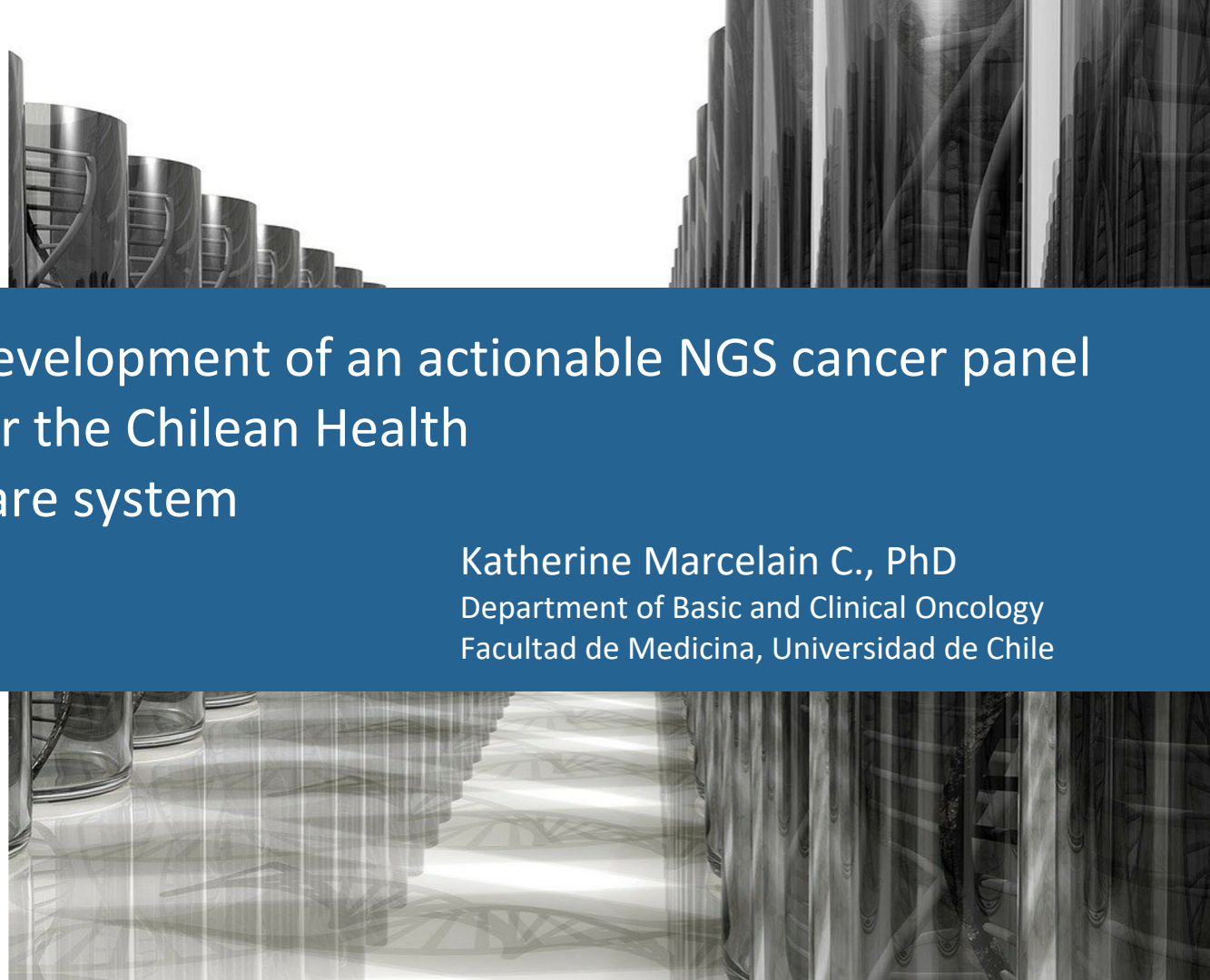
05-07-2020

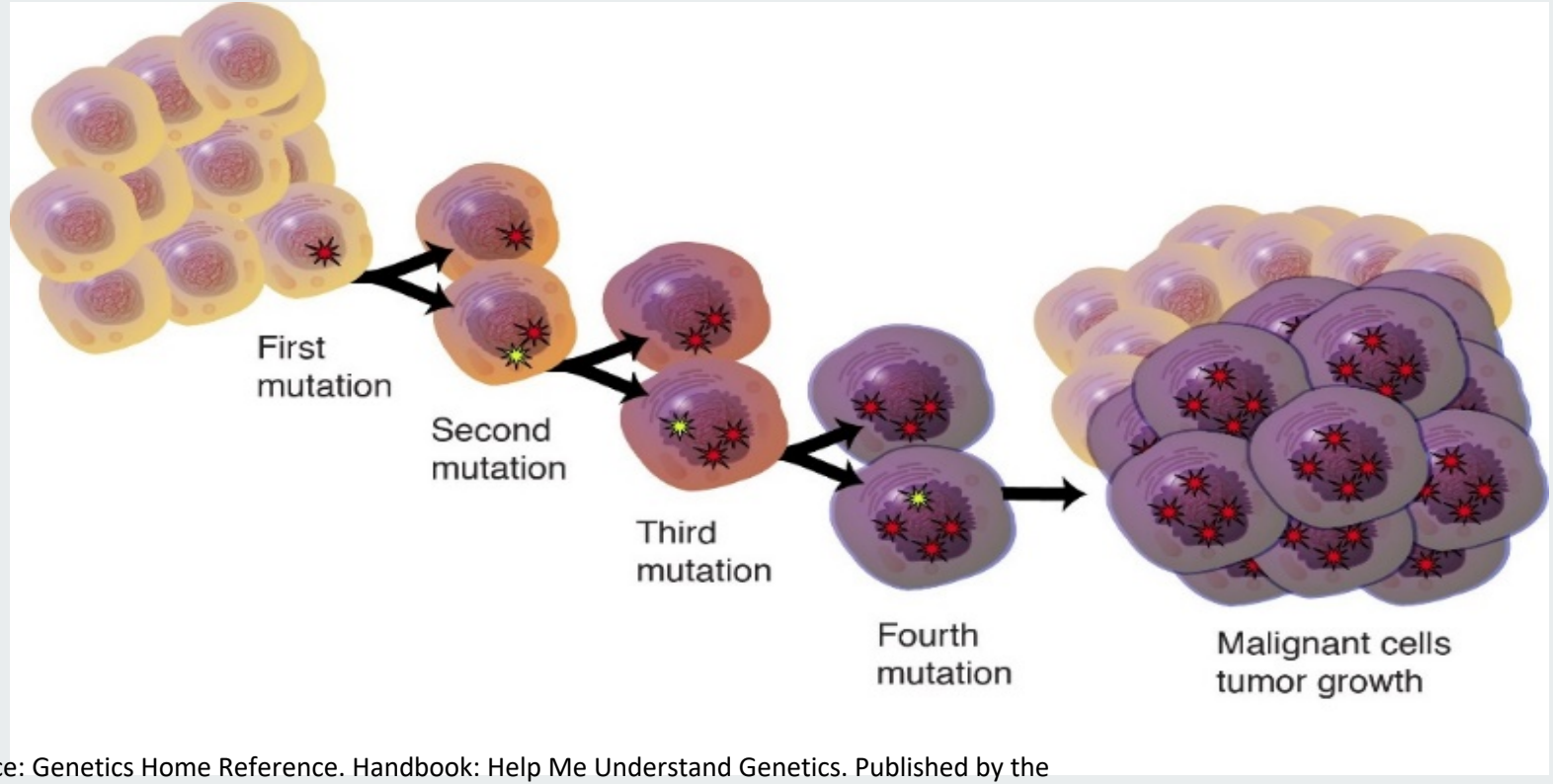
Development of an actionable NGS cancer panel for the Chilean Health Care system

Katherine Marcelain C., PhD
Department of Basic and Clinical Oncology
Facultad de Medicina, Universidad de Chile

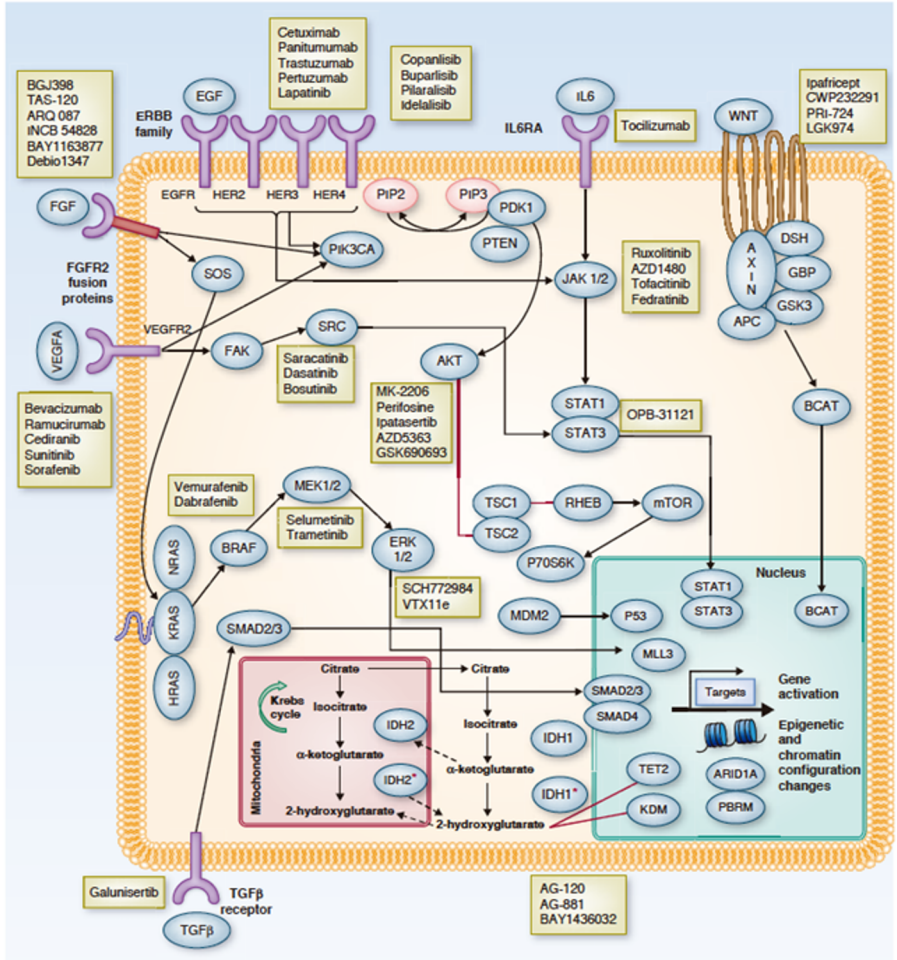


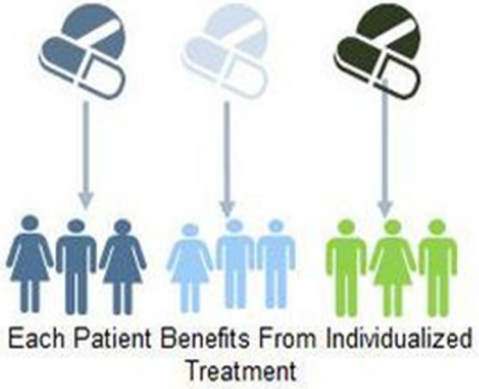
Global Genomic Medicine Collaborative

Genomic Medicine in Oncology treatment



Reference: Genetics Home Reference. Handbook: Help Me Understand Genetics. Published by the Lister Hill National Center for Biomedical Communications, US National Library of Medicine, National Institutes of Health, Department of Health & Human Services. June 4, 2012.



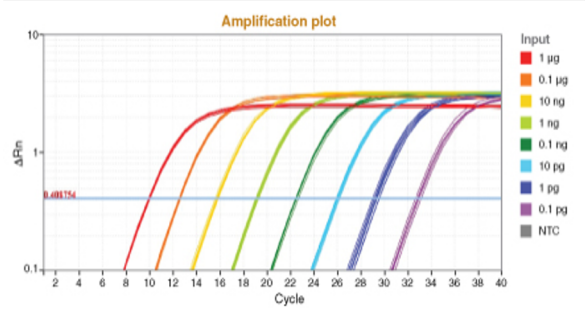


Many Targeted therapies, many biomarkers.

Some of these biomarkers are specific gene mutations

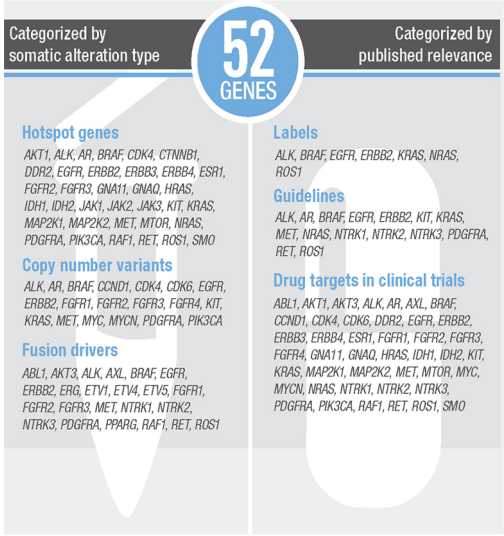
(SNV, Indels, Fusions, Amplifications)

Current Methods for detection of somatic mutations in solid tumours in the clinical practice



RT-qPCR
Few mutations in one or a couple of genes
Example: Cobas (Roche)

$$
U$ 500



NGS
Medium size panels
Ex. Oncomine Focus Assay (Thermo)

$$$
U$2,000

NGS
Large panels
Foundation One CDx

$$$$$
U$2,200 – 4,230

Design and validation of a 25 genes NGS panel for treatment indication in Solid Tumours

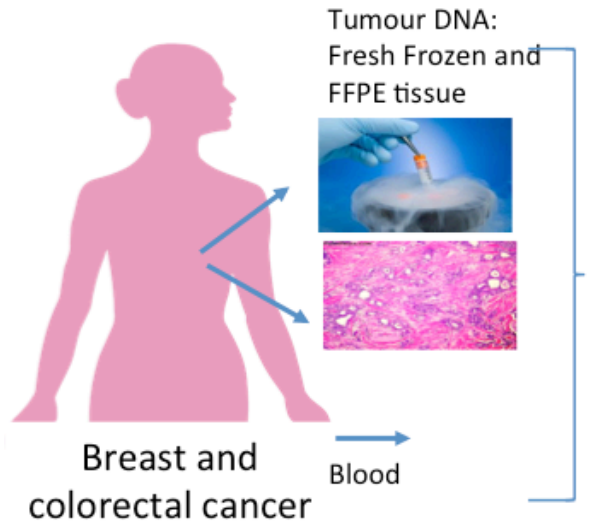
Currently **only 18 genes** are FDA or NCCN-recommended biomarkers for solid tumours (Level A).
(Level B: Standard of care; Level C: Clinical evidence)

Custom Panel adapted to local requirements (Chile and Latinoamerican countries): mostly FDA or NCCN-recommended biomarkers + in late trials. For solid tumours

TumorSec
(Hibridization Capture)

GENE	REGION	MUT TYPE	DRUGS	TUMOR TYPE	EVIDENCE
AKT1	all exons	Point	AZD-5363	BC, OV, Endom	B
ALK	Target	Point	Crizotinib, inh ALK	LUNAD	B
ARID1A	all exons	Point	inh ATM, erlotinib	BC, OV	C
BRAF	all exons	Point	Vemurafenid, dabrafenib, cetuximab, etc	MEL, NSCLC, CRC, THY	A
BRCA1	all exons	Point	Olaparib	OV, BC, CRC, MEL, SAR, PRO	A
BRCA2	all exons	Point	Olaparib	OV, BC, CRC, MEL, SAR, PRO	A
Cdk4	all exons	Amplification	Palbociclib/Abemaciclib	liposarc, MEL	B
EGFR	Target	Point/Amplif	Erlotinib, gefitinib, neratinib, osimertinib, etc	NSCLC	A
ERBB2	Target	Amplification	Trastuzumab	BC, Gastric	A
ESR1	Target	Point	Palbociclib	BC	B
IDH2	Target	Point	Enasidenib	AML	A
KIT	Target	Point	Nilotinib, imatinib, dasotinib,	MEL, GIST, AML	A
KRAS	all exons	Point	Cetuximab, erlotinib, regorafenib, etc	CRC, Panc, NSCLC	A
MET	Target	Point/Amplif	Foretinib, Rilotumumab	Papilary RCC, MEL, NSCLC	B
MTOR	all exons	Point	mTOR inhibitors	RCC	B
NRAS	all exons	Point	EGFR inhibitors	CCR	A
PDGFRA	Target	Point	Imatinib, Sunitinib	GIST	A,B
PI3KCA	all exons	Point/Amplif	Buparlisib, Serabelisib, Alpelisib, Copanlisib	BC	A
PTCH1	all exons	Point	Vismodegib	MDB, SC	B
PTEN	all exons	Point	Everolimus	Various	B
ROS1	Target	Point	Crizotinib	NSCLC	C
SMO	Target	Point	Vismodegib	Basal CC	B
TP53	all exons	Point	Prognosis	various	A
TSC1	all exons	Point	MTOR inh, Everolimus	RCC, Bladder C	A
TSC2	all exons	Point	MTOR inh	CNS, RCC	A, B

Optimization of protocol and Bioinformatic Flow works



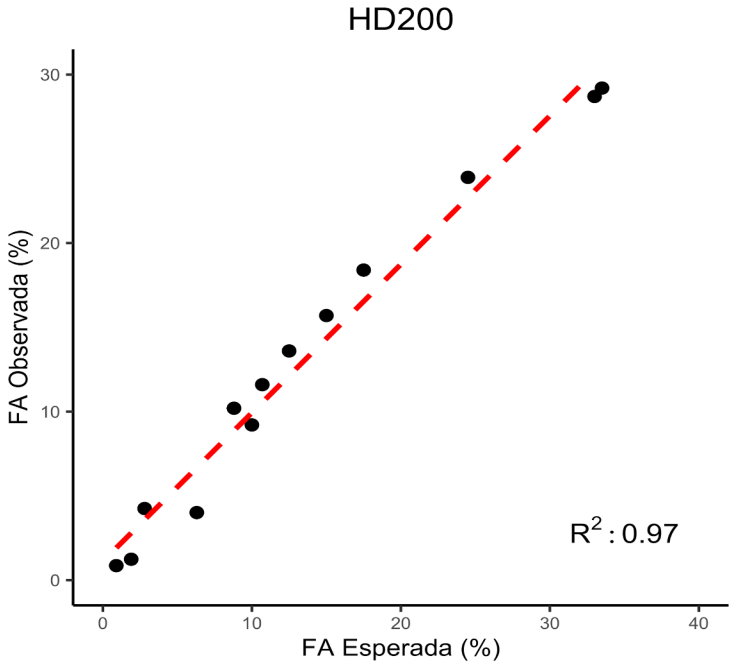
Optimization for using in FFPE tissues

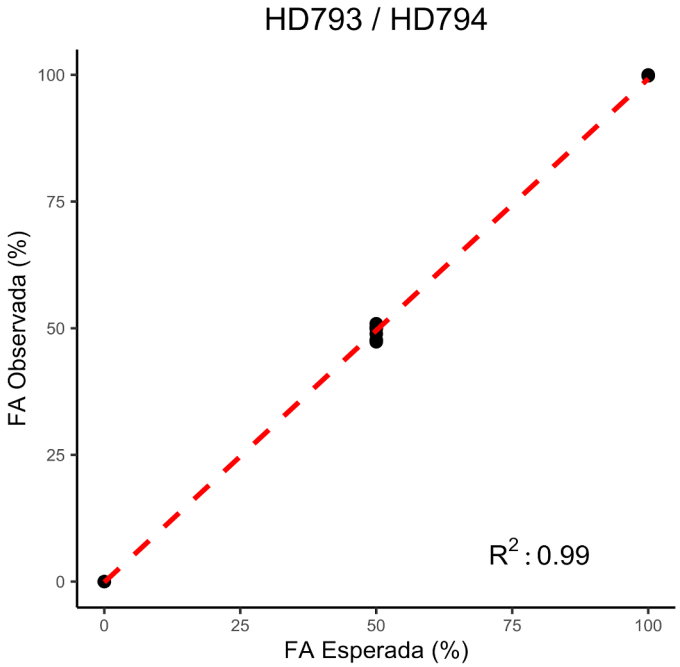
Discart germline mutations without a blood sample

TumorSec FFPE*

***FFPE**: Formalin-Fixed Paraffin Embedded tissues

Analytical Precission of TumorSec





Technical Validation

Repeatability (inter-run)

*same library, different run (3 samples)

Reproducibility (intra-run)

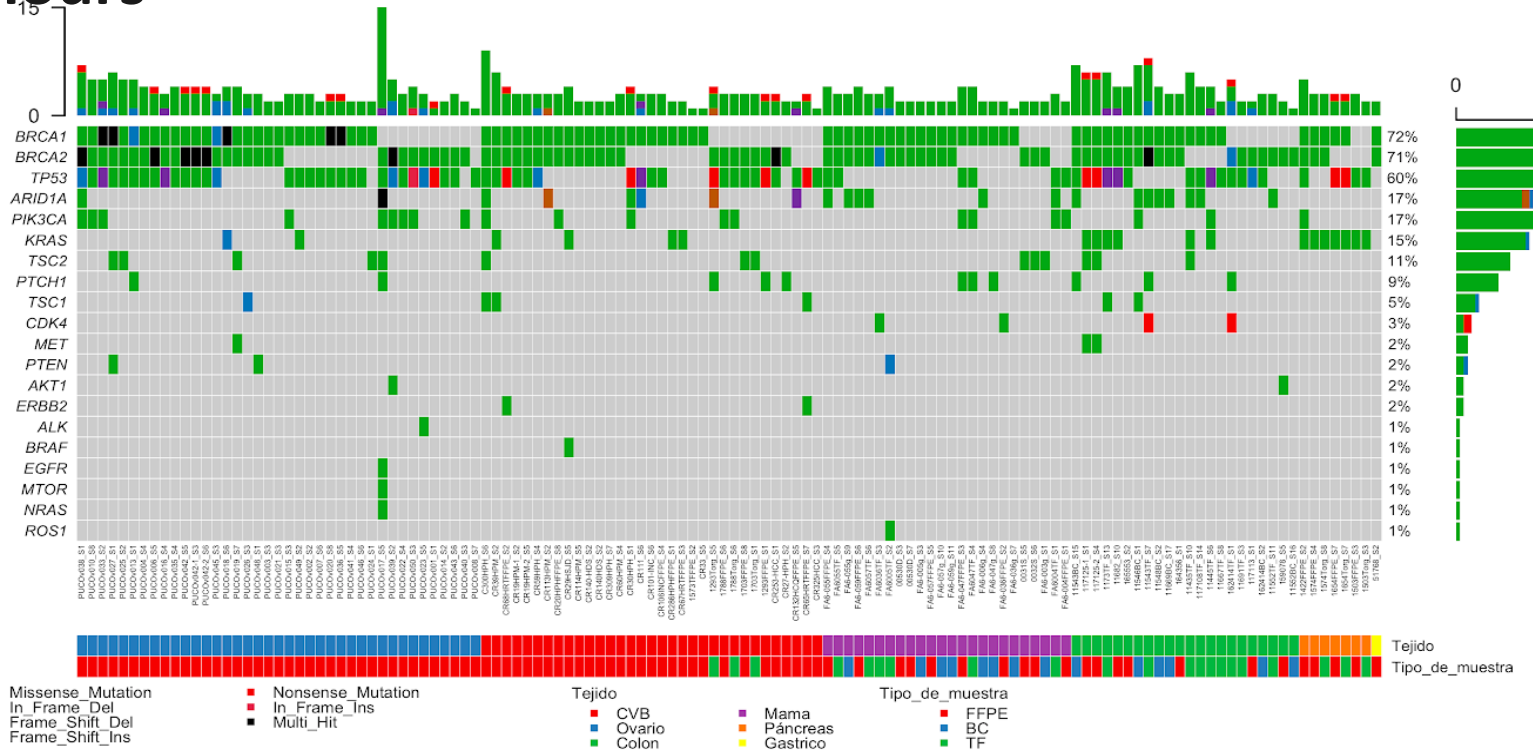
*different library, same run (3 samples)

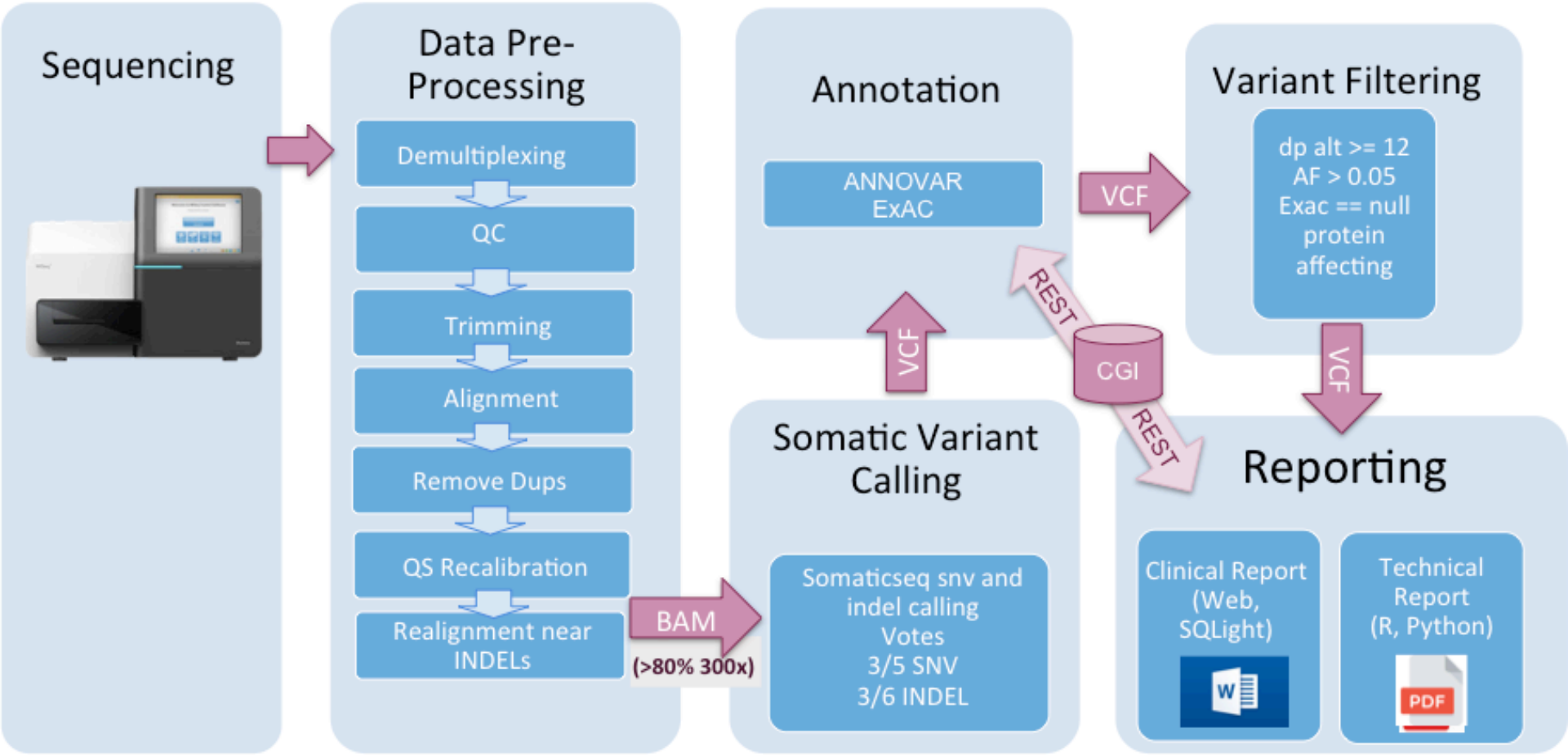
Reproducibility (inter e intra-run)

*different libraries, different runs (1 sample)

100% concordance

Identification of mutations in different types of solid tumours




Sequencing
Data Pre-Processing
Demultiplexing
QC
Trimming
Alignment
Remove Dups
QS Recalibration
Realignment near INDELs
BAM
(>80% 300x)
Somatic Variant Calling
Somaticseq snv and indel calling
Votes
3/5 SNV
3/6 INDEL
VCF
Annotation
ANNOVAR
ExAC
VCF
Variant Filtering
dp alt >= 12
AF > 0.05
Exac == null
protein affecting
VCF
REST
CGI
REST
Reporting
Clinical Report (Web, SQLight)
Technical Report (R, Python)
PDF

Laboratorio
Genómica
Del Cáncer

Reporte TumorSec: Control de calidad de los datos generados.

En el siguiente reporte se presentan diversas métricas de calidad correspondiente a la corrida 191002_TumorSec este informe fue generado el día 03/10/19 por el pipeline bioinformático de TumorSec desarollado por el laboratorio de Genómica del Cáncer, Universidad de Chile. Estas métricas representan una guía para verificar la calidad de los resultados obtenidos por cada muestra en la secuenciación.

2.- Control de calidad de la corrida:

2.1.- Información de la corrida:

Nombre kit	MiSeq Standard Reagent Kit V2
Longitud de Lecturas	2x150 bp
Maximum Output	5.1 Gb
Cantidad de Lecturas	24-30 Millones
Calidad de Lecturas	80% > Q30.
Fecha	02-10-2019
ID_Flow Cell	CGMN9
Modo	Paired End
Equipo	MiSeq
N° Serie	M03158
Ciclos	2x150
Kit Preparación Librería	SeqCap EZ HyperCap Roche
Regiones Blanco	326,00
Largo Total Regiones Blanco (pb)	88.277,00
Calidad de Lecturas	87.24 % > Q30

Tabla 1: Información de la corrida

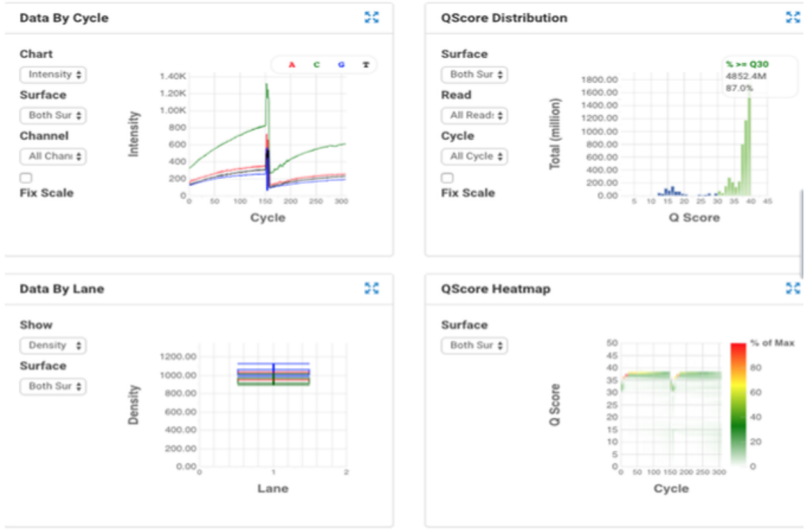
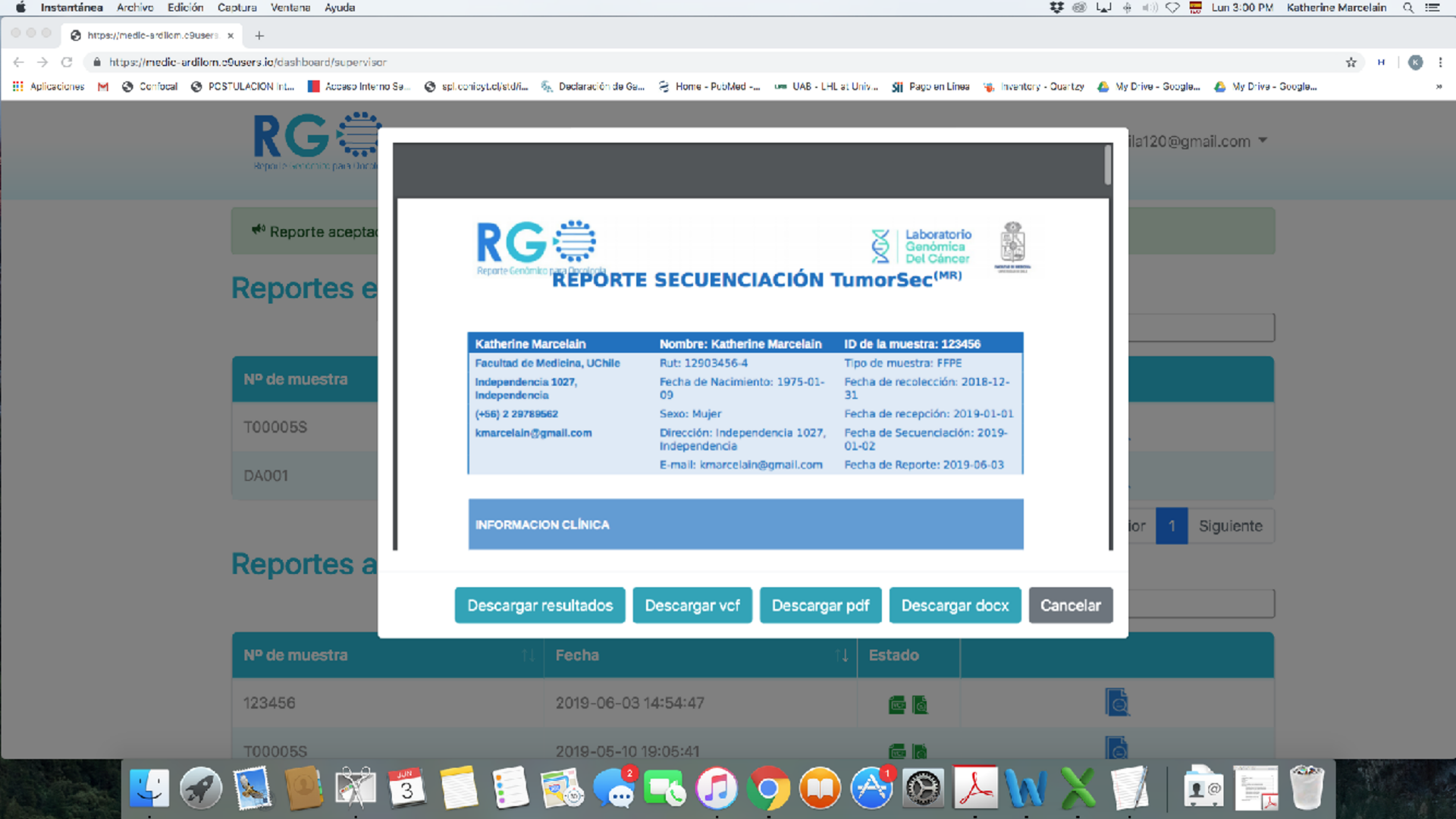


Imagen 1: Métricas de BaseSpace Illumina MiSeq.


Instantánea Archivo Edición Captura Ventana Ayuda
Lun 3:00 PM Katherine Marcelain
https://medic-ardilom.c9users.io/dashboard/supervisor
Aplicaciones Confocal PCSTULACION InL... Acceso Interno Se... spl.conicyt.cl/std/i... Declaración de Ga... Home - PubMed -... UAB - LHL at Univ... Pago en Línea Inventory - Quartzy My Drive - Google... My Drive - Google...
Reporte aceptad
Reportes e
Nº de muestra
T00005S
DA001
Siguiente
Reportes a
Nº de muestra
Fecha
Estado
123456
2019-06-03 14:54:47
T00005S
2019-05-10 19:05:41
REPORTE SECUENCIACIÓN TumorSec(MR)
Laboratorio Genómica Del Cáncer
Katherine Marcelain
Nombre: Katherine Marcelain
ID de la muestra: 123456
Facultad de Medicina, UChile
Rut: 12903456-4
Tipo de muestra: FFPE
Independencia 1027, Independencia
Fecha de Nacimiento: 1975-01-09
Fecha de recolección: 2018-12-31
(+56) 2 29789562
Sexo: Mujer
Fecha de recepción: 2019-01-01
kmarcelain@gmail.com
Dirección: Independencia 1027, Independencia
Fecha de Secuenciación: 2019-01-02
E-mail: kmarcelain@gmail.com
Fecha de Reporte: 2019-06-03
INFORMACION CLÍNICA
Descargar resultados
Descargar vcf
Descargar pdf
Descargar docx
Cancelar

Acknowledgments

DPTO. ONCOLOGIA BASICO CLINICO

- Katherine Marcelain
- Ricardo Verdugo
- Olga Barajas (Oncologist)
- Mónica Ahumada (Oncologist)
- Jessica Toro (Bq)
- Evelin González (Bioinformatician)
- Paola González (Tech)
- Daniela Diez (Study coordinator)
- Valentina Garate (Study coordinator GBC)
- Ignacio Maureira (Ms. Genetics)
- Nicolás Miranda (Ms Genetics)
- Nicole Castillejo (Student)
- Vania Montecinos (Study Coordinator Assistant)

Roche

- Mauricio Salvo

ISPCH Instituto de Salud Pública

- Jorge Fernández
- Profesionales Lab. De Genética Molecular ISP.

BTUCH BIOBANCO DE TEJIDOS Y FLUIDOS UNIVERSIDAD DE CHILE

- Iván Gallegos (Pathologist)
- Alicia Colombo (Biobank Director)
- Profesionales Biobanco.

FALP Juntos contra el cáncer

- Eva Bustamante (PhD)
- Ana María Carrasco (MD)
- Johanna Wettlin
- Equipo médico

Federal Ministry of Education and Research

CONICYT Ministerio de Educación Gobierno de Chile

FONDEF Fondo de Fomento al Desarrollo Científico y Tecnológico

CEMP

Pfizer

Roche