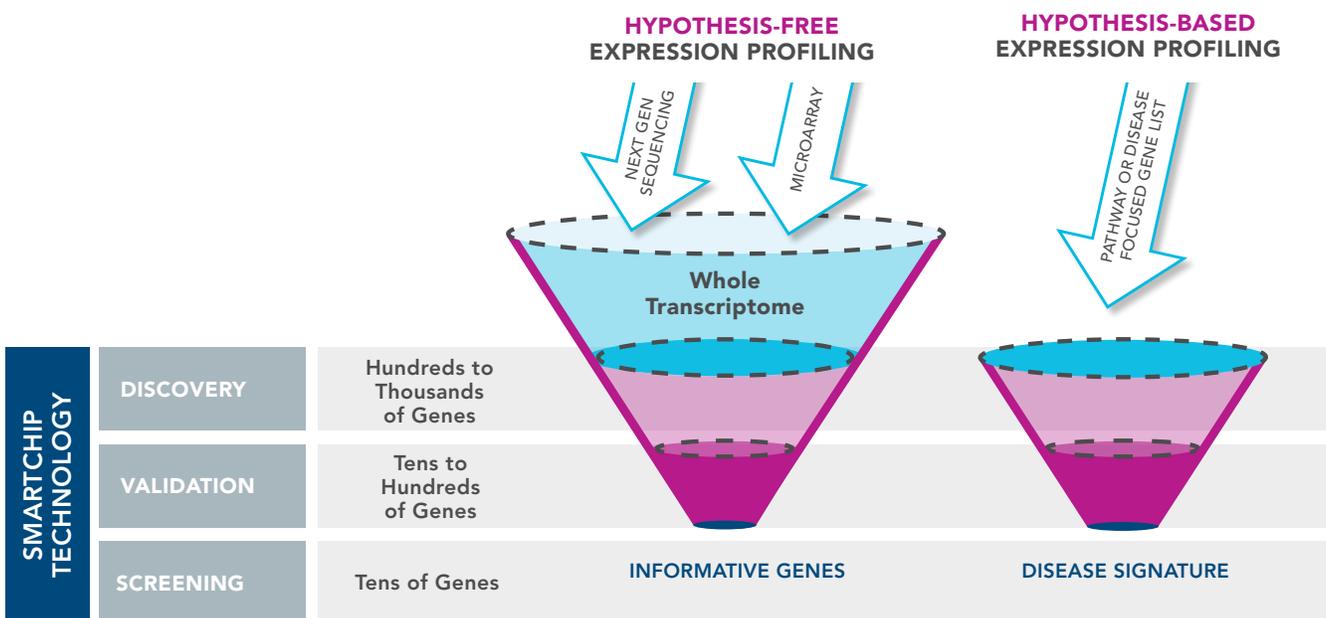

One SmartChip real-time PCR platform from discovery through screening.

High-Throughput PCR Reactions Employ Standard Techniques

## ATTAIN BIGGER EXPERIMENTS WITHOUT BIGGER WORKLOADS

THE SMARTCHIP SYSTEM is a complete high-density, high-throughput real-time PCR solution made possible by key innovations in nanoliter real-time PCR. At the heart of the system is the SmartChip Nanowell Chip. With 72x72 nanoscale-wells, each with an effective reaction volume of 100 nL, the SmartChip Nanowell Chip is a complete revolution in genomic analysis. This configuration allows completion of 5,184 nanoscale quantitative real-time PCR reactions in just over 2 hours, with the same high-quality data you would expect from traditional quantitative real-time PCR experiments. The SmartChip Nanowell Chip is available as either a SmartChip Panel with validated assays or a SmartChip Custom Panel with customer-defined assays. Upstream and downstream workflows from loading and running the SmartChip Panel use well-established laboratory techniques and off-the-shelf, cost-effective reagents. Even loading the SmartChip Panel with the cDNA/Real-Time Master-Mix is a simple 10-20 minute process and yields high-precision data. In contrast, microfluidics or complicated reagent loading workflows can negatively impact both data, quality and hands-on time.

A single SmartChip Nanowell Chip is equivalent to > thirteen 384-well plates. The ~1 square inch metal-alloy chip allows gene expression profiling on multiple pathways or on a disease panel in a single 2-hour experiment.
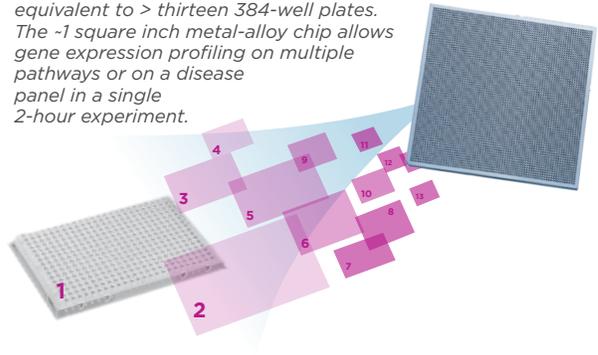
Dynamic range and sensitivity are required for validation of biological signatures, which are often limited with hybridization arrays or next generation sequencing, respectively. Real-time PCR does not have such limitations. Current real-time PCR technologies can be limiting with only 96 to 384 genes analyzed at a time. The SmartChip System enables the validation of larger sets of putative markers so that more informative genes can be analyzed in a single run. In addition, the ability to customize smaller gene sets, in the range of tens to hundreds, allows you to use SmartChip technology throughout the validation process by further validating markers with many samples per chip.

FROM PURIFIED RNA TO DATA WITH < 1 HOUR HANDS-ON TIME

| 120 MIN	20 MIN	~2 HRS	15 MIN
PURIFY RNA	PREPARE cDNA	LOAD SMARTCHIP PANEL	RUN REAL-TIME PCR	ANALYZE DATA
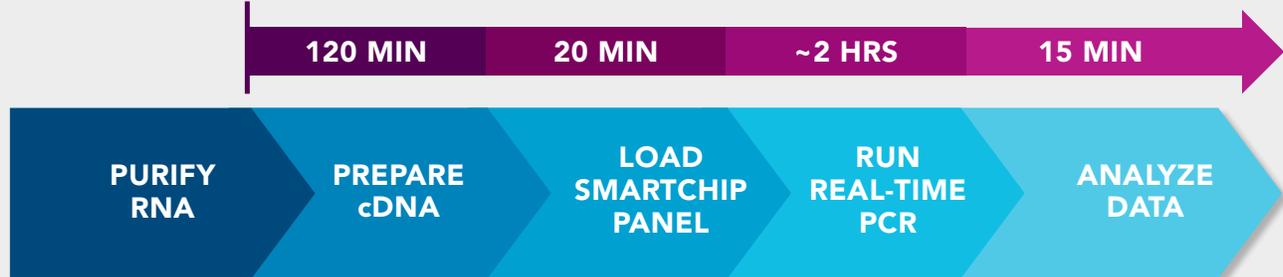
Example workflow for preparing and running a SmartChip Panel with a single RNA sample using the SmartChip Core System. Simply reverse transcribe the RNA to cDNA using standard protocols, prepare a cocktail of cDNA and real-time PCR master-mix and load onto the

SmartChip Panel using the SmartChip Nanodispenser. The SmartChip Cycler performs thermal cycling and data collection. The SmartChip Multisample Nanodispenser is used for up to 384 samples.

Breakthrough Technology Delivers Experimental Flexibility

EXPERIENCE THE ADVANTAGES OF A CUSTOMIZABLE PLATFORM

DISCOVERY

VALIDATION

SmartChip Nanodispenser

Sample

SmartChip Multisample Nanodispenser

SmartChip Panel

SmartChip Cycler

2 HOURS

SmartChip qPCR Software
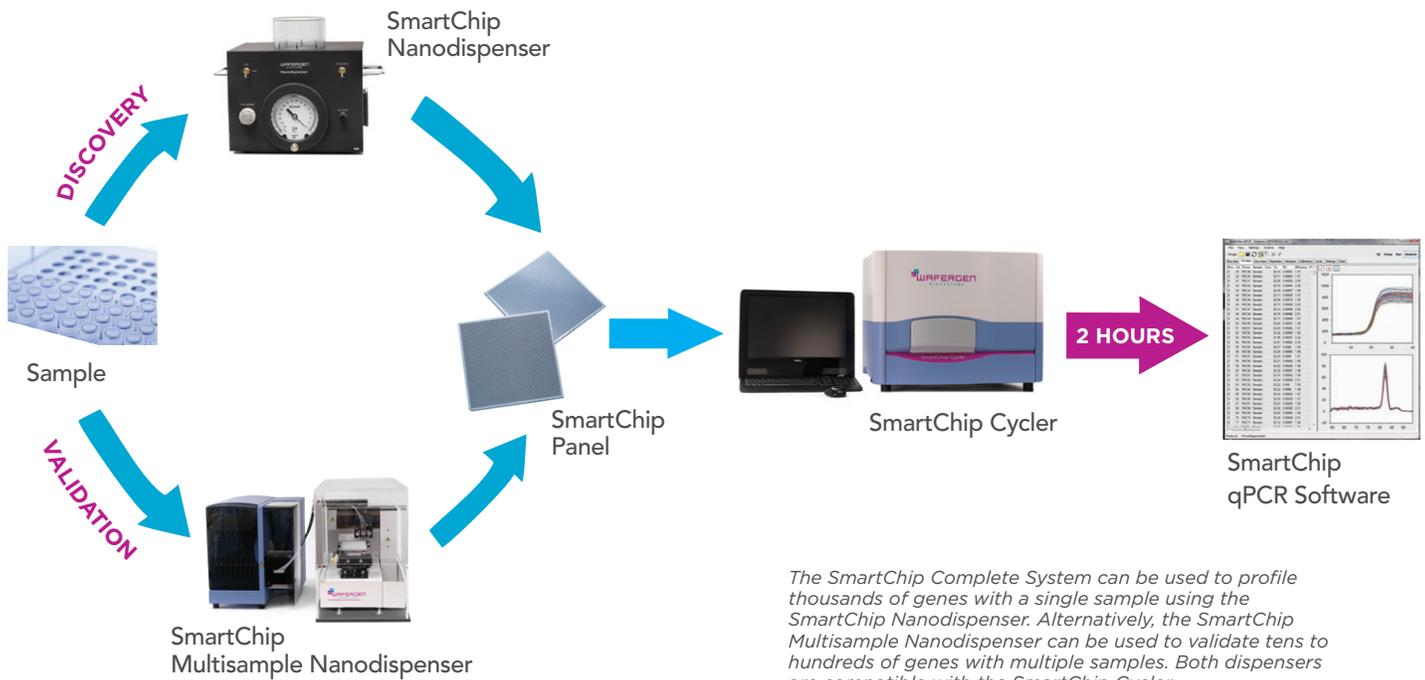
The SmartChip Complete System can be used to profile thousands of genes with a single sample using the SmartChip Nanodispenser. Alternatively, the SmartChip Multisample Nanodispenser can be used to validate tens to hundreds of genes with multiple samples. Both dispensers are compatible with the SmartChip Cycler.

The SmartChip Nanodispenser

SINGLE-STEP LOADING: Dispense a solution of cDNA and Real-Time PCR Master-Mix for an entire 5,184 well SmartChip Panel in one easy step that takes less than 10 minutes.

The SmartChip Multisample Nanodispenser

SAMPLE FLEXIBILITY: Enables automated loading of up to 384 samples on a single SmartChip Panel.

PROVEN PERFORMANCE: Demonstrated precision at nanoliter volumes.

RELIABLE RESULTS: Active evaporation control and chip cooling station.

QUICK LOADING: Prepare an entire 72x72 SmartChip Panel in as little as 10 minutes.

The SmartChip Cycler

FAST RESULTS: Thermal cycle and collect data on the 5,184 nanowell SmartChip in ~ 2 hours.

EASY OPERATION: Powerful and intuitive tools with the SmartChip qPCR software for data collection and analysis.

TEMPERATURE PRECISION: Effective temperature control to produce intrachip Ct standard deviations < 0.1.

The SmartChip qPCR Software

AUTOMATED ANALYSIS: Automated well finding, Ct determination and exportable results.

INTUITIVE INTERFACE: Simple data entry and analysis tools.

Rigorously Tested Assays for Discovery and Validation

## OBTAIN QUALITY RESULTS WITH COMPREHENSIVE PANELS

Assay Validation

Every real-time SYBR® Green PCR assay contained within a SmartChip Panel undergoes extensive quality control steps to ensure the assay functions reproducibly at the nanoliter scale.

| SmartChip Panel Assay Validation Process	
Specifications	**Criteria**
Strict bioinformatics criteria	■ Maximize primer specificity ■ Minimize primer-dimers ■ Targeted annealing T_m ■ Short amplicon length

Meets functional requirements	■ Minimum 5-log dynamic range
	■ Specificity
	  – Melt analysis
	  – Gel analysis

Target verification	■ Assays sequenced to ensure specific targeted transcript is amplified

Low Variability

The SmartChip System is designed to generate precise data. Sample loading, temperature uniformity and fluorescence uniformity have all been controlled to yield high precision across the 5,184 SmartChip Nanowell Chip.
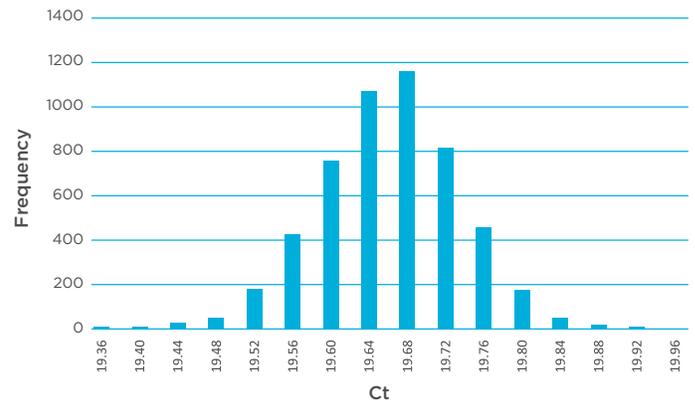
Low variance of Ct values for positive control DNA dispensed across each of the 5,184 wells. The standard deviation of Cts is < 0.1.

### SmartChip Human Oncology Panel

- Ideal for oncology disease-related gene expression profiling.
- 968 gene-specific assays covering 16 functional groups in quadruplicate.
- Includes 11 endogenous and 6 exogenous controls.

Mean C_ts (N=754)
$y = 1.0063x - 0.1177$
$R^2 = 0.9794$
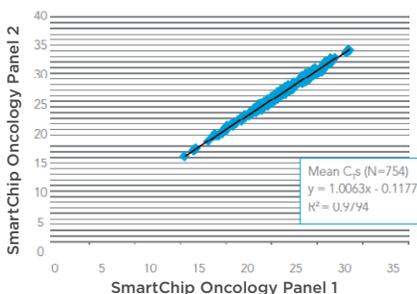
Correlation between replicate SmartChip Human Oncology Panels using 100 pg/well of total RNA from frozen lung tumor.

SmartChip Human microRNA Panel

- Ideal for comprehensive profiling of microRNA targets.
- 778 microRNA specific assays designed to the human miRBase version 14.0 in quadruplicate.
- Includes 12 endogenous and 6 exogenous controls.

Mean C_ts (N=755)
$y = 0.9686x + 0.4054$
$R^2 = 0.9942$
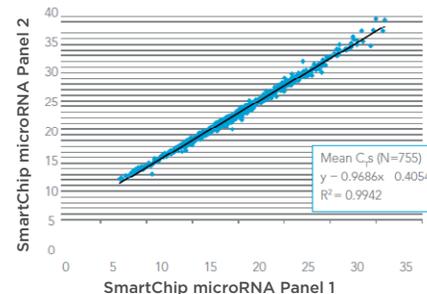
Correlation between replicate SmartChip Human microRNA Panels using 200 pg/well of total RNA from commercially available artificial template pool.

Customized Services for Experimental Versatility

DISCOVER REAL-TIME PRODUCTIVITY

SmartChip Custom Panels

SmartChip Custom Panels enable you to profile many samples on smaller sets of genes in a validated workflow. Develop your own application-specific real-time PCR assay panel, choose from our library of assays, or let us develop a panel for you. WaferGen Biosystems can design, optimize, and deliver SmartChip Custom Panels with tens to hundreds of assays repeated across the chip, saving you time and money on your real-time PCR validation studies.

Number of Samples	Number of Genes	Number of Replicates
384	3	4
192	6	4
96	12	4
48	24	4
24	48	4
12	96	4
6	192	4
3	384	4

SmartChip Custom Panels can be printed in a variety of formats depending on the number of genes, samples, and replicates needed for your study.

SmartChip Services

Get started on your high-throughput gene expression studies today with SmartChip Services. WaferGen Biosystems perform SmartChip Services in a dedicated facility using the latest prevalidated SmartChip Panels or Custom Panels for your validation studies. Most projects are completed in 1 or 2 weeks, depending on the number of samples submitted.

SERVICES INCLUDE:

- Assistance with study design
- Incoming quality control on sample
- Data generation
- Project analysis

Visit www.wafergen.com to learn about new SmartChip Panels

High-Density, High-Throughput Real-Time PCR—Now a Reality.

ACHIEVE COST-EFFECTIVE, QUALITY RESULTS WITH UNCOMPLICATED WORKFLOWS

☐ Unique combination of the high-throughput nature of microarrays with the sensitivity, precision, and dynamic range of quantitative real-time PCR in a single platform.

☐ Ideal for both gene expression discovery and target validation of data from next generation sequencing or microarray experiments.

☐ Nanoscale high-density reactions ensure that cost reduction and fast results are realized.

DISCOVER THE PLATFORM OF CHOICE FOR GENOMIC ANALYSIS

Contact your local sales representative: **sales@wafergen.com**

For assistance on SmartChip Panel Services, contact **510-651-4450** or **smartchipservices@wafergen.com**

For support: **support@wafergen.com**

For general information: **info@wafergen.com**

SMARTCHIP SYSTEMS

PART NO.	PRODUCT NAME
420-000001	The SmartChip Core System: SmartChip Cycler, SmartChip Nanodispenser and SmartChip qPCR Software
420-000002	The SmartChip Multisample Dispenser
420-000003	The SmartChip Cycler
420-000004	The SmartChip Nanodispenser

SMARTCHIP PANELS

PART NO.	PRODUCT NAME
430-000001-1	SmartChip Human microRNA Panel, 1 panel
430-000001-6	SmartChip Human microRNA Panel, 6 panels
430-000002-1	SmartChip Human Oncology Panel, 1 panel
430-000002-6	SmartChip Human Oncology Panel, 6 panels

SMARTCHIP CUSTOM PANELS

PART NO.	PRODUCT NAME
440-000001	SmartChip Custom Panels, 12 genes/panel
440-000002	SmartChip Custom Panels, 24 genes/panel
440-000003	SmartChip Custom Panels, 48 genes/panel
440-000004	SmartChip Custom Panels, 96 genes/panel
440-000005	SmartChip Custom Panels, 192 genes/panel
440-000006	SmartChip Custom Panels, 384 genes/panel

SMARTCHIP PANEL SERVICES

PART NO.	PRODUCT NAME
450-000001	SmartChip Human microRNA Panel Service, per sample
450-000002	SmartChip Human Oncology Gene Panel Service, per sample

Visit us at **www.wafergen.com** for more information.

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