FRONTAGE

COMPREHENSIVE GENOMIC SERVICES SUPPORTING ONCOLOGY STUDIES

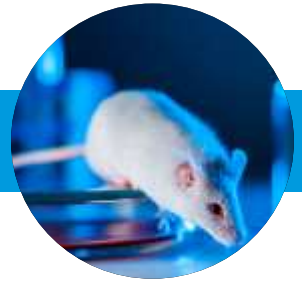
FEBRUARY 2022

INTEGRATED DRUG DEVELOPMENT SERVICES

DMPK

- In Vitro ADME Screening
- In Vitro ADME Development Studies
- In Vivo Services
- Metabolite Syntheses and Radiolabel/ Isotope Services
- QWBA

Safety and Toxicology



- IND Enabling Studies
- General Toxicology
- Genetic Toxicology
- Toxicokinetics
- Safety Pharmacology
- DART
- SEND

Bioanalytical and Genomics

- Biologics (ADC, Mab, Proteins, Peptides)
- Biomarker Services (ADA, Immunogenicity)
- Genomics
- Oligo, Gene and Cell Therapy

Product Development

- Organic Chemistry
- Analytical Services
- Formulation Development
- CTM Manufacturing
- GMP Commercial Stability
- Small Molecules and Biologics
- IND and ANDA

Early Stage Clinical

- Clinical Centers in US and China
- Phase I: SAD, MAD, BA, BE, hAME, Food Effect, DDI
- Biometrics, Data Management, Medical writing

Central Lab

- Clinical Collection Kits
- Sample Tracking
- Local Lab Normalization
- Biorepository
- Logistics
- Scientific Operations
- Clinical, PK/PD
- COVID-19 Testing

OPERATIONS IN NORTH AMERICA & CHINA

North America

- **Exton, PA (3) (HQ)**
- Concord, OH
- Vancouver, Canada
- Secaucus, NJ
- Monmouth Junction, NJ
- Palo Alto, CA
- Hayward, CA (2)
- Deerfield Beach, FL
- Chicago, IL

China

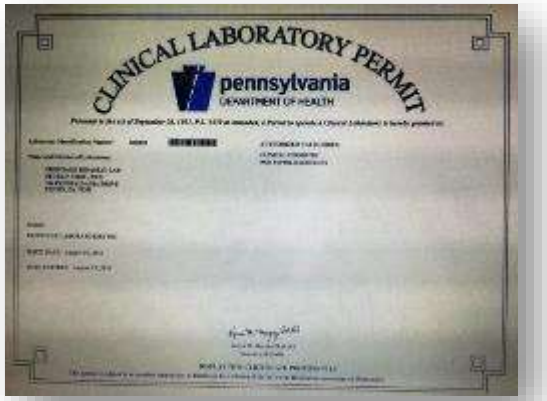
- **Shanghai (4) (HQ)**
- Suzhou (4)
- Zhengzhou
- Wuhan
- Yantai

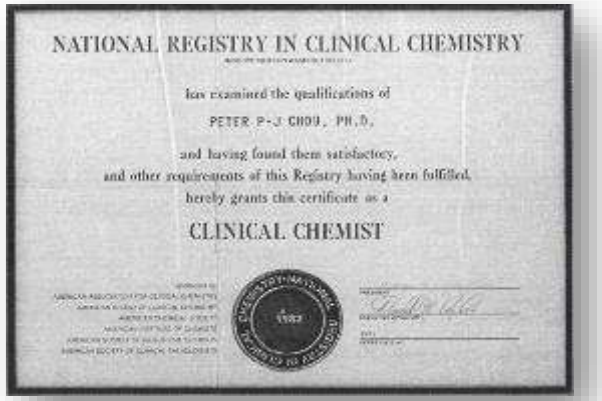
QAU - GXP LABORATORY

- On-site independent Quality Assurance Unit
- Quality standard: FDA/OECD GLPs and related guidelines
- Electronic data handling complies with FDA 21 CFR part 11
- SOP’s on-line in ZenQMS
- Periodic inspections from QAU, clients and QA consulting firms
- Strict QC process (technical, QC specialist, management and QA)
- Data qualified for regulatory submissions
- Systematic GLP/technical/SOP trainings

GLP-COMPLIANT, CLIA CERTIFIED LABORATORY

- Supporting Both Pre-Clinical and Clinical Development Programs
  - Method Development/Optimization/Transfer
  - Method Validation
  - Sample Analysis
- Assays Supported in our CLIA-Certified,
- GLP-Compliant Lab:
  - Biomarker Assays
  - PK / ADA / NAb
  - Genome sequencing and genotyping





A COMPREHENSIVE SET OF GENOMIC SERVICES SUPPORTING DRUG DEVELOPMENT

- Sequence analysis of DNA and RNA
- Quantification of DNA and RNA

Oncology

- ctDNA or solid tumor DNA sequencing: WGS, exome and gene panel
- RNA/DNA sequencing panels for detection of gene fusions, translocations, copy number variation, SNPs, Indels, tumor mutational burden, microsatellite instability
- Epigenomic analysis: DNA methylation and chromatin modification

Pharmacogenomics

- Mutations that alter protein sequences
- Structural variations (CNV, fusion, TL)
- Changes in gene expression level or mRNA processing
- Changes in small RNA profiles (miRNA)
- Solid and liquid biopsy mutation analysis
- Changes in the epigenome (mC)

Pharmacodynamics

- Changes in target gene expression
- DNA sequence changes by gene editing

Pharmacokinetics

- mRNA therapeutics
- siRNA therapeutics
- Viral vectors / DNA vaccine
- CRISPR/Cas9

Safety

- Biodistribution
- Viral shedding

Other

- Microbiome analysis

FRONTAGE SAMPLE PROCESSING EQUIPMENT

Automated liquid handling

- D — Biomek 4000 Liquid Handler

Sample Processing

- E — MP FastPrep-24

RNA/DNA Extraction

- E — KingFisher Flex

- D — Chemagic 360-D

Quantification and QC

- E — Fragment Analyzer

- D — Bioanalyzer

FRONTAGE GENOMICS EQUIPMENT

E Exton, PA
D Deerfield, FL

Next-Generation Sequencing

- Ilumina MiniSeq

E
- Illumina NextSeq 550

E
- Illumina NextSeq 2000

D
- 10x Chromium Controller

D

ddPCR

- QX200

E
D

qPCR

- QuantStudio 5

D
- QuantStudio 7Flex

E
- BioRad C

D
- Fluidigm Biomark

D

Scanners and Plate Readers

- Luminex MAGPIX

D
- BioTek Synergy LX

D
- Axon Genepix 4000B Microarray Scanner

D
- Nanosight NS300 (exosome and nanoparticle sizing)

D

Flow Cytometry

- Beckman Coulter Navios EX

E
- BD FacsCelesta

E
- Beckman Coulter Cytoflex

D

Immunoassays

- Quanterix Simoa

E
- MSD

E
- Luminex LX100

D
- Spectramax

E

ELISPOT

- ImmunoSpot S6UA

E

COMPREHENSIVE ASSAY PLATFORMS

Discovery; Pre-Clinical and Clinical Studies; patient diagnostic testing

Genomic DNA extraction/QC

- Quantification with qPCR or ddPCR

- Genotyping with qPCR or ddPCR

- Genotyping by PCR and Sanger sequencing

- WGS/WES

- Target capture and NGS

- Genotyping by amplicon sequencing with NGS

ctDNA extraction/QC

- WGS/WES by NGS

- Target capture and NGS

- Quantification and genotyping with qPCR or ddPCR

RNA extraction/QC

- RNA-seq

- Quantification and genotyping with qPCR or ddPCR

- Target capture and RNA-seq

Cell culture, lavage fluid, processed tissue

- ELISA; MSD

- Surface and intracellular
  - Immunophenotyping
  - Cellular activation
  - Rare cell populations
  - Receptor Occupancy

- Immunospot Assays

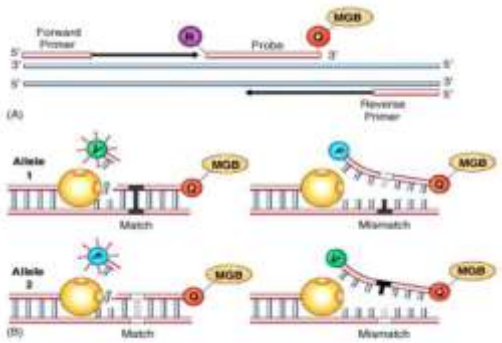
PHARMACOGENOMICS: TAQMAN AND HRM ASSAYS

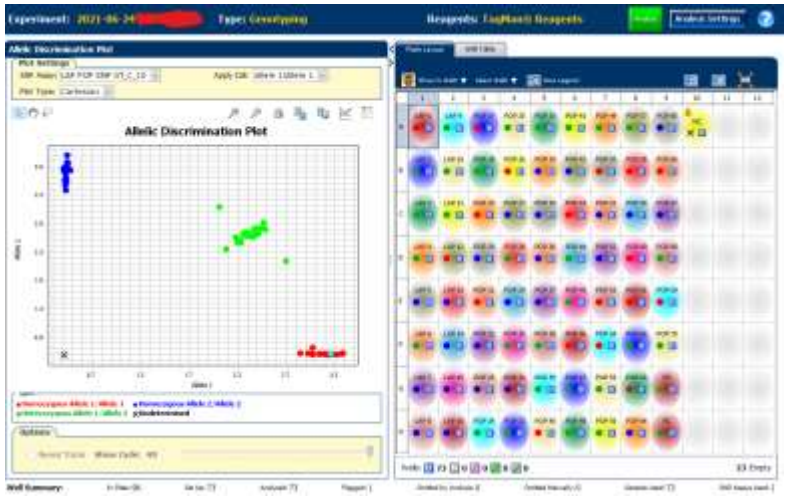
# of target genes	1s	10s	100s	1000s	All genes
Known variants?	Yes / No	Yes / No	No	No	No

qPCR

SNP analysis using Taqman assays

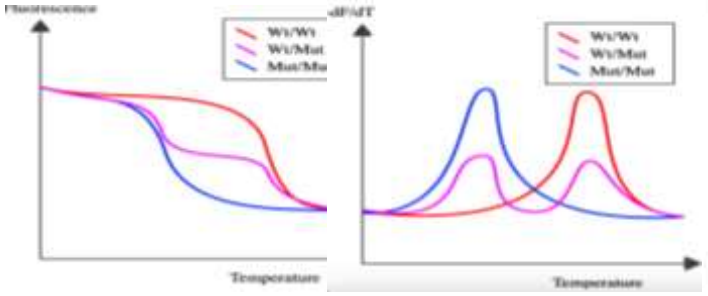
- Two Taqman probes with two different dyes are used in the same qPCR reaction
  - Probe 1 (Fam) matches Wt sequence
  - Probe 2 (Vic) matches Mut sequence
- Wt/Wt: Fam only
- Mut/Mut: Vic only
- Wt/Mut: Fam + Vic

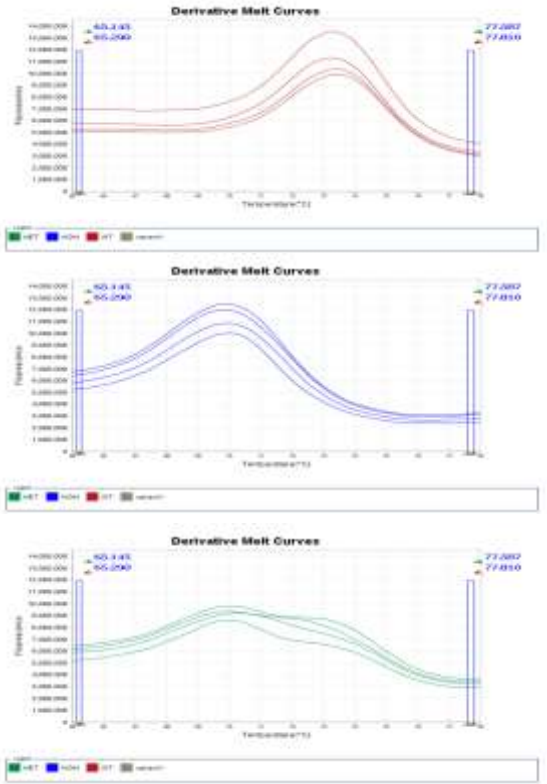




SNP analysis using HRM

- High resolution melting analysis
  - After PCR, temperature is raised to denature dsDNA
  - Fluorescent dye binds dsDNA
  - PCR products from different alleles denature at different temperatures
- Wt/Wt vs. Mut/Mut: two distinct melting curves
- Wt/Mut: a combination of the two melting curves





PHARMACOGENOMICS: AMPLICON SEQUENCING

# of target genes	1s	10s	100s	1000s	All genes
Known variants?	Yes / No	Yes / No	No	No	No

Amplicon sequencing: NGS sequencing of PCR products

Analysis of gene editing results

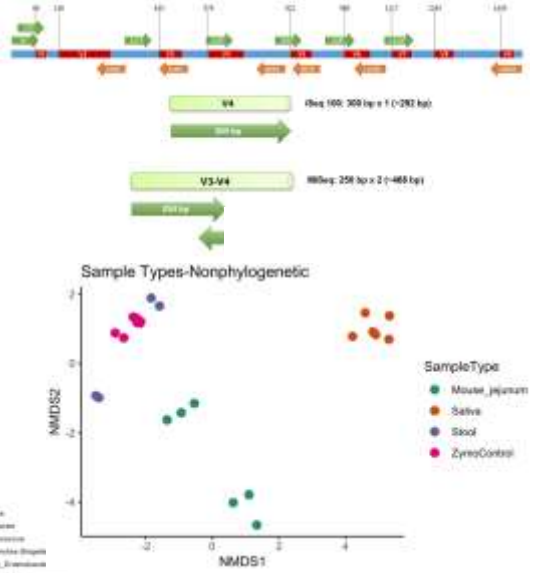
- Gene editing by CRISPR/Cas or ZnF results in highly heterogenous sequence and structural changes at the target site
- Editing efficiency can be highly variable

Editing results: SNPs, indels, etc.
Editing efficiency: % of target cells edited

Microbiome Analysis using Metagenomics

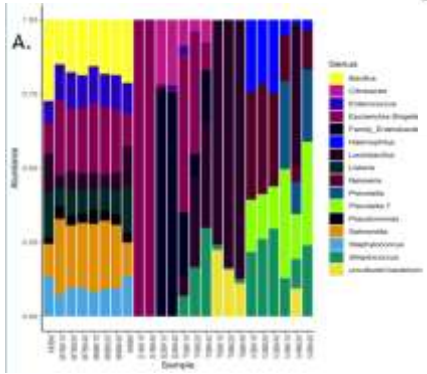
16s rDNA sequencing

- The 16s rRNA gene contains hypervariable regions (HVR) flanked by highly conserved regions
- Conserved regions allow PCR amplification
- HVRs provide diversity information

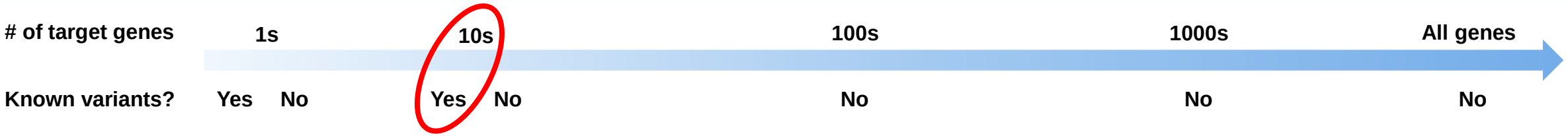


Sample Types

Stool/Feces
Tissue Biopsies
Cells
Saliva
Bronchial Lavage
Sputum
Buccal Swabs
Oral Biofilms
Soil and Plants
Food Items



PHARMACOGENOMICS: HIGH-THROUGHPUT TAQMAN ASSAY



High throughput qPCR using customized plates

- Preloaded PCR plates with duplex Taqman assays
- Highly customizable
- Suited for the analysis of a moderate number of known SNPs
- E.g.: 12 SNPs on one plate; each represented 32 times in a 384-well plate

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
A	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
B	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
C	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
D	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
E	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
F	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
G	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
H	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
I	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
J	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
K	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
L	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
M	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
N	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
O	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
P	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12

PHARMACOGENOMICS: TARGET CAPTURE AND NGS

# of target genes	1s	10s	100s	1000s	All genes
Known variants?	Yes / No	Yes / No	No	No	No

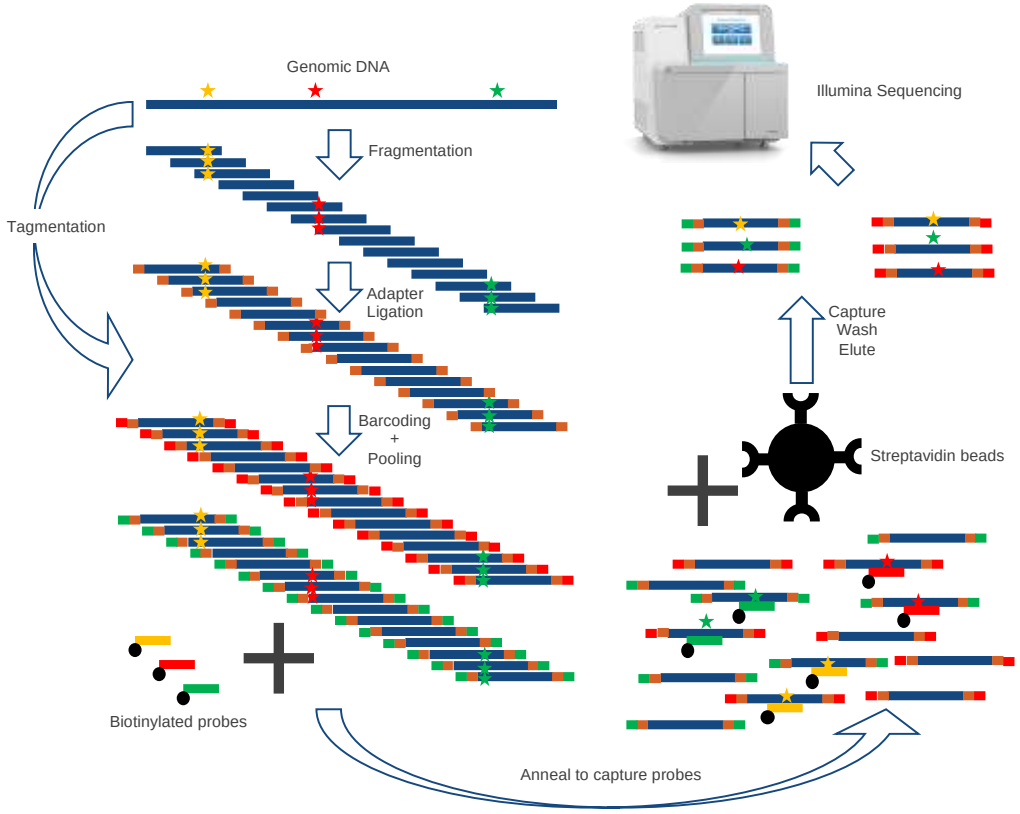
Target capture and NGS

Deep sequencing of a gene panel

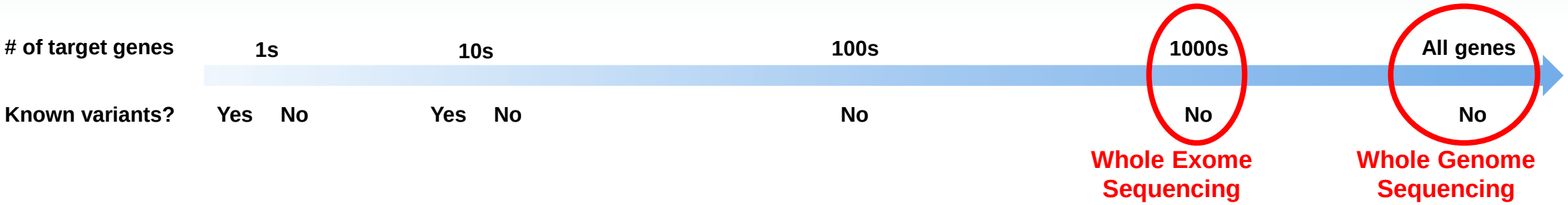
- Selectively deep sequencing of a subset of genes or loci
- Flexible target selection and sequencing depth
  - Customize panels to meet diverse needs
  - Commercially available panels

- DME profiling panels
- Oncogene panels
  - Tumor biopsy: tumor genomic DNA
  - **Liquid biopsy: ctDNA sequencing**

DNA Extraction from Edited Cells → Genomic Library → Target Capture → Target Enrichment → NGS Sequencing

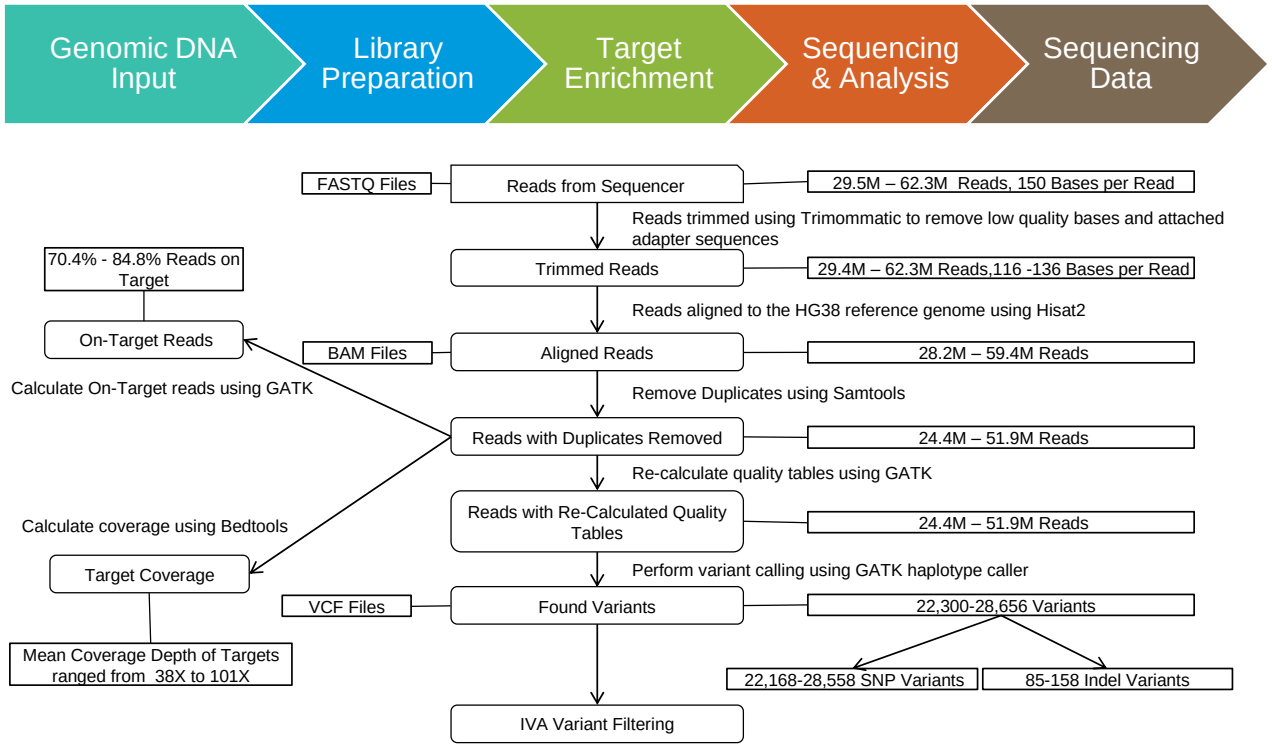


PHARMACOGENOMICS: WHOLE-EXOME SEQUENCING AND WHOLE GENOME SEQUENCING



Whole Exome Sequencing (WES)

- Capture and sequence all annotated exons in the genome
- Roche panel: ~43Mb
- Illumina Nextera: 37Mb



PHARMACOGENOMICS: BIOINFORMATIC ANALYSIS FOR VARIANT IDENTIFICATION

- Is it real a variant or caused by an error in sequencing or post processing?
- How common is this variant among patients with similar diseases and in the world at large in general?
- How might it affect the patient?

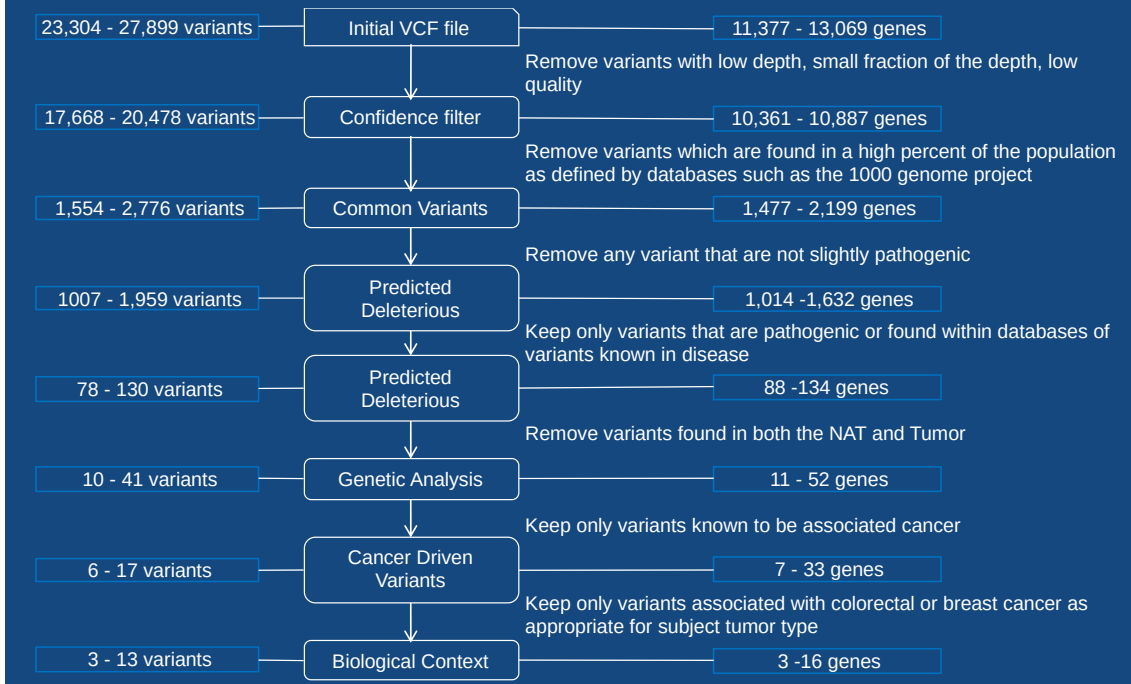


Table I. Number of variants after each filtering step

Cancer type	Colorectal	Colorectal	Colorectal	Colorectal	Colorectal	Breast	Breast	Breast	Control	Control
subject	20568	20567	20569	20574	20577	20576	20575	20573	control male	control female
initial	25,791	23,304	25,052	23,960	23,384	26,229	27,899	23,432	32,364	32,321
Confidence Filter	20,478	17,990	18,598	18,395	18,160	18,402	17,668	18,486	24,988	15,076
Common Variants	2,776	1,711	1,868	1,757	1,664	1,671	1,554	1,718	1,864	465
Predicted Deleterious	1,959	1,099	1,234	1,117	1,069	1,063	1,007	1,093	1,170	310
Predicted Deleterious	130	92	91	113	105	78	101	98	96	21
Genetic Analysis	19	14	10	15	15	16	41	14	0	0
Cancer Driven Variants	9	10	7	9	14	10	27	6	0	0
Biological Context	7	9	7	9	13	6	12	3	0	0

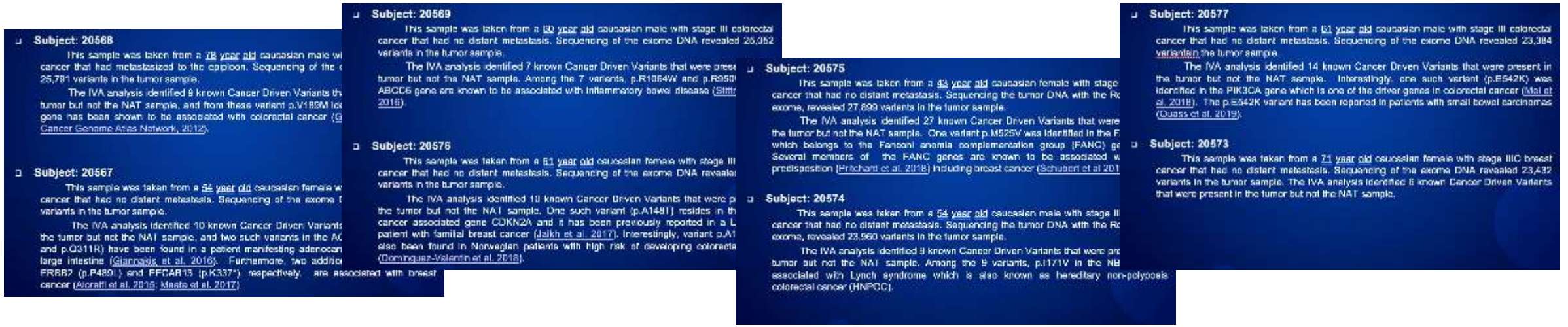
Table II. Number of genes after each filtering step

Cancer type	Colorectal	Colorectal	Colorectal	Colorectal	Colorectal	Breast	Breast	Breast	Control	Control
subject	20568	20567	20569	20574	20577	20576	20575	20573	control male	control female
initial	12,232	11,423	12,028	11,676	11,377	12,327	13,069	11,462	13,974	13,987
Confidence Filter	10,887	10,523	10,709	10,640	10,483	10,537	10,361	10,593	12,733	9,471
Common Variants	2,199	1,654	1,779	1,685	1,584	1,593	1,477	1,625	1,557	289
Predicted Deleterious	1,632	1,123	1,242	1,149	1,078	1,071	1,014	1,094	988	203
Predicted Deleterious	134	104	109	123	120	88	116	127	102	25
Genetic Analysis	21	15	11	15	19	17	52	17	0	0
Cancer Driven Variants	9	11	7	9	17	11	33	7	0	0
Biological Context	7	10	7	9	16	7	15	3	0	0

PHARMACOGENOMICS: BIOINFORMATIC ANALYSIS FOR VARIANT IDENTIFICATION

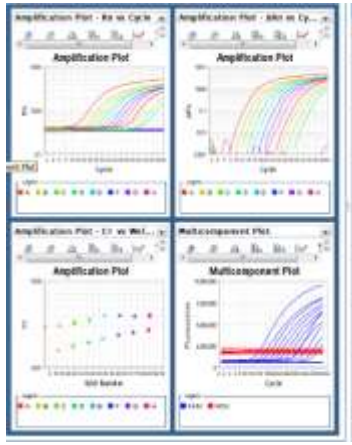
Table I. Overview of patient and number of biologically-relevant cancer-driven variants

Patients	Cancer type	Gender	Age	Cancer Stage	Histologic Tumor Type	# Cancer Driven Variants
Control 1	None	Male	N/A	N/A	N/A	0
Control 2	None	Female	N/A	N/A	N/A	0
20568	Colorectal	Male	78	III	Adenocarcinoma	7
20567	Colorectal	Female	54	III	Adenocarcinoma	10
20569	Colorectal	Male	60	III	Adenocarcinoma	7
20576	Breast	Female	61	IIIC	Invasive ductal carcinoma	7
20575	Breast	Female	43	IIIB	Invasive carcinoma of no special type (NST)	15
20574	Colorectal	Male	54	III	Adenocarcinoma	9
20577	Colorectal	Male	61	III	Adenocarcinoma	16
20573	Breast	Female	71	IIC	Invasive carcinoma of no special type (NST)	3

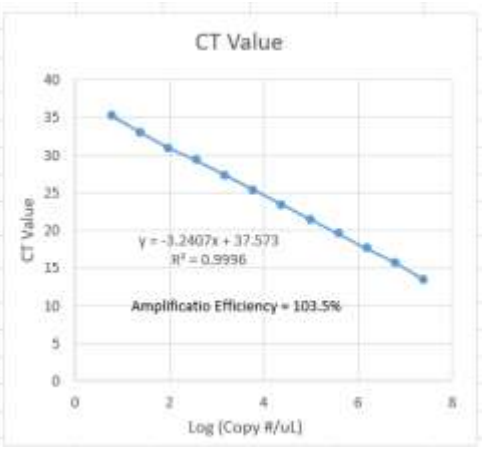


QUANTIFICATION OF DNA BY QPCR AND DDPCR

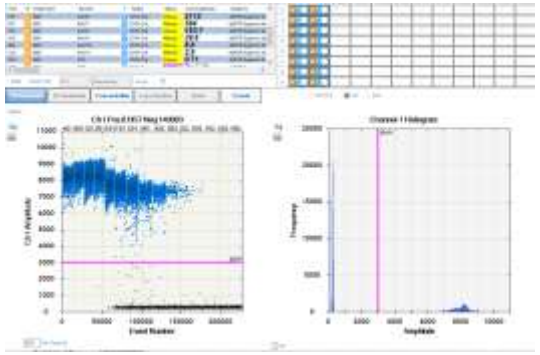
qPCR quantification of PAAV2–HRGFP in human genomic DNA

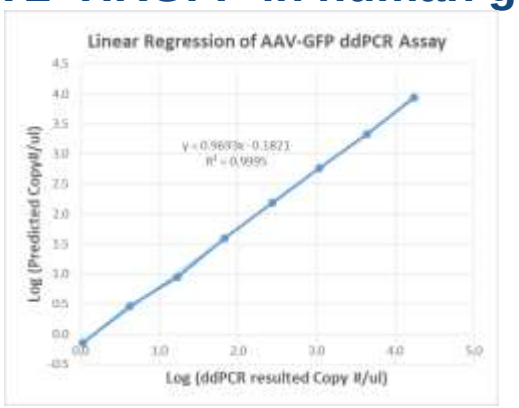


Copies/ul	Log (DNA	CT Value
2.5E+07	7.39794	13.3631
6250000	6.79588	15.6817
1562500	6.19382	17.5814
390625	5.59176	19.5394
97656.3	4.9897	21.3869
24414.1	4.38764	23.3951
6103.5	3.78558	25.3155
1525.9	3.18352	27.2408
381.5	2.58146	29.3202
95.4	1.9794	30.8899
23.8	1.37734	33.0302
6.0	0.77528	35.2121

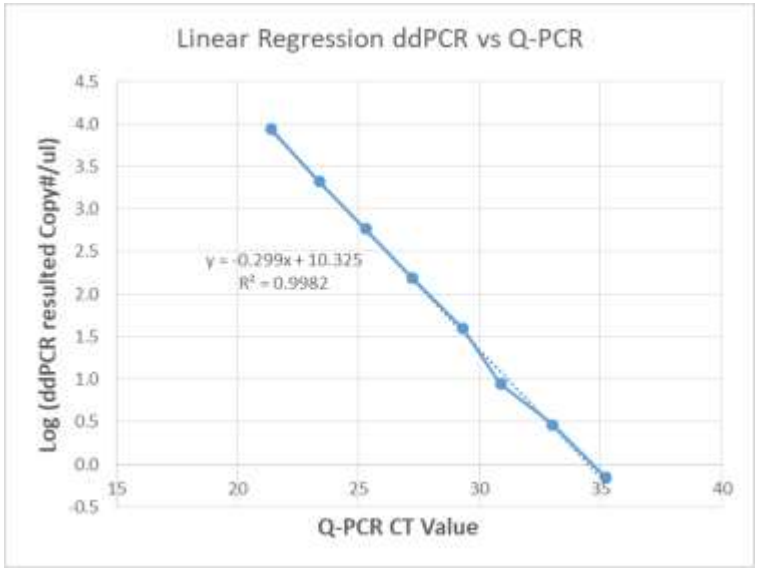


ddPCR quantification of PAAV2–HRGFP in human genomic DNA



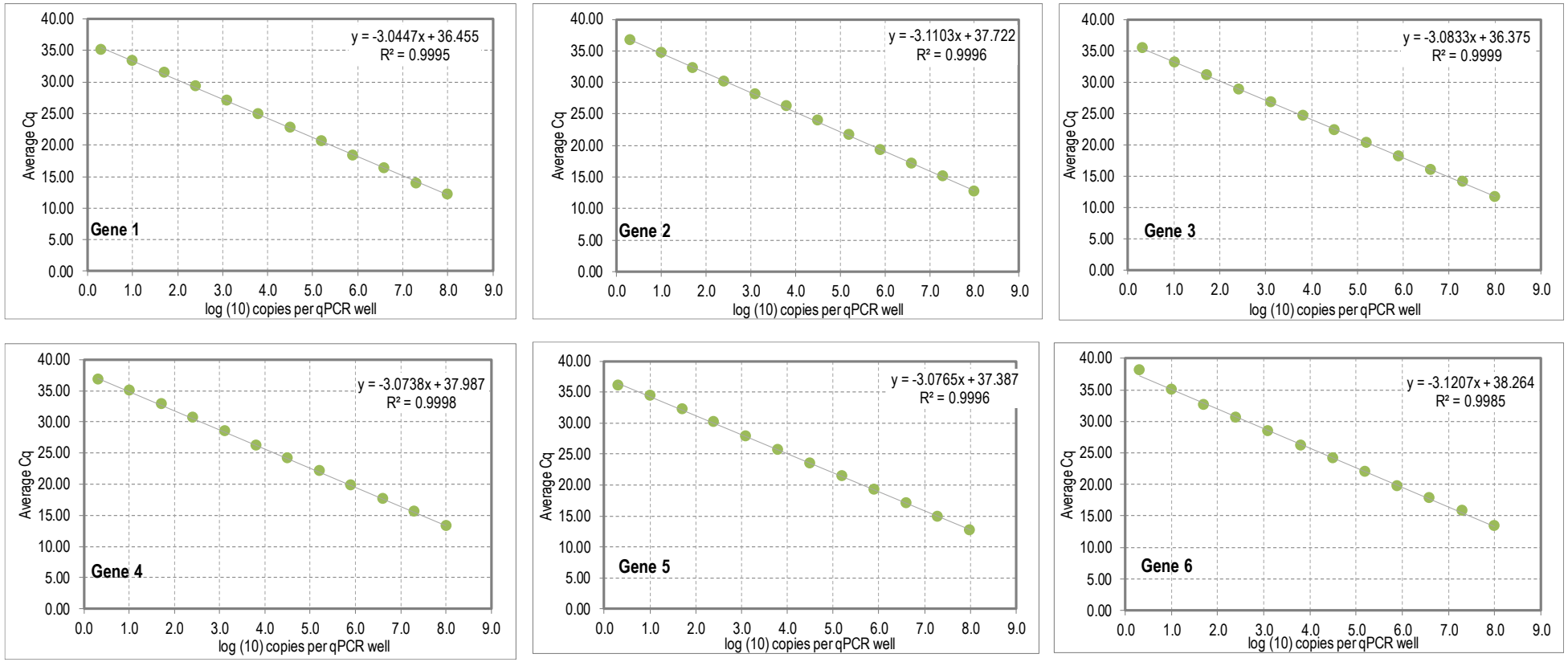


Consistency between qPCR and ddPCR results



QUANTIFICATION OF RNA BY RT-QPCR AND RT-DDPCR

RT-qPCR analysis of the expression levels of 6 human genes



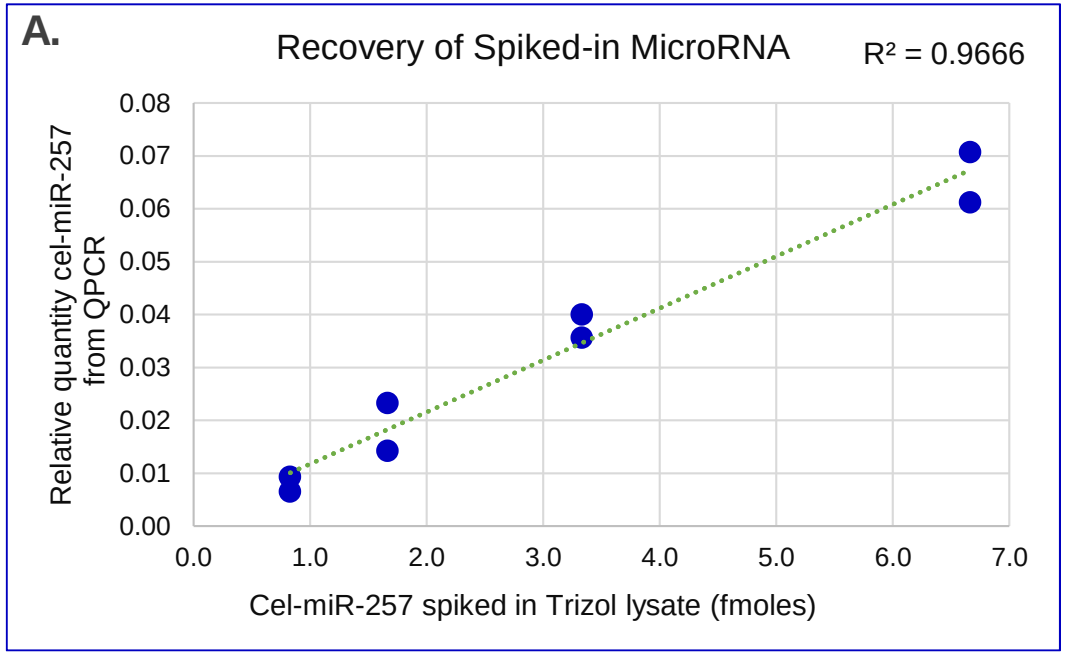
Linear dynamic range: 10,000,000X

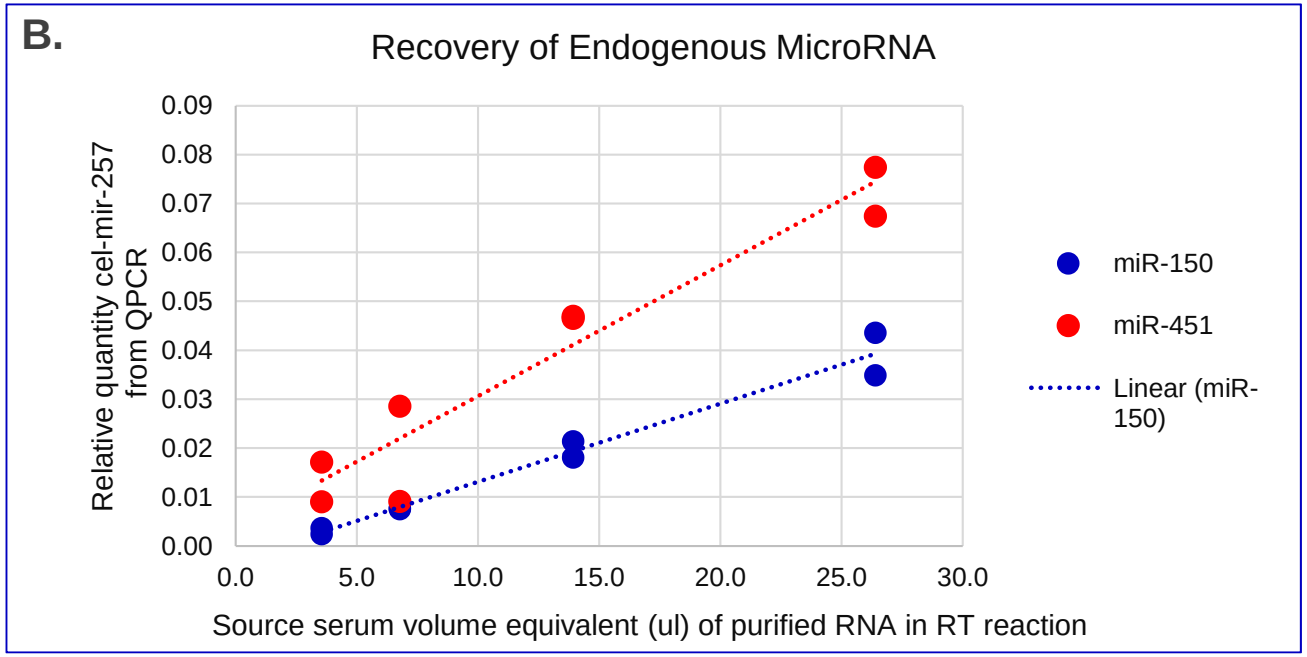
Limit of detection: Typically 10 copies of cDNA per qPCR well

QUANTIFICATION OF SMALL RNA (MIRNA) BY RT-QPCR

Quantitative Recovery of Endogenous and Spiked-in MicroRNA

Mass of both exogenous and endogenous microRNAs in the purified RNA was linear to the volume of serum used.





Relative quantity for panel A is based on $2^{(Ct_{con} - Ct_{sample})}$, where Ct_{con} and Ct_{sample} represent the mean Ct value of a positive control RNA added directly to the RT reaction and for the spike in the extracted RNA sample, respectively.

Relative quantity for panel B is based on $2^{(Ct_{tissue} - Ct_{sample})}$, where Ct_{tissue} and Ct_{sample} represent the mean Ct value of a positive control tissue RNA pool and of the spike in the extracted RNA sample, respectively.

TRANSCRIPTOME ANALYSIS BY RNA-SEQ

From Extraction To Analysis Report Through Numerous QC Checkpoints

- Optimized sample preparation protocols for limiting amounts of RNA, DNA, protein, and degraded starting materials (FFPE)
- Parsimonious consumption of samples and derivatives at each processing point

- Efficient workflows established for each service to ensure rapid turnarounds
- All GLP/ GCLP equipment undergoes continuous validation, calibration and maintenance schedule

- Customizable data analysis services, tailored to experimental objectives
- Post project support available with preparation of materials for regulatory submission

MIRNA PROFILING BY MIRNA-SEQ

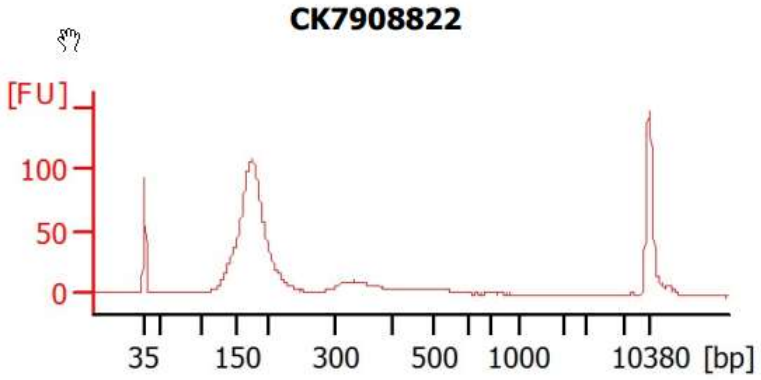
Isolation and sequencing of miRNAs from serum

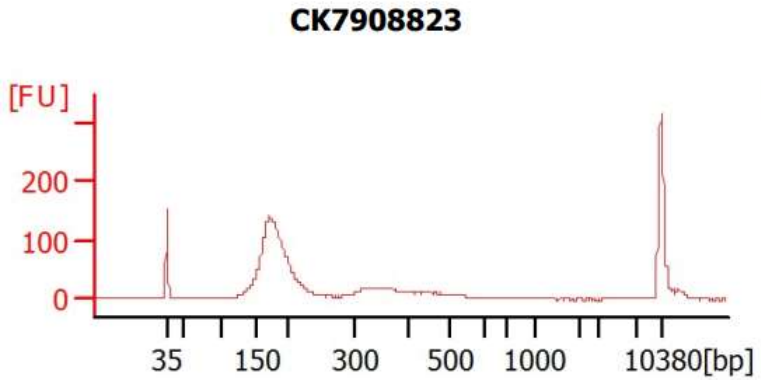
	100 ul – RepA	100 ul – RepB	200 ul – RepA	200 ul – RepB	400 ul – RepA	400 ul – RepB	800 ul – RepA	800 ul – RepB
Input Reads	37.46	35.36	37.78	33.29	20.44	32.58	33.39	20.59
Pass Quality Filter Reads	36.13	34.09	36.45	32.06	19.76	31.40	32.29	19.89
Too-short (< 17 bp) Reads	7.39	5.94	6.01	5.69	3.46	7.43	7.51	3.99
3'-Adapter Only Reads	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00
5'-Adapter Containing Reads	4.13	4.71	4.41	4.62	2.54	3.18	3.17	2.13
Non-Adapter Reads	0.12	0.34	0.14	0.17	0.09	0.24	0.10	0.09
N reads	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Reads after Trimming	24.46	23.08	25.88	21.58	13.66	20.54	21.49	13.68
Reads Count Pass Filter (>5)	23.48	22.13	24.97	20.96	13.39	19.96	21.10	13.44
Genome and mRNA	10.69	10.32	13.66	13.48	10.30	15.25	16.58	10.94
tRNA	0.31	0.22	0.32	0.25	0.20	0.49	0.29	0.13
rRNA	2.28	2.05	2.26	2.21	1.22	1.95	1.46	0.91
snoRNA	0.01	0.01	0.00	0.01	0.00	0.01	0.01	0.00
Mature MicroRNA	1.14	1.36	1.50	2.28	1.89	1.69	2.20	1.62
Pri-miRNA	1.17	1.38	1.53	2.29	1.91	1.73	2.23	1.63
piRNA	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.00
Ensembl cDNA - release 80	0.84	0.79	0.84	0.93	0.62	0.83	0.76	0.57

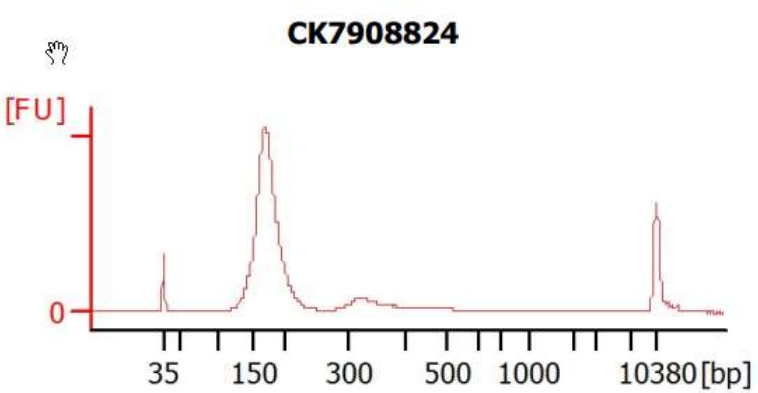
Mature.miRNA.Name	Mature.miRNA. Accession	100ul RepA	200ul RepA	400ul RepA	800ul RepA	100ul RepB	200ul RepB	400ul RepB	800ul RepB	Ave.RPM
hsa-miR-486-5p	MIMAT0002177	16241.4	20489.3	37072.9	34690.6	18077.8	30282.7	27028.2	31648.6	26941.4
hsa-miR-320a	MIMAT0000510	12851.9	14680.3	24999.0	16945.1	13784.7	21485.9	12751.0	29374.5	18359.0
hsa-miR-423-5p	MIMAT0004748	9582.1	9428.6	16266.7	7323.5	15573.8	18351.5	4213.5	13356.1	11762.0
hsa-miR-92a-3p	MIMAT0000092	6416.4	6076.9	8172.7	7151.5	5204.2	8781.5	9201.1	3716.0	6840.1
hsa-miR-22-3p	MIMAT0000077	4914.6	4700.1	7487.8	8324.3	9437.1	6967.1	5108.6	6934.2	6734.2
hsa-let-7a-5p	MIMAT0000062	5397.3	5557.4	8738.1	3374.8	5782.0	8703.1	4570.7	3202.5	5665.7
hsa-miR-122-5p	MIMAT0000421	3192.4	3268.8	5277.6	2717.9	5392.7	5438.7	1740.8	3457.9	3810.9
hsa-let-7b-5p	MIMAT0000063	2444.4	2686.3	3568.7	1327.4	4172.7	4055.8	1221.6	1837.2	2664.3
hsa-miR-320b	MIMAT0005792	1926.6	2300.9	3092.1	2517.0	2731.6	2888.0	1887.7	3743.3	2635.9
hsa-let-7f-5p	MIMAT0000067	2120.9	2021.5	4401.2	1810.7	2217.1	3130.8	2133.0	1749.4	2448.1
hsa-miR-10b-5p	MIMAT0000254	2624.8	1559.8	3276.7	1826.9	2003.1	3178.1	1870.6	1368.8	2213.6
hsa-miR-451a	MIMAT0001631	1700.9	1202.6	1445.3	1721.2	2958.1	2382.7	1482.1	1317.8	1776.4
hsa-let-7d-3p	MIMAT0004484	1440.5	1598.6	2606.2	1318.2	2015.3	2943.1	1198.7	821.0	1742.7
hsa-miR-148a-3p	MIMAT0000243	1006.3	1409.6	2576.9	1449.1	2214.1	2840.7	740.6	1374.0	1701.4
hsa-miR-10a-5p	MIMAT0000253	1925.6	1074.9	2427.0	1502.5	1774.0	2398.1	1399.2	845.5	1668.3
hsa-miR-26a-5p	MIMAT0000082	1608.1	755.1	884.6	1061.0	980.8	1350.6	1584.0	865.0	1136.2
hsa-let-7g-5p	MIMAT0000414	767.1	534.2	1236.0	764.6	729.0	654.9	946.4	735.1	795.9
hsa-let-7i-5p	MIMAT0000415	612.1	496.3	963.6	804.1	894.0	651.4	795.3	573.9	723.8
hsa-miR-24-3p	MIMAT0000080	521.7	412.3	361.9	474.8	632.6	411.7	578.2	493.7	485.8
hsa-miR-99b-5p	MIMAT0000689	440.5	253.3	636.9	559.7	514.6	575.4	392.7	271.6	455.6
hsa-miR-25-3p	MIMAT0000081	413.0	393.0	458.4	421.9	512.7	366.0	532.0	338.8	429.5
hsa-miR-629-5p	MIMAT0004810	250.6	229.2	596.8	591.3	241.5	495.1	300.8	632.1	417.2
hsa-miR-378a-3p	MIMAT0000732	252.5	212.9	544.1	559.7	518.6	389.6	349.6	383.7	401.3
hsa-miR-375	MIMAT0000728	417.3	294.5	412.4	524.5	393.5	492.5	312.5	361.6	401.1
hsa-miR-320c	MIMAT0005793	518.8	393.5	279.6	189.4	618.0	478.4	300.2	418.6	399.6
hsa-miR-30d-5p	MIMAT0000245	242.5	275.9	452.8	397.7	406.5	275.4	506.2	416.4	371.7
hsa-let-7c-5p	MIMAT0000064	459.4	398.9	394.8	170.8	423.1	667.0	282.0	168.2	370.5
hsa-miR-192-5p	MIMAT0000222	297.3	210.7	274.9	408.2	723.0	296.5	289.6	215.5	339.5
hsa-miR-151a-3p	MIMAT0000757	39.0	185.3	412.6	318.7	322.6	305.8	116.6	847.3	318.5
hsa-miR-185-5p	MIMAT0000455	248.0	175.2	416.2	321.3	141.8	296.7	365.2	482.9	305.9

CTDNA METHYLATION ANALYSIS BY TARGET CAPTURE AND BISULFITE SEQUENCING

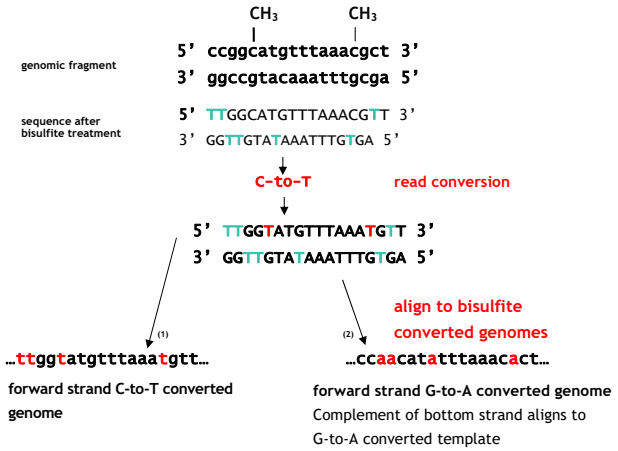
ctDNA extraction from plasma and QC



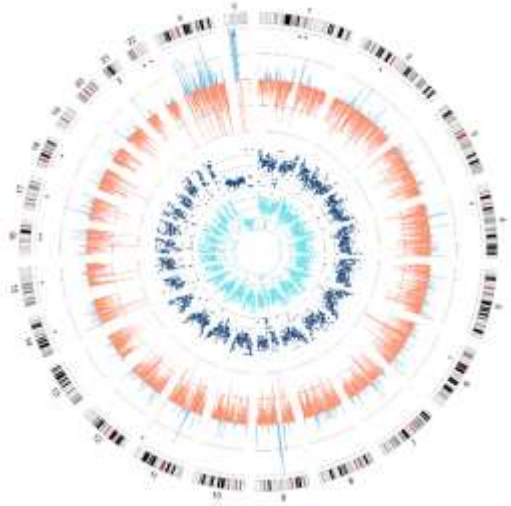




Bisulfite library preparation



Sequencing and data analysis



Most regions were hypomethylated in PDAC vs. normal samples.

The outer Circos visualization shows the difference in % methylated CpGs between PDAC and Normal patients for each 1 Mbase tile in the genome. The blue and red bars indicate regions with higher and lower % methylation in PDAC vs. Normal, respectively. Regions with FDR < 0.1 are indicated by *. The gridlines indicate a methylation difference of 5%.

The inner scatter plots show the average number of methylated CpGs in each region across all samples for PDAC (dark blue; n=6) and Normal (light blue; n=6) groups. The gridlines indicate 50 methylated CpGs.

METHOD VALIDATION FOR GENOMICS STUDIES

- FDA recognizes that "*the new sequencing technologies used in genomic testing can examine millions of DNA variants at a time, and thus* ***warrant a flexible approach to oversight*** *that is adapted to the novel and evolving nature of these tests*".

- We develop NGS method validation plans with the following considerations:
  - Elements to be included in validation: Guidance from FDA and other regulatory agencies
  - "Gold standard": Validation procedures in FDA-approved assays, peer-reviewed publications and industry best practices
  - Specific parameters to be validated and thresholds to be met: Defined in consultation with sponsors to meet indications for use and project-specific needs

THANK YOU

U.S. Headquarters

China Headquarters

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