

Estudios moleculares en cáncer ¿Qué necesitamos saber?

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Laboratorio de Diagnóstico Molecular y Biomarcadores

Servicio de Anatomía Patológica

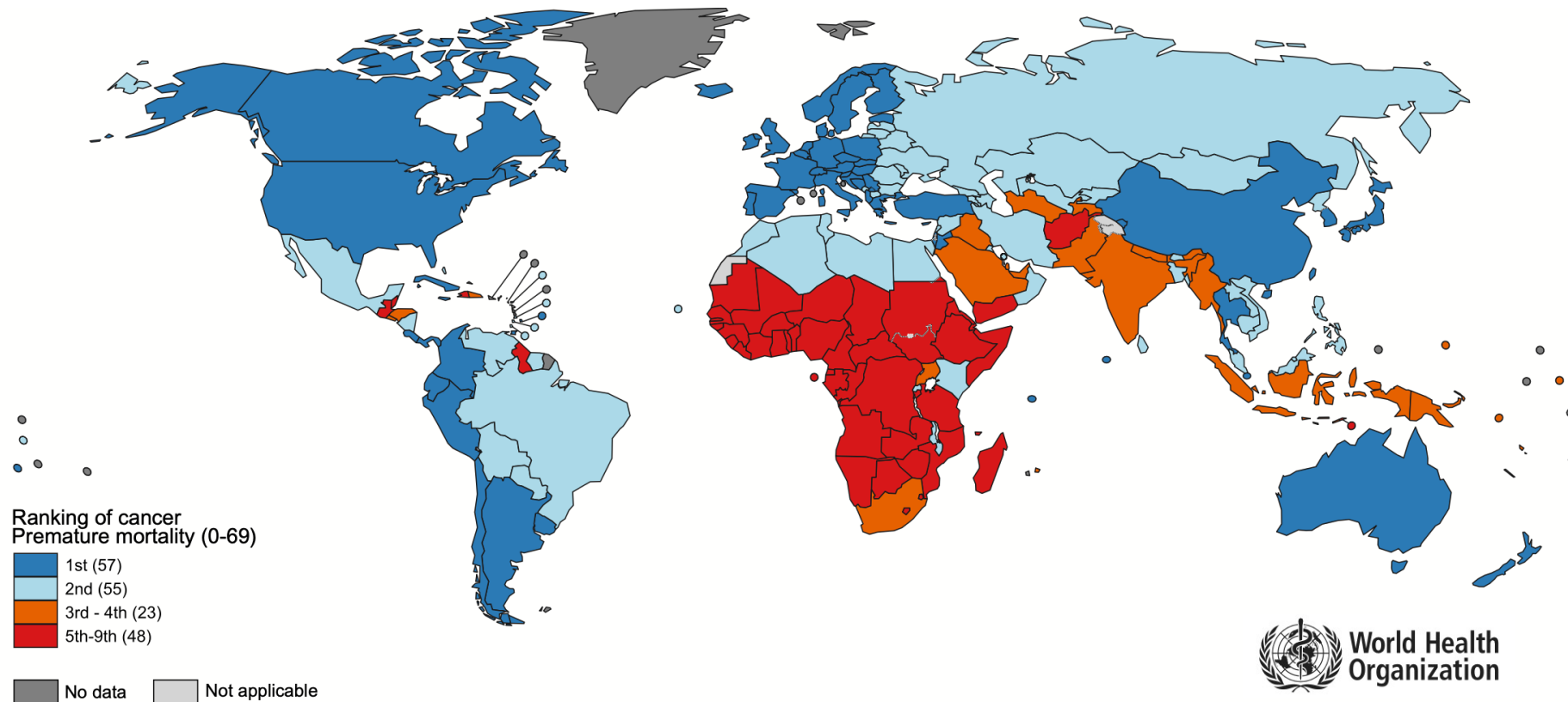
Clínica Alemana de Santiago

Declaración de intereses

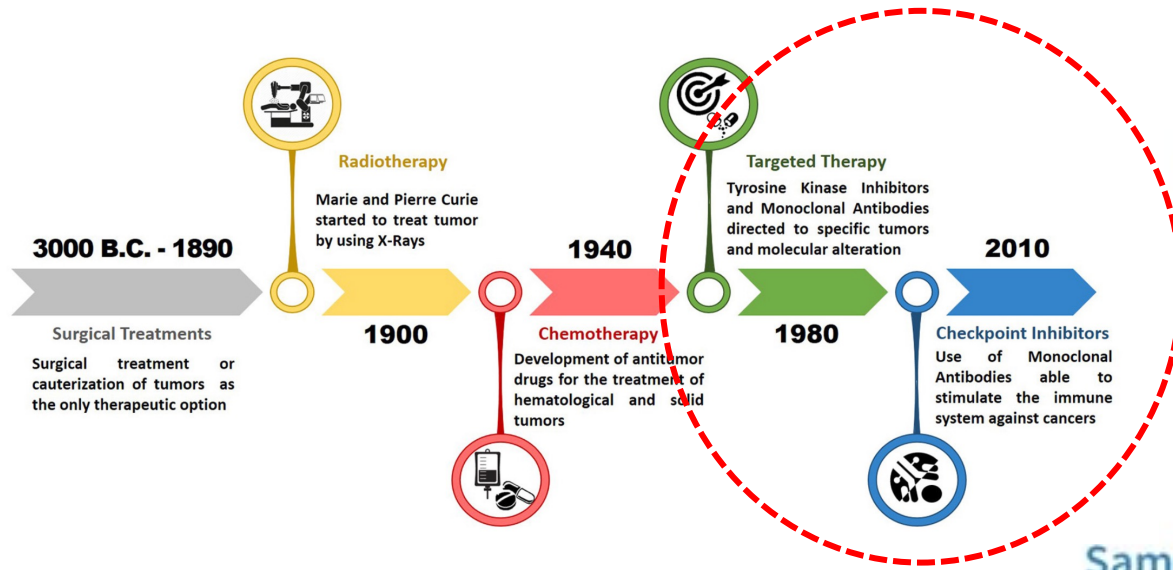
- Declaro no tener conflicto de interés en esta presentación

Cáncer

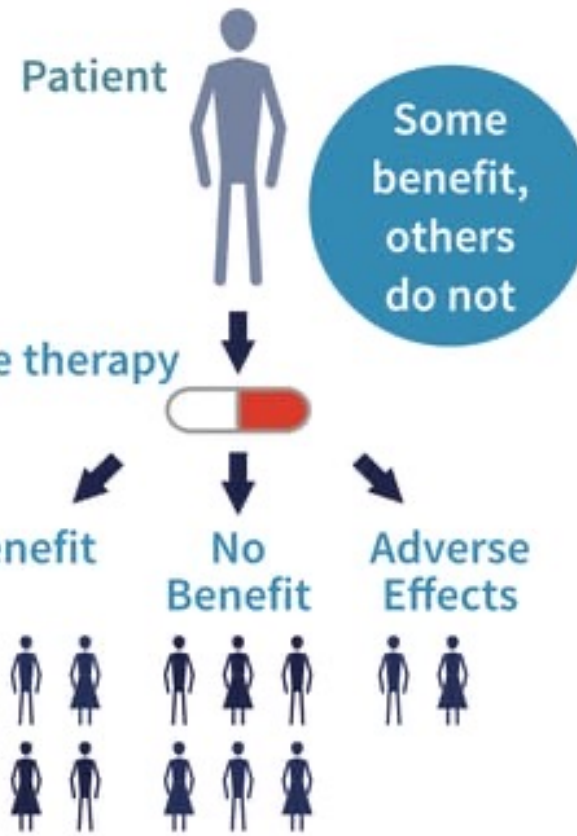
- Una de las principales causas de muerte a nivel mundial, 10 millones de muertes en 2020.
- Se estiman 19.3 MM de nuevos casos en 2020 y 28.4 MM en 2040.



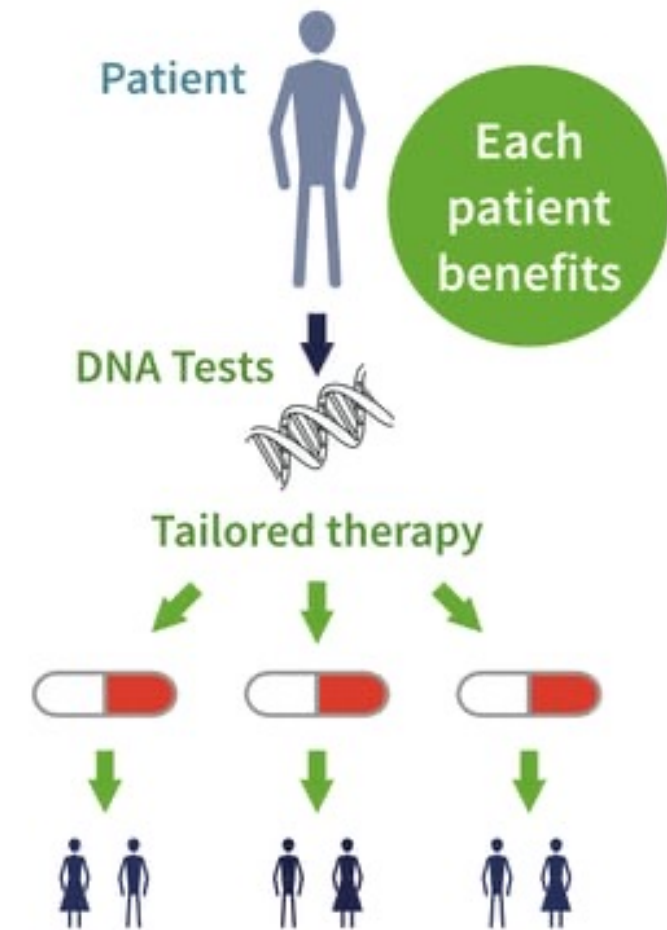
Medicina de precisión



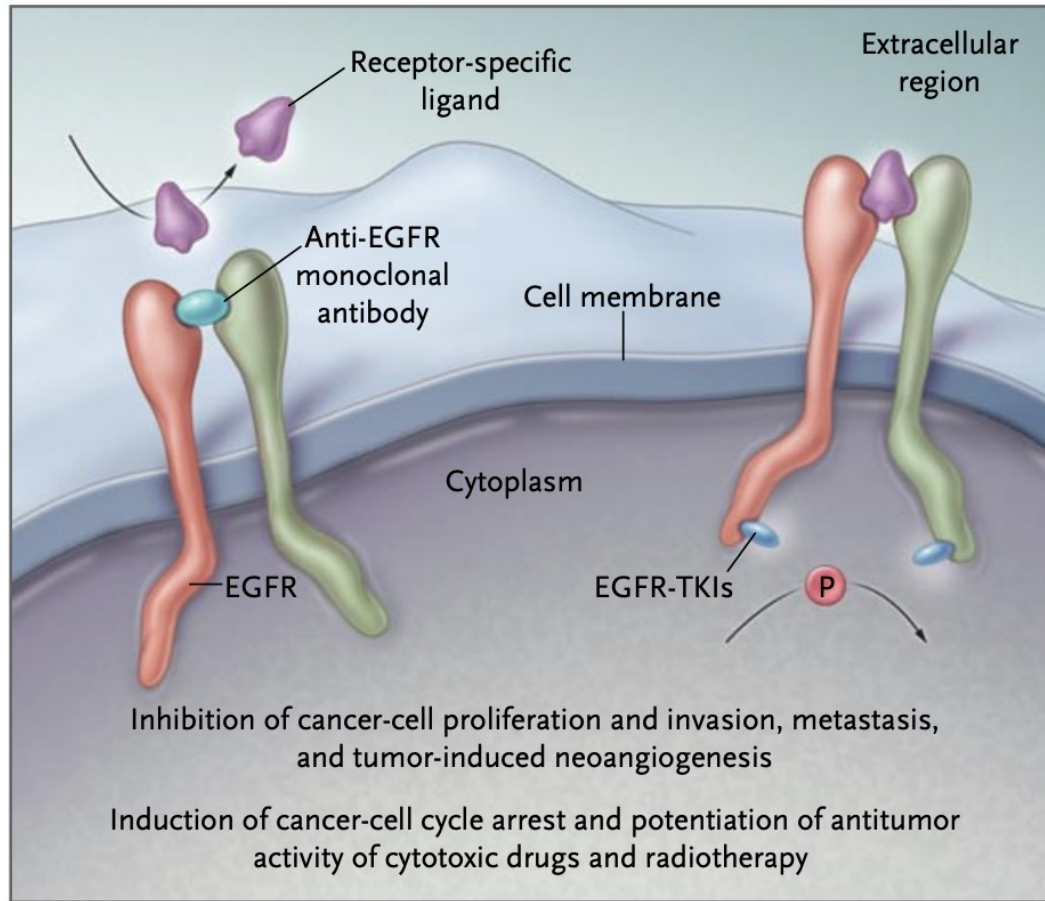
Without precision medicine



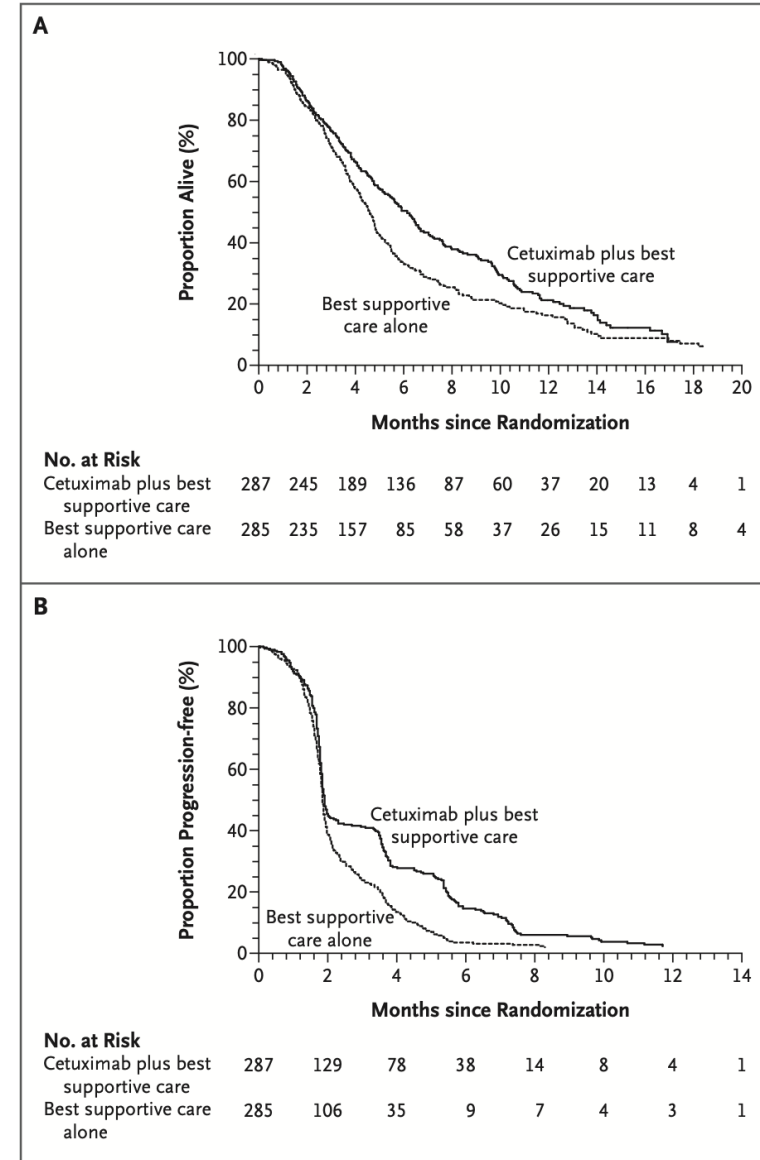
With precision medicine



Medicina de precisión

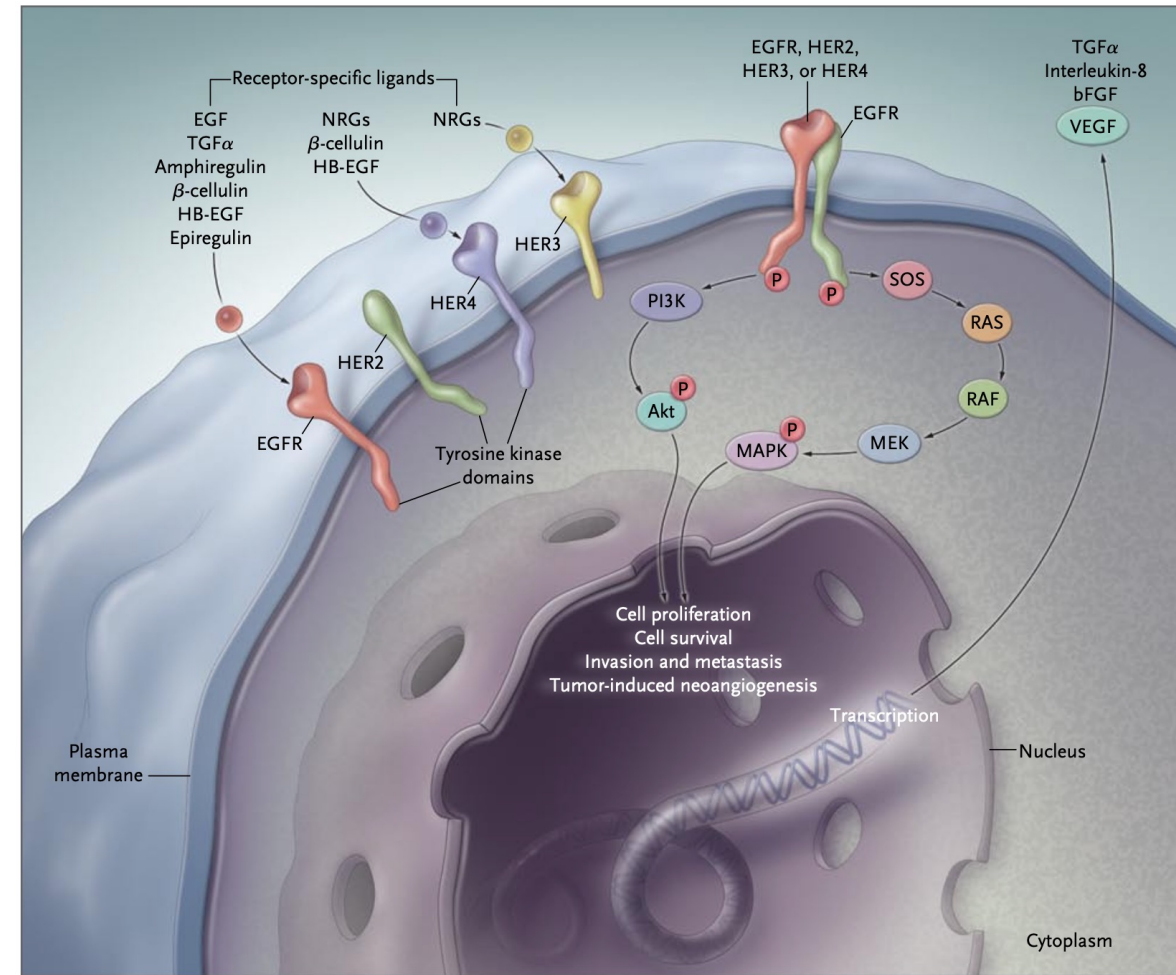
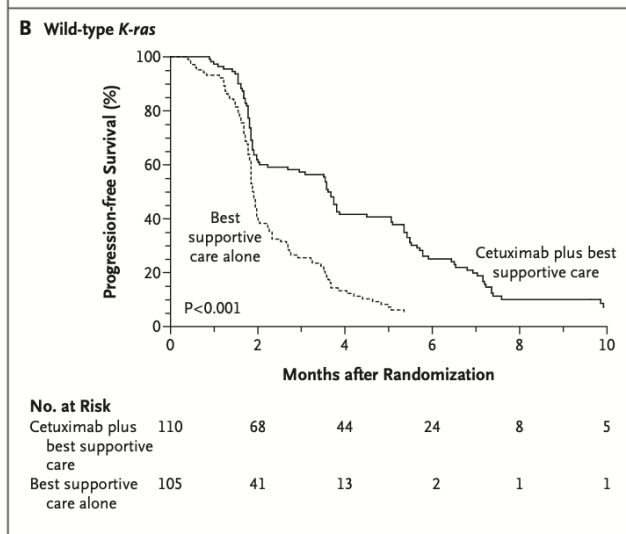
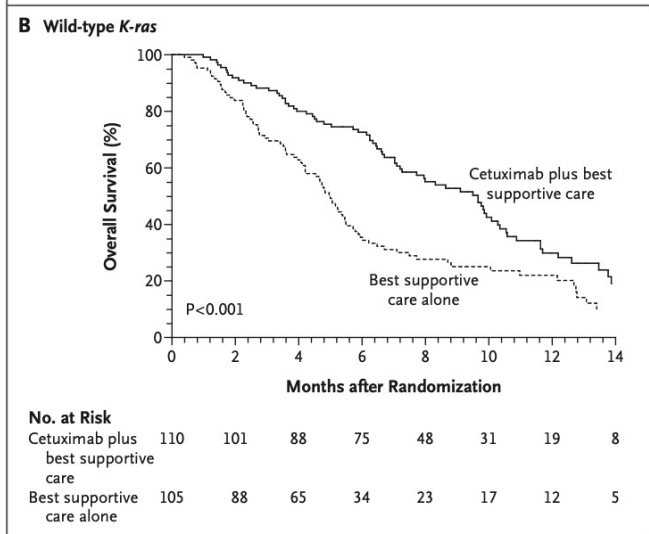
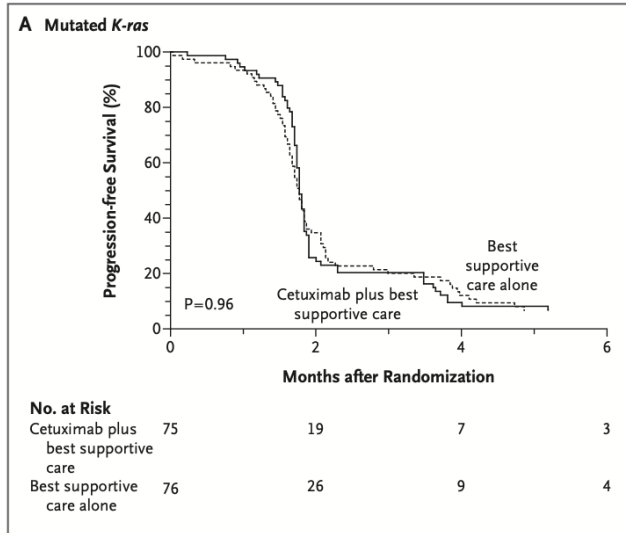
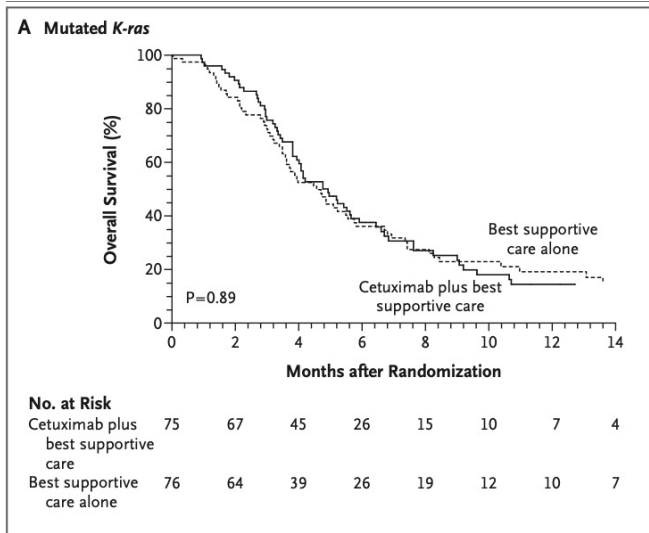


Ciardello et al. N Engl J Med 2008

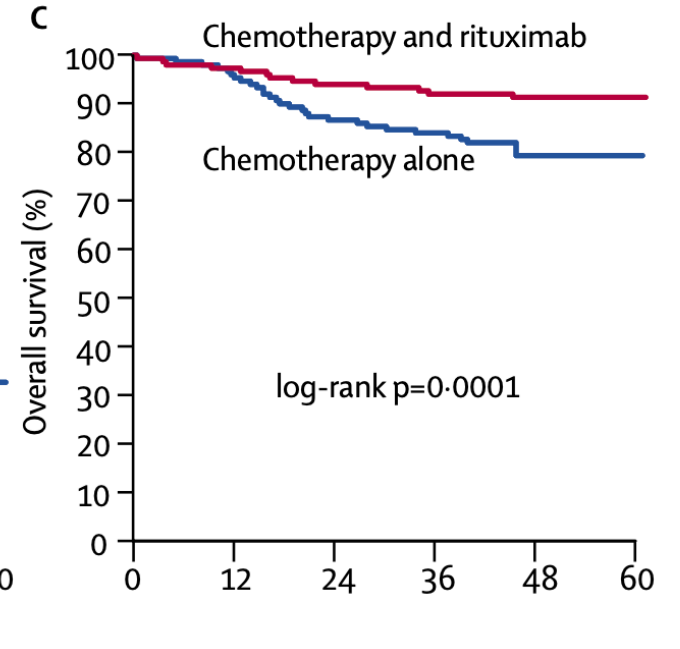
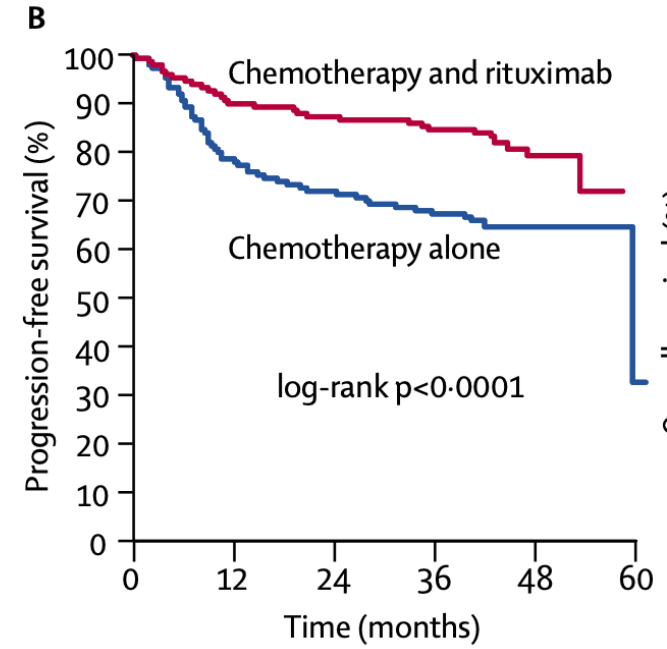
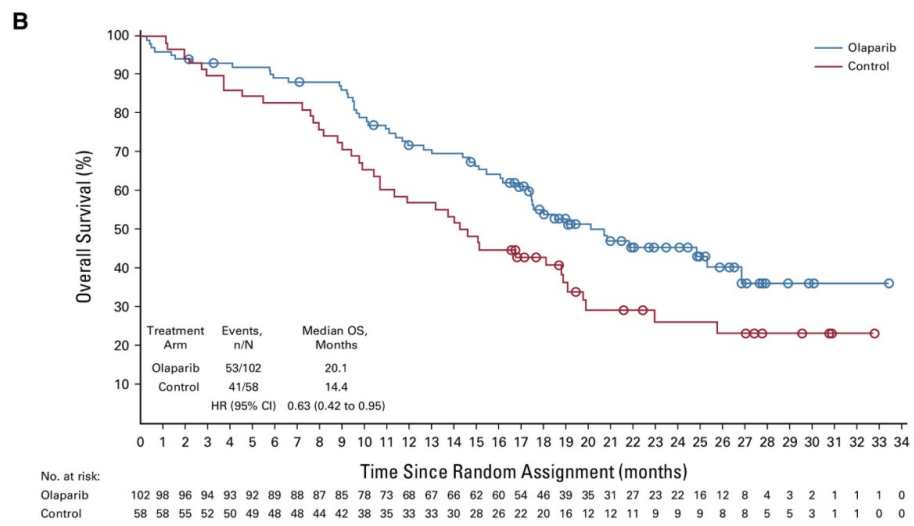
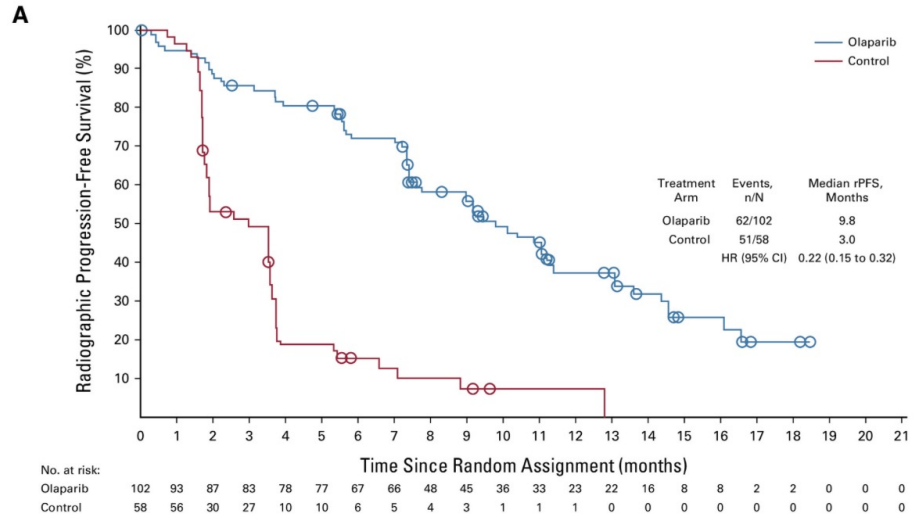


Jonker et al. N Engl J Med 2007

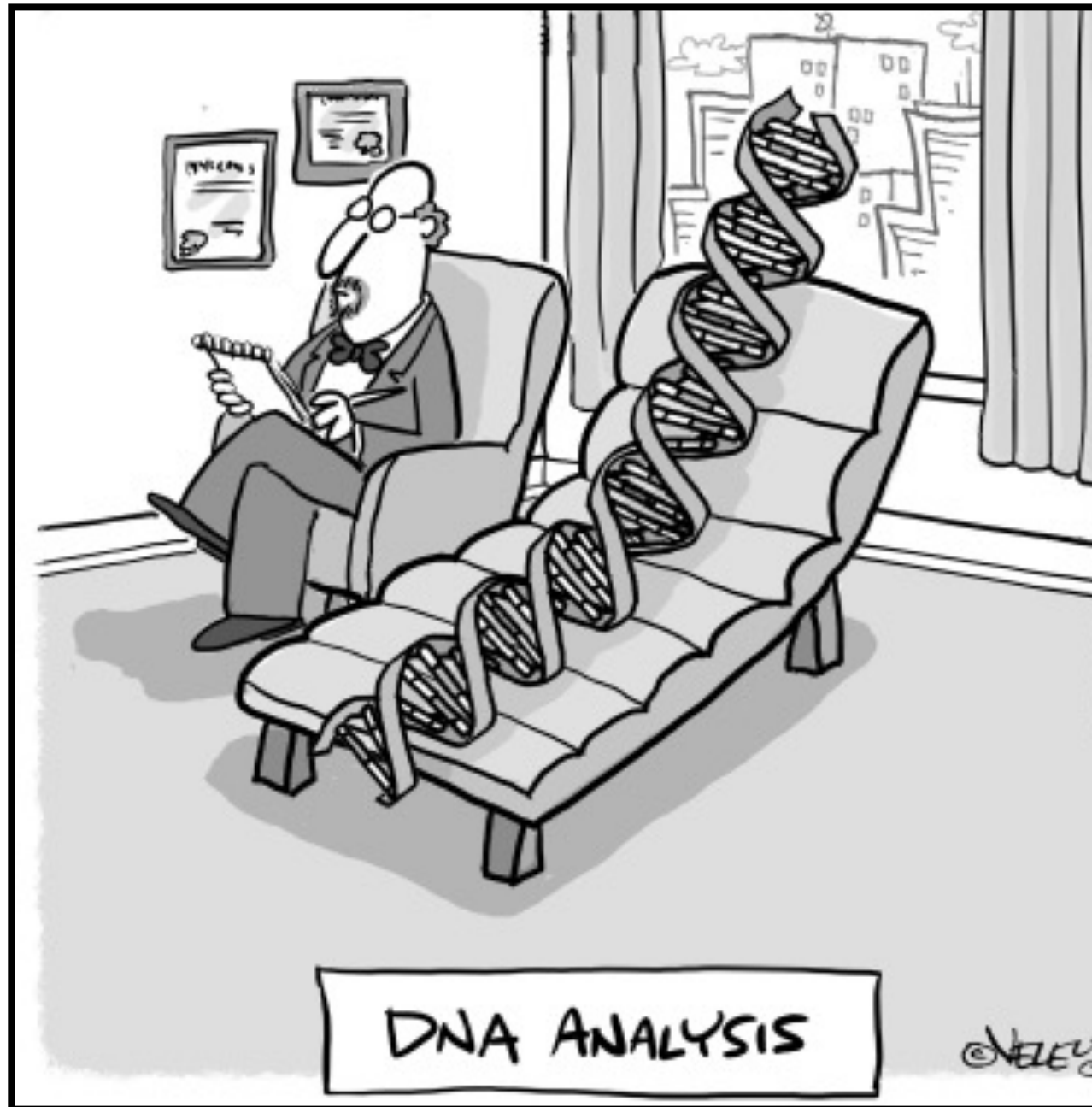
Medicina de precisión



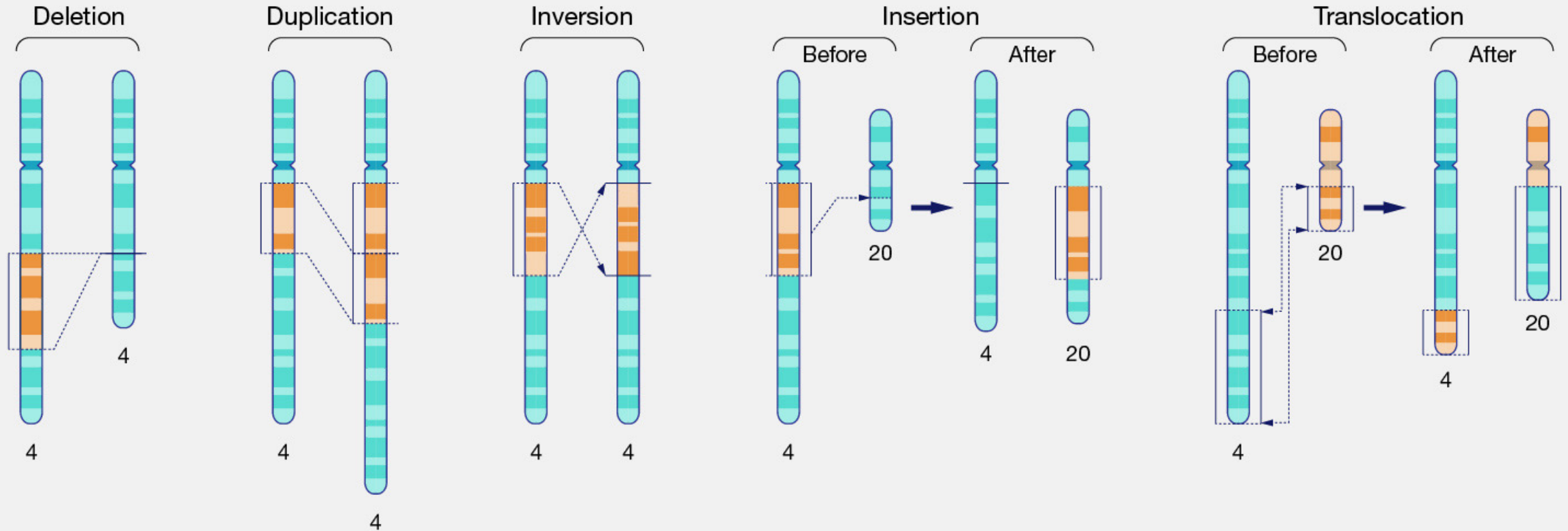
Medicina de precisión



Pfreundschuh et al. Lancet Oncol 2006



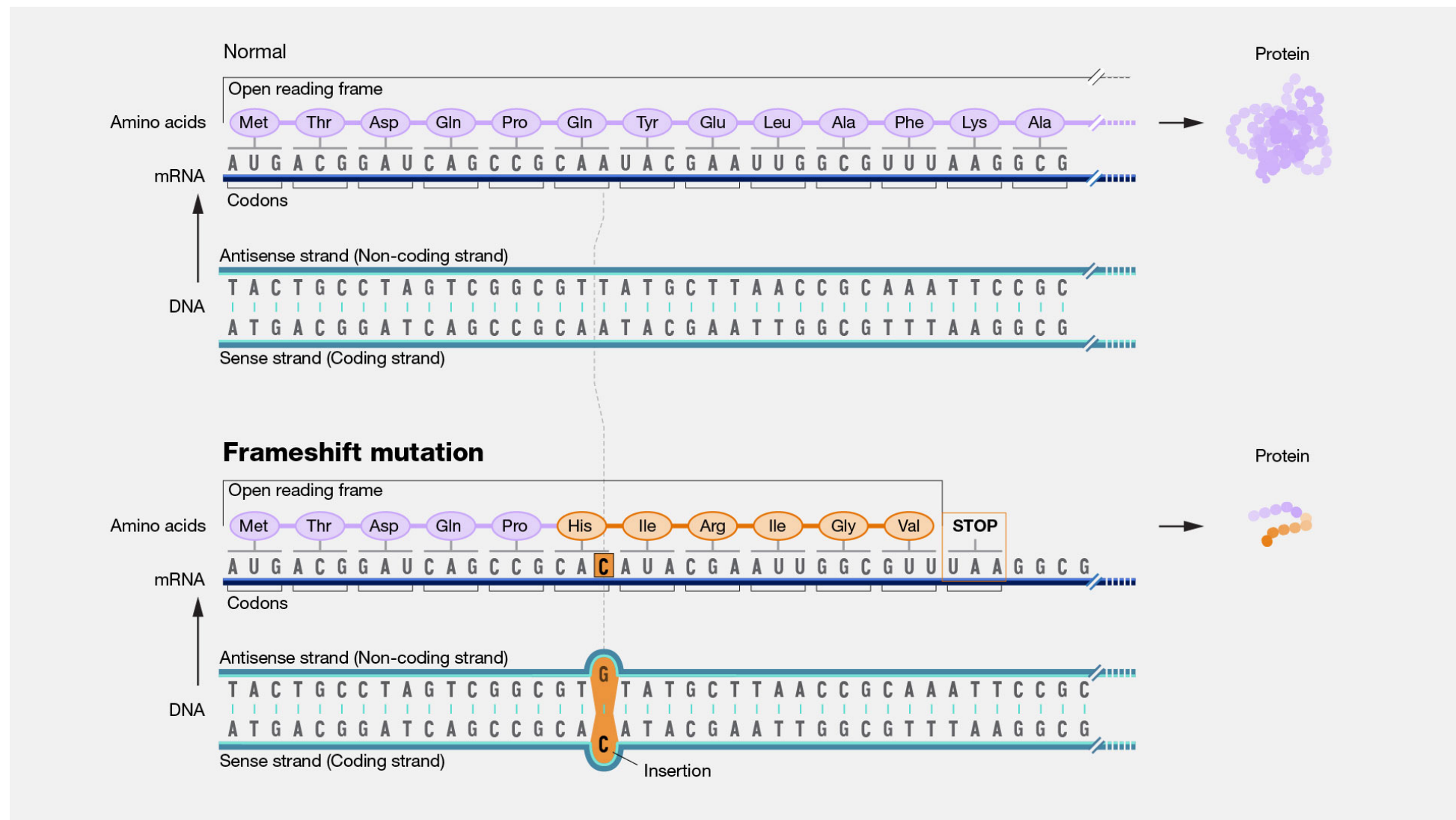
Alteraciones genéticas en cáncer



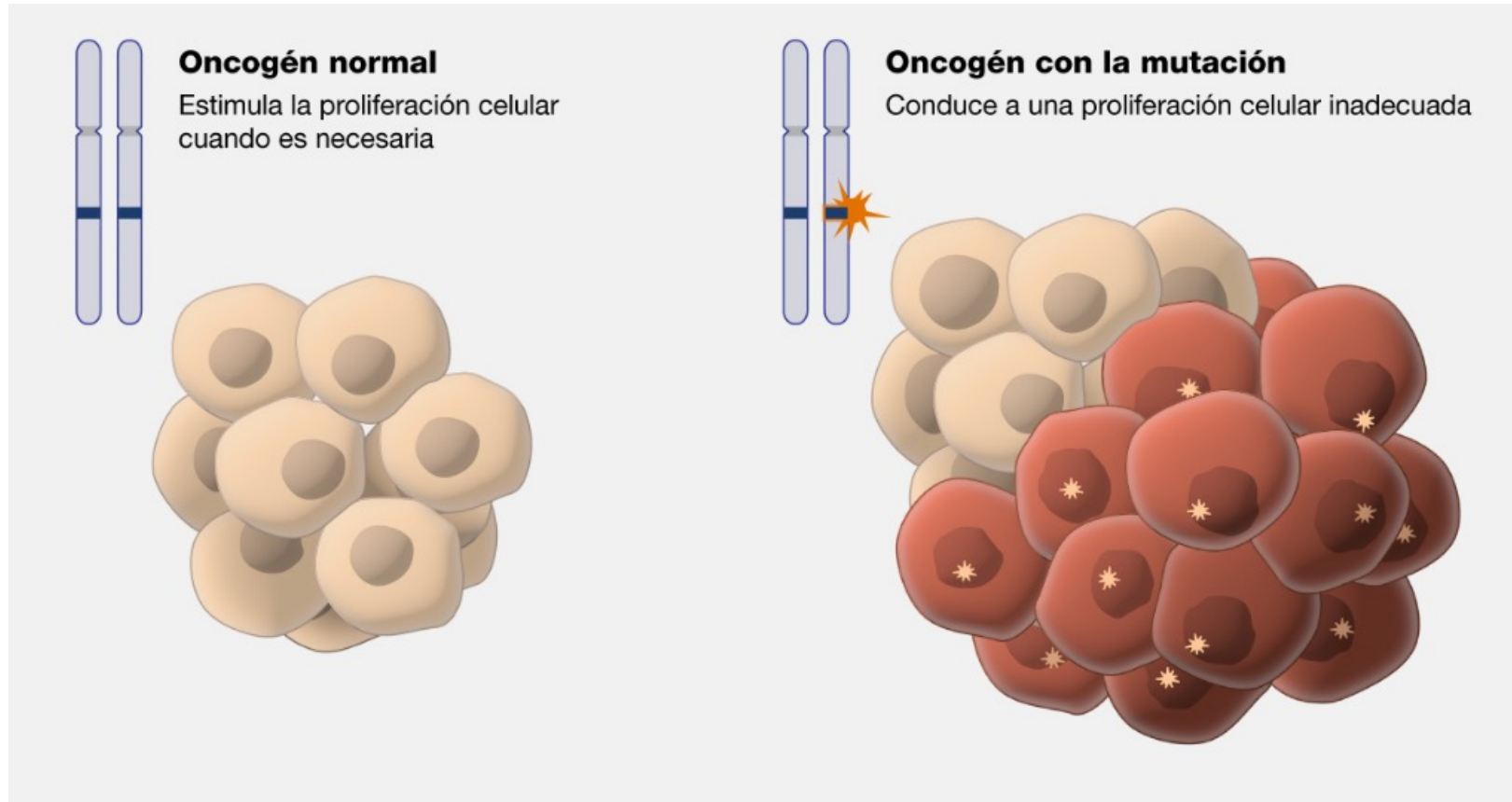
Alteraciones genéticas en cáncer



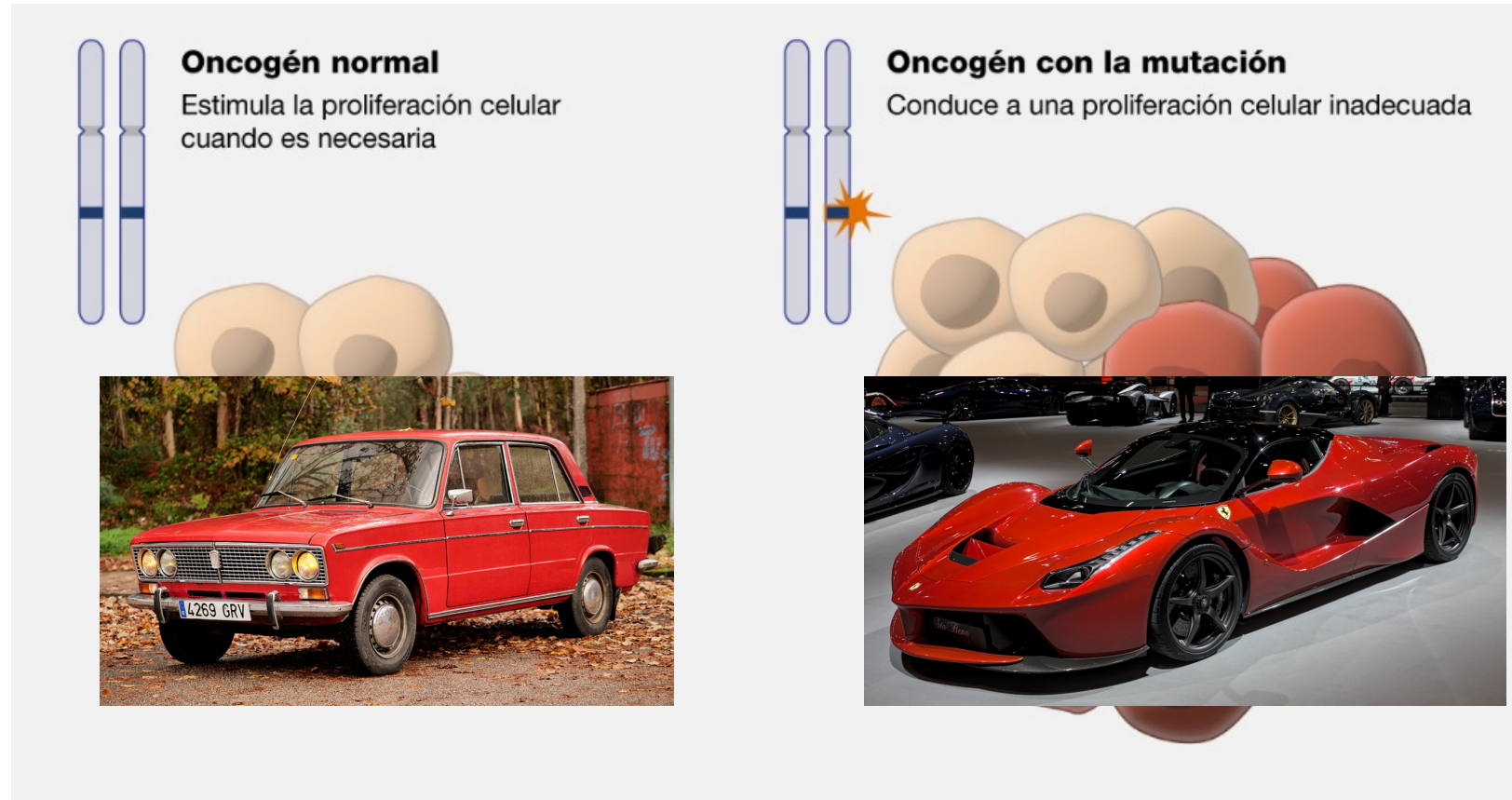
Alteraciones genéticas en cáncer



Efecto de alteraciones genéticas



Efecto de alteraciones genéticas



The diagram is split into two panels. The left panel shows two normal chromosomes with a blue band on the lower arm, representing a normal oncogene. Below them are two simple, round cells. A photograph of a red Lada sedan is shown at the bottom. The right panel shows two chromosomes with a blue band on the lower arm and a yellow starburst on the upper arm, representing a mutated oncogene. Below them is a cluster of several larger, more irregular cells. A photograph of a red Ferrari sports car is shown at the bottom.

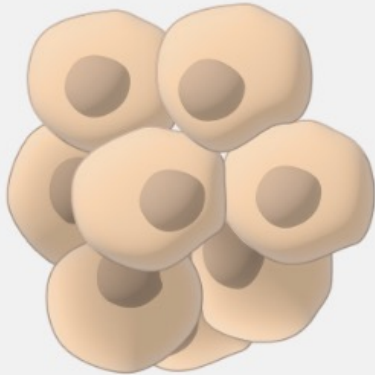
Oncogén normal
Estimula la proliferación celular cuando es necesaria

Oncogén con la mutación
Conduce a una proliferación celular inadecuada

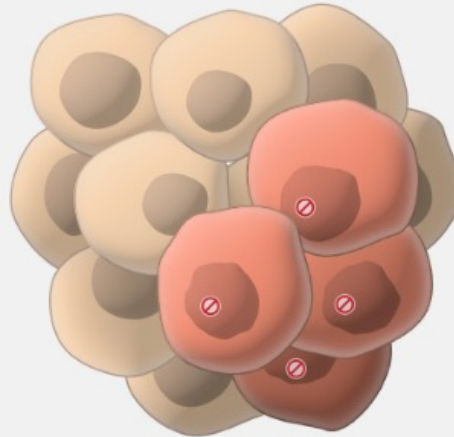
Efecto de alteraciones genéticas

Gen supresor de tumores normal

Retrasa la proliferación celular

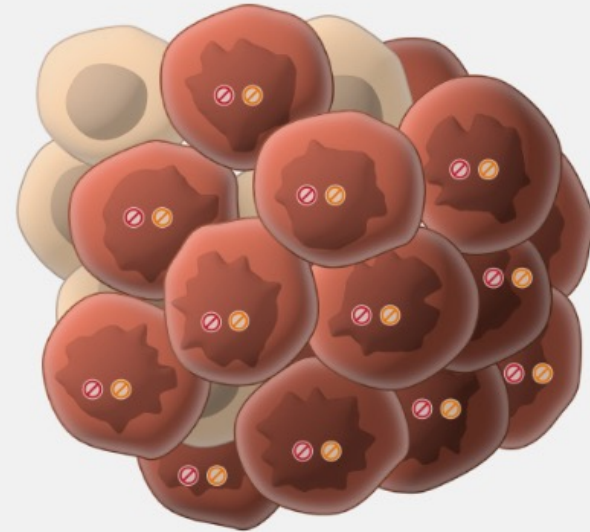


Un gen supresor de tumores con la mutación



Dos genes supresores de tumores con la mutación

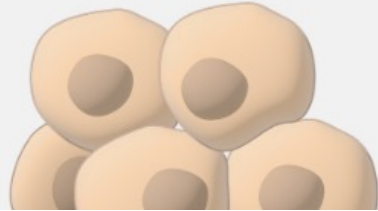
Genera imposibilidad de detener la proliferación celular



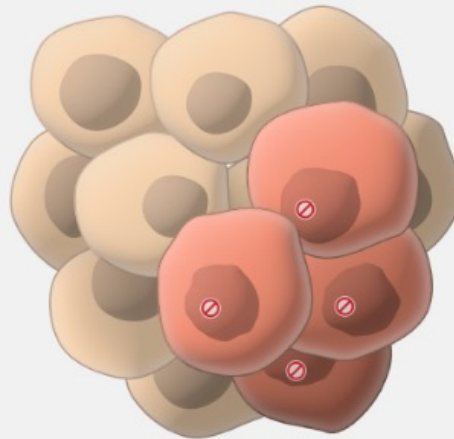
Efecto de alteraciones genéticas

Gen supresor de tumores normal

Retrasa la proliferación celular

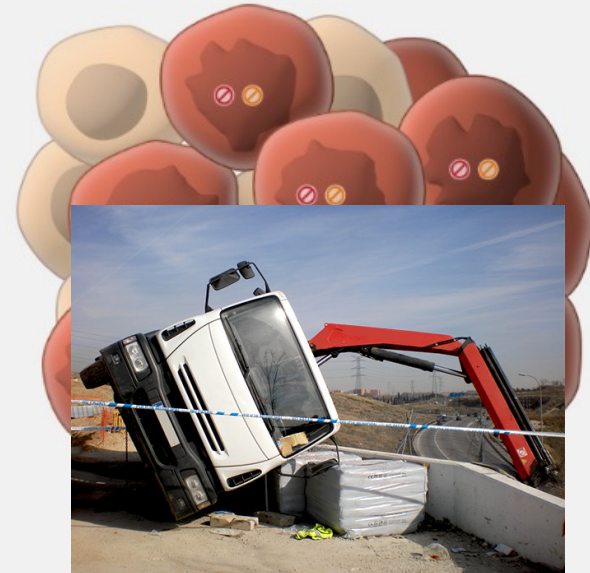


Un gen supresor de tumores con la mutación



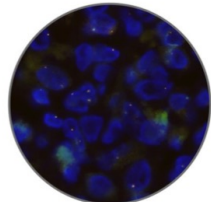
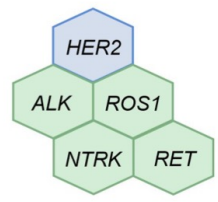
Dos genes supresores de tumores con la mutación

Genera imposibilidad de detener la proliferación celular




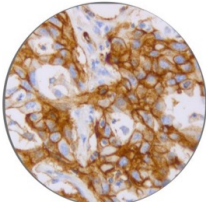
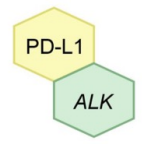
¿Cómo se estudian las alteraciones?

FISH: chromosomes

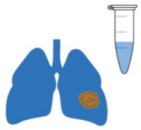
- fusions
- amplifications

IHC: proteins

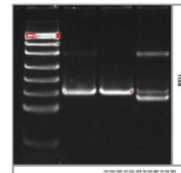
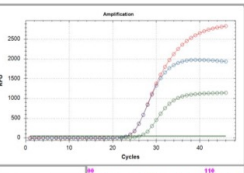
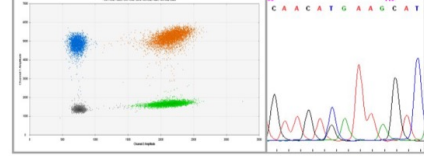




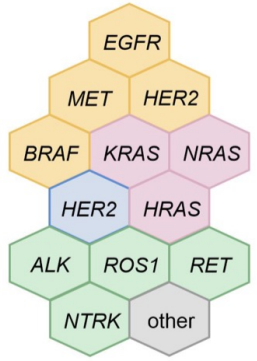
- expression
- fusions

PCR: DNA/RNA

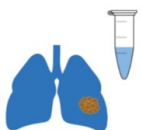


- micromutations
- fusions
- amplifications


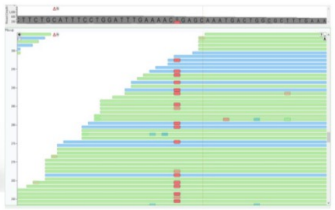




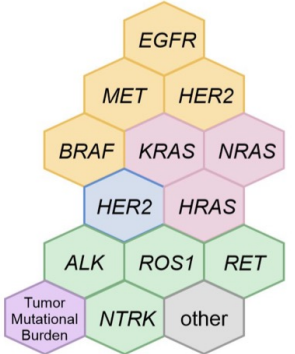


NGS: DNA/RNA

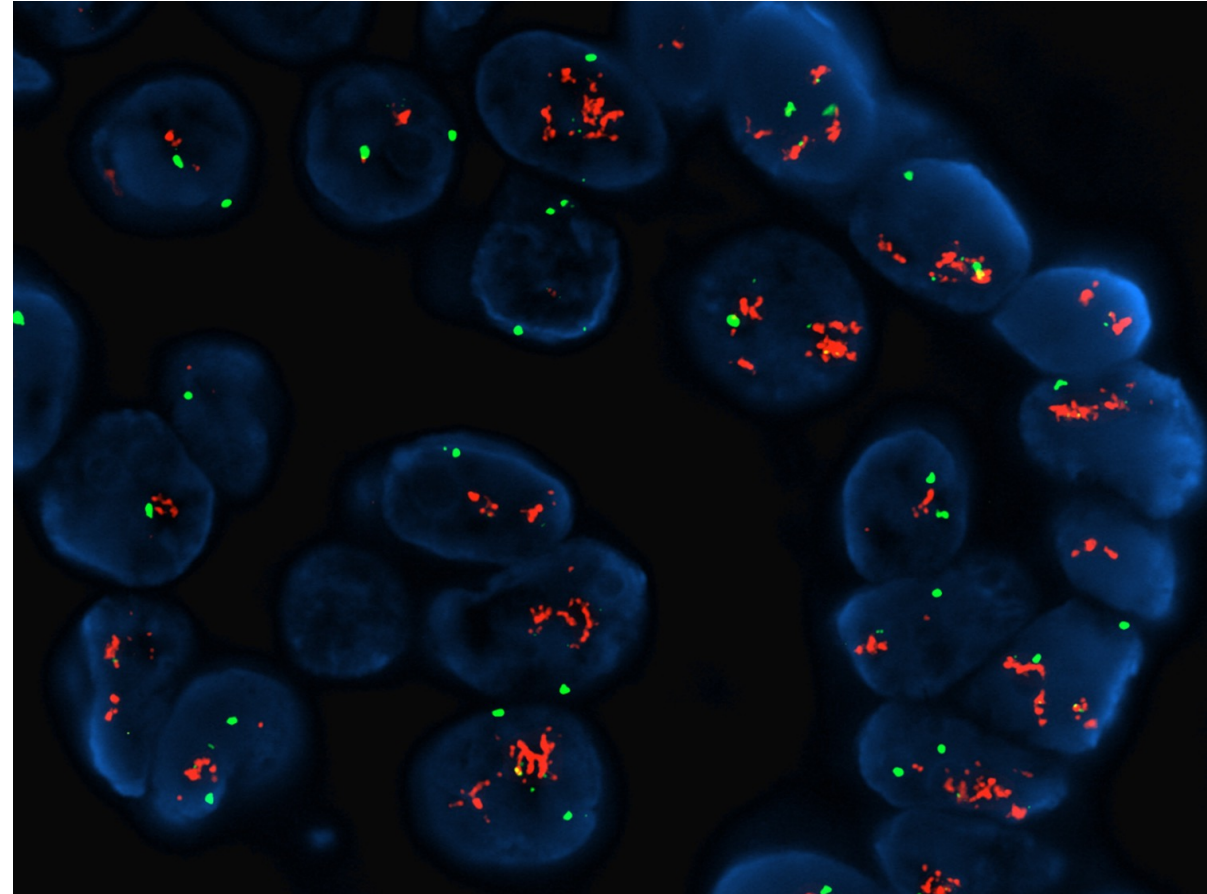
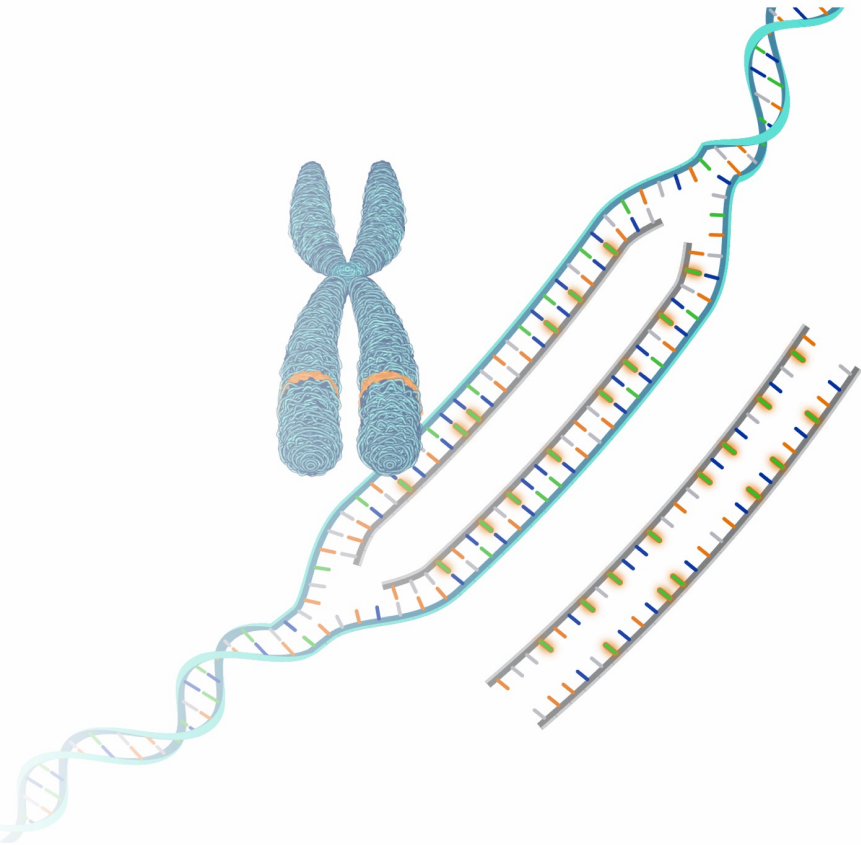


- micromutations
- fusions
- amplifications
- genetic profile

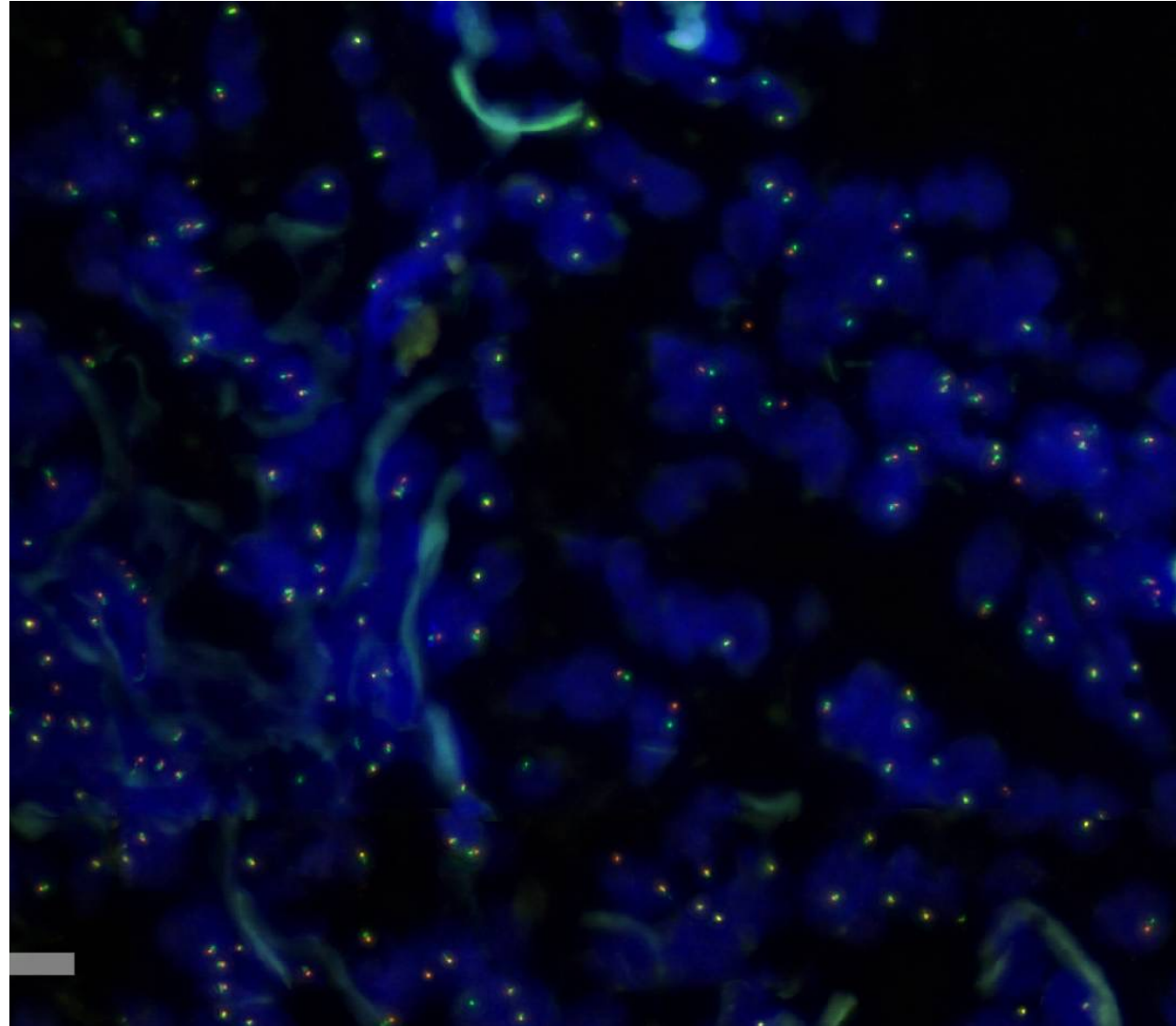
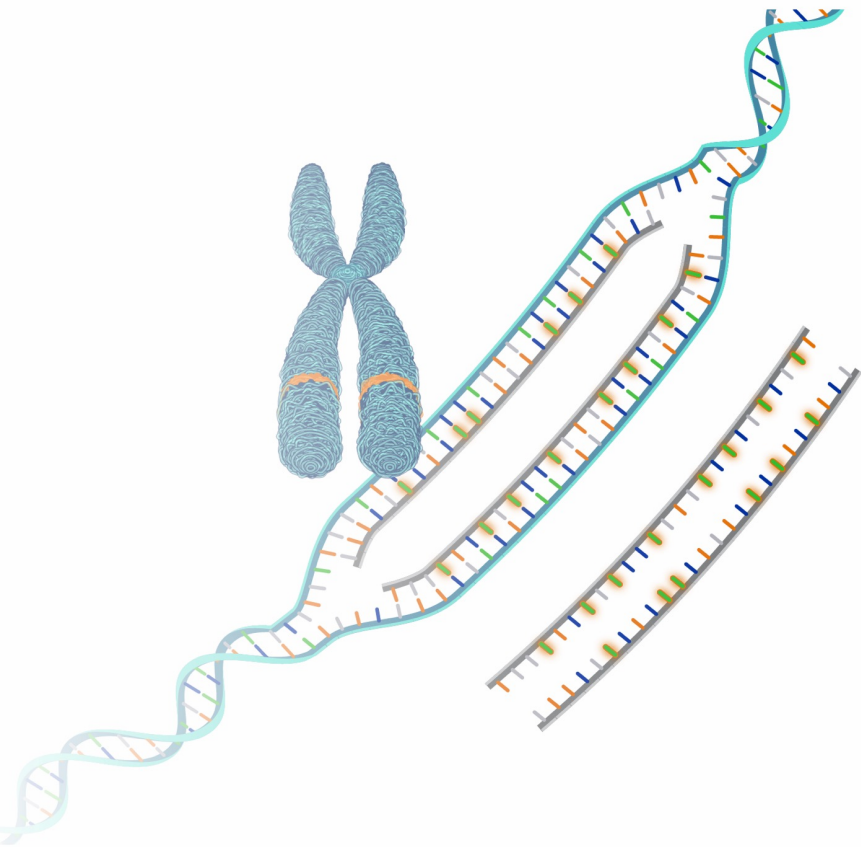


Hibridación in-situ fluorescente

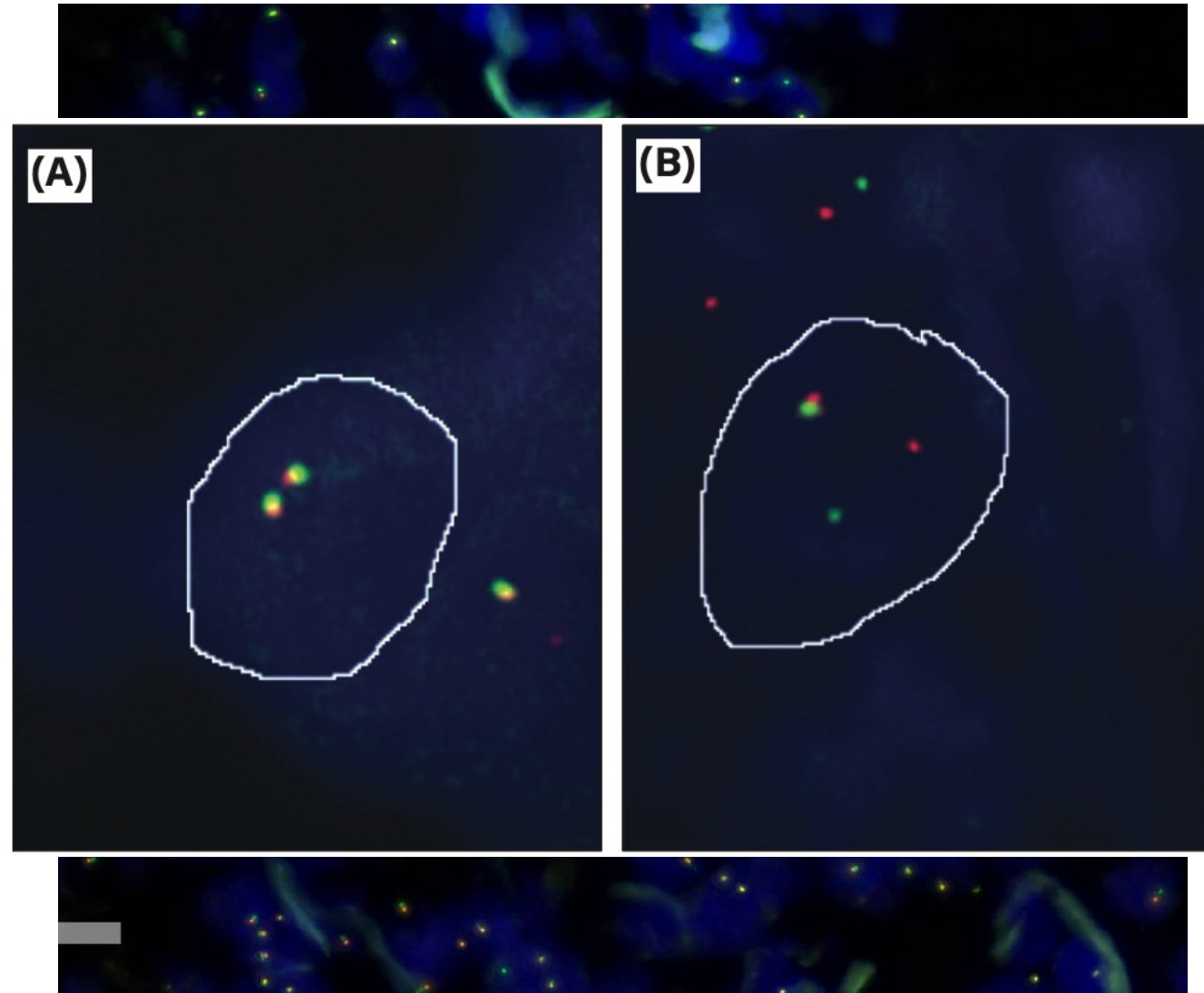
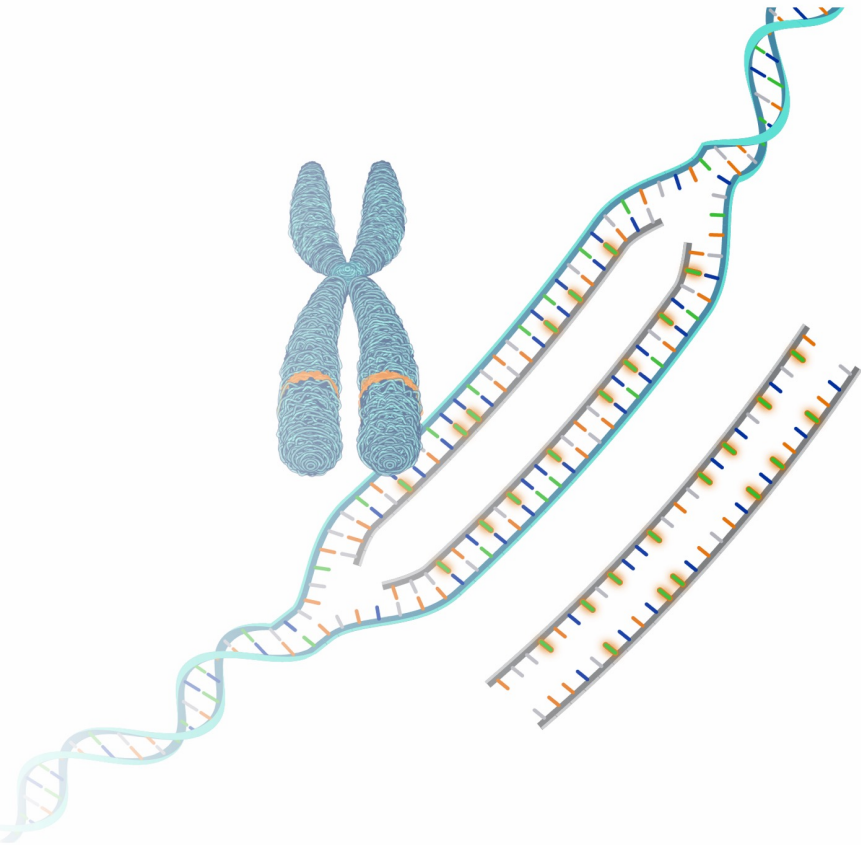


FISH Her2 DAKO

Hibridación in-situ fluorescente

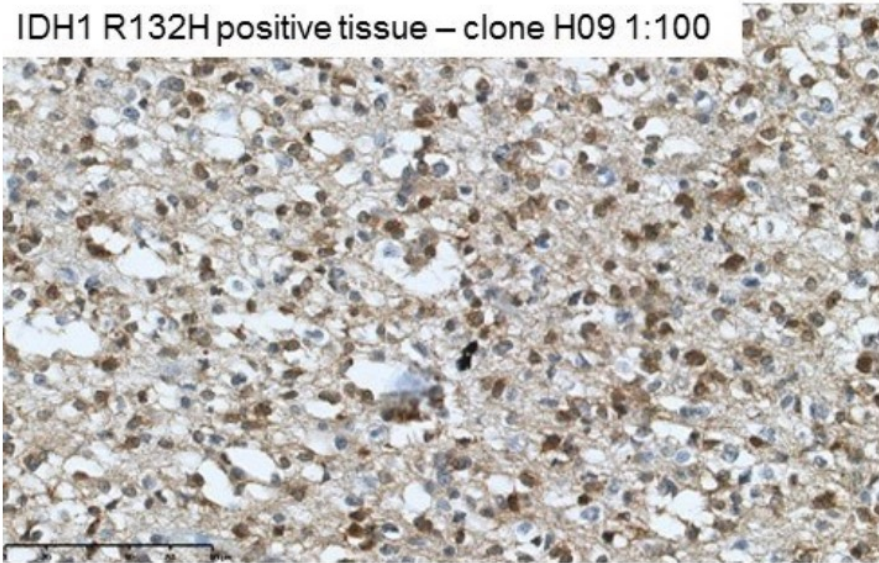


Hibridación in-situ fluorescente

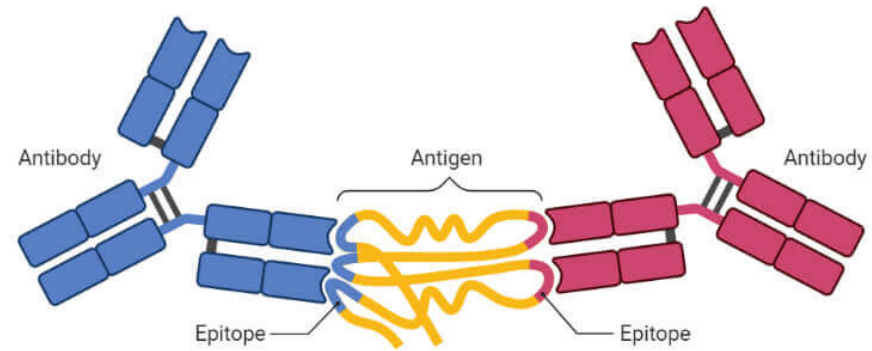
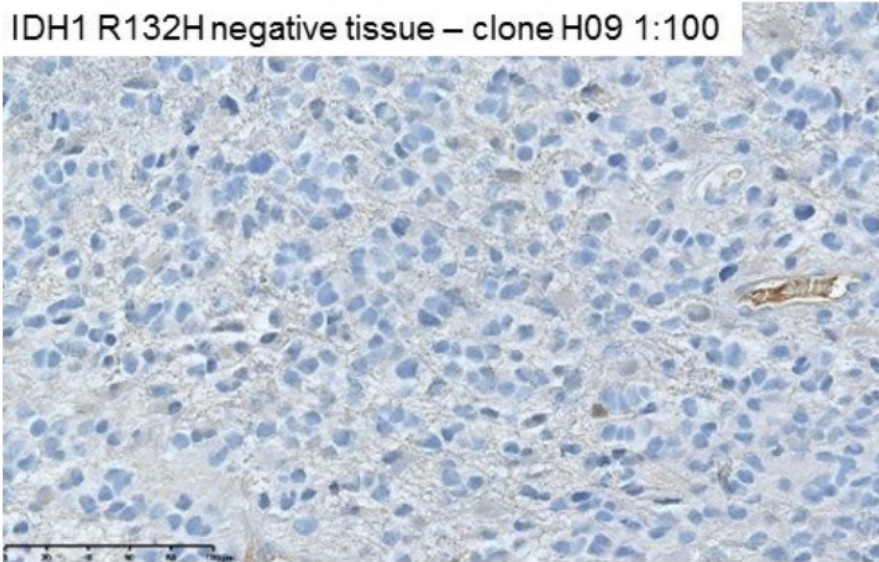


Inmunohistoquímica

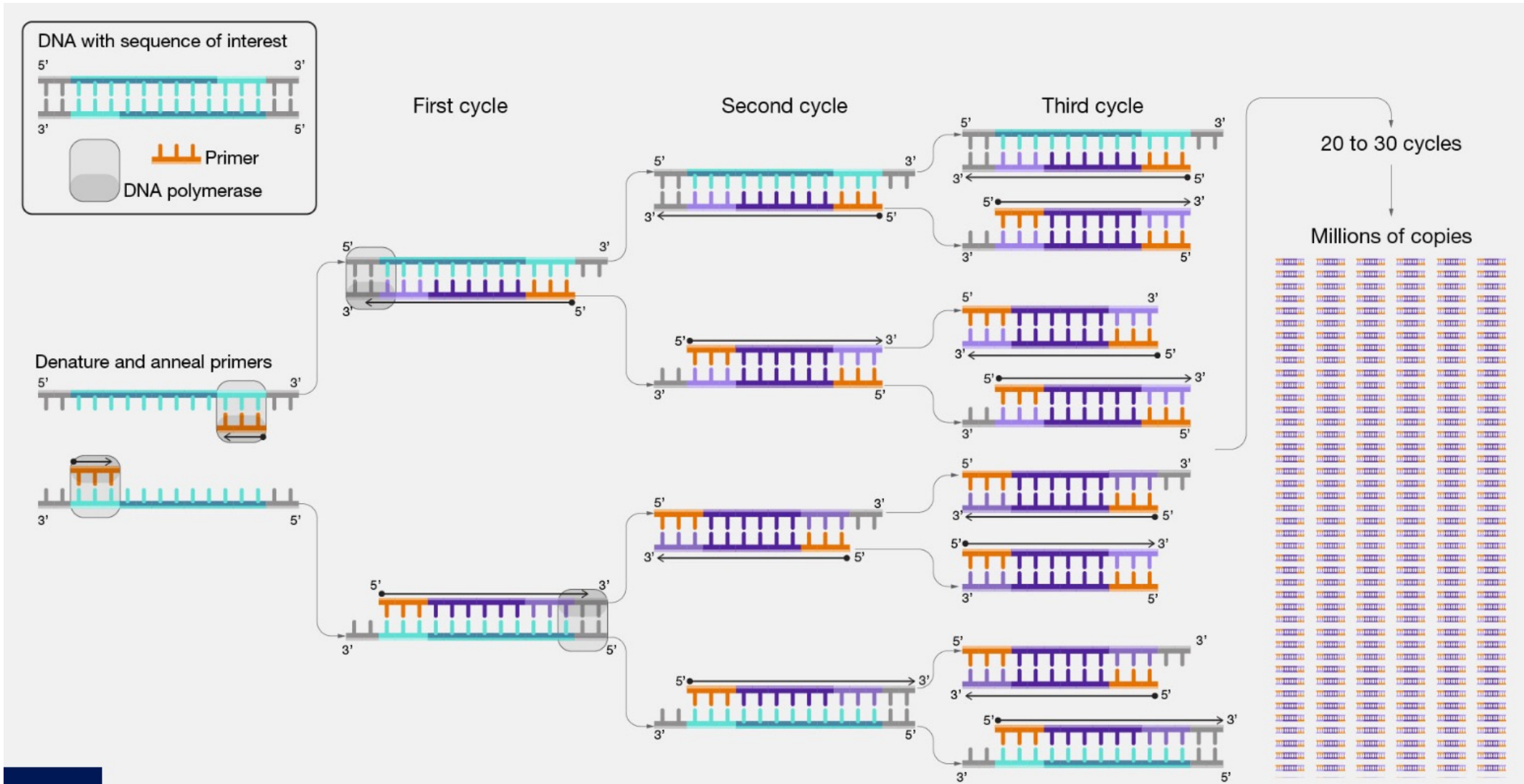
IDH1 R132H positive tissue – clone H09 1:100



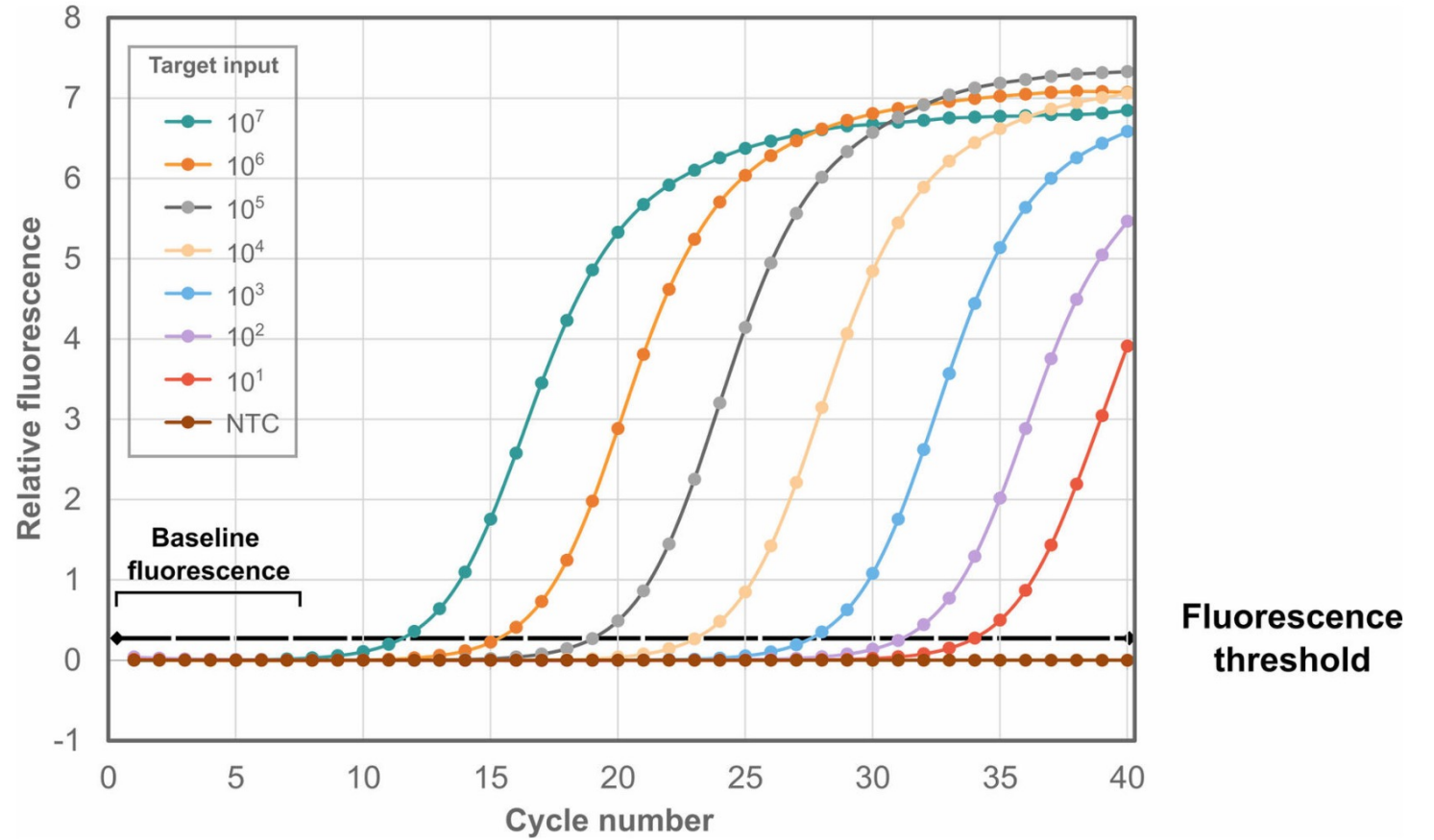
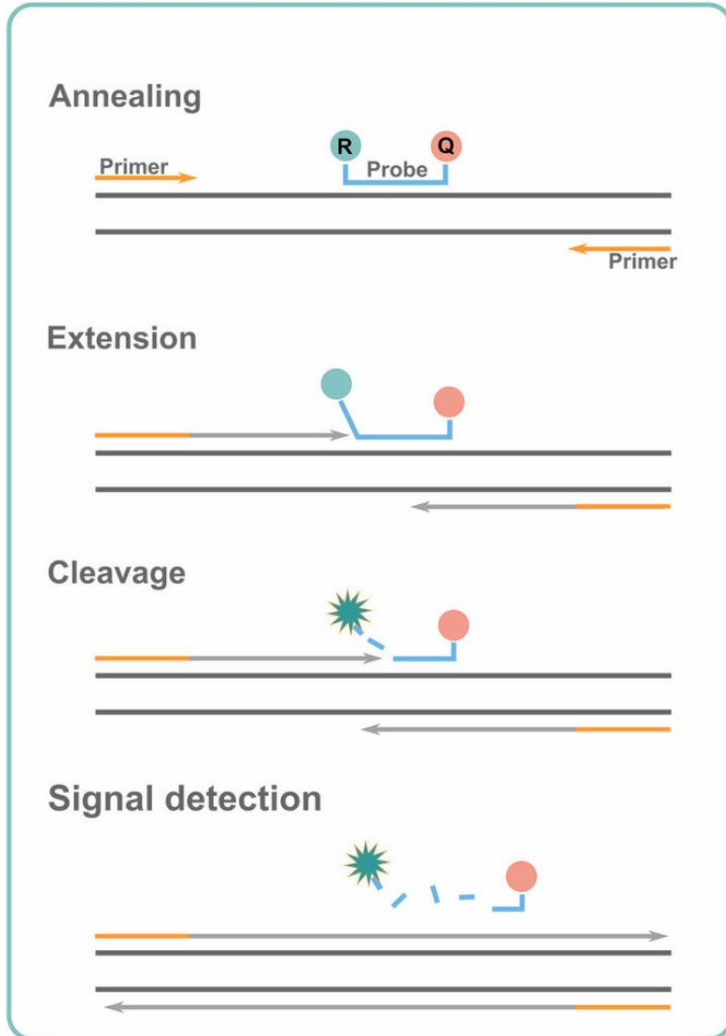
IDH1 R132H negative tissue – clone H09 1:100



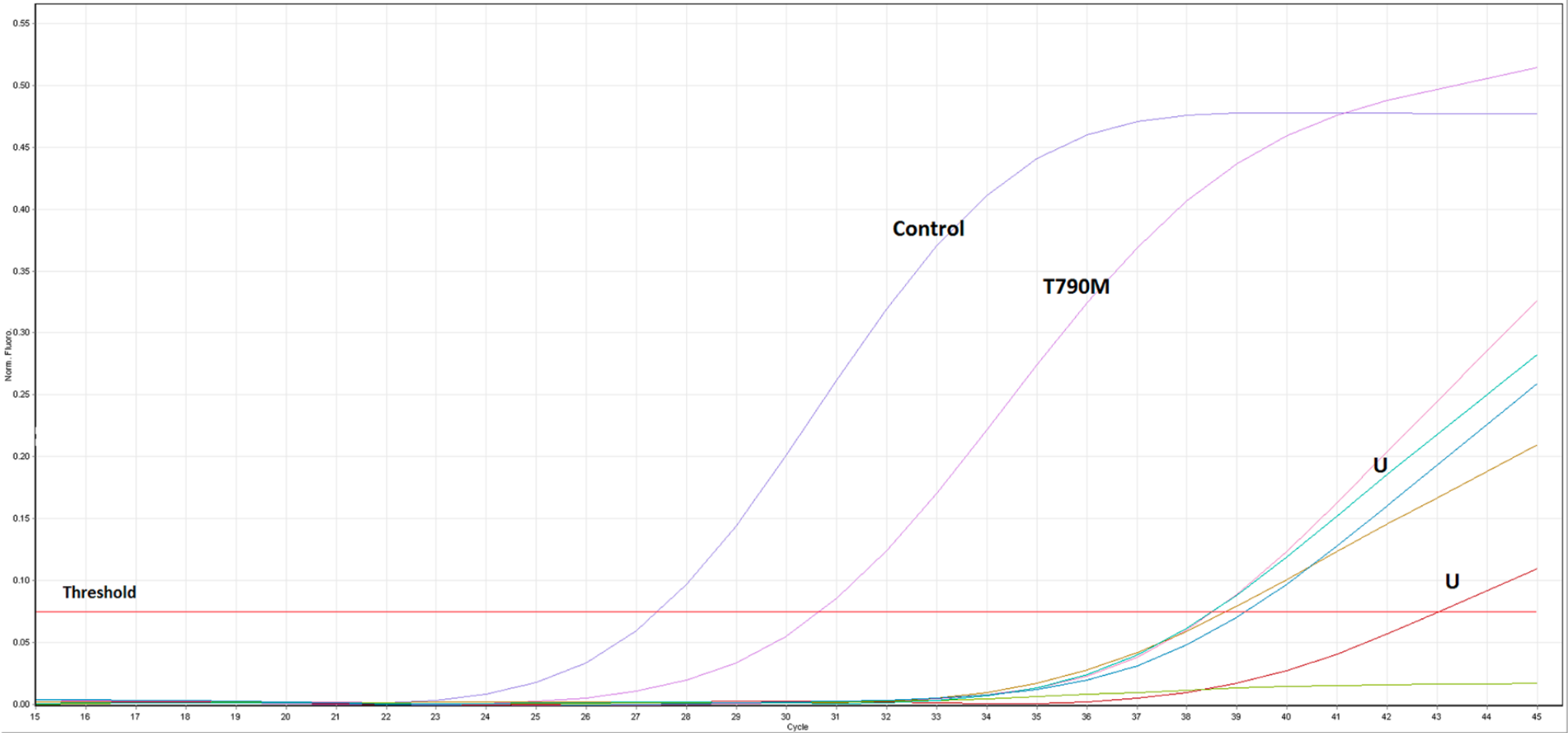
PCR



qPCR



qPCR



EGFR Mutation Test cobas

Secuenciación

Determinar el orden preciso de nucleótidos en una molécula de ADN

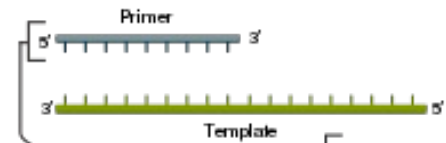
Determinar el orden de las 4 bases nitrogenadas que componen una hebra de ADN



Secuenciación Sanger

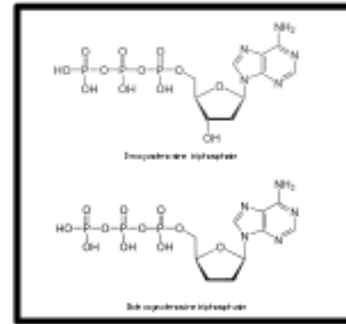
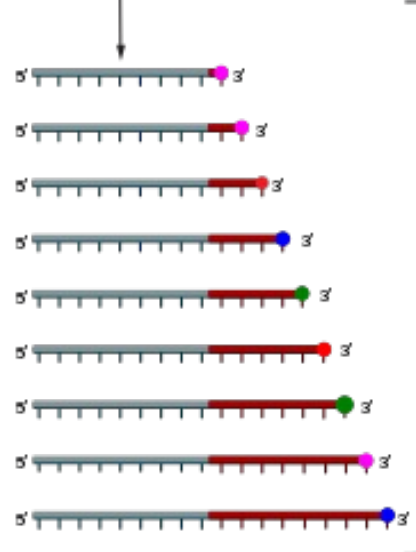
1 Reaction mixture

- ▶ Primer and DNA template
- ▶ DNA polymerase
- ▶ ddNTPs with flouochromes
- ▶ dNTPs (dATP, dCTP, dGTP, and dTTP)

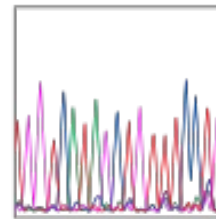
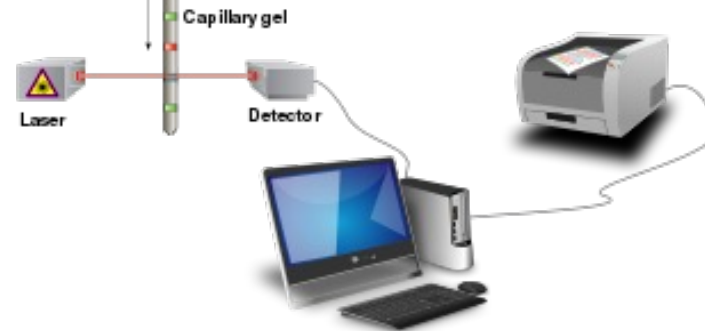


- ddNTPs
- ddTTP (red)
- ddCTP (blue)
- ddATP (green)
- ddGTP (magenta)

2 Primer elongation and chain termination

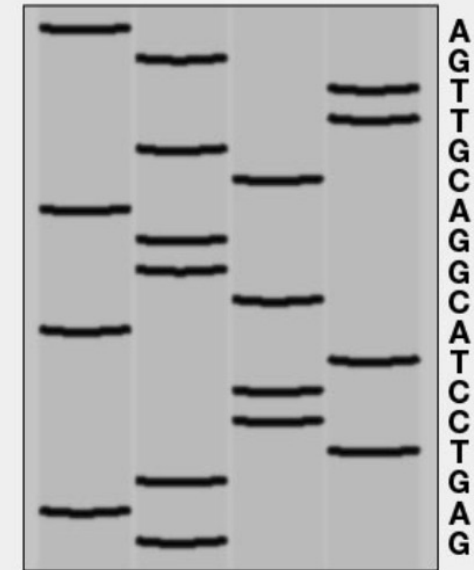
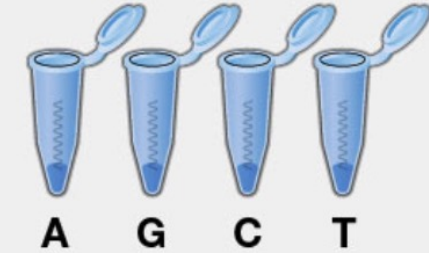


3 Capillary gel electrophoresis separation of DNA fragments

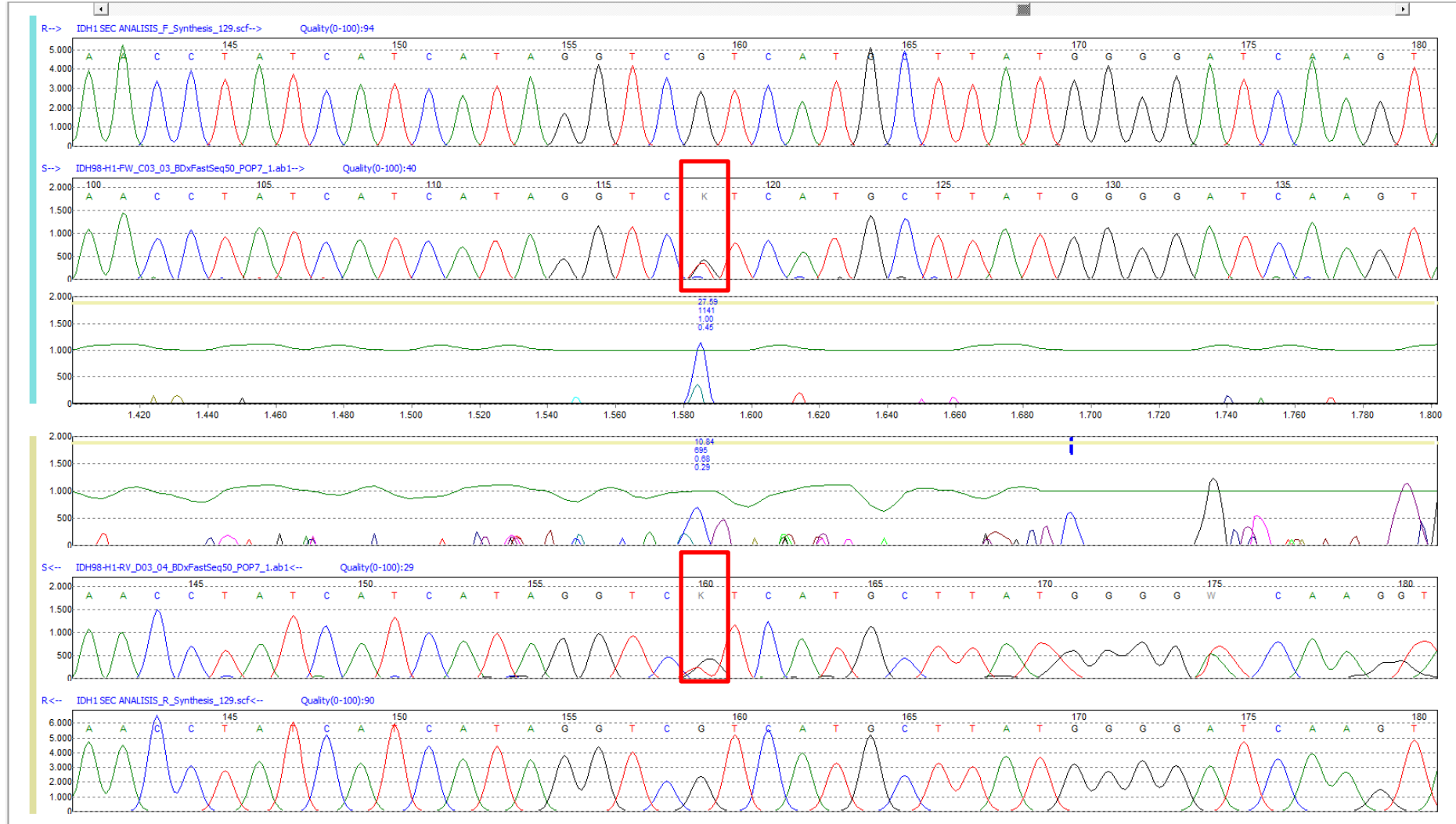


Chromatograph

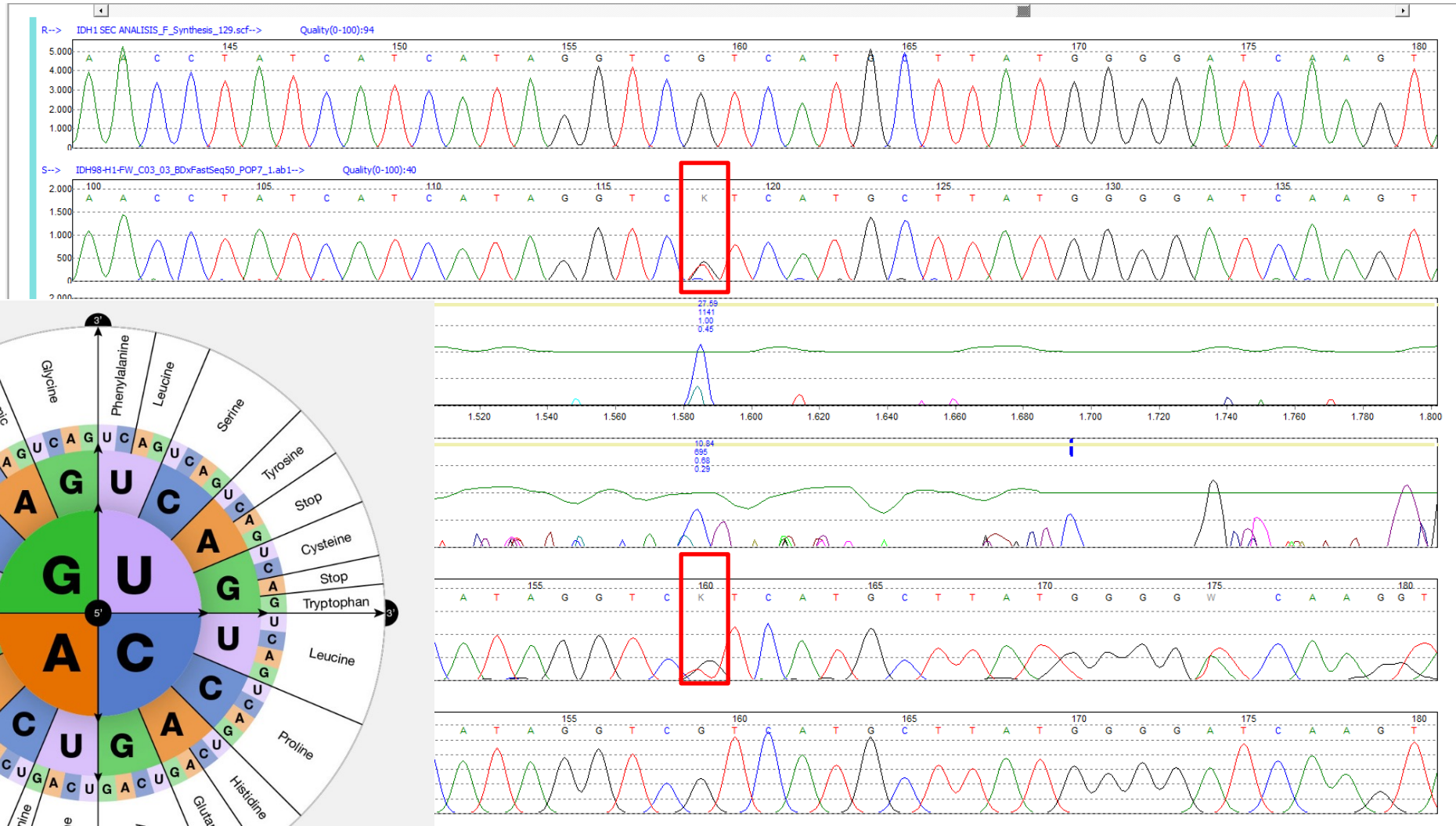
4 Laser detection of flouochromes and computational sequence analysis



Secuenciación Sanger

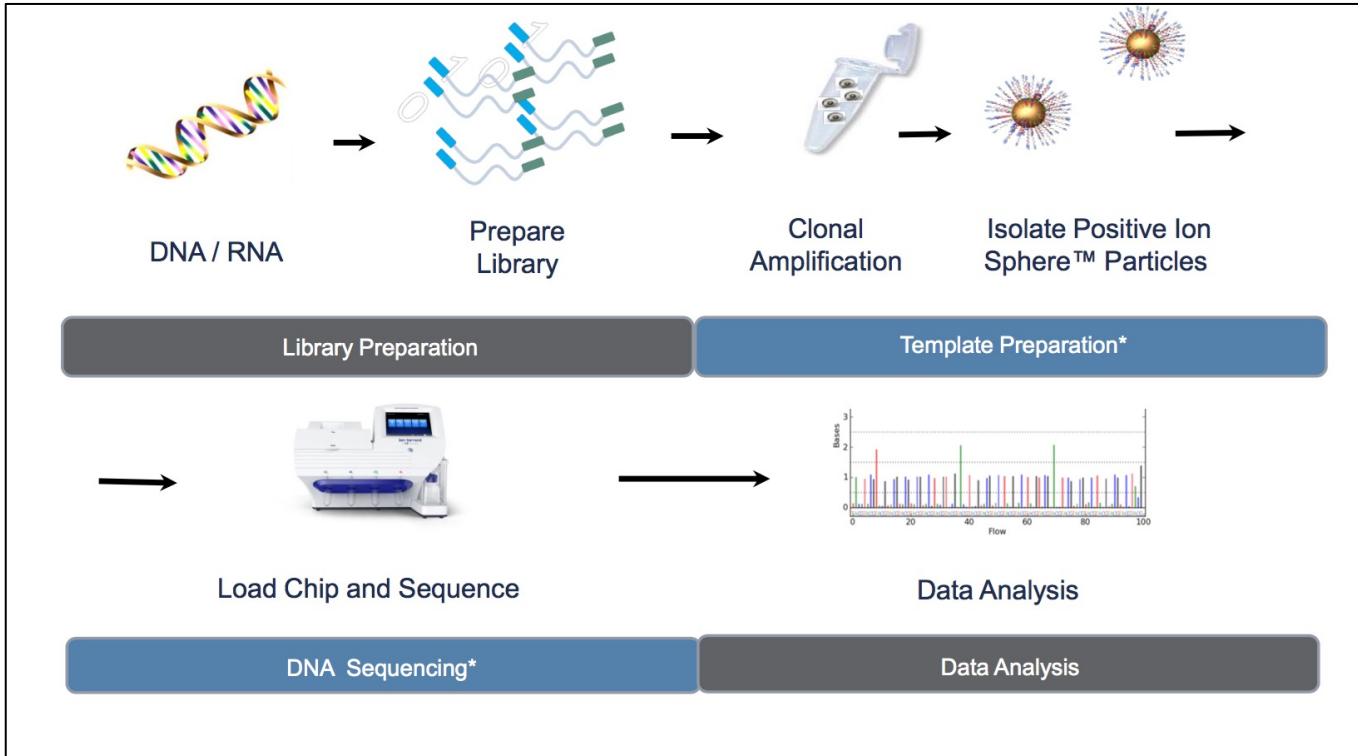


Secuenciación Sanger

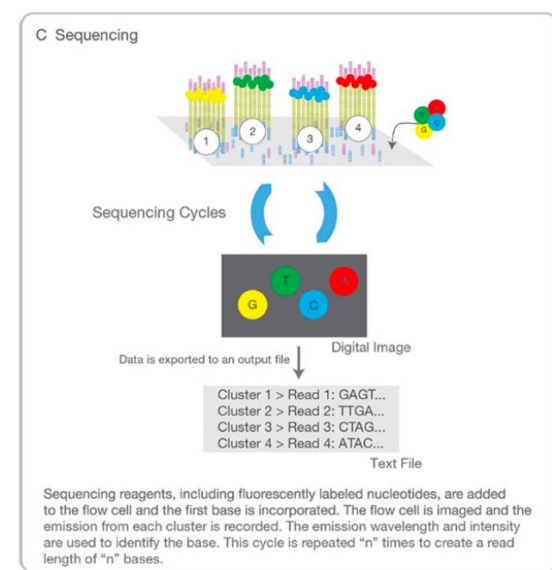
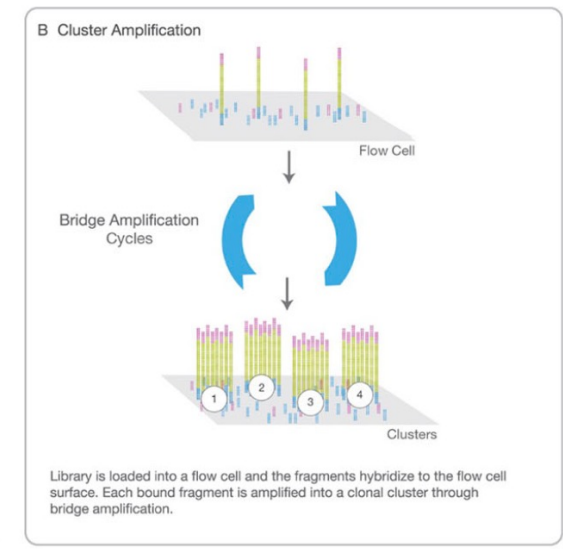
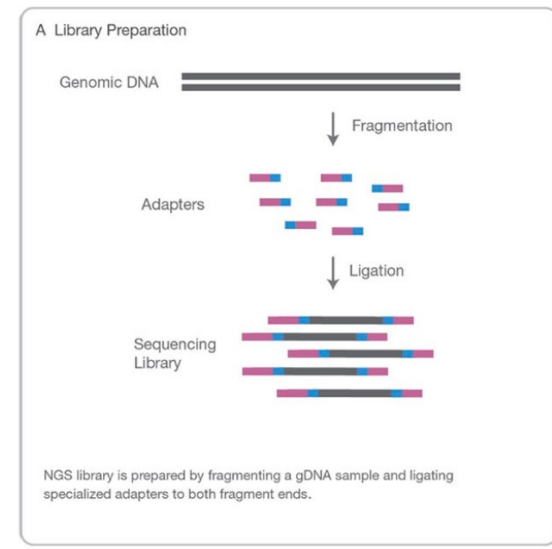


IDH 1: **R132L** (c.395G>T; p.Arg132Leu)

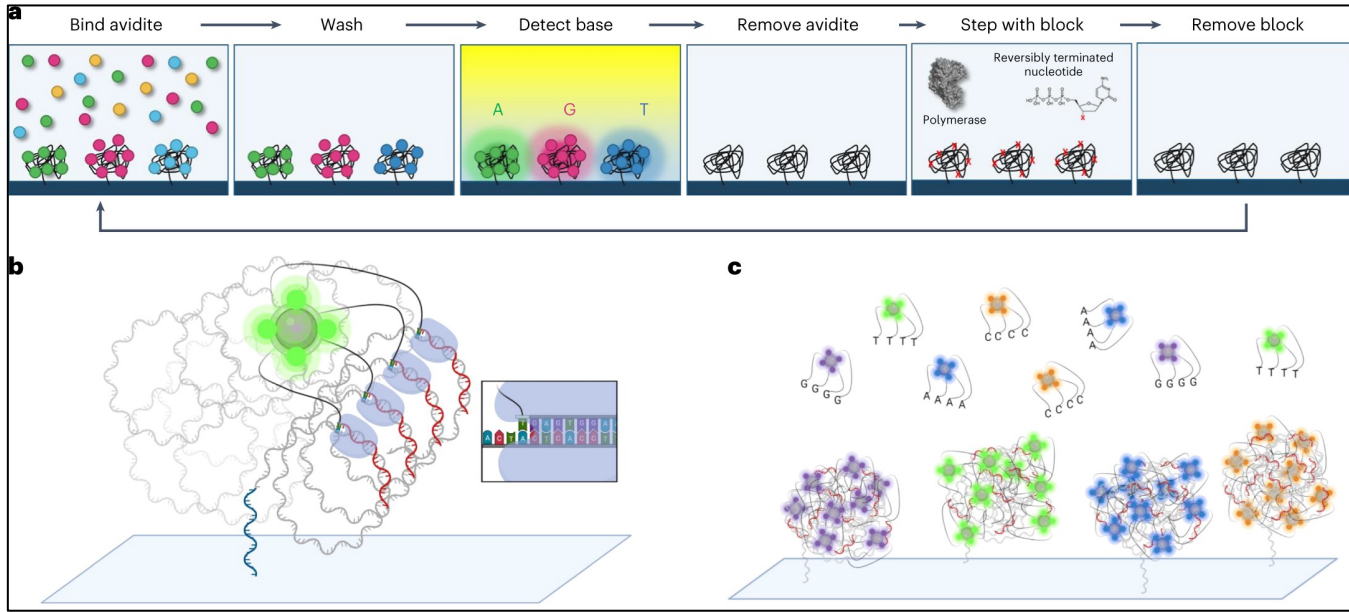
Secuenciación NGS



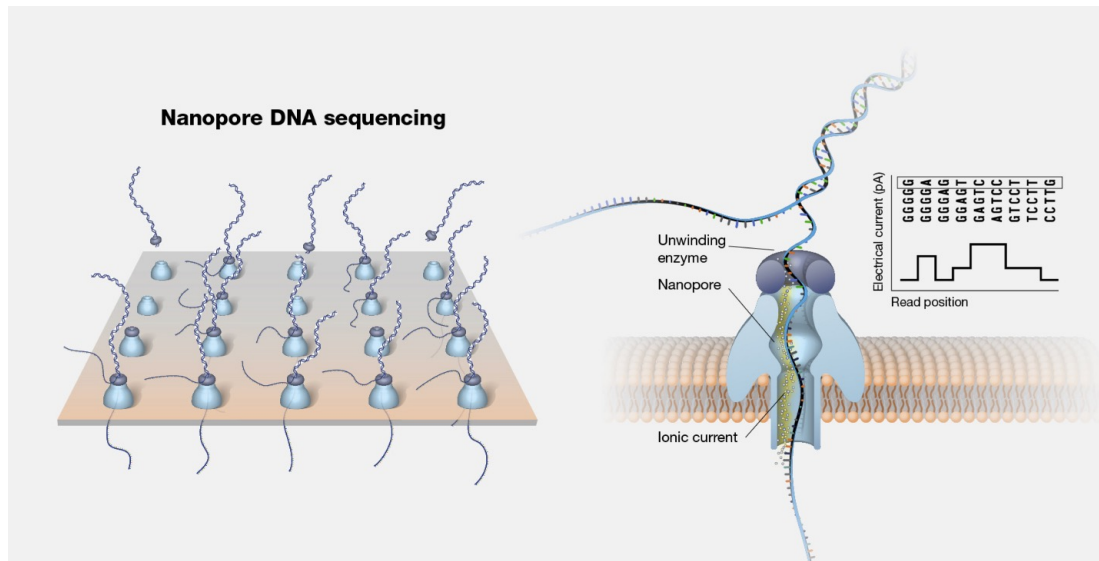
ThermoFisher Ion Torrent



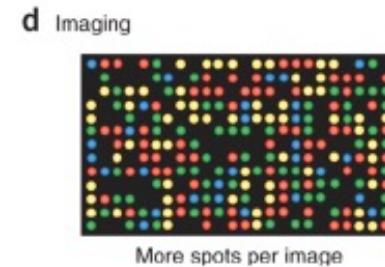
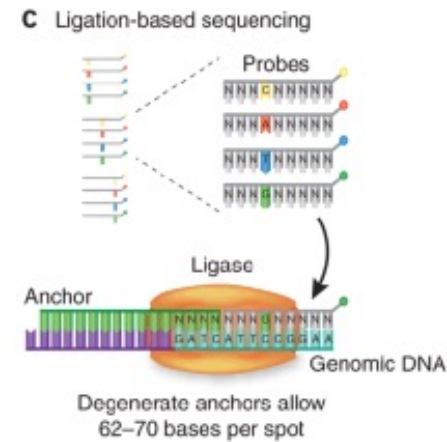
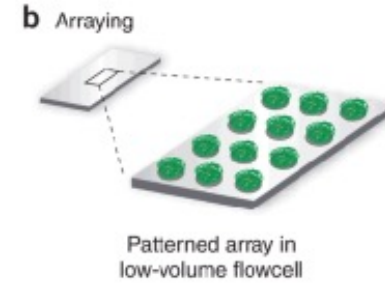
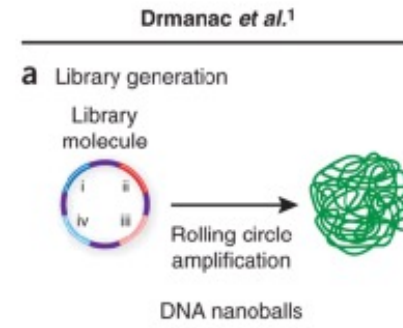
Secuenciación NGS



Element Biosciences SBA



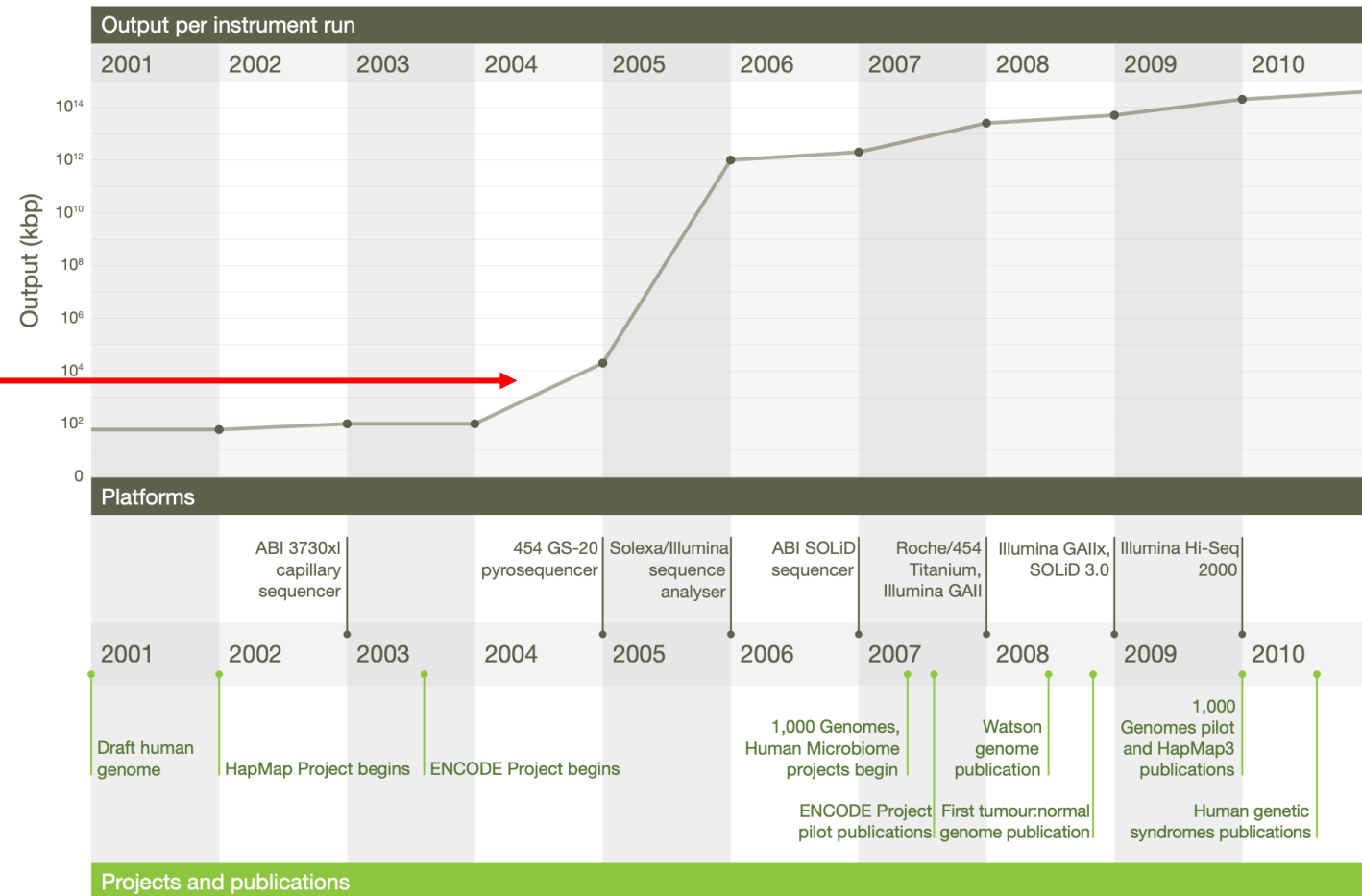
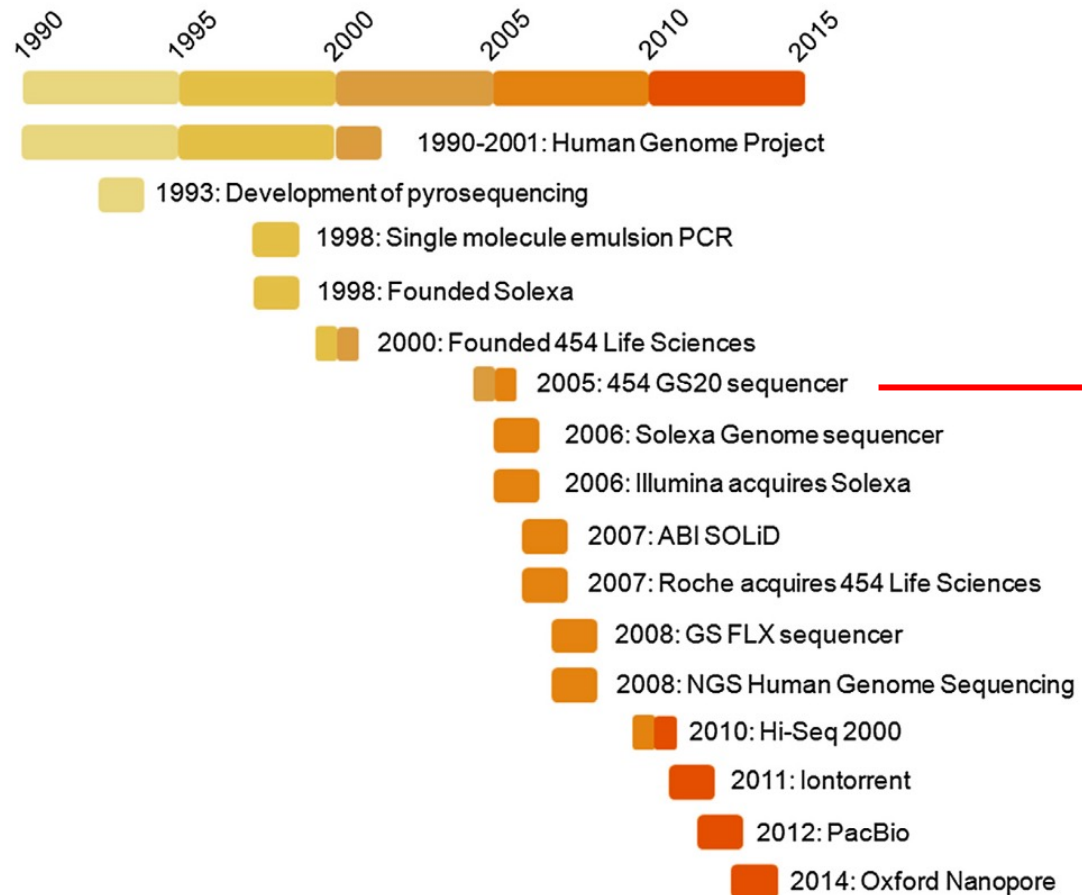
Oxford ONT



MGI SBS

Secuenciación NGS

Mayor velocidad y volumen de información

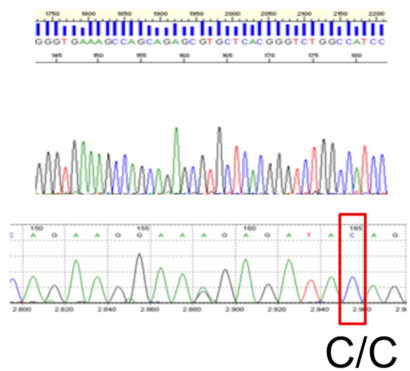


Secuenciación NGS

Mayor sensibilidad

Sanger Sequencing

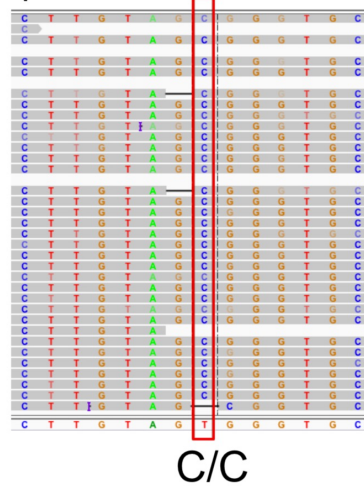
- La señal proviene de la población completa de moléculas.



100% señal C

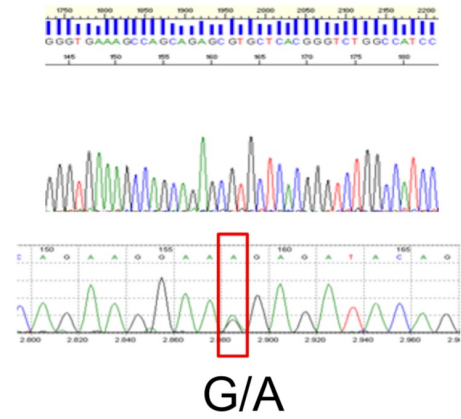
Next Generation Sequencing

- El basecalling es para cada molécula, clonalmente amplificada. Call por Consenso



Sanger Sequencing

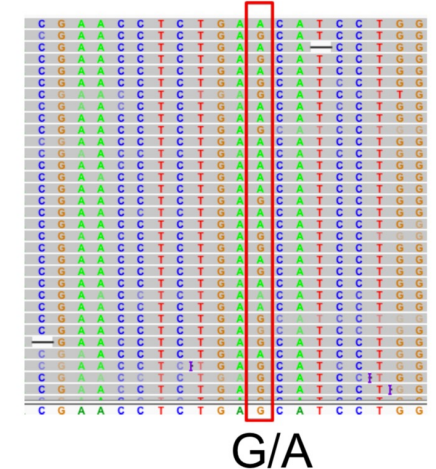
- La señal proviene de la población completa de moléculas.



50% señal G/ 50% señal A

Next Generation Sequencing

- El basecalling es para cada molécula, clonalmente amplificada. Call por Consenso

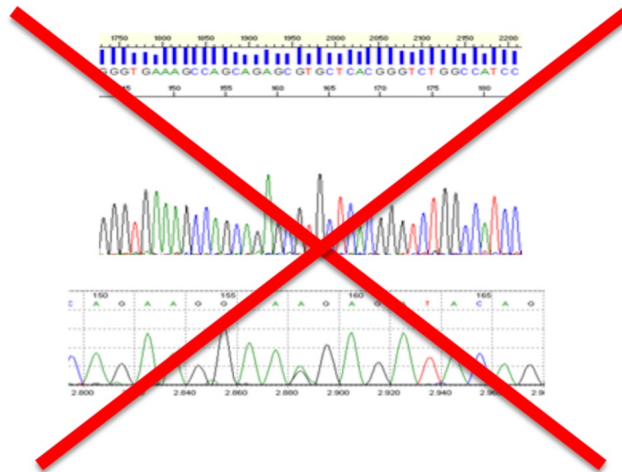


Secuenciación NGS

Mayor sensibilidad

Sanger Sequencing

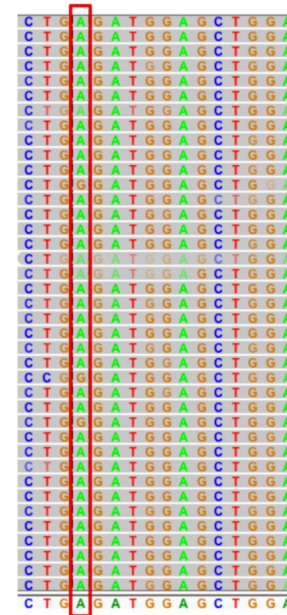
- La señal proviene de la población completa de moléculas.



No distingue señal del ruido

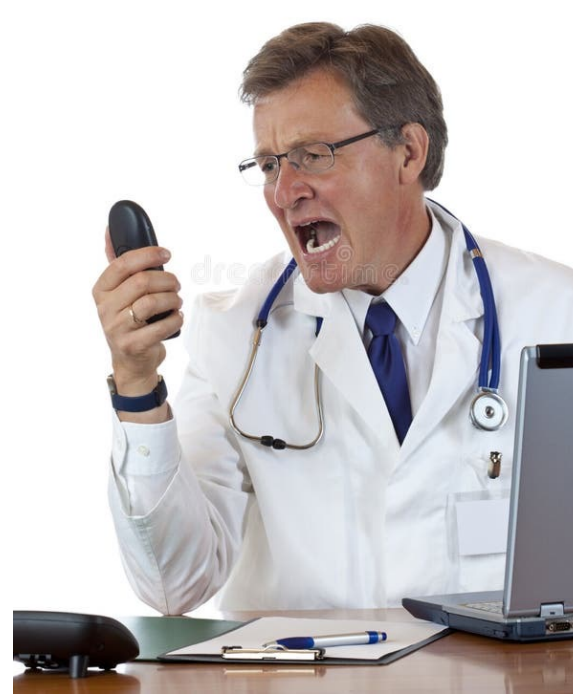
Next Generation Sequencing

- El basecalling es para cada molécula, clonalmente amplificada.
Call por Consenso

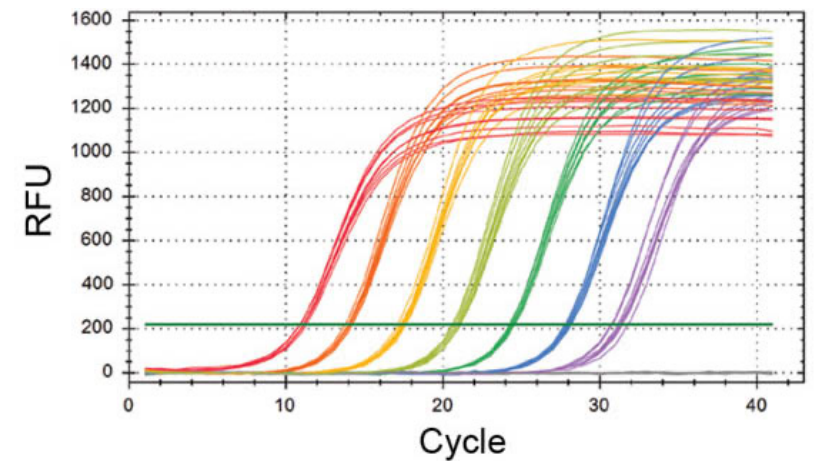


10% señal G/ 90% señal A

¿Cuánto demora?

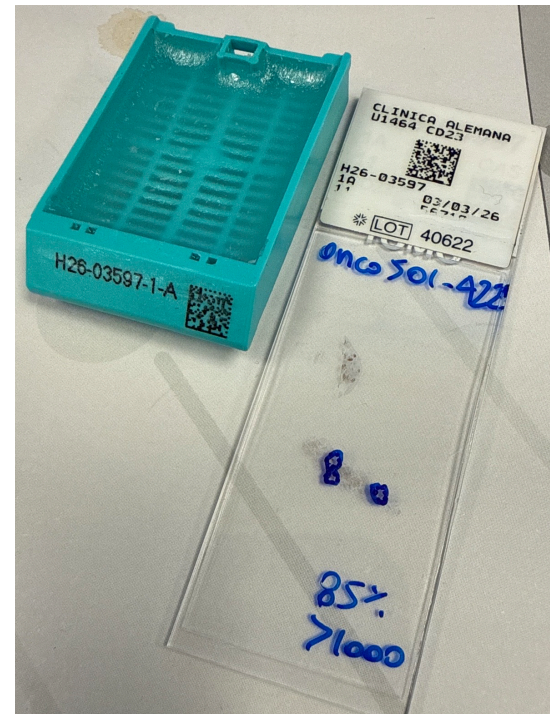
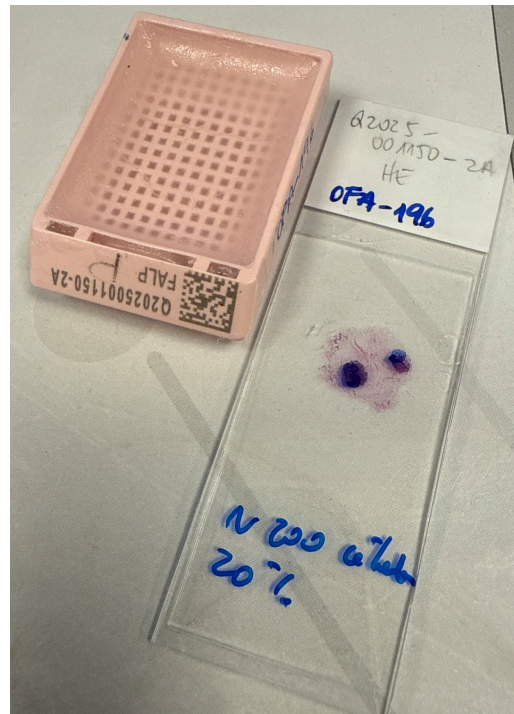


Flujo de trabajo NGS



Flujo de trabajo NGS

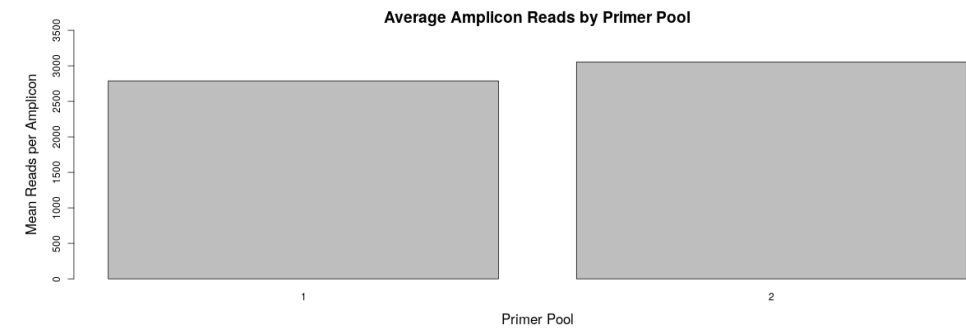
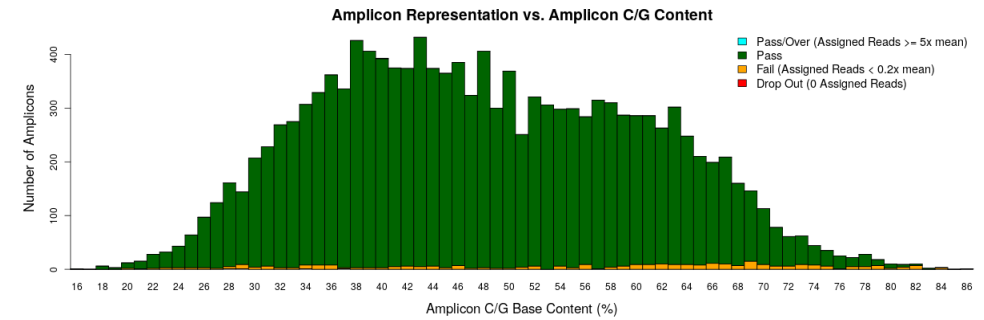
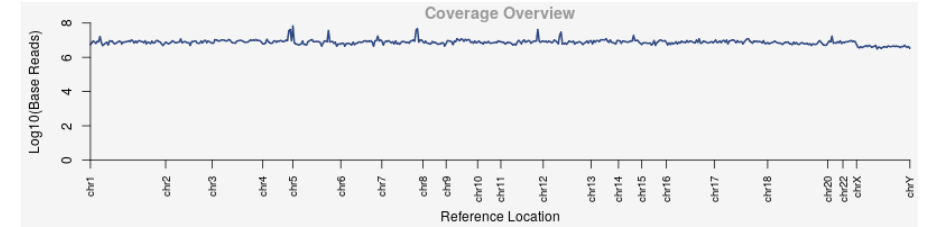
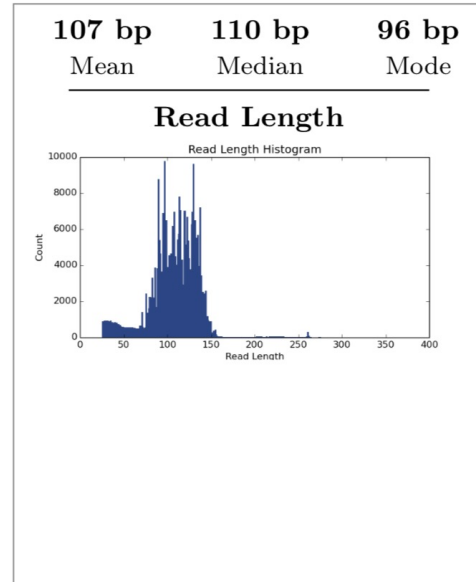
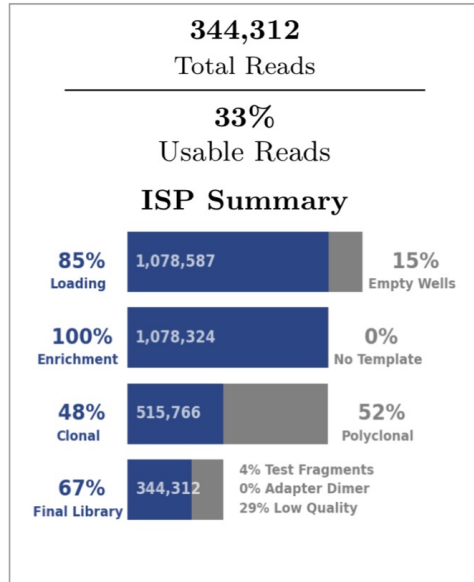
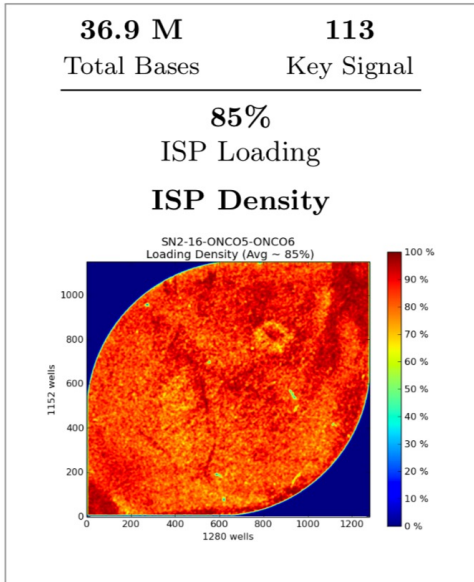
- Mayor tiempo con muestras escasas o difíciles



Flujo de trabajo NGS

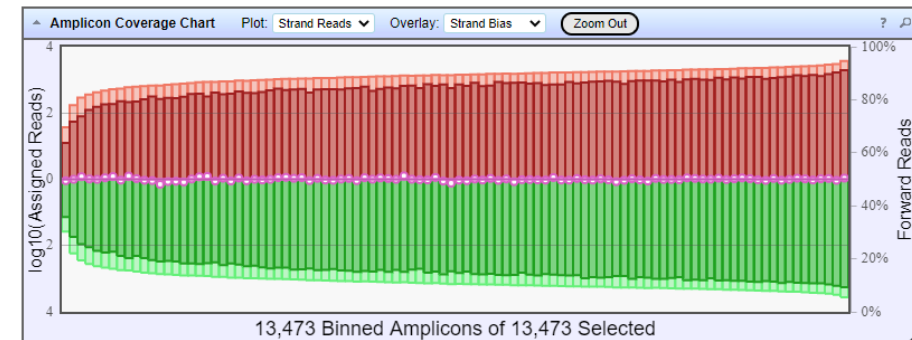


Revisión parámetros preanalíticos



Barcode Name	Sample	Mapped Reads	On Target	Mean Depth	Uniformity
IonXpress_009	ONCO17	232,224	98.82%	1,063	96.53%
IonXpress_010	ONCO18	187,562	98.03%	862.7	100.00%

1 items per page 1 - 2 of 2 items



Filtrado de variantes

Filter Options

Variants

- Filtered In Variants (8334)
- Hidden Variants (0)
- Filtered Out Variants (0)

Samples

- DNA Sample: ONCO501-208_v1
 - Gender : Male
 - Percentage Cellularity : 20
 - Sample Type : DNA
- Fusions Sample: ONCO501-208_RNA_v1
 - Gender : Male
 - Percentage Cellularity : 20
 - Sample Type : RNA

Chromosome

All

Filter Chains

No Filter

No filters selected

Save Filter Chain



Location in exonic

Variant Type in INDEL, LONGDEL, MNV, SNV

Variant Effect in missense, nonframeshiftInsertion, nonframeshiftDeletion, nonframeshiftBlockSubstitution, nonsense, stoploss, frameshiftInsertion, frameshiftDeletion, frameshiftBlockSubstitution

0.0 <= 5000Exomes EuropeanAmerican MAF(20161108) <= 0.1

UCSC Common SNPs = Not In

My Variants = Not In

__Location__1 in utr_5, splicesite_5, splicesite_3, upstream

__Variant Type__1 in INDEL, LONGDEL, MNV, SNV

__Variant Effect__1 in unknown

0.0 <= __5000Exomes EuropeanAmerican MAF(20161108)__1 <= 0.1

__UCSC Common SNPs__1 = Not In

__My Variants__1 = Not In



Filter Options

Variants

- Filtered In Variants (23)
- Hidden Variants (0)
- Filtered Out Variants (8311)

Samples

- DNA Sample: ONCO501-208_v1
 - Gender : Male
 - Percentage Cellularity : 20
 - Sample Type : DNA
- Fusions Sample: ONCO501-208_RNA_v1
 - Gender : Male
 - Percentage Cellularity : 20
 - Sample Type : RNA

Chromosome

All

Filter Chains

CAS FILTER ONCO161-...

Filter chain query applied:

Location AND Variant Type AND Variant Effect AND 5000Exomes EuropeanAmerican MAF(20161108) AND

Visualización de variantes

Analysis Results

MyVariants Download Visualize Selected Variants Send to Report Role Switch To Generate Report

Analysis Name: ONCO22_v1_4e4c0faf-be79-4398-86f9-57c8a23...

To learn more about reviewing your results, visit the help guide.

Summary Functional Population Ontologies Pharmacogenomics Somatic QC

Search Go Preferences

Classification	Locus	Genes	Type	Ref	Genotype	Variant Effect	Coverage	% Frequency	Phred QU...	Coding	Amino Acid Change	dbSNP	COSMIC/NCBI	Variant ID	Oncomine Variar
Unclassified	chr17:7579472	TP53	SNV	G	G/C	missense	678	C=98.53, T=0.00	11933.9	c.215C>G	p.Pro72Arg	rs1042522		COSM45985	
Unclassified	chr19:17945696	JAK3	SNV	C	C/T	missense	728	36.13	2726.99	c.2164G>A	p.Val722Ile	rs3213409		COSM34213	
Unclassified	chr12:25398285	KRAS	SNV	C	C/A	missense	1818	A=35.31, G=0.00, T=0.00	6636.48	c.34G>T	p.Gly12Cys	rs121913530		COSM516;COSM518;COSM51	
Unclassified	chr17:7573976	TP53	SNV	T	T/A	nonsense	1565	23.58	2348.43	c.1051A>T	p.Lys351Ter	rs141402957			
Unclassified	chr7:55211088	EGFR	SNV	A	A/G	missense	1999	22.66	2817.32	c.331A>G	p.Met111Val				
Unclassified	chr4:153245449	FBXW7	SNV	T	T/A	missense	1401	20.06	1600.59	c.1742A>T	p.Gln581Leu				
Unclassified	chr22:24134064	SMARCB1	SNV	C	C/A	missense	550	18.36	549.456	c.215C>A	p.Thr72Lys				
Unclassified	chr5:112175589	APC	SNV	C	C/T	missense	1152	7.12	164.548	c.4298C>T	p.Pro1433Leu				
Unclassified	chr13:49033890	RB1	SNV	TAGAACATAT TAGAACATATCA'	missense	753	T=0.00, TAGAACATATCACC=	32.1352	c.2039T>C	p.Ile680Thr	rs201046651			COSM870	

20 items per page

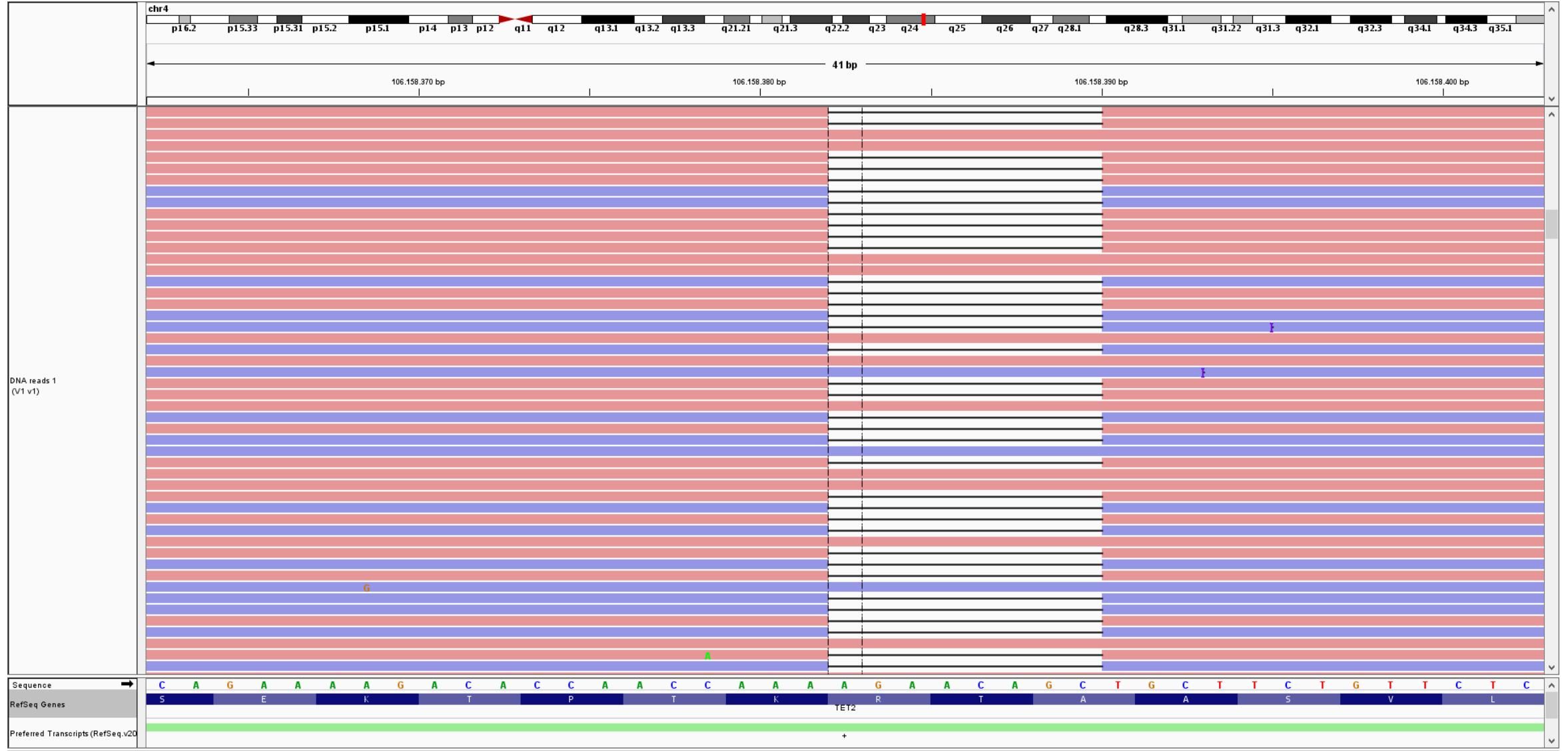
1 - 9 of 9 items

CONFIRMAR!!

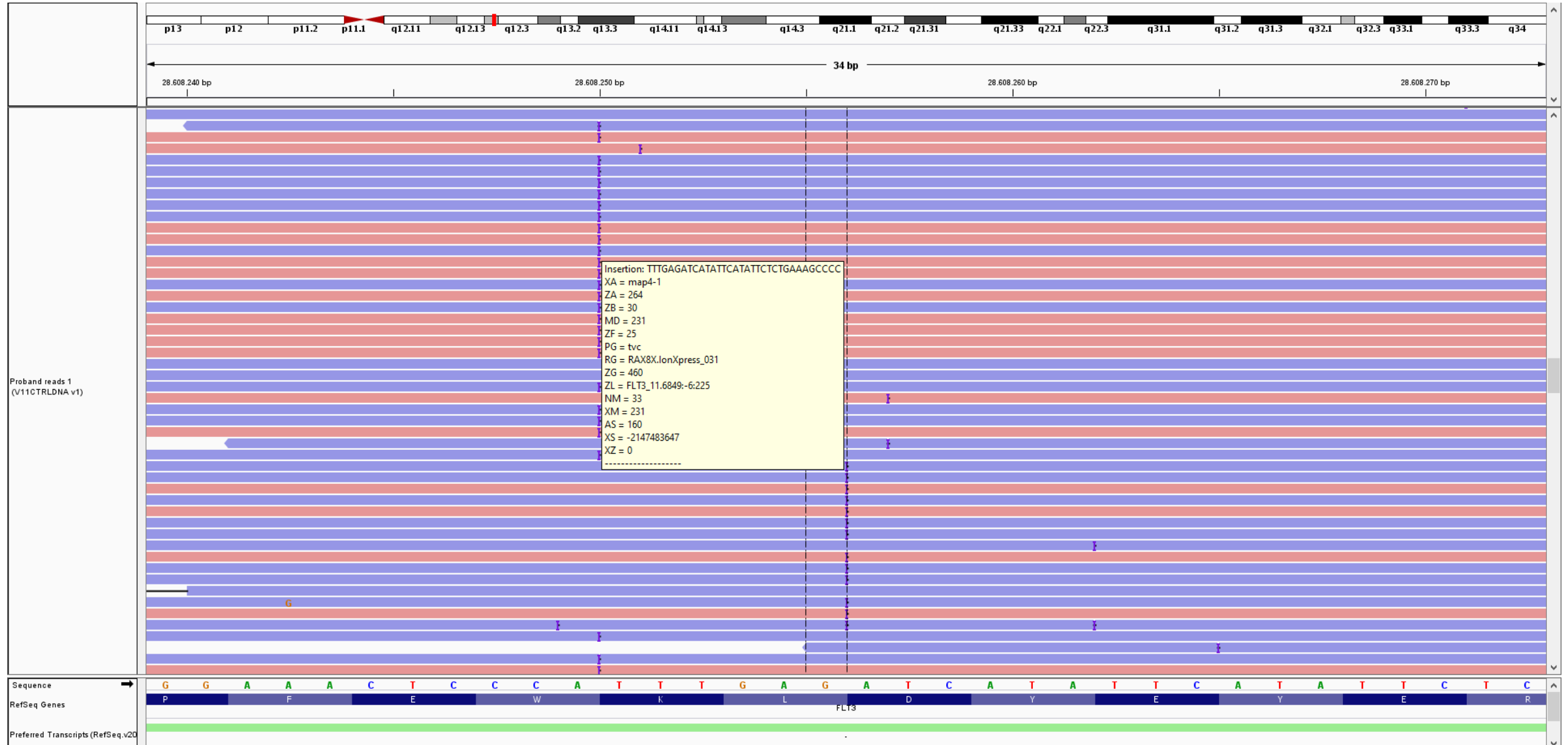
Visualización de variantes



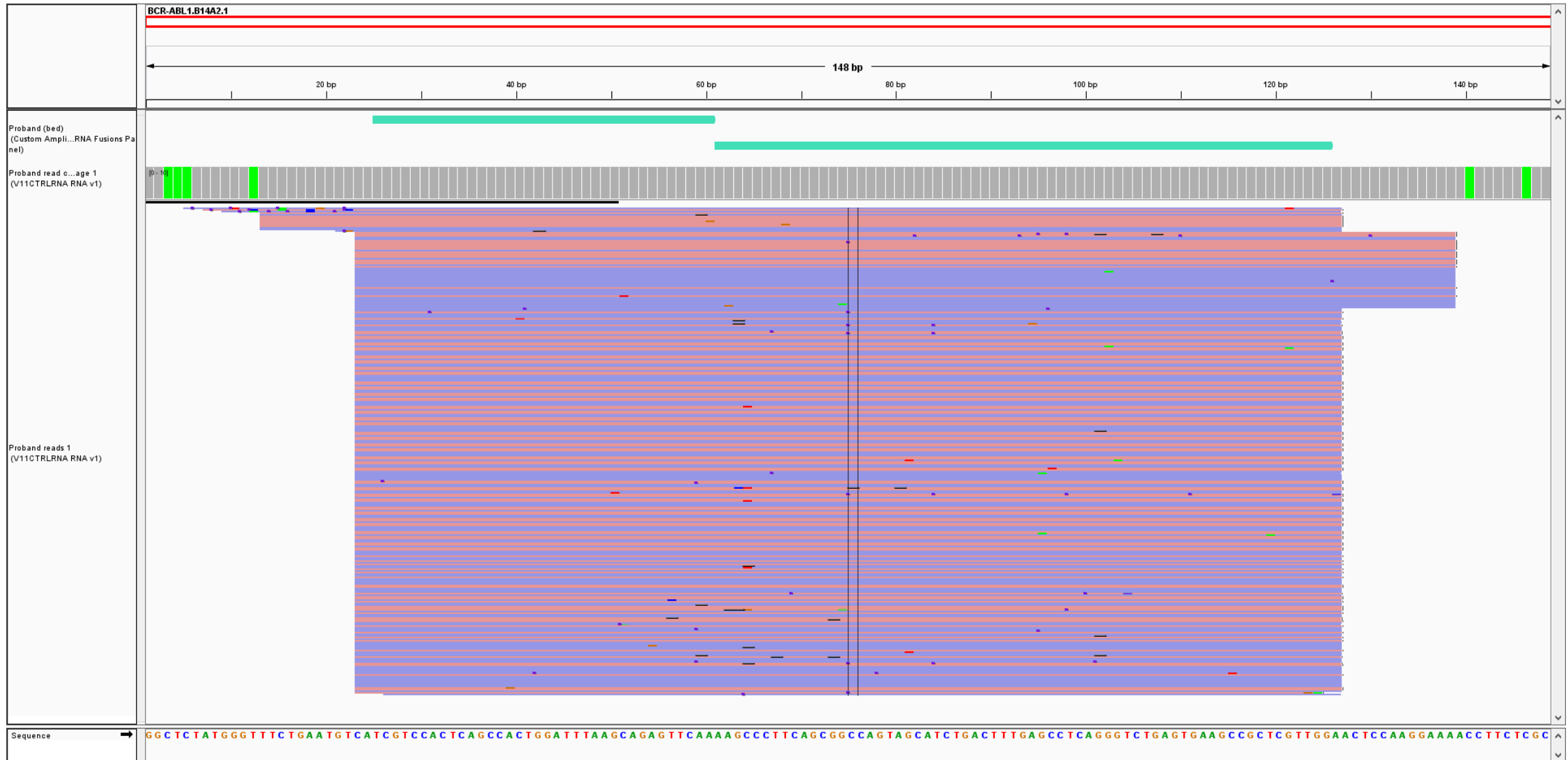
Visualización de variantes



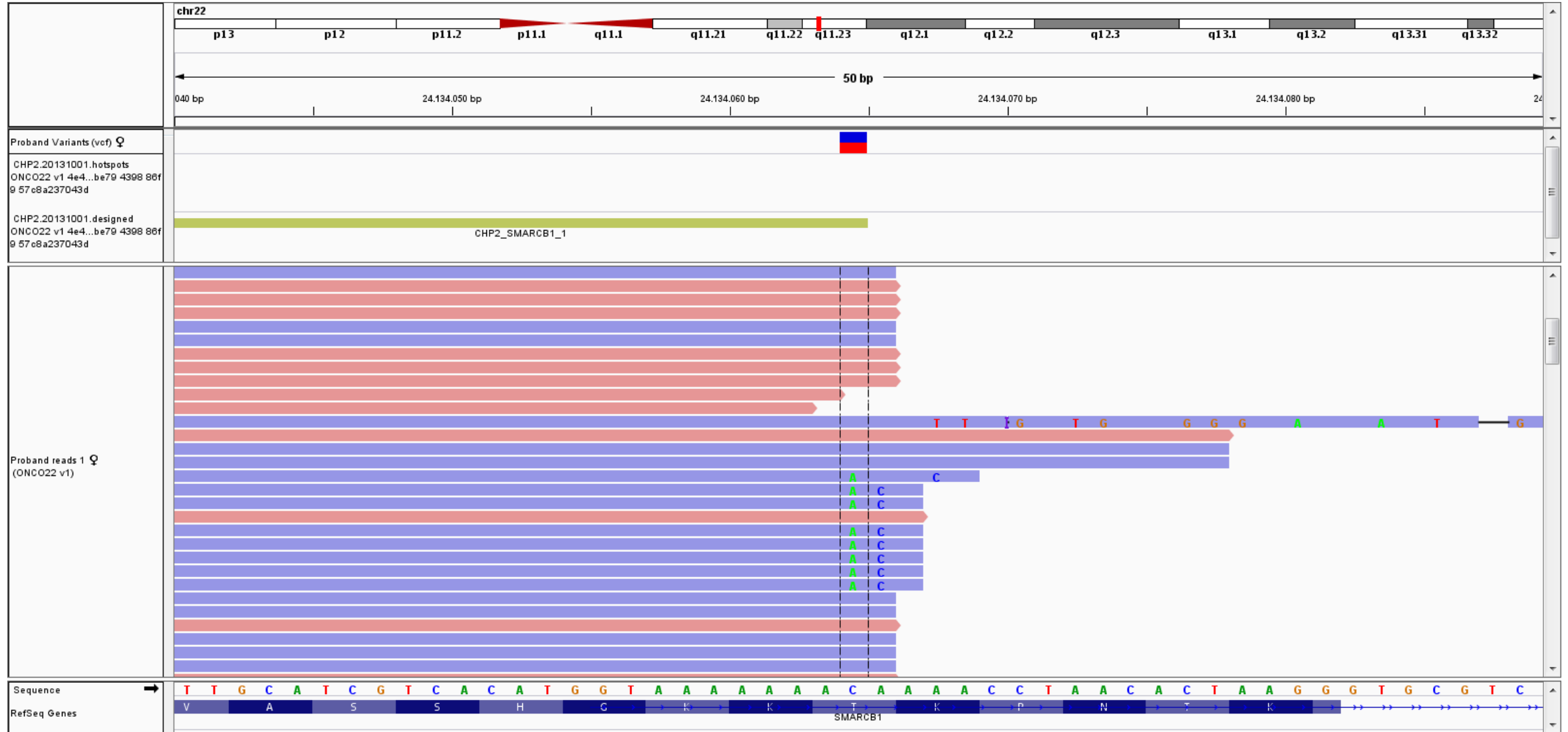
Visualización de variantes



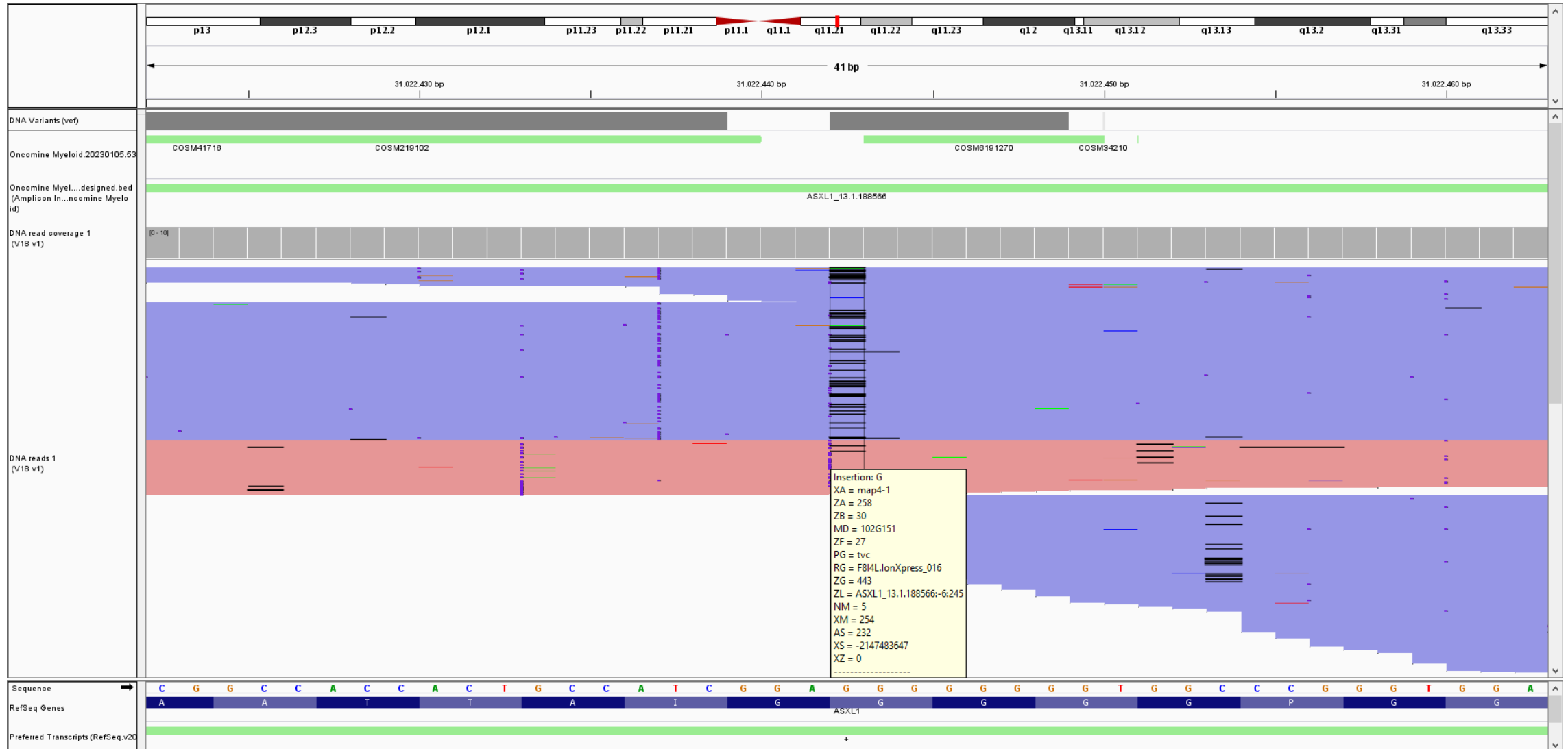
Visualización de variantes



Visualización de variantes



Visualización de variantes



Interpretación clínica

Analysis Results

MyVariants Download Visualize Selected Variants Send to Report Role Switch To Generate Report

Analysis Name: ONCO22_v1_4e4c0faf-be79-4398-86f9-57c8a23...

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Summary Functional Population Ontologies Pharmacogenomics Somatic QC

Search Go Preferences

Classification	Locus	Genes	Type	Ref	Genotype	Variant Effect	Coverage	% Frequency	Phred QU...	Coding	Amino Acid Change	dbSNP	COSMIC/NCBI	Variant ID	Oncomine Variar
Unclassified	chr17:7679472	TP53	SNV	C	G/G	missense	679	0-99.59, T=0.00	14933.9	c.245G>C	p.Pro72Arg	rs1042522		COSM45985	
Unclassified	chr19:17945696	JAK3	SNV	C	C/T	missense	728	36.13	2726.99	c.2164G>A	p.Val722Ile	rs3213409		COSM34213	
Unclassified	chr12:25398285	KRAS	SNV	C	C/A	missense	1818	A=35.31, G=0.00, T=0.00	6636.48	c.34G>T	p.Gly12Cys	rs121913530		COSM516;COSM518;COSM51	
Unclassified	chr17:7573976	TP53	SNV	T	T/A	nonsense	1565	23.58	2348.43	c.1051A>T	p.Lys351Ter	rs141402957			
Unclassified	chr7:55211088	EGFR	SNV	A	A/G	missense	1999	22.66	2817.32	c.331A>G	p.Met111Val				
Unclassified	chr4:153245449	FBXW7	SNV	T	T/A	missense	1401	20.06	1600.59	c.1742A>T	p.Gln581Leu				
Unclassified	chr22:21494884	SMARCB1	SNV	G	G/A	missense	558	18.99	548.458	c.245G>A	p.Thr72Lys				
Unclassified	chr5:442475588	APC	SNV	G	G/T	missense	4452	7.42	1644.548	c.4288G>T	p.Pro1433Leu				
Unclassified	chr12:18388888	RB1	SNV	T	TAGAACATAT TAGAACATATG	missense	753	T=0.00, TAGAACATATCACC=	32.4352	c.2989T>G	p.Ile888Thr	rs201046651		COSM870	

20 items per page

1 - 9 of 9 items



NIH National Library of Medicine National Center for Biotechnology Information

ClinVar Search ClinVar by gene Advanced

NIH National Library of Medicine National Center for Biotechnology Information

dbSNP Search SNP Advanced



FILTER OPTIONS

ESTUDIO DE MUTACIONES PANEL CAS-ONCO50 B23-00040 DE LA MUESTRA H23-01525

Diagnóstico:
MUTACIONES DETECTADAS:

-MUTACIÓN A767_V769dup EN EGFR (Frec.: 64%; c.2300_2308dup; p.Ala767_Val769dup; rs727504263).

ESTUDIO DE MUTACIONES PANEL CAS-ONCO161 B21-01841 DE LA MUESTRA H21-18952

Diagnóstico:
ALTERACIONES DETECTADAS:

-MUTACIÓN R175H EN GEN TP53 (Frecuencia: 65%; c.1669C>T; p.Gln557Ter; rs28934578).
-MUTACIÓN Q557* EN GEN ARID1A (Frecuencia: 68%; c.1669C>T; p.Gln557Ter).
-MUTACIÓN V270I EN GEN SMO (Frecuencia: 83%; c.808G>A; p.Val270Ile; rs111694017).
-AMPLIFICACIÓN DEL GEN EGFR (114.3 copias)
-AMPLIFICACIÓN DEL GEN MYC (14.0 copias)
-AMPLIFICACIÓN DEL GEN FLT3 (5.2 copias)

ESTUDIO DE MUTACIONES PANEL CAS-ONCO501 B25-00359 DE LA MUESTRA H25-15713

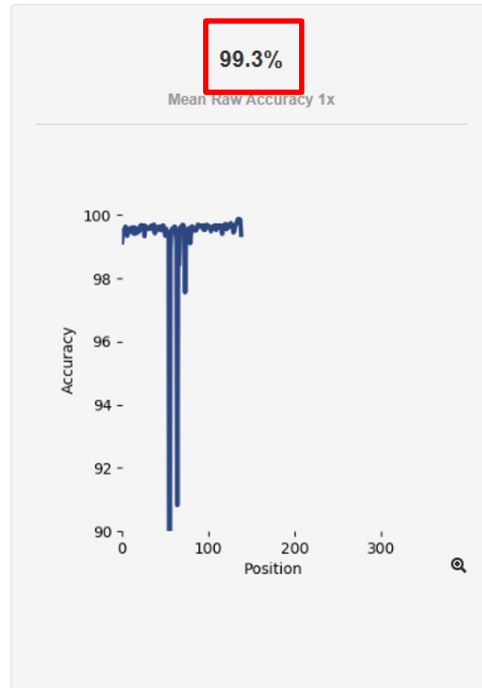
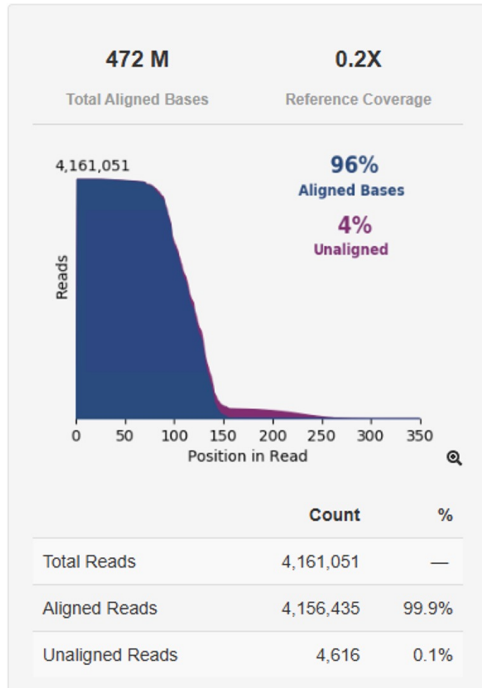
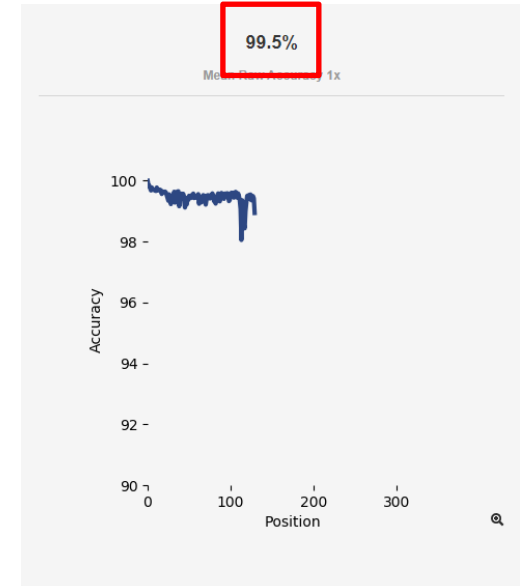
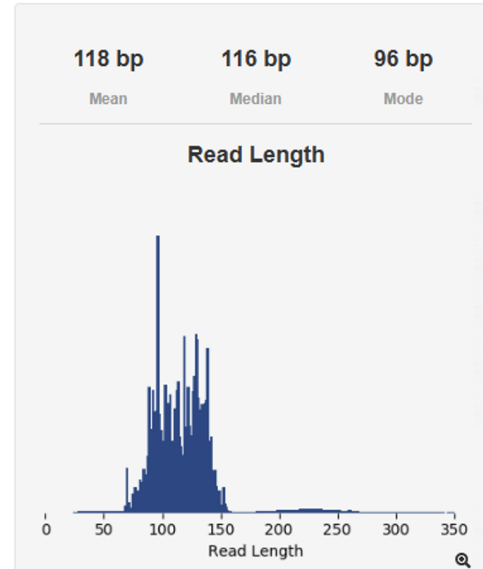
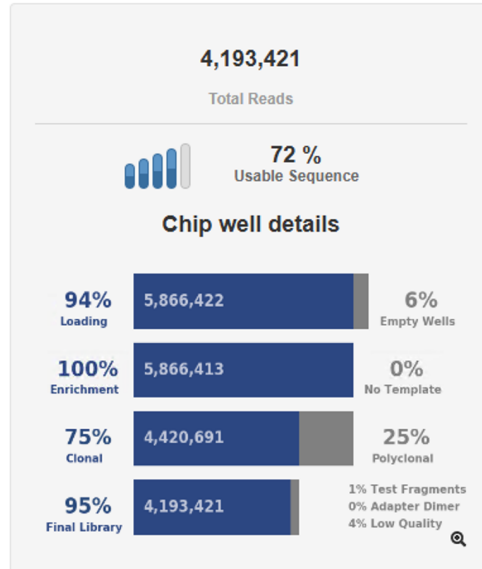
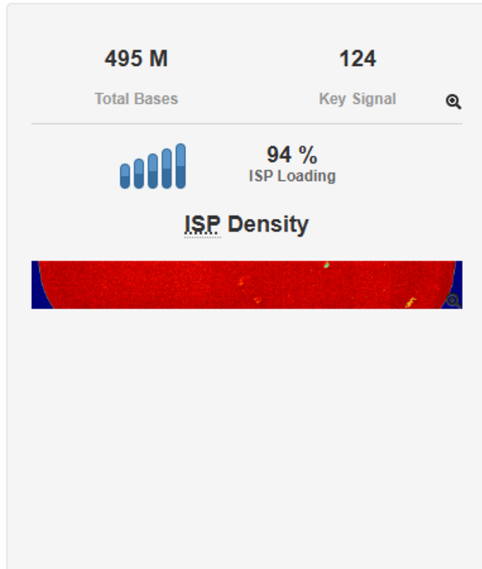
Diagnóstico:
ALTERACIONES DETECTADAS (por orden de frecuencia):

-CARGA MUTACIONAL TUMORAL: 71.75 mut/Mb (ver comentario).
-INESTABILIDAD MICROSATELITAL: DETECTADA/ALTA (Ver comentario).
-MUTACIONES R2471Dfs* EN KMT2D, R58* EN CDKN2A, G826Efs* EN SPEN, P327Lfs* EN BTK, R273C EN TP53, K1108Nfs* EN RICTOR, S813L EN SMARCA4, N2002Mfs* EN SPEN, A182Lfs* EN MARCO, R271* EN TNFAIP3, P262Hfs* EN PSD, R318H EN TP63, T169Dfs* EN TNFRSF14, G416Afs* EN TCF7L2, M296* EN PALB2, R80* EN CDKN2A, R210* EN PPP6C, G289Vfs* EN NOTCH3, G139Dfs* EN LRRIQ3, G95* EN BCOR, S1203Afs* EN PTCH1, G325R EN RAD54L, Q1334del EN ARID1A, S485Hfs* EN BAP1, R406* EN MSH2, c.2921+1G>A EN ATM, R1447* EN SMARCA4 Y R320* EN DNMT3A.

Experiencia del equipo es fundamental

- Permite resolver problemas con la muestra
- Permite optimizar el pre analítico
- Permite interpretar mejor los hallazgos
- Contexto clínico es primordial

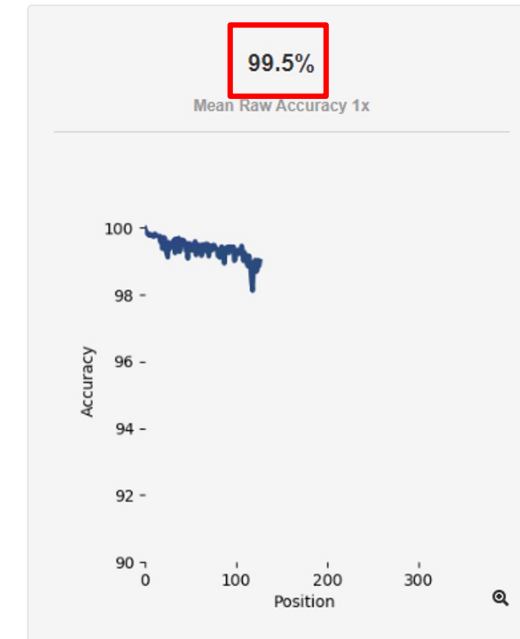
Experiencia del equipo es fundamental



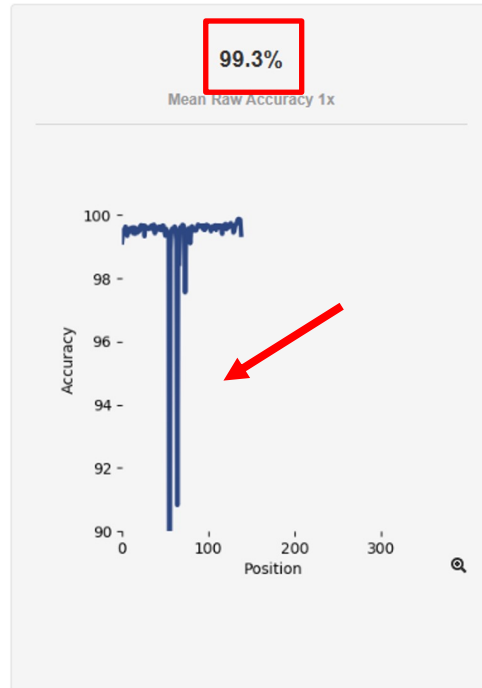
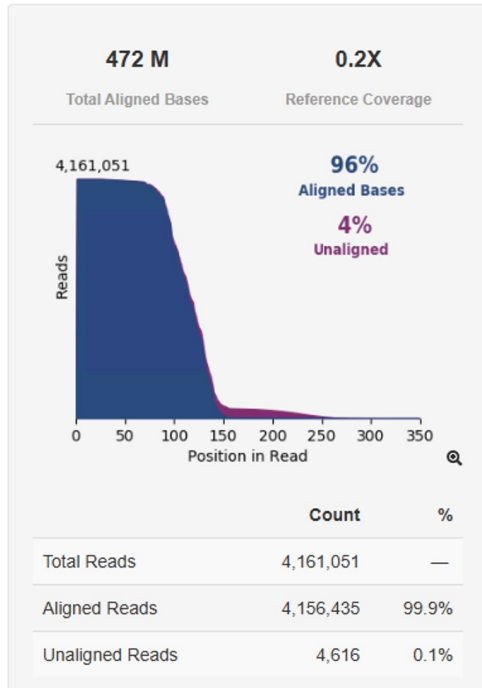
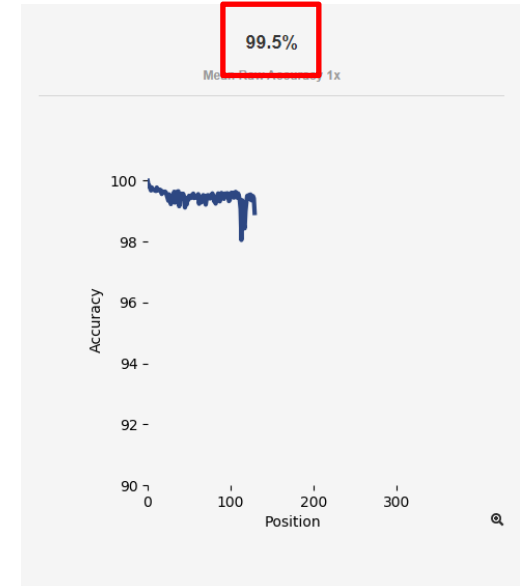
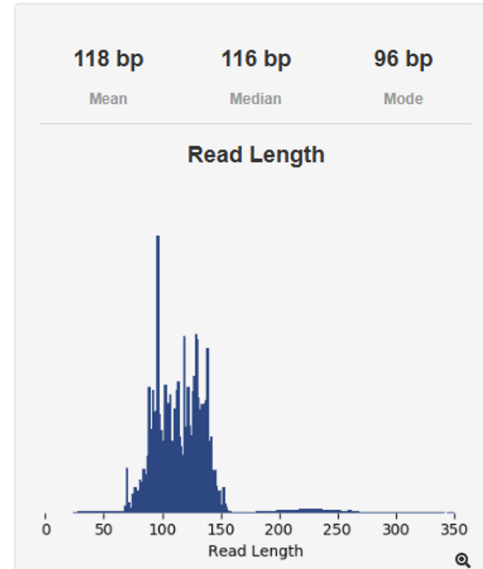
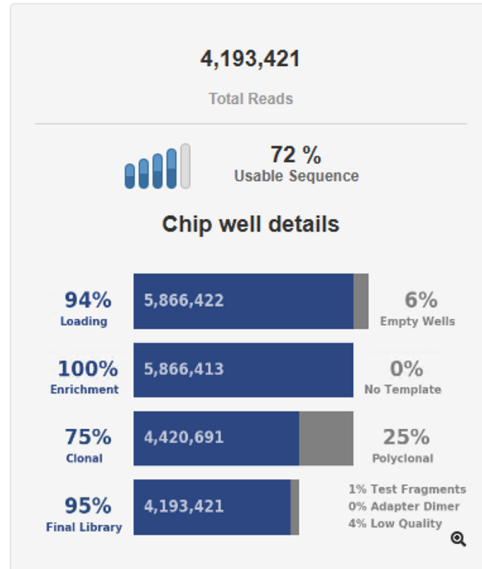
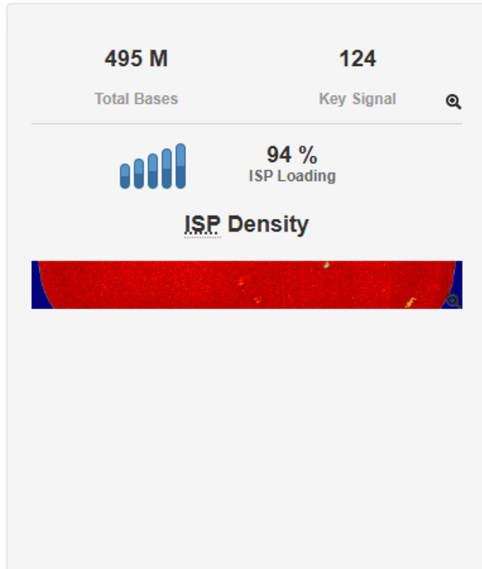
451 M AQ17 Total Bases

Alignment Quality

	AQ17	AQ20	Perfect
Total Number of Bases [bp]	451 M	429 M	390 M
Mean Length [bp]	111	108	101
Longest Alignment [bp]	352	352	316
Mean Coverage Depth [x]	0.1	0.1	0.1



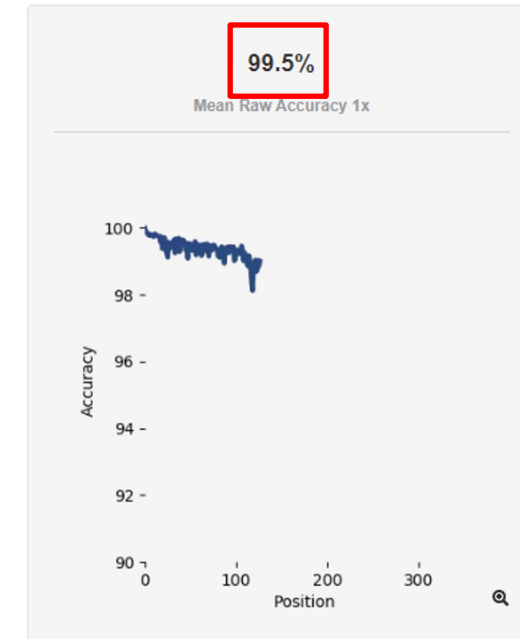
Experiencia del equipo es fundamental



451 M AQ17 Total Bases

Alignment Quality

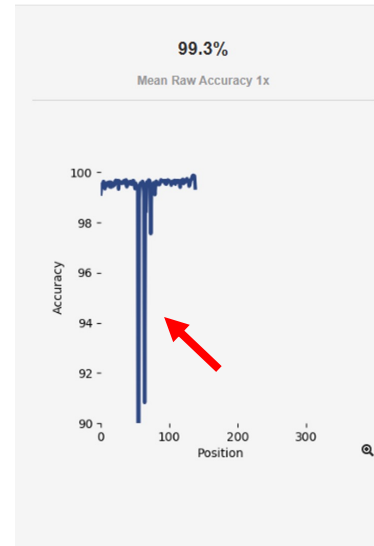
	AQ17	AQ20	Perfect
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Mean Length [bp]	111	108	101
Longest Alignment [bp]	352	352	316
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Experiencia del equipo es fundamental

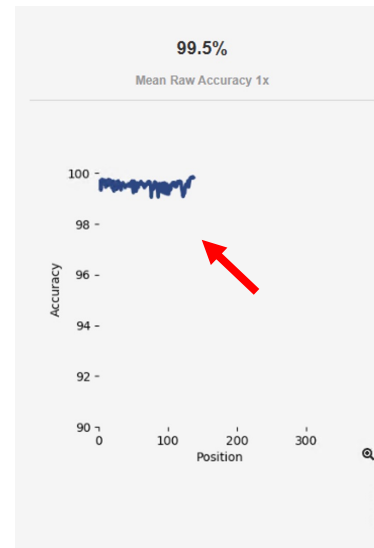
chr7:55242464	EGFR	INDEL	AGGAATTAAC	AGGAATTAAGAC	nonframeshiftDel	1913			28583.8	c.2235_2249delGG	p.Glu746_Ala750del
chr17:7578368	TP53	SNV	CACCATCGC	CACCATCGCTAT	missense	1905			10274.0	c.524G>A	p.Arg175His
chr9:80409429	GNAQ	INDEL	G	G/GA	frameshiftInsertio	1989	39.72		4400.69	c.684_685insT	p.Leu229SerfsTer5
chr13:49039214	RB1	INDEL	G	G/GA	frameshiftInsertio	1981	37.51		2591.62	c.2296_2297insA	p.Thr766AsnfsTer29
chr7:116403184	MET	INDEL	G	G/GA	frameshiftInsertio	1958	22.32		760.969	c.2503_2504insA	p.Thr835AsnfsTer16
chr13:28608335	FLT3	INDEL	C	C/CT	frameshiftInsertio	1992	15.51		377.853	c.1720_1721insA	p.Ser574LysfsTer14
chr5:112175769	APC	INDEL	CGGA	CGGA/CGGAA	frameshiftInsertio	1987		CA=0.00, CGA=0.00, CGGAA=3.07, CGG=0.05	99.5764	c.4483_4484insA	p.Ser1495LysfsTer19

chr7:55242464	EGFR	INDEL	AGGAATTAAC	AGGAATTAAGAC	nonframeshiftDel	1913	28583.8	c.2235_2249delGG	p.Glu746_Ala750del	
						AAAACATCTCCGAA/ AAAACATCTCCGAA/ AAACATCTCCGAAA/ AAACATCTCCGAAA/ AAACATCTCCGAAA/ AATCTCCGAAAGCC. AGGAATTAAGAGAA/ GGGAATTAAGAGAA/				
chr17:7578368	TP53	SNV	CACCATCGC	CACCATCGCTAT	missense	1905	10274.0	c.524G>A	p.Arg175His	
						CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC C=0.00, GACCATCGCTATCTC				
chr9:80409429	GNAQ	INDEL	G	G/GA	frameshiftInsertioi	1989	39.72	4400.69	c.684_685insT	p.Leu229SerfsTer5
chr13:49039214	RB1	INDEL	G	G/GA	frameshiftInsertioi	1981	37.51	2591.62	c.2296_2297insA	p.Thr766AsnfsTer29
chr7:116403184	MET	INDEL	G	G/GA	frameshiftInsertioi	1958	22.32	760.969	c.2503_2504insA	p.Thr835AsnfsTer16
chr13:28608335	FLT3	INDEL	C	C/CT	frameshiftInsertioi	1992	15.51	377.853	c.1720_1721insA	p.Ser574LysfsTer14
chr5:112175769	APC	INDEL	CGGA	CGGA/CGGAA	frameshiftInsertioi	1987	99.5764	c.4483_4484insA	p.Ser1495LysfsTer19	
						CA=0.00, CGA=0.00, CGGAA=3.07, CGG=0.05				



Corrida 1

chr7:55242464	EGFR	INDEL	AGGAATTAAC	AGGAATTAAGAC	nonframeshiftDel	1980	26235.4	c.2235_2249del	p.Glu746_Ala750del
						AAAAC=1.26, AAAC=76.36, A=0.00, GGGAATTAAGAGAA/			
chr17:7578368	TP53	SNV	CACCATCGC	CACCATCGCTAT	missense	1881	9350.62	c.524G>A	p.Arg175His
						CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC CACCATCGCTATCTC C=0.00, GACCATCGCTATCTC			



Corrida 2

Experiencia del equipo es fundamental

Analysis Results

Analysis Name: ONCO50-170_v1_f36777dc-8e5b-4241-944a-a84...

MyVariants Download Visualize Selected Variants Send to Report Role Switch To Generate Report

To learn more about reviewing your results, visit the [help guide](#).

Summary Functional Population Ontologies Pharmacogenomics Somatic QC

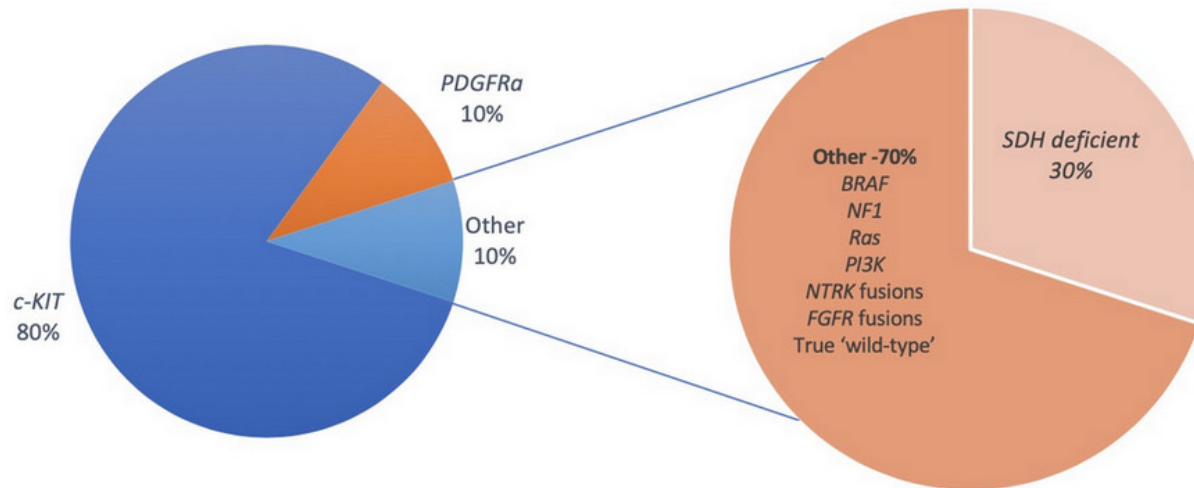
Search Go Preferences

Classification	Locus	Genes	Type	Ref	Genotype	Variant Effect	Coverage	% Frequency	Phred QU...	Coding	Amino Acid Change	dbSNP	COSMIC/NCBI	Variant ID	Oncomine Variar
Unclassified	chr9:139399408	NOTCH1	INDEL	GCAC	GCAC/G	nonframeshiftDel	971	1.44	11.5252	c.4732_4734del	p.Val1578del	rs761020817		COSM13047	
Unclassified	chr9:21971131	CDKN2A	SNV	G	G/A	missense	249	1.20	6.07957	c.227C>T	p.Ala76Val	rs587776716 ...(2)		COSM13766	

20 items per page

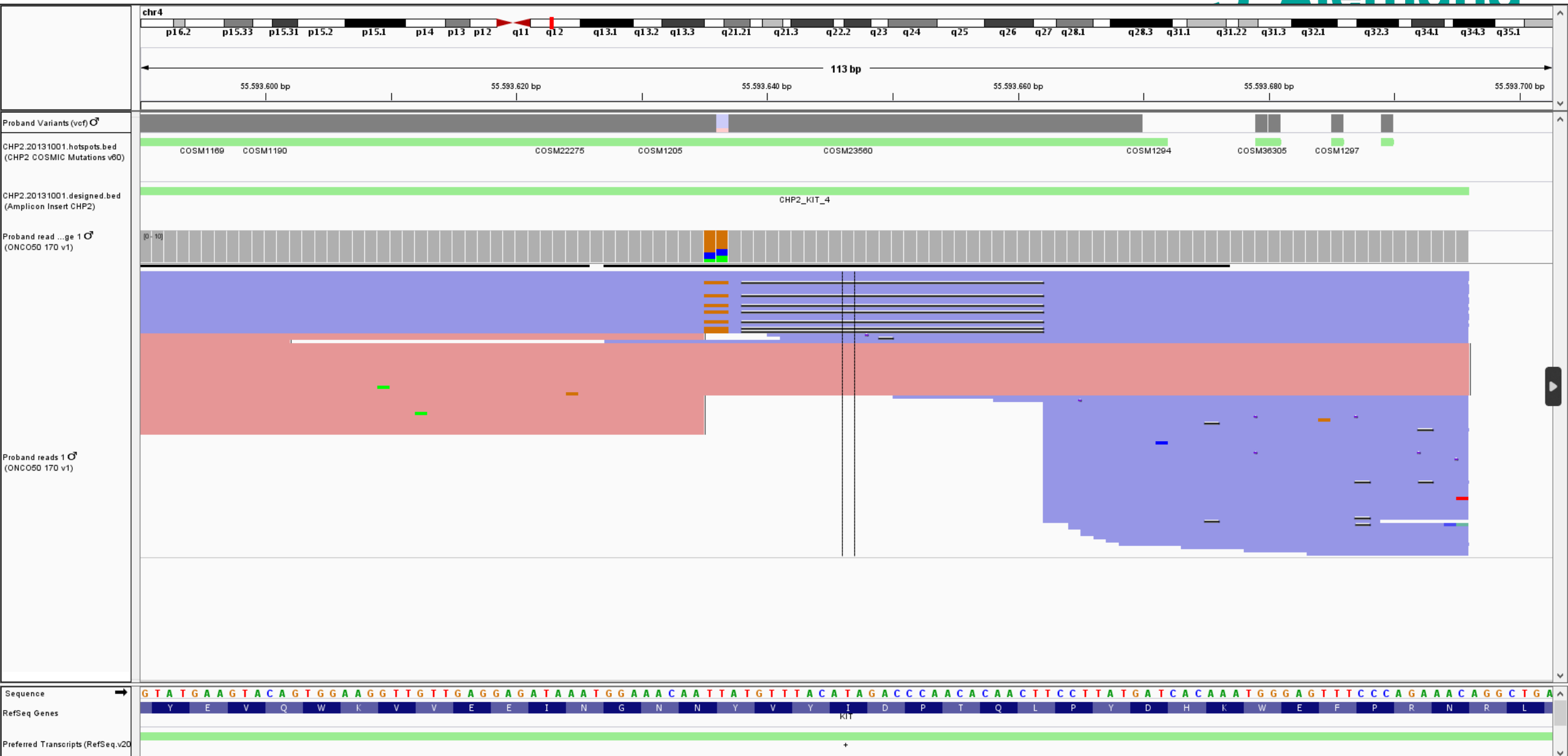
1 - 2 of 2 items

GIST genetic variability



Revisar genes relevantes!!

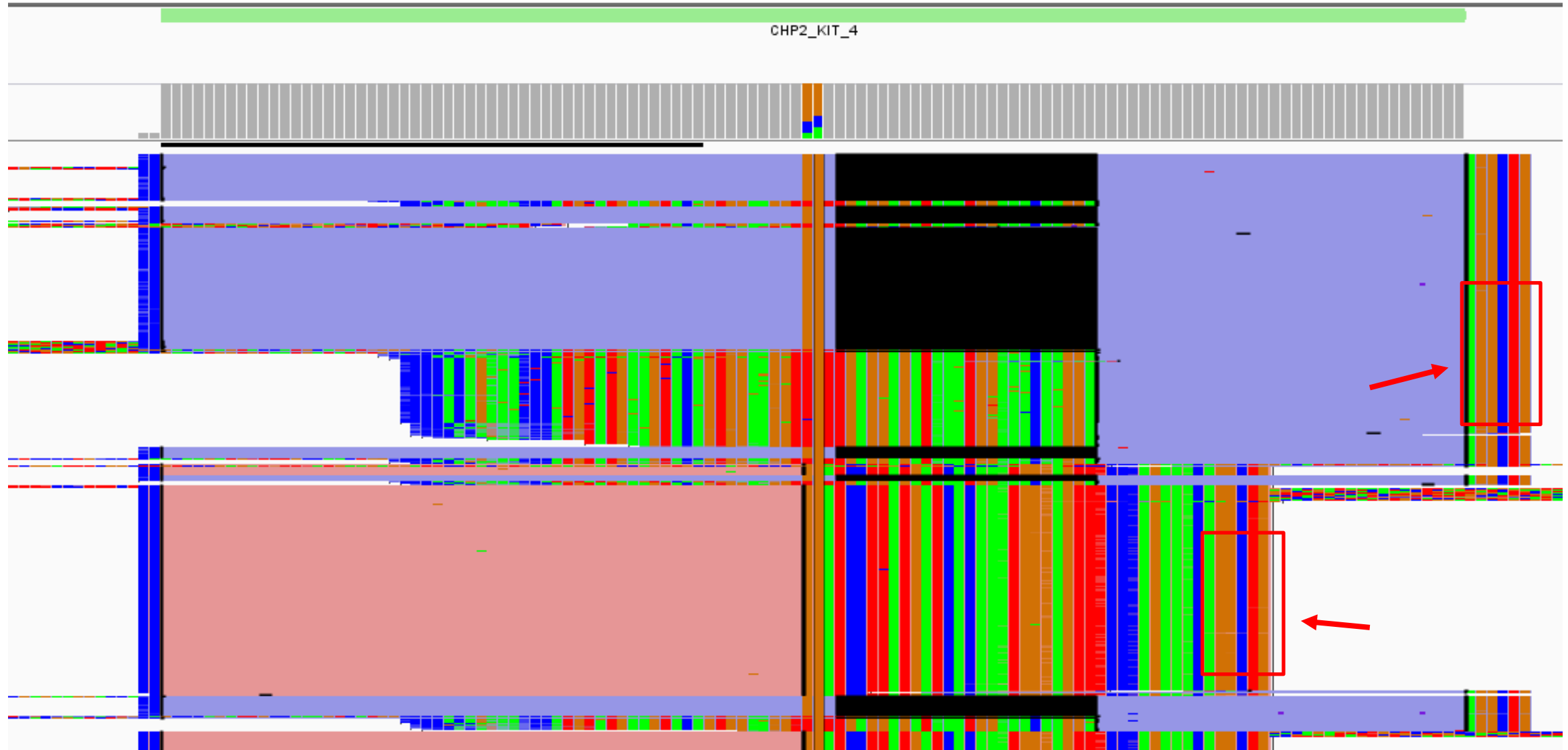
Experiencia del equipo es fundamental



Experiencia del equipo es fundamental



Experiencia del equipo es fundamental



Experiencia del equipo es fundamental

Analysis Name: ONCO50-170_v1_f36777dc-8e5b-4241-944a-a84...

To learn more about reviewing your results, visit the help guide.

Summary Functional Population Ontologies Pharmacogenomics Somatic **QC**

KIT Go Preferences

	Classification	Locus	Genotype	Ref	Type	No Call Reason	Genes	P-Value	Phred QUAL Score	Raw Coverage	Coverage	Allele Coverage
<input type="checkbox"/>	Unclassified	chr4:55593636	/	T	NOCALL	&STDBIAS0.999977>0.95&STDBIASPVAL0<1	KIT	0.00001	5699.14	7015	1995	T=1463, G=532
<input type="checkbox"/>	Unclassified	chr4:55561763	C/C	C	REF		KIT	0.00001	87.2886	8625	1999	C=1999, G=0
<input type="checkbox"/>	Unclassified	chr4:55561764	G/G	G	REF		KIT	0.00001	63.5153	8623	2000	G=1998, A=2
<input type="checkbox"/>	Unclassified	chr4:55592178	C/C	C	REF		KIT	0.00001	87.0732	6486	1994	C=1994, CTGCCTA=0
<input type="checkbox"/>	Unclassified	chr4:55592202	A/A	A	REF		KIT	0.00001	87.2906	6491	1999	A=1999, T=0
<input type="checkbox"/>	Unclassified	chr4:55593431	G/G	G	REF		KIT	0.00001	87.3325	7163	2000	G=2000, A=0
<input type="checkbox"/>	Unclassified	chr4:55593464	A/A	A	REF		KIT	0.00001	87.2033	7152	1997	A=1997, C=0
<input type="checkbox"/>	Unclassified	chr4:55593481	A/A	A	REF		KIT	0.00001	63.514	7127	2000	A=1998, G=2
<input type="checkbox"/>	Unclassified	chr4:55593583	AACCCATGTATGAAC	AACCCATGTATGAAC	REF		KIT	0.00001	86.1953	9494	1974	AACCCATGTATGAAGT=
<input type="checkbox"/>	Unclassified	chr4:55593586	CCATGTATGAAGTAC	CCATGTATGAAGTAC	REF		KIT	0.00001	72.0213	9487	1966	CCATGTATGAAGTACAG TCATGTATGAAGTACAG
<input type="checkbox"/>	Unclassified	chr4:55593587	CATGTATGAAGTACA	CATGTATGAAGTACA	REF		KIT	0.00001	86.0799	9486	1972	CATGTATGAAGTACAGT CGAAGTACAGTGG=0, C CTGG=0, C=0
<input type="checkbox"/>	Unclassified	chr4:55593588	ATGTATGAAGTAC/AT	ATGTATGAAGTAC	REF		KIT	0.00001	62.5726	9494	1974	ATGTATGAAGTAC=1972, CTGTATGAAGTAC=2, AA
<input type="checkbox"/>	Unclassified	chr4:55593589	TGTATGAAGTACAGT	TGTATGAAGTACAGT	REF		KIT	0.00001	86.0714	9479	1971	TGTATGAAGTACAGTGG TGTGGAA=0, TGAA=0, T
<input type="checkbox"/>	Unclassified	chr4:55593591	TATGAAGTACAGTGC	TATGAAGTACAGTGC	REF		KIT	0.00001	60.5506	6967	1387	TATGAAGTACAGTGGAA AATGAAGTACAGTGGAA T=0

FILTER OPTIONS

SEND FEEDBACK

Delección no fue reportada por el software por NOCALL (strand bias >0.95)

Debido al mapeo incorrecto el software no llama la variante



Revisión y adaptación del algoritmo de análisis

Experiencia del equipo es fundamental

Analysis Results

Analysis Name: ONCO50-170_Output MNV

MyVariants Download Visualize Selected Variants Send to Report Role Switch To Generate Report

To learn more about reviewing your results, visit the help guide

Summary Functional Population Ontologies Pharmacogenomics Somatic QC

Search Go Preferences

Classification	Locus	Genes	Type	Ref	Genotype	Variant Effect	Coverage	% Frequency	Phred QU...	Coding	Amino Acid Change	dbSNP	COSMIC/NCBI	Variant ID
Unclassified	chr4:55593633	KIT	INDEL	AATTATGTTT/ AATTATGTTTAC/	nonframeshiftBlockSubstitution		9813	44.43	50.0	c.1701_1727del	p.Asn567_Leu576delinsLysAsp	rs1016976398 ...(17)		
Unclassified	chr9:139399408	NOTCH1	INDEL	GCAC	GCAC/G	nonframeshiftDeletion	971	1.44	11.5252	c.4732_4734del	p.Val1578del	rs761020817		COSM13047
Unclassified	chr9:21971131	CDKN2A	SNV	G	G/A	missense	249	1.20	6.07957	c.227C>T	p.Ala76Val	rs587776716 ...(2)		COSM13766

1 - 3 of 3 items



KIT: N567_L576delinsKD, Variante patogénica

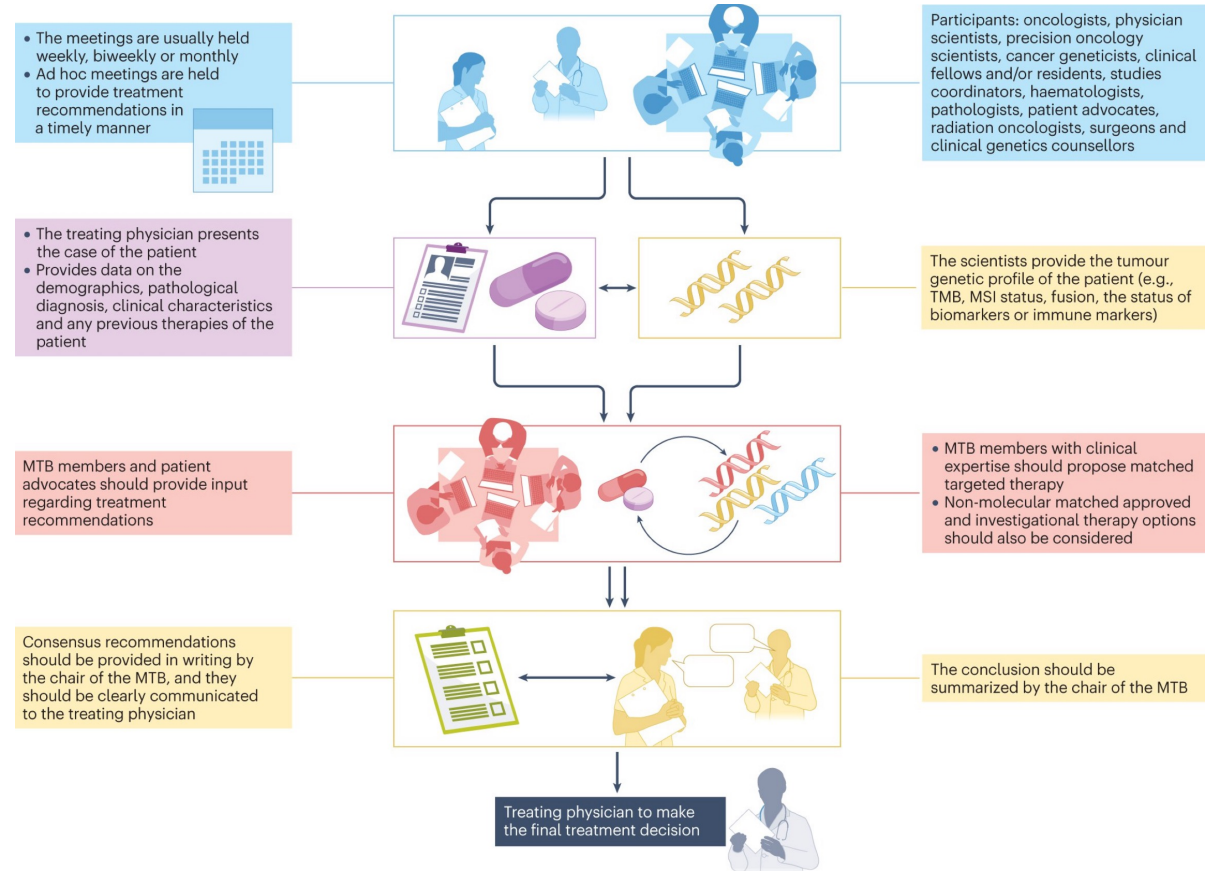
Trabajo en equipo es fundamental



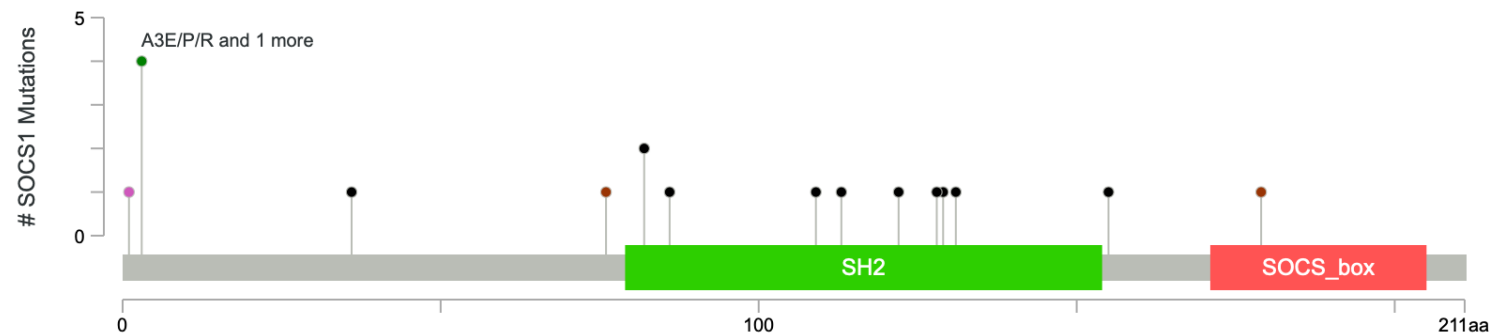
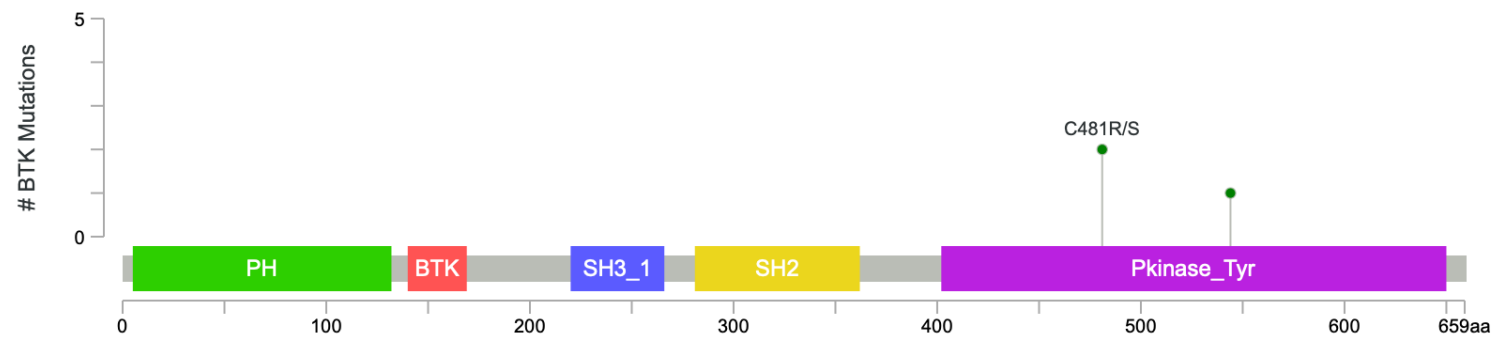
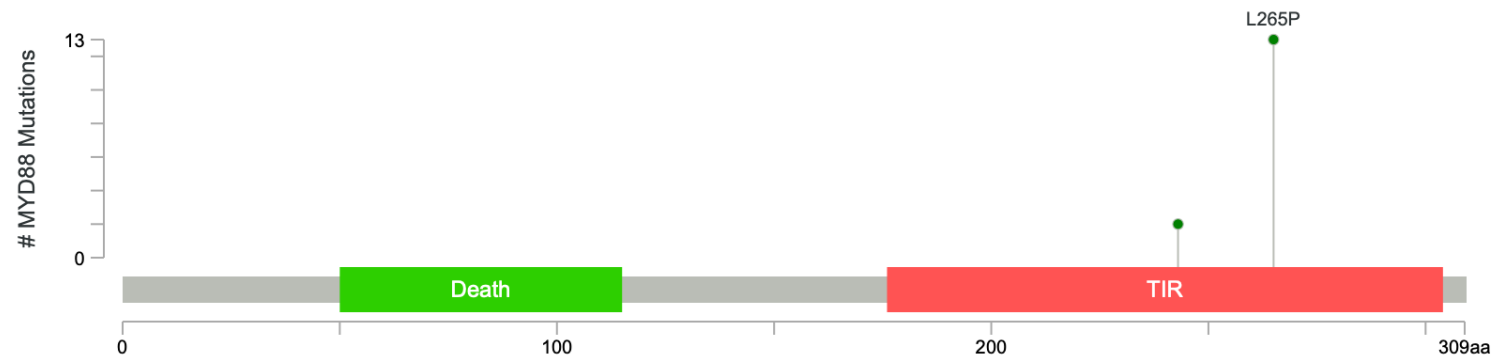
Mejor toma de decisión clínica



Comité Molecular de Tumores



Mejor toma de decisión clínica



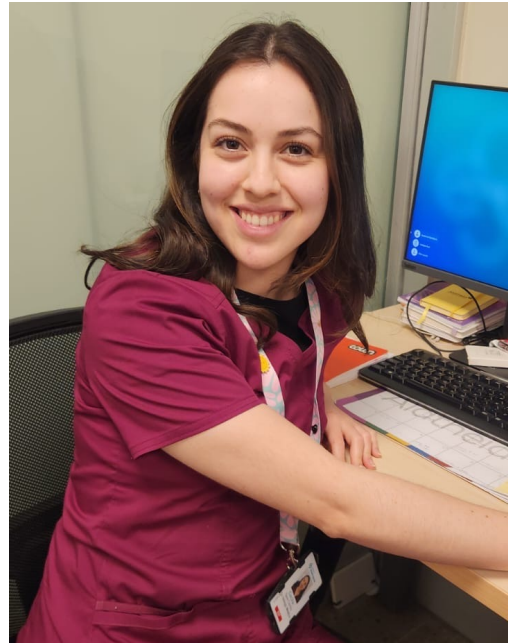
Mejor toma de decisión clínica



Para llevar a casa

- El estudio de alteraciones moleculares es cada vez más relevante en medicina de precisión
- NGS permite el estudio simultáneo de biomarcadores con utilidad clínica
- La experiencia en el flujo de trabajo es crítica para obtener resultados confiables
- El análisis de variantes debe incluir un proceso de visualización y contextualización clínica
- Los resultados de un NGS deben contextualizarse biológica y clínicamente
- El máximo beneficio clínico del NGS se logra integrando competencias

El equipo de Diagnóstico Molecular



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