

SmartChip™ Real-Time PCR System

Where throughput meets flexibility

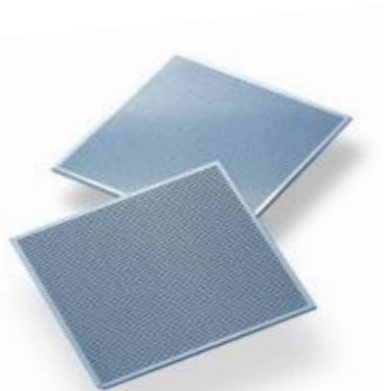
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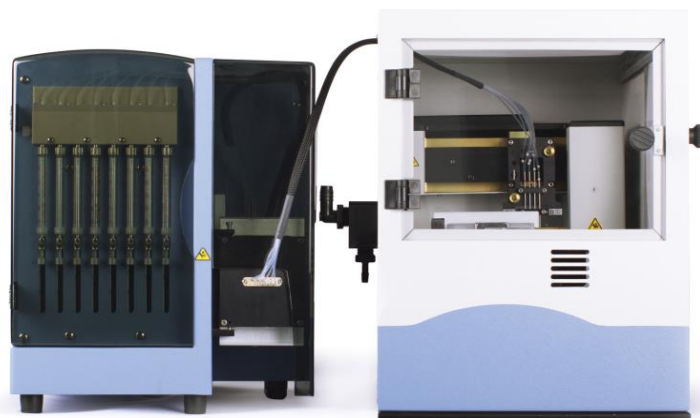
that's
GOOD
science!®

The SmartChip Real-Time PCR System

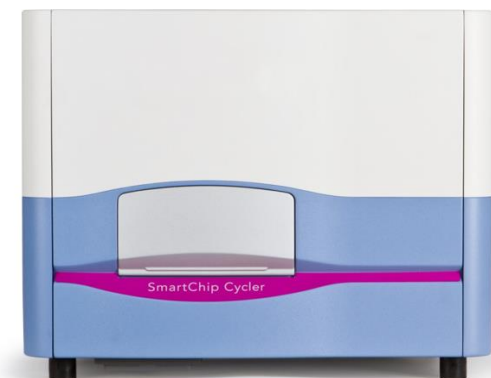
Genotyping (GT) and gene expression (GX) analysis



5,184 100-nl
reactions

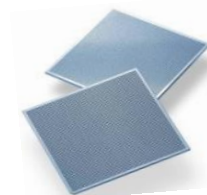


Dispense samples
or assays in just
40 minutes each



From dispense to data
in less than two hours

SmartChip technology



High-throughput platform enables
5,184 100-nl reactions on a single chip

Flexible, sensitive, and cost-effective

- Best-in-class open platform
- Flexible chip configuration
- “Smart volume” provides sensitive PCR analysis over an extensive dynamic range
- 3–10 ng/μl input requirement per 100-nl well
- Pre-amplification optional
- 100-nl reactions significantly reduce reagent costs versus standard 10-μl reactions

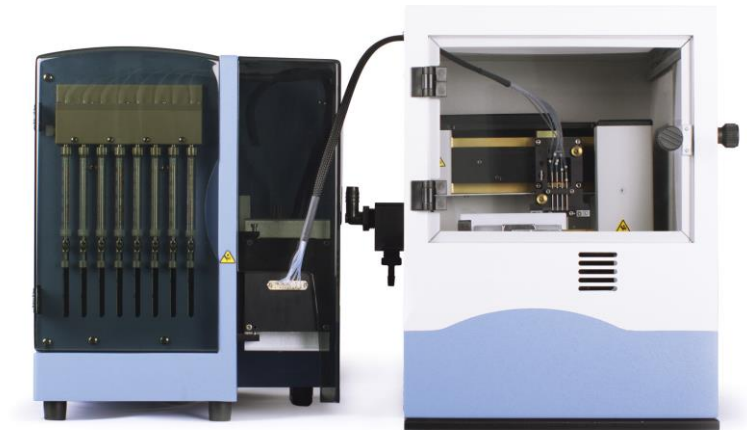
Assays	Samples
12	384
24	216
36	144
48	108
54	96
72	72
80	64
96	54
120	42
144	36
216	24
248	20
296	16
384	12

SmartChip MultiSample NanoDispenser (MSND)

Simple, automated sample and assay dispensing

Quick automated reaction setup

- Precision nl-volume dispensing in 40 minutes with just 10 minutes of hands-on time
- Decreased human error and reaction variability
- Environmentally controlled, enclosed system

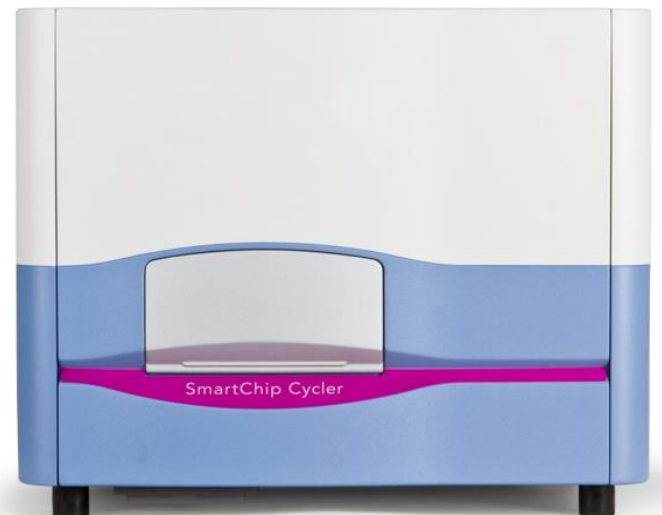


SmartChip Real-Time PCR Cycler

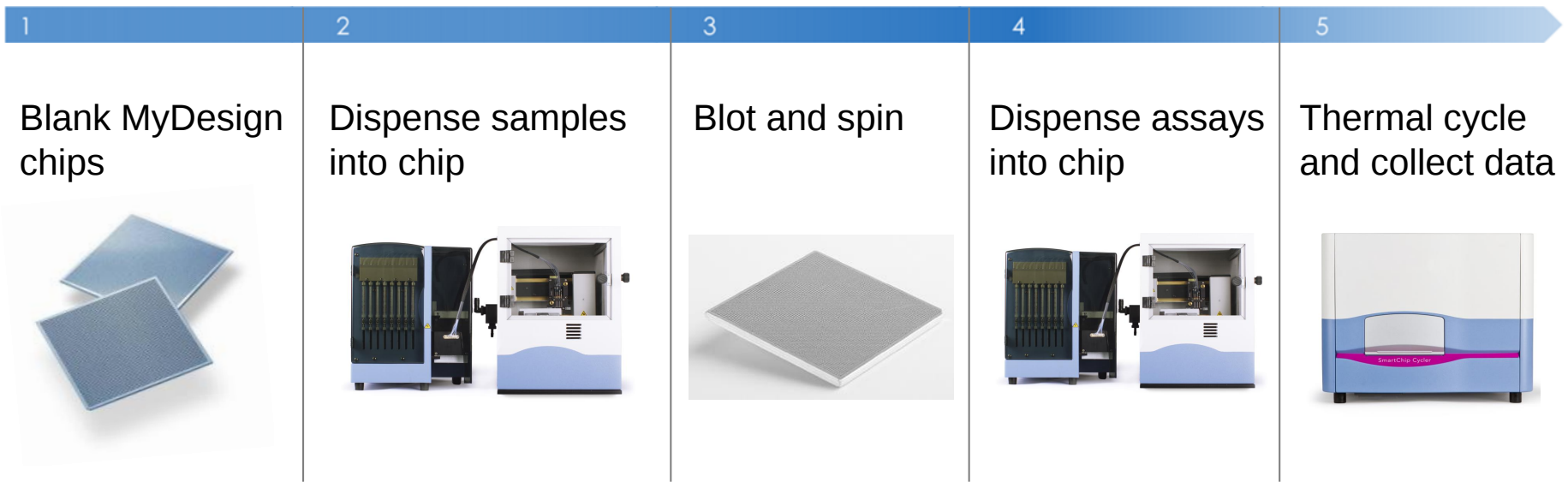
Sensitive, high-throughput real-time PCR analysis

Sensitive, high-throughput PCR analysis

- Fast real-time genotyping (GT) and gene expression (GX) analysis in two hours
- CCD camera and optics
 - FAM (475 EX / 520 EM)
 - VIC (520 EX / 565 EM)
 - ROX (543 EX / 676 EM)
 - SYBR (475 EX / 550 EM)
- Integrated analysis software



MyDesign workflow



One flexible system, from discovery to screening

Biomarker discovery on MyDesign chips

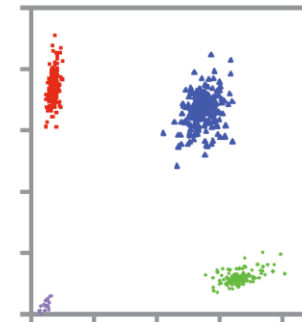
Quickly change configurations to test different numbers of samples and assays in your laboratory

Assays	Samples
12	384
24	216
36	144
48	108
54	96
72	72
80	64
96	54
120	42
144	36
216	24
248	20
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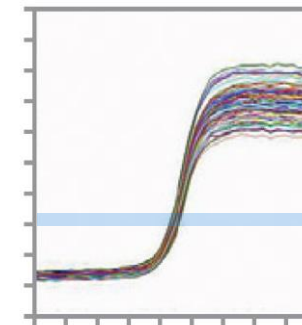
Finalized
panel

Biomarker screening on MyDesign chips

Quick, high-throughput biomarker screening on validated assays

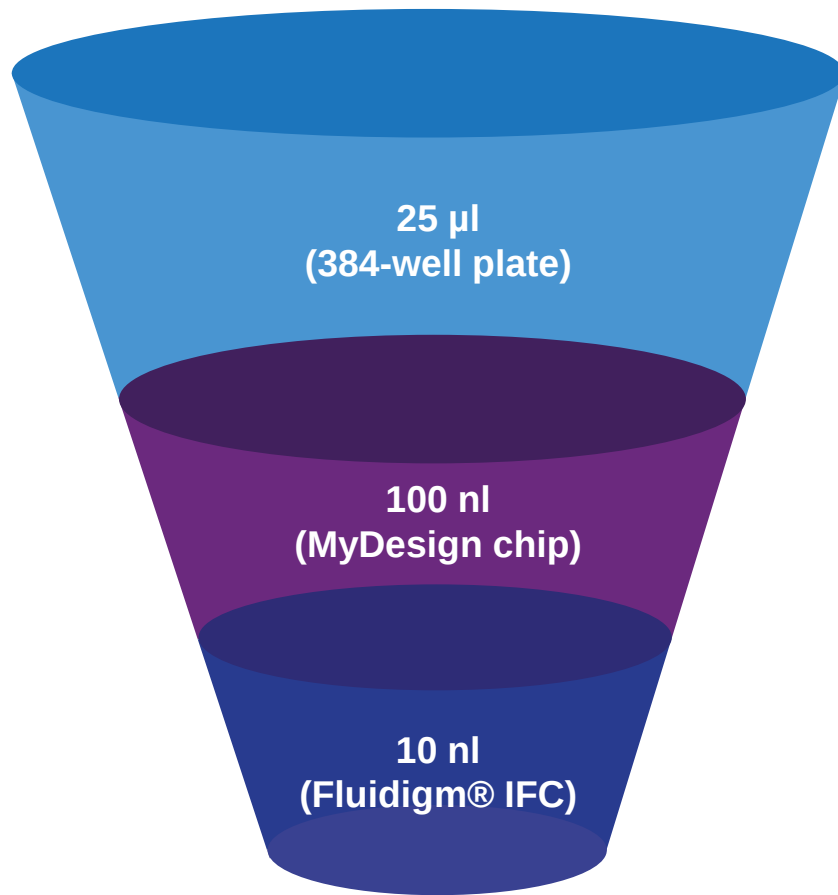


Genotyping



Gene
expression

100 nl: decreasing reaction costs while preserving sensitivity and decreasing time to data

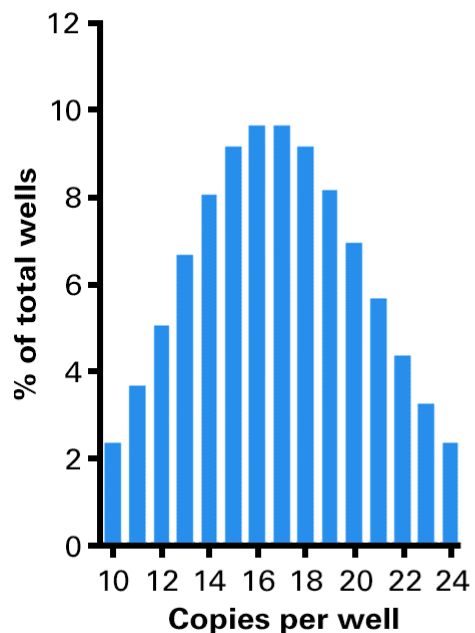


- Significant reagent savings: scaling down from 25 µl to 100 nl
- SmartChip technology delivers sensitivity and a broad linear dynamic range without pre-amplification, staying above the Poisson limit
- Small additional reagent savings if moving to reactions <100 nl, but at the cost of requiring pre-amplification

“Smart” reaction volume

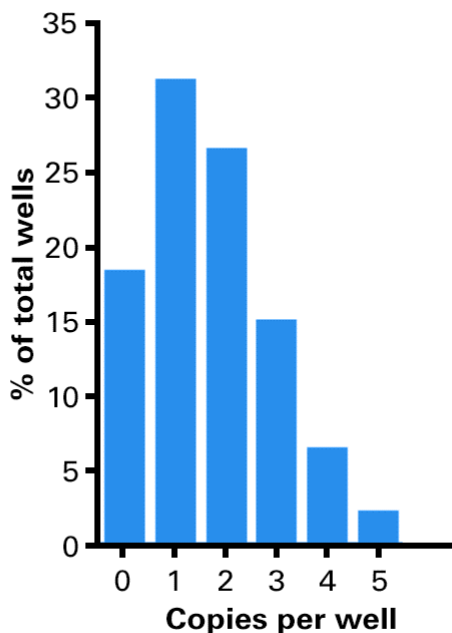
Distribution of human gDNA at 0.5 ng/μl

100 nl SmartChip reactions



3–10 ng/μl requirement

10 nl Fluidigm reactions



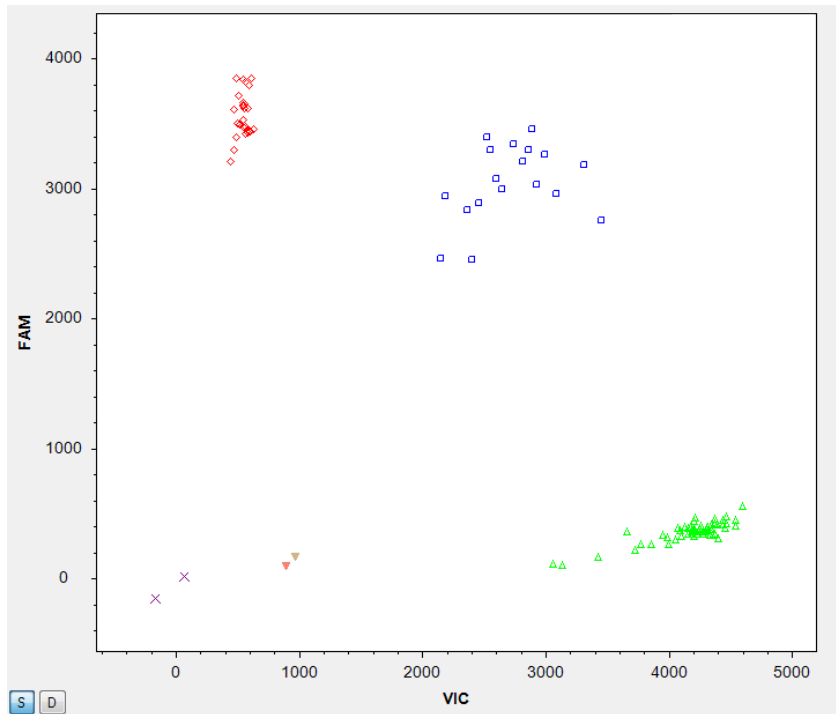
60 ng/μl requirement

>18% of 10 nl reactions lack a single copy of target

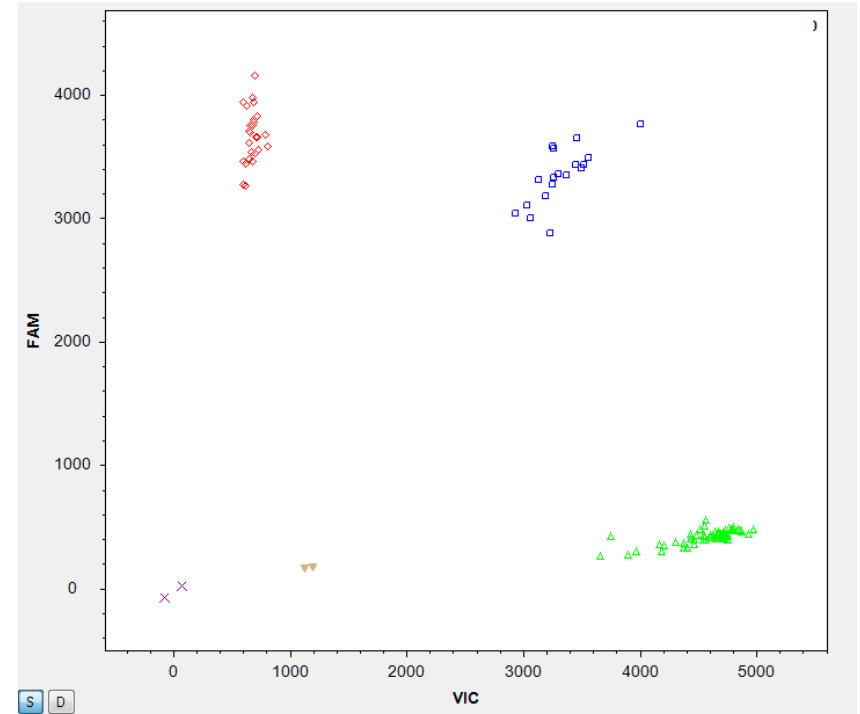
Consistent detection requires pre-amplification or excessive sample input

SmartChip GT is sensitive

1 ng/ μ l sample concentration



5 ng/ μ l sample concentration



System demonstrates robust calling with as little as 1 ng/ μ l

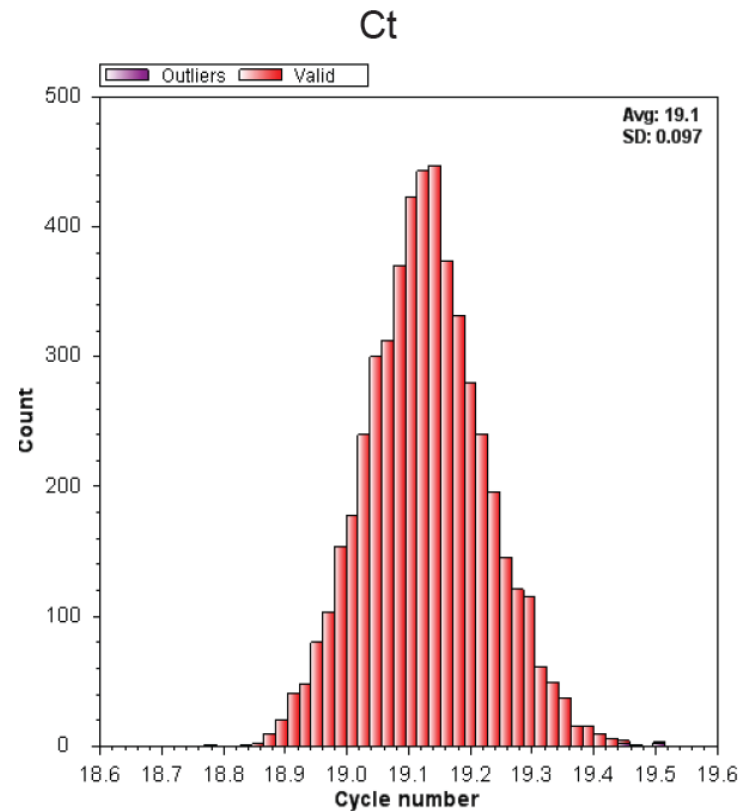
Consistent performance across users and days

Customer data

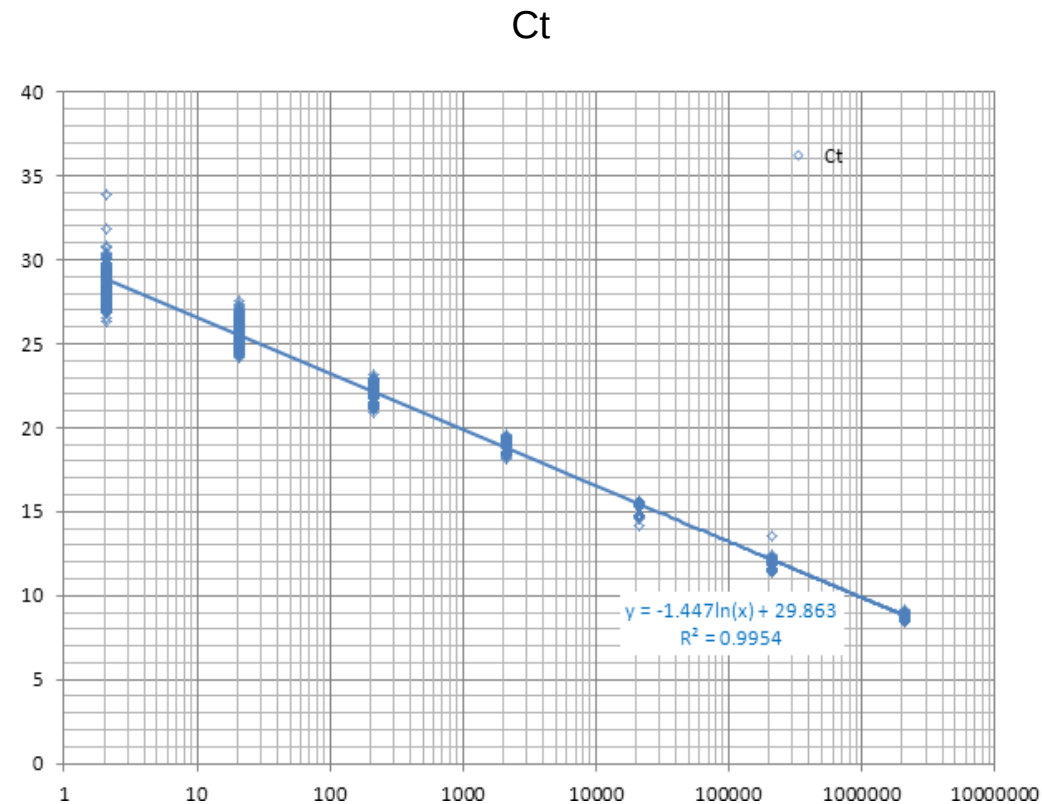
FAM/FAM	VIC/VIC	VIC/FAM	Not called	NTC	Call rate (%) ▲
0	10248	0	140	196	98.65
6075	919	3276	118	196	98.86
2	10297	0	89	196	99.14
0	10325	0	63	196	99.39
10136	0	191	61	196	99.41
2354	2910	5071	53	196	99.49
23	9379	934	52	196	99.50
1238	4620	4484	46	196	99.56
1022	4989	4335	42	196	99.60
0	10347	4	37	196	99.64
840	5533	3978	37	196	99.64
4	10351	0	33	196	99.68
692	5798	3865	33	196	99.68
1957	3306	5092	33	196	99.68
6993	380	2982	33	196	99.68
6959	396	3002	31	196	99.70
4	10354	0	30	196	99.71
289	7274	2796	29	196	99.72
617	6062	3680	29	196	99.72
4	10358	0	26	196	99.75
4	10174	184	26	196	99.75
0	10359	4	25	196	99.76
10260	8	98	22	196	99.79
3	10348	18	19	196	99.82

- >10,000-sample real-world study
- Chips run by multiple operators on multiple days
- >99% average call rate
- Reproducible detection of extremely low-frequency alleles (< 0.1%)

SmartChip GX is reproducible over an excellent dynamic range



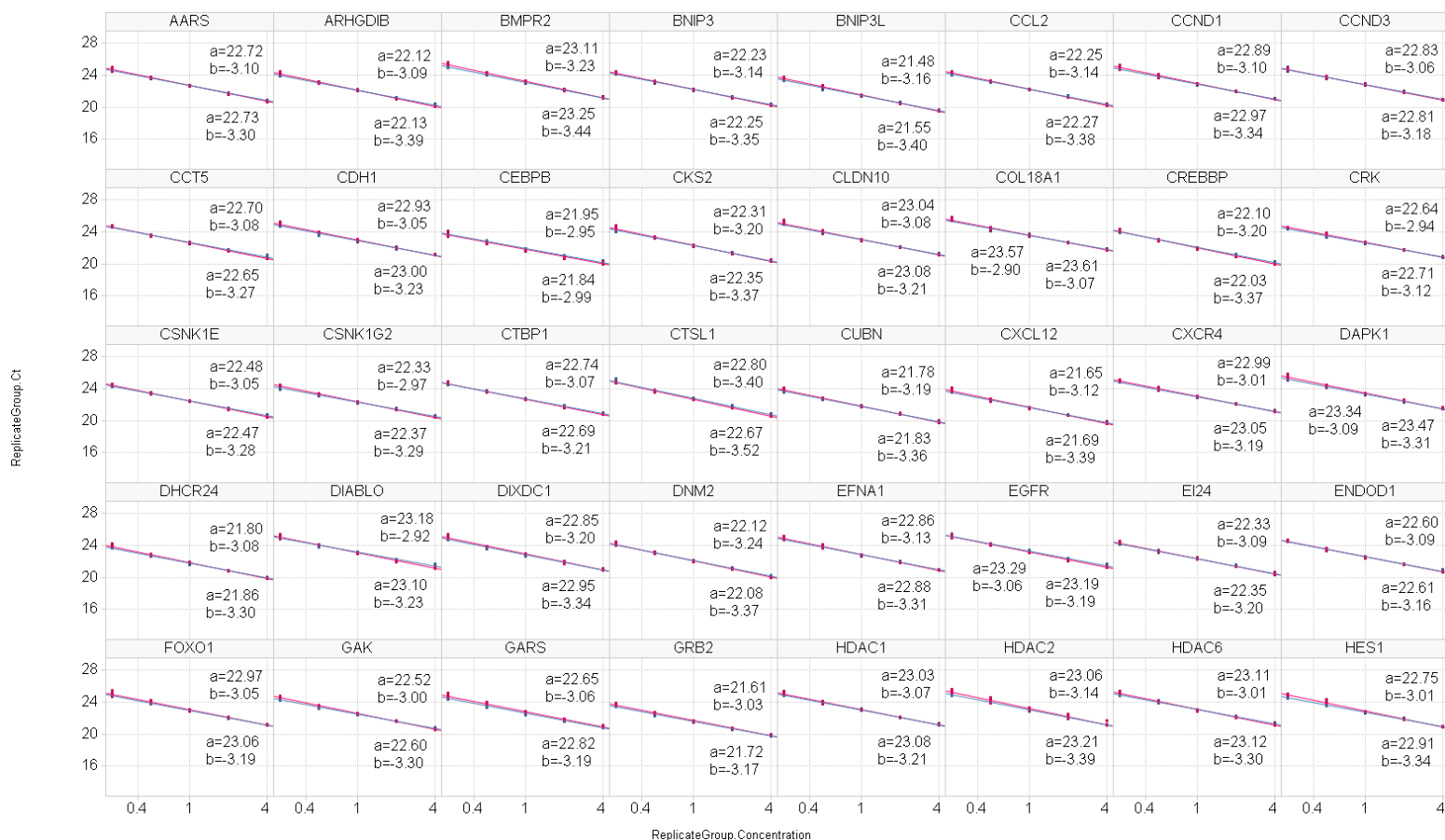
SmartChip PCR uniformity
across 5,184 nanowells



Titration of lambda DNA
copies per 100-nl reaction

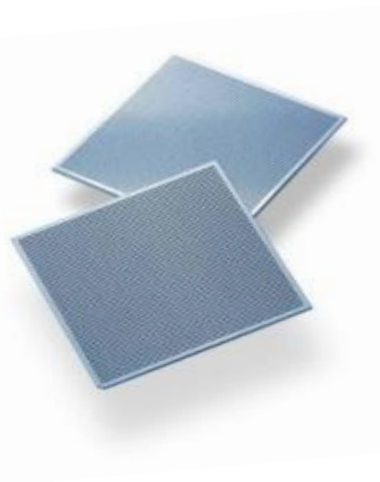
SmartChip GX is consistent

Consistent, reproducible data from systems/operators (n=3)
and chip replicates (n=2)



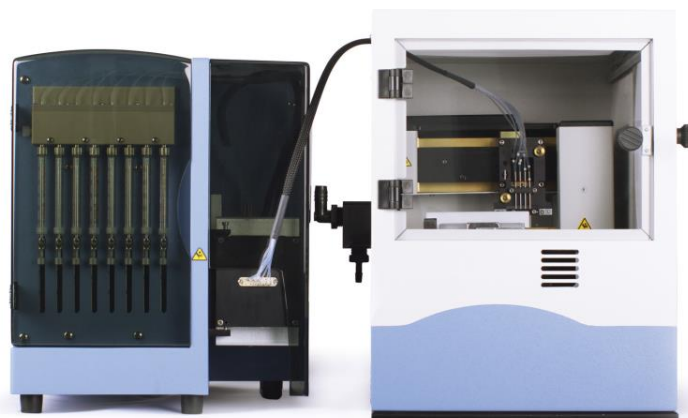
The SmartChip Real-Time PCR System

Multifunctional,
flexible, and
adaptable



5,184-nanowell
pre-printed or blank
chips

Automated, high-throughput,
and cost-efficient



SmartChip MultiSample NanoDispenser

Dispense samples or
assays in just 40
minutes each

Sensitive, accurate,
and reproducible



From dispense to data in
less than two hours

SmartChip Real-Time PCR System

- Multifunctional, flexible, and adaptable
 - GT and GX analysis
 - Adaptable
 - Move from low- to high-throughput experiments without additional validation
 - Multiple assay and sample formats
- Sensitive, consistent, and accurate
 - Accurately detects low sample concentration (3–10 ng/μl) with excellent dynamic range
 - Pre-amplification is unnecessary (60 ng total for 96 reactions)
 - Within-chip, chip-to-chip, and system-to-system reproducibility
- Automated, high-throughput, and cost-efficient
 - 5,184 100-nl reactions decrease reagent and consumable costs
 - Easy and fast workflow with limited hands-on time
 - Integrated software for easy analysis



CUSTOMERS & APPLICATIONS

Pathogen detection— antibiotic resistance genes (ARG)

- 23 publications used the SmartChip Real-Time PCR System to perform ARG profiling
 - 3–4 groups (China, Michigan State, Finland)
 - 9 publications in the last 2 years
- Bacteria can acquire ARGs over time due to selective pressure
 - Overuse of antibiotics in humans
 - Antibiotics given to livestock
 - Waste from humans/livestock end up in water, soil, produce, etc., in the environment
- Researchers collect these environmental/patient samples to look for ARGs



Clinical biomarker discovery & screening

- 16 publications (from 11 institutions) used the SmartChip Real-Time PCR System to screen for cancer biomarkers
- Long noncoding RNA panel expression profiling (>1,707-assay panel) as biomarkers of malignancy
- Oncology panels, custom lung cancer panel (173-assay panel)
- miRNA biomarker assay panels:
 - >300-assay panel: temporal studies of healthy individuals (plasma, serum, T- & B-cell subsets)
 - 1,100-assay panel for quality control of biological specimens



PRESS RELEASE

FOR IMMEDIATE RELEASE
Reference: IBBL-PR-010714

Luxembourg, 1st July 2014

**Luxembourg's biobank collaborates with
US National Cancer Institute**

Research projects investigate how tissue processing methods can affect
downstream results



Detection of fungal infection

- Canadian Grain Commission
 - SYBR® green assay panel to assess *Fusarium* head blight in Canadian wheat
 - Large number of samples, screening for multiple markers/species of infection

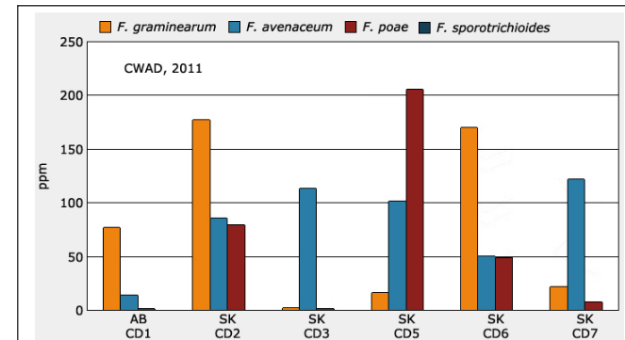
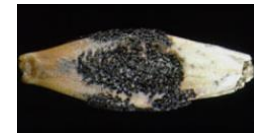


Figure 27. Distribution of toxic *Fusarium* species infecting Canada Western Amber Durum wheat collected in Prairie crop districts during the 2011 Harvest Sample Program

▼ Figure 27: table

Province	Crop district	Samples	Fusarium graminearum	Fusarium avenaceum	Fusarium poae	Fusarium sporotrichioides
Alberta	1	1	77,5	14,3	1,8	0
Saskatchewan	2	2	177,2	86,3	79,9	0
Saskatchewan	3	2	2,3	113,4	1,8	0
Saskatchewan	5	2	16,7	101,6	206,0	0
Saskatchewan	6	3	170,5	50,3	49,4	0
Saskatchewan	7	5	22,3	121,9	8,3	0



Women's Health – BV Panel

- Molecular test panel for detection of pathogens related to bacterial vaginitis
 - Improved sensitivity and specificity
 - Reasonable test cost
 - Faster turnaround time to a complete result
 - Easier for the laboratory to perform, preferably with automation available

19 microorganisms

BV PANEL TARGETS	
<i>Atopobium vaginae</i>	<i>Mobiluncus curtisii</i>
<i>Bacteriodes fragilis</i>	<i>Mobiluncus mulieris</i>
<i>Candida albicans</i>	<i>Mycoplasma genitalium</i>
<i>Candida glabrata</i>	<i>Mycoplasma hominis</i>
<i>Candida krusei</i>	<i>Neisseria gonorrhoeae</i>
<i>Candida parapsilosis</i>	<i>Prevotella bivia</i>
<i>Candida tropicalis</i>	<i>Trichomonas vaginalis</i>
<i>Chlamydia trachomatis</i>	<i>Ureaplasma urealyticum</i>
<i>Gardnerella vaginalis</i>	Human albumin
HSV1	RNaseP
HSV2	β -globulin

Covers bacterial, yeast, protozoan, fungal and viral pathogens + 3 internal positive controls

Circulating RNAs

- Growing interest in circulating RNAs – NIPT, heart disease, alzheimers
- Organ-specific circulating (or cell-free) RNA in blood that will provide early detection & disease monitoring in critical and hard-to-detect areas
- Initial striation of patients by NGS, qPCR used to confirm NGS data and perform kinetic studies to determine dosing or administration of medicines

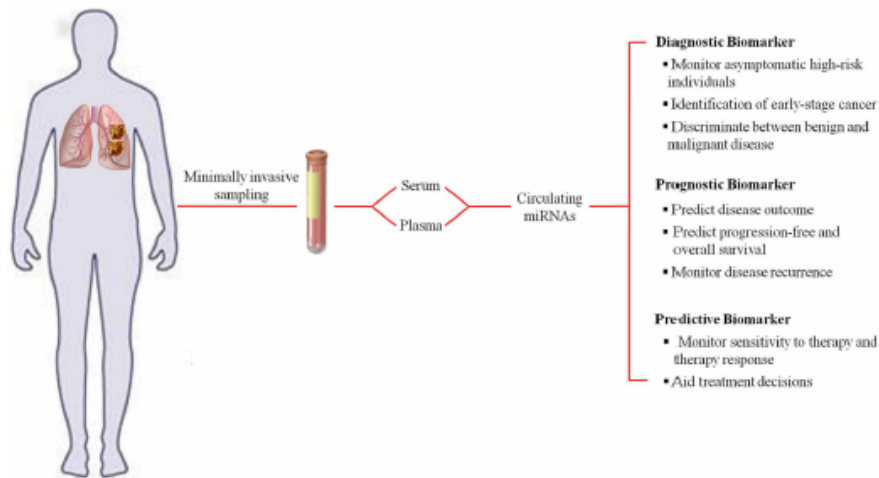
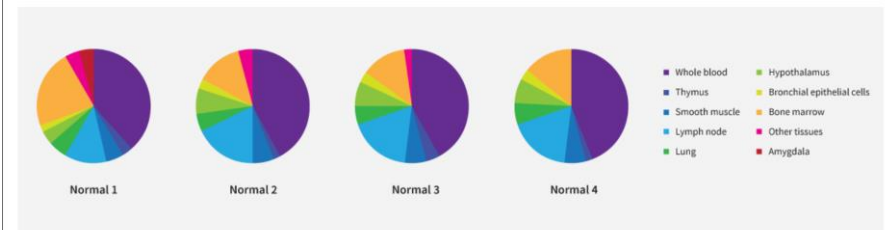


FIGURE 1 | Representation of the diagnostic, prognostic, and predictive uses of circulating miRNAs as a biomarker using lung cancer as an example.

Tissue-Specific RNA in the Blood of Healthy Individuals is Reproducible. Deviations can Indicate a problem.



Results of circulating RNA in unique tissues is consistent from normal individual to normal individual

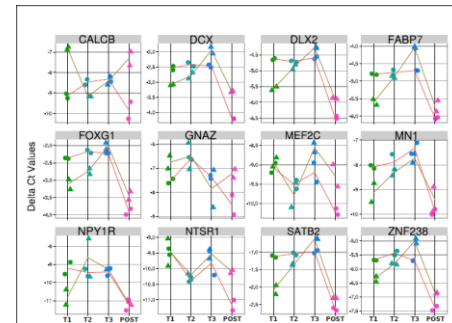


Fig. 4. Time course of fetal brain-specific genes, measured by qPCR. Plot

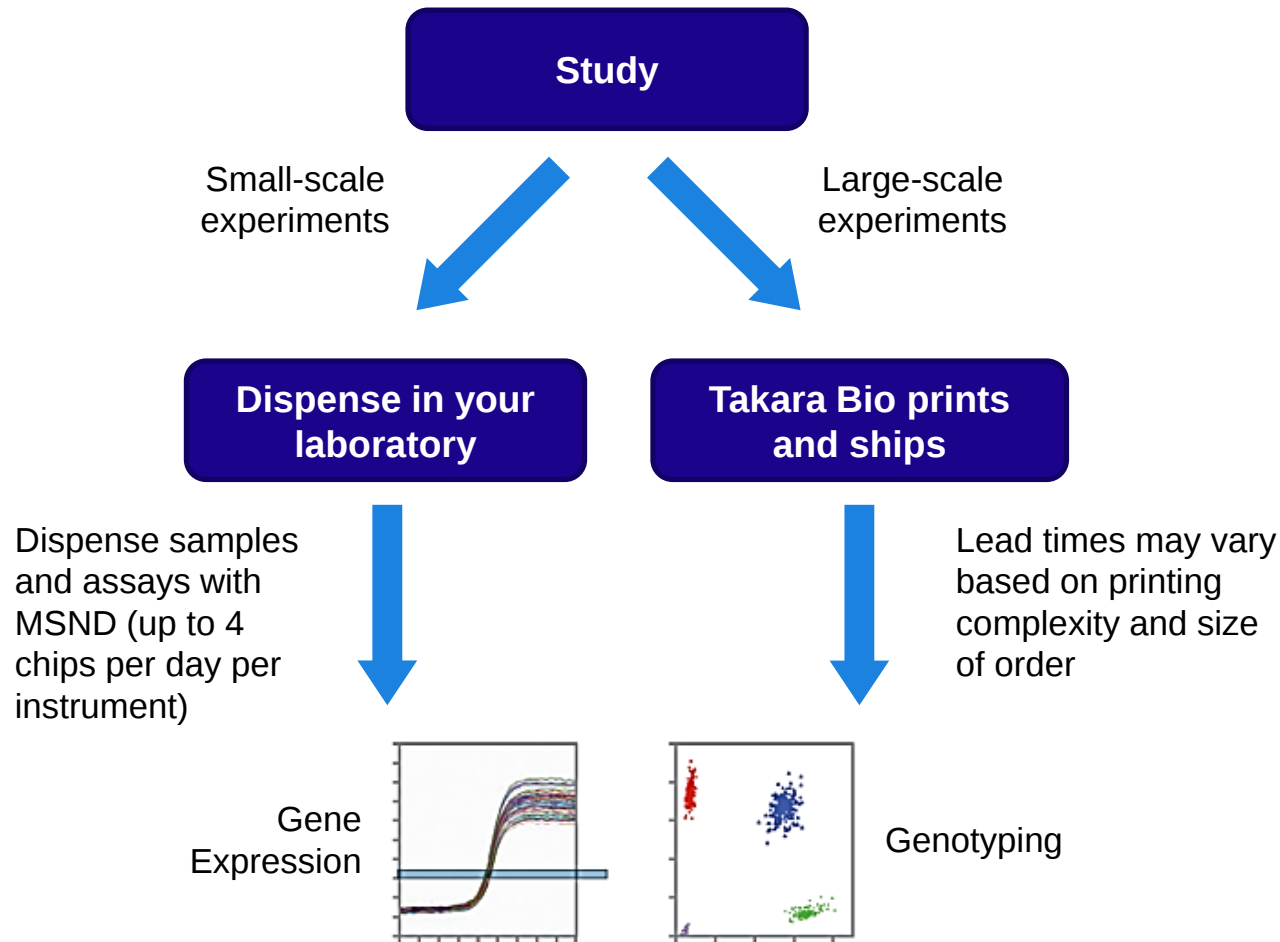
Genotyping – TaqMan SNP assays

- Red cell patient genotyping panels:
 - Red Cell Genotyping Panel (44 antigens reported)
 - Rh antigens & Rh variant panel
 - Common panel (24 antigens reported)
- Mouse genotyping panels:
 - Breeding and genetic tracking of strains in mouse colonies
 - Applicable to other livestock, eg. fisheries management and wildlife species tracking
- Pharmacogenomics (PGx) panels:
 - Study of how genes affect a person's response to drugs
 - Combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses tailored to a person's genetic makeup

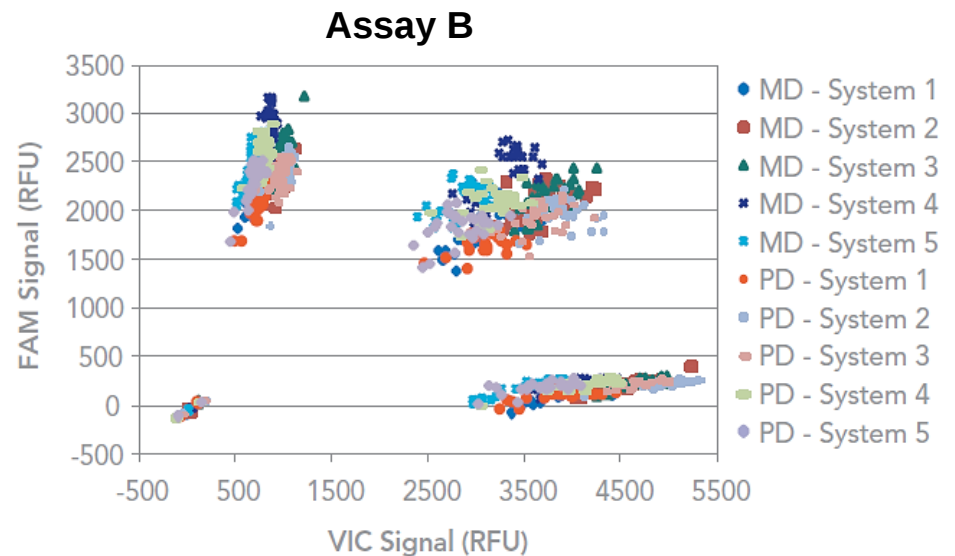
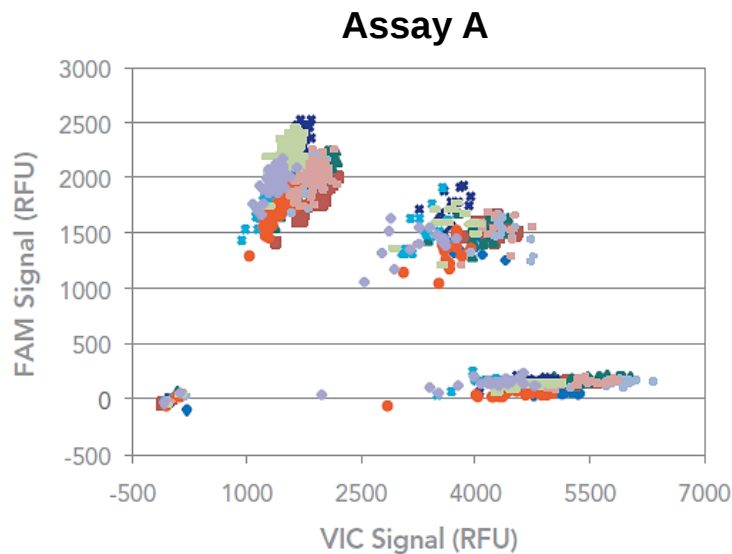


PRE-PRINTED CHIPS

Move from low- to high-throughput experiments with no additional validation



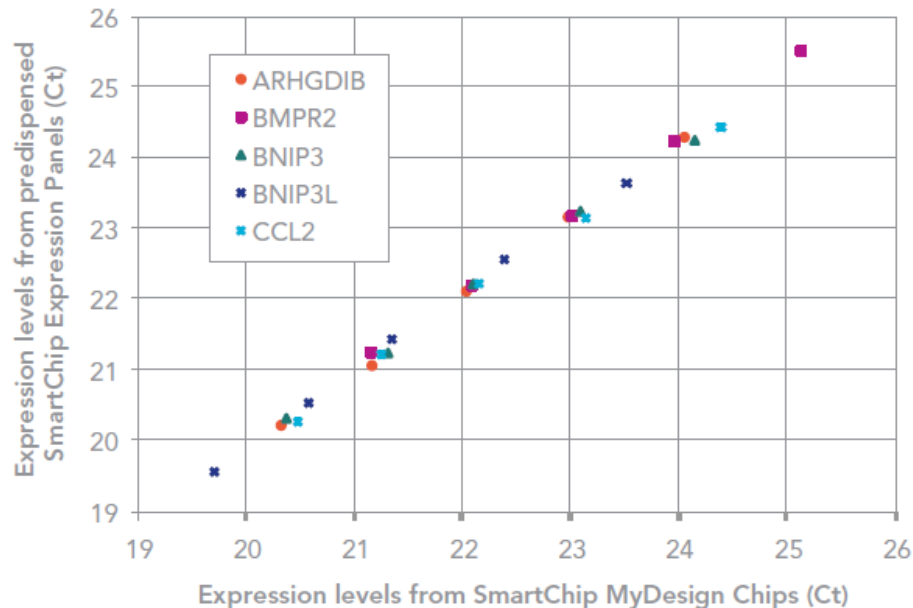
Consistent performance between GT workflows



System	MyDesign Chips		Predispensed Panels	
	Call Rate	Concordance	Call Rate	Concordance
1	99.4%	100%	98.7%	99.98%
2	97.4%	99.98%	99.5%	100%
3	99.5%	99.96%	99.6%	100%
4	99.6%	99.98%	99.6%	100%
5	99.6%	99.98%	99.4%	99.98%

- Cluster plots across five systems demonstrating high call and concordance rates

Consistent performance between GX workflows



- Nearly linear correlation between Ct values from MyDesign chips and predispensed GX experiments

Gene	Ct Std Dev	R ² of Linear Correlation
ARHGDIB	0.08	0.998
BMPR2	0.10	0.999
BNIP3	0.08	0.999
BNIP3L	0.09	0.998
CCL2	0.07	0.999

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science!®