

II Jornadas de Genómica Clínica
La Revolución Genómica en la Medicina Clínica: Estrategias Preventivas, Diagnósticas
y Tratamientos

Viernes 27/10/2023 - 9 a 18hs
Facultad de Ciencias Exactas y Naturales - UBA.

**Exomas germinales y tumorales en la práctica clínica de tumores
gastrointestinales**

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Unidad de Investigación Traslacional GENUIT

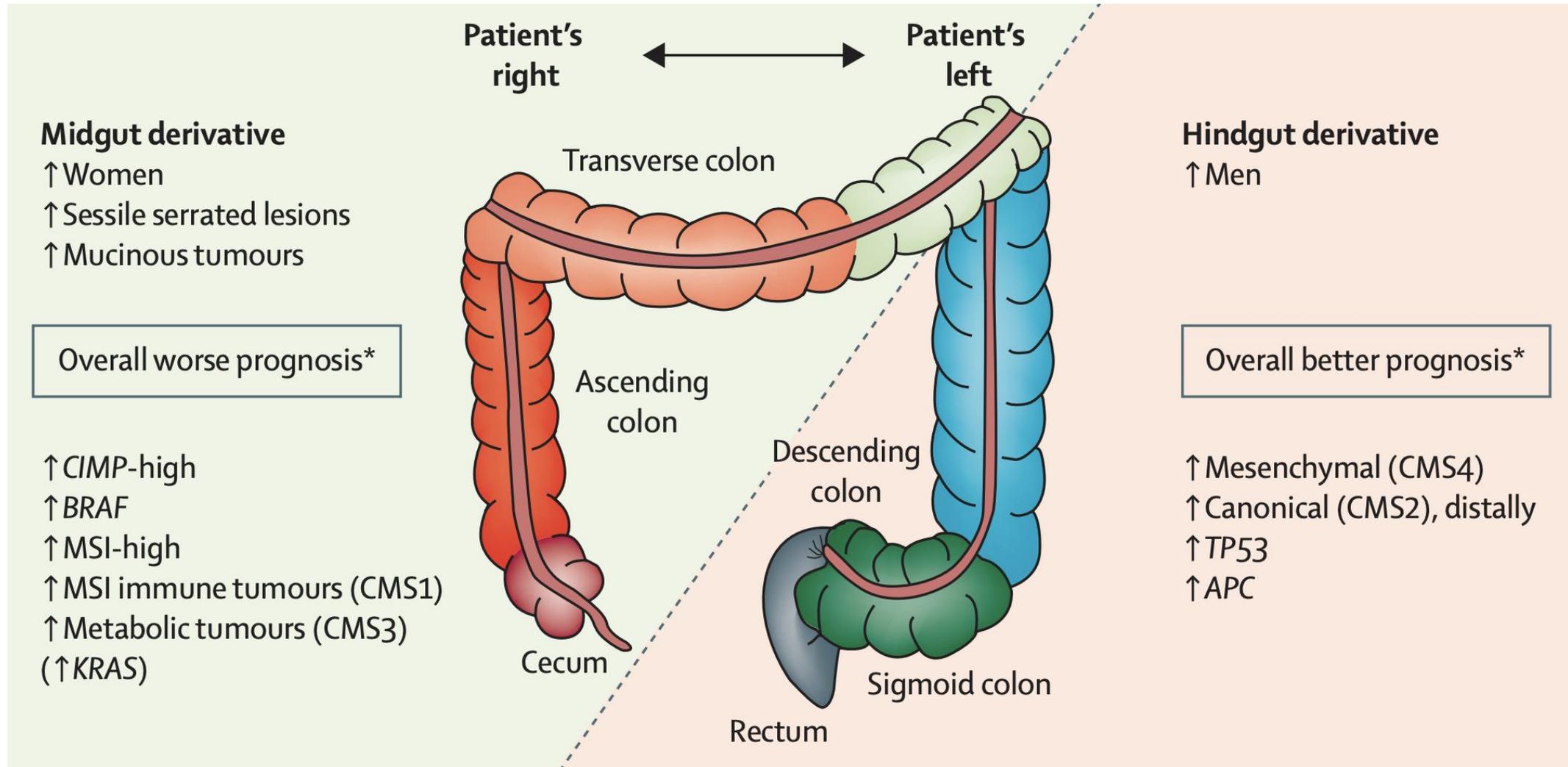
Hospital de Gastroenterología "Dr. C. B. Udaondo" - IATTGI



GENUIT


IATTGI

Un órgano muchas enfermedades



Un órgano muchas enfermedades

KRAS Wild-Type and *KRAS* Mutant Pancreatic Ductal Adenocarcinoma: Are These One in the Same or Separate Entities?

July 19, 2023

Dae Won Kim, MD; Mahati Paravathaneni, MD; and Todd Knepper, PharmD

Table. *KRAS*-Mutated Versus *KRAS* Wild-Type Pancreatic Cancer

	<i>KRAS</i> mutant PDAC	<i>KRAS</i> wild-type PDAC
Prevalence	90%	10%
MSI-high	0.7%	4.7%
TMB-high	1.0%	5%
Targetable oncogenic mutations (<i>BRAF</i> , <i>BRCA</i> , and <i>PALB2</i>)	Less frequent	More frequent
Targetable oncogenic fusions (<i>ALK</i> , <i>BRAF</i> , <i>FGFR2</i> , <i>MET</i> , <i>NRG1</i> and <i>RET</i>)	0%-1%	19%-67%



WES germinal



- ¿Variante patogénica?
- Vigilancia en la familia
- Sensible a tratamientos

NCCN guidelines:
Cancer de Páncreas
Ovario, Colorrectal

15% de todos los
diagnósticos de cáncer
hay variantes
germinales en su
mayoría accionables



WES tumoral



- Predicción de respuesta al tto
- Predicción de la sobrevida
- Indicaciones agnósticas
- Ayuda a caracterizar variantes germinales.



Utilidad del WES germinal en Cáncer

Búsqueda de variantes germinales de predisposición al cáncer

Búsqueda de variantes germinales por sensibilidad a tratamientos

Muestra “normal” para extracción de variantes germinales sobre WES somático

Valoración de AF para cálculo de LOH (pérdida de heterocigosidad) sobre muestra somática

Cáncer hereditario

Variantes germinales:

Síndromes hereditarios

Síndrome de Lynch: **MLH1 MSH2(EPCAM) MSH6 PMS2**

Síndrome polipósico: **APC MUTYH**

Li-Fraumeni: **TP53**

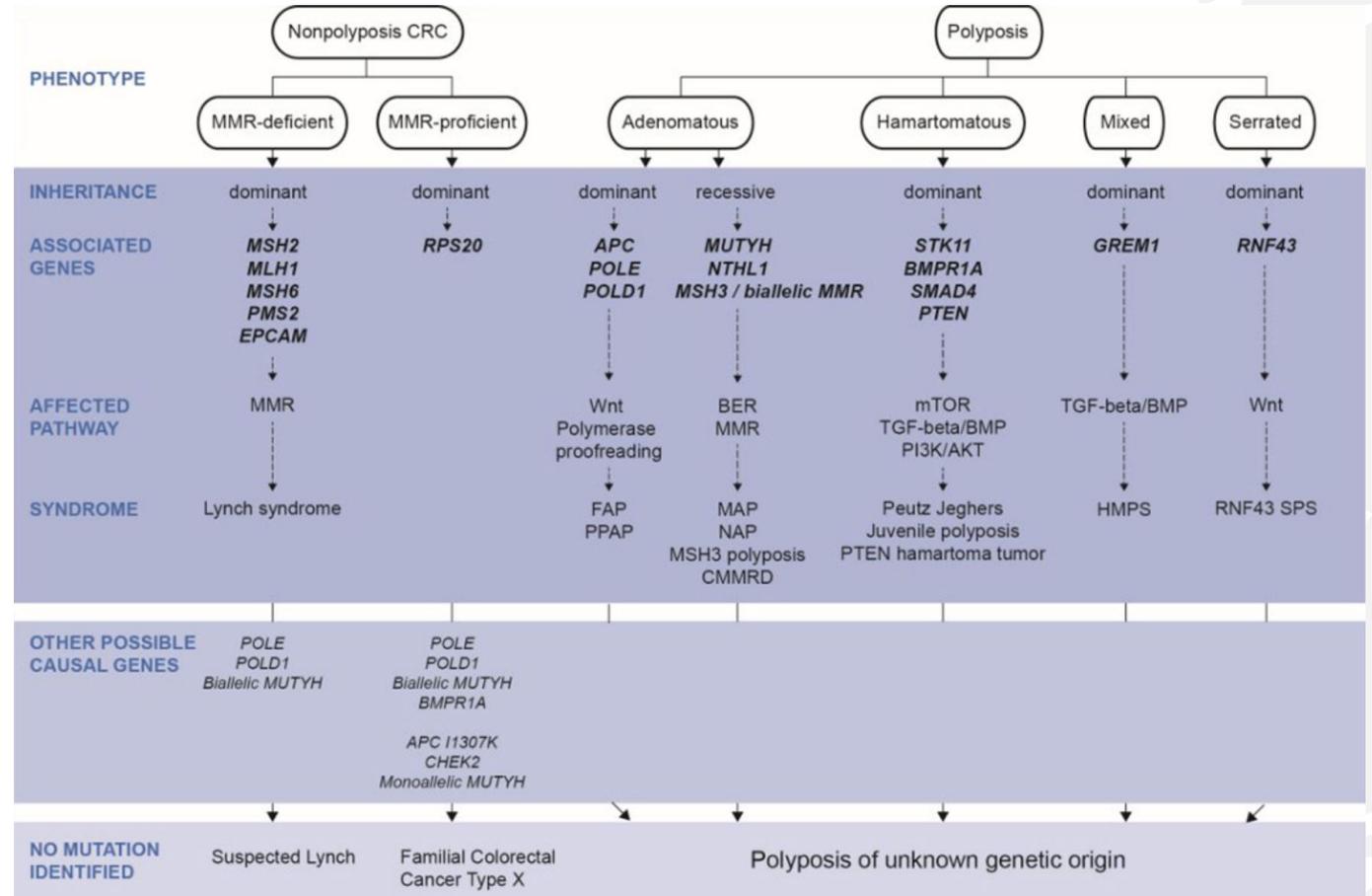
Bloom Síndrome: **NBN**

Anemia de Fanconi: **FANCA/B/C**

Poliposis Juvenil: **SMAD4 BMPR1A**

Síndrome de Peutz-Jeghers: **STK11**

Síndrome Hamartomatoso: **PTEN**



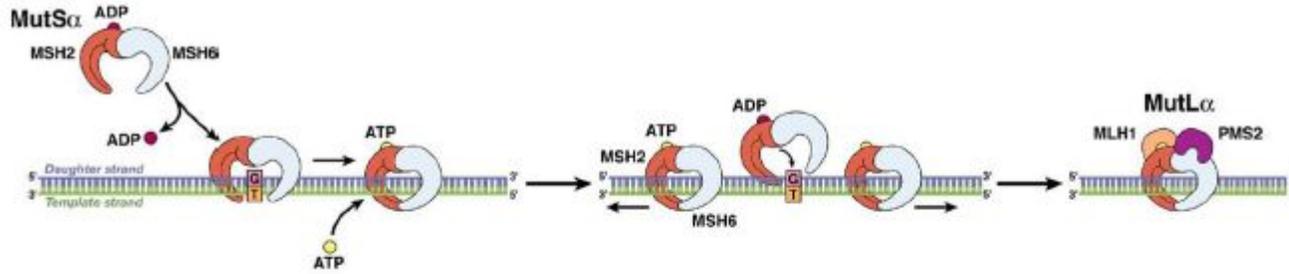
Cáncer Gástrico Difuso: **CDH1**

PDAC: **BRCA1/2 PALB2 CHEK1 ATM CDKN2A**

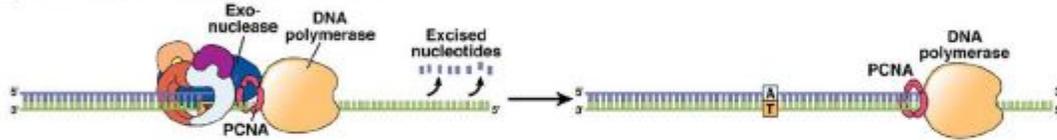
Síndrome mama-ovario: **BRCA1/2 PALB2**

Proteínas reparadoras del ADN

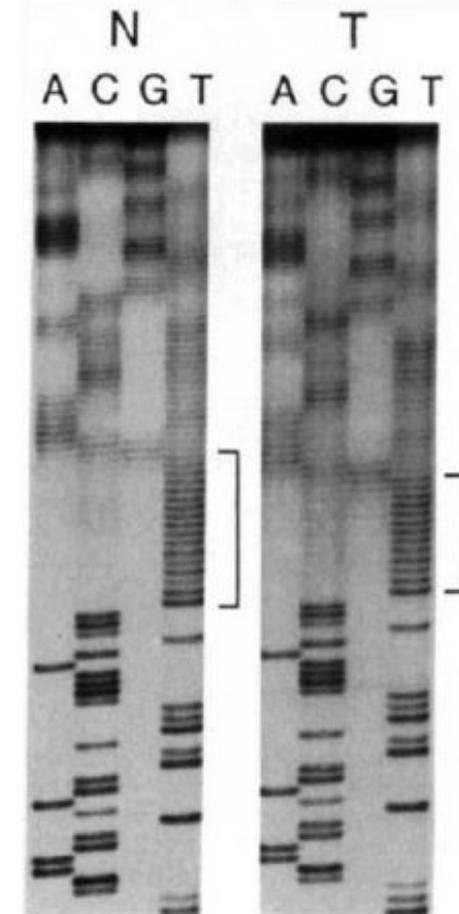
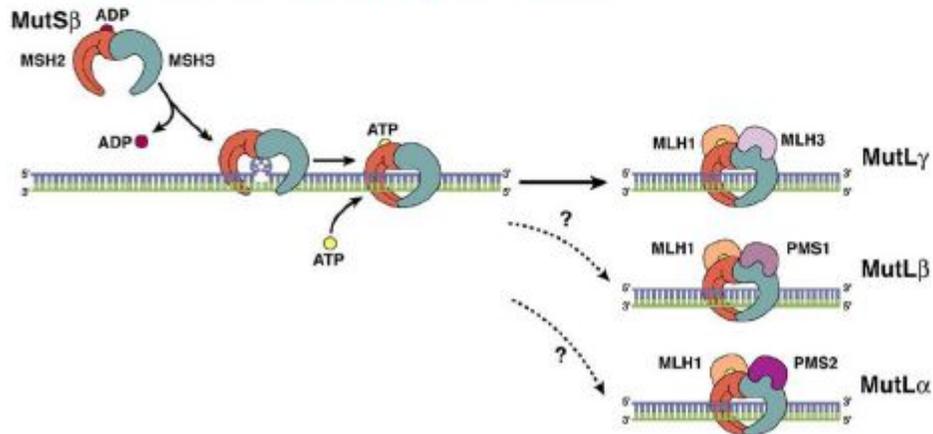
A Single mismatch



B Exonuclease complex and resynthesis

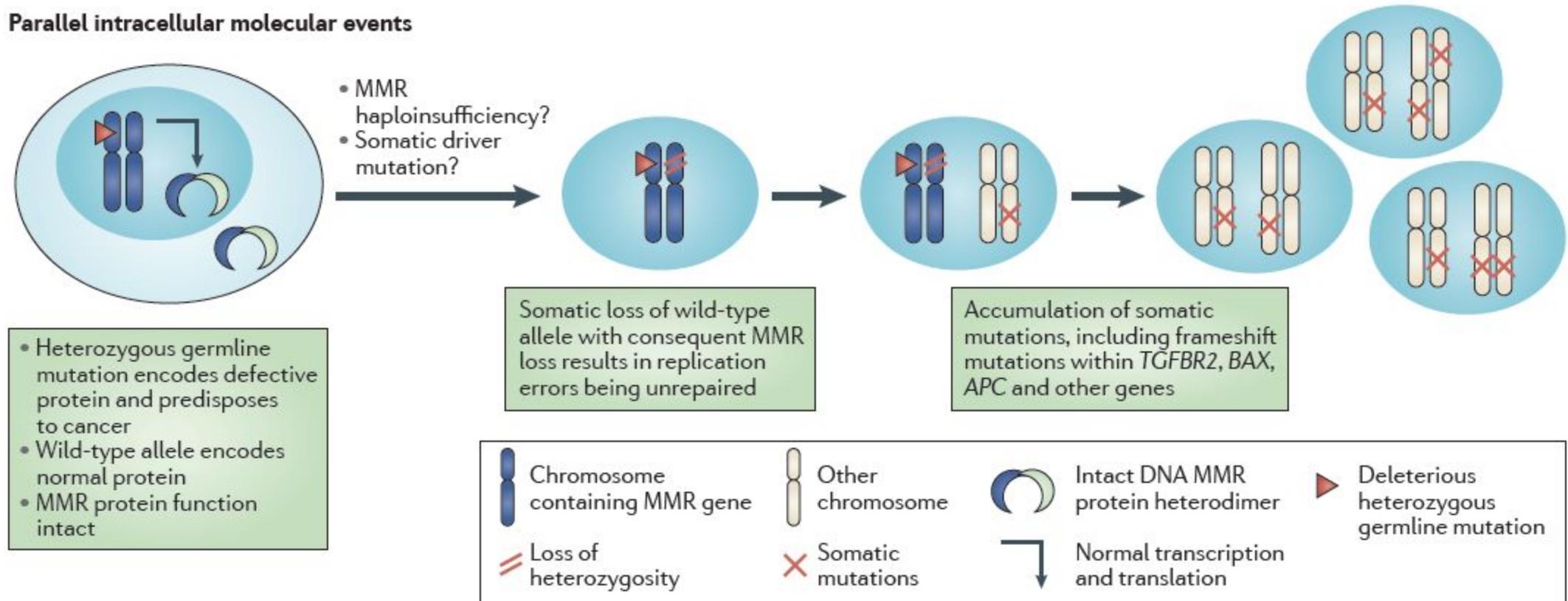


C Insertion/deletion loop and variations in MutL complexes

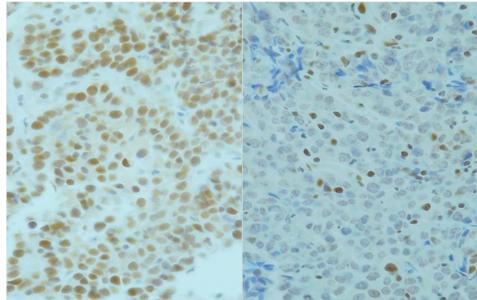


Mecanismo molecular en el desarrollo de la enfermedad

Parallel intracellular molecular events



Lynch Syndrome



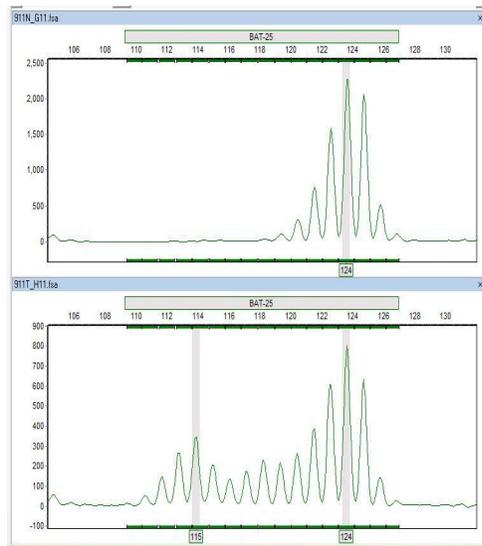
Expresión
Conservada

Déficit en la
expresión

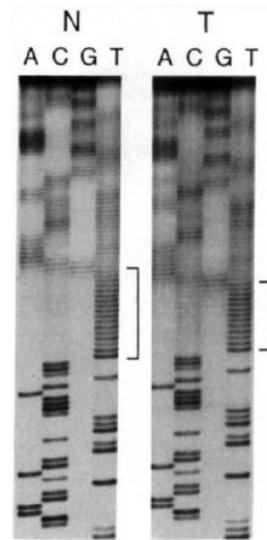
Cual es la primer sospecha ante una variantes candidata en los genes MMR de reparación del ADN si tenemos pérdida de expresión en el tumor de alguna proteína de reparación e inestabilidad de microsatélites?

La información somática es determinante para la clasificación de variantes germinales de predisposición al cáncer.

Qué podría aportar tener el WES somático?



Inestabilidad de Microsatelites



High TMB
MSI signature
LOH o variante puntual confirmando segundo hit

Sensibilidad a tratamientos:

Inhibidores de PARP (Mecanismo de letalidad sintética)

PDAC BRCA1/2 germinal indicación de Olaparib en mantenimiento: (POLO trial)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer

Talia Golan, M.D., Pascal Hammel, M.D., Ph.D., Michele Reni, M.D.,
Eric Van Cutsem, M.D., Ph.D., Teresa Macarulla, M.D., Ph.D.,
Michael J. Hall, M.D., Joon-Oh Park, M.D., Ph.D., Daniel Hochhauser, M.D., Ph.D.,
Dirk Arnold, M.D., Ph.D., Do-Youn Oh, M.D., Ph.D.,
Anke Reinacher-Schick, M.D., Ph.D., Giampaolo Tortora, M.D., Ph.D.,
Hana Algül, M.D., Ph.D., M.P.H., Eileen M. O'Reilly, M.D.,
David McGuinness, M.Sc., Karen Y. Cui, M.D., Ph.D., Katia Schlienger, M.D., Ph.D.,
Gershon Y. Locker, M.D., and Hedy L. Kindler, M.D.

Patients were eligible if they were 18 years of age or older and had histologically or cytologically confirmed pancreatic adenocarcinoma and a **documented deleterious or suspected deleterious germline mutation in BRCA1 or BRCA2.**

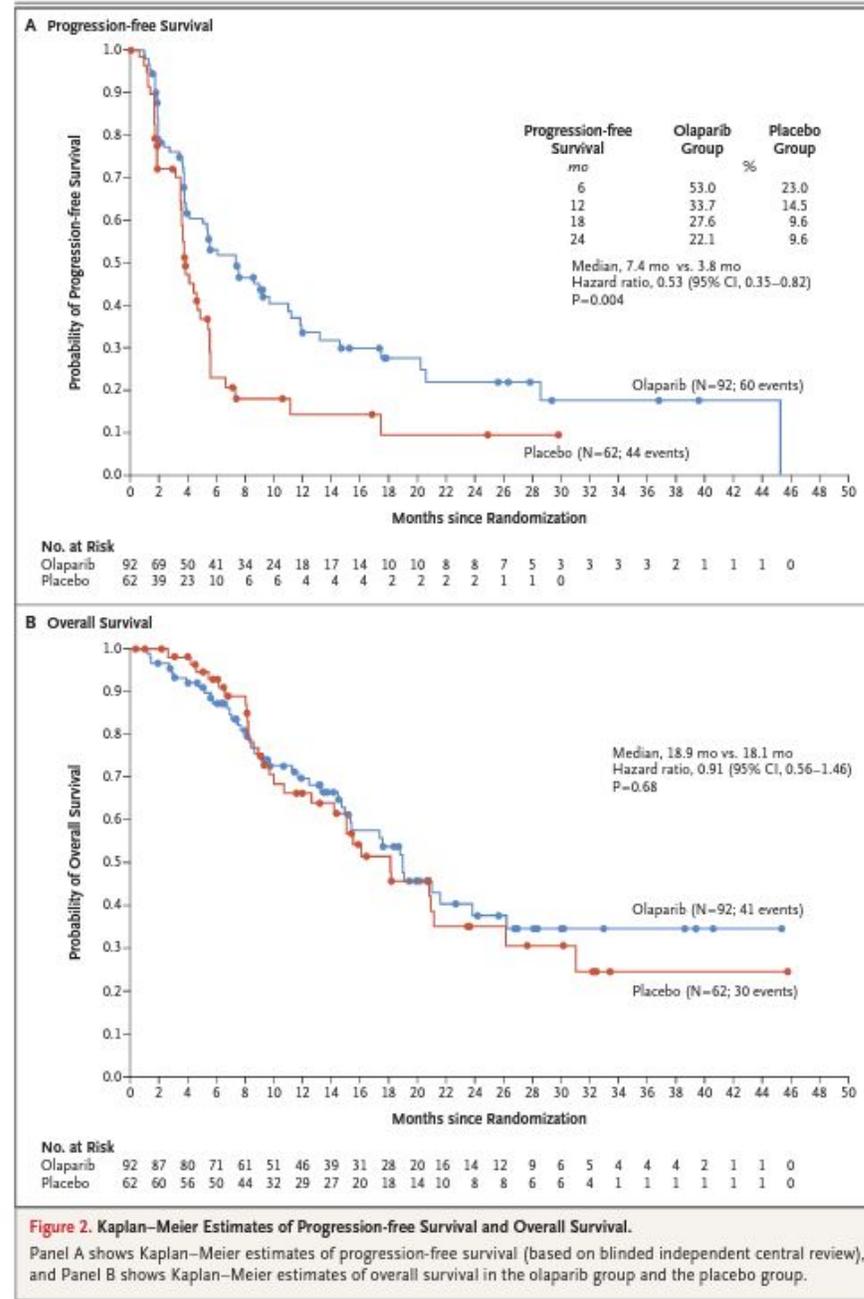
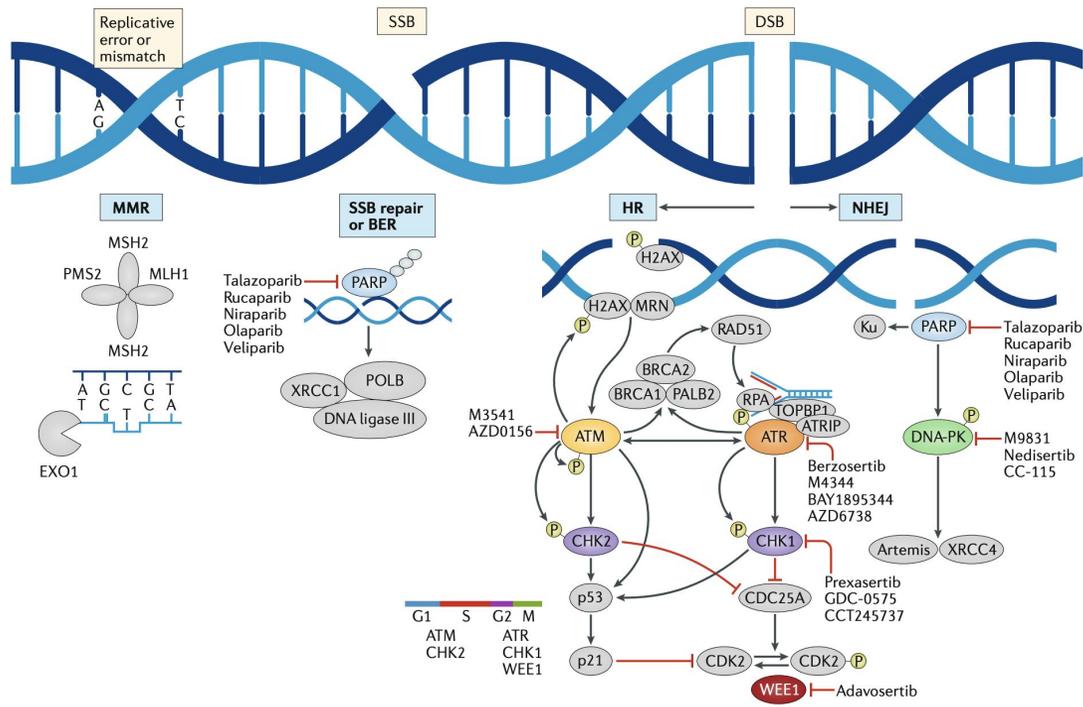


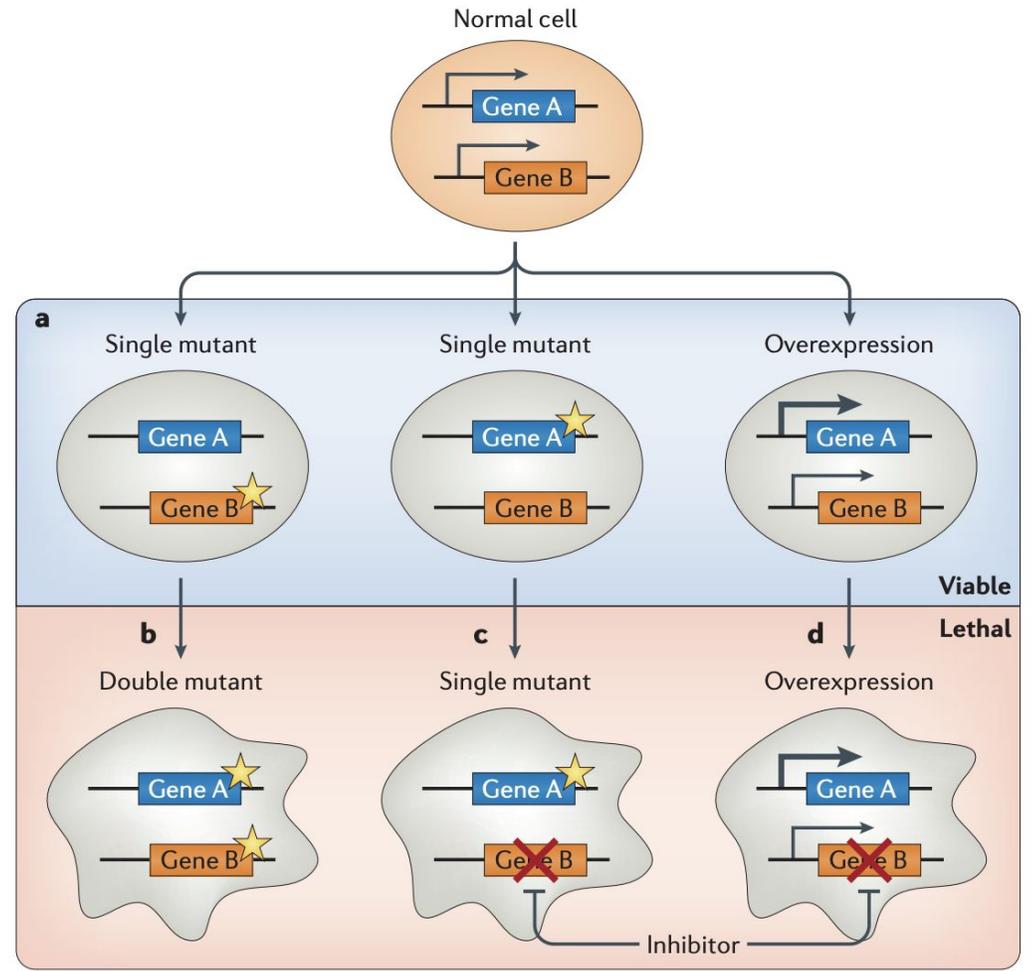
Figure 2. Kaplan–Meier Estimates of Progression-free Survival and Overall Survival.

Panel A shows Kaplan–Meier estimates of progression-free survival (based on blinded independent central review), and Panel B shows Kaplan–Meier estimates of overall survival in the olaparib group and the placebo group.

DNA damage response pathways



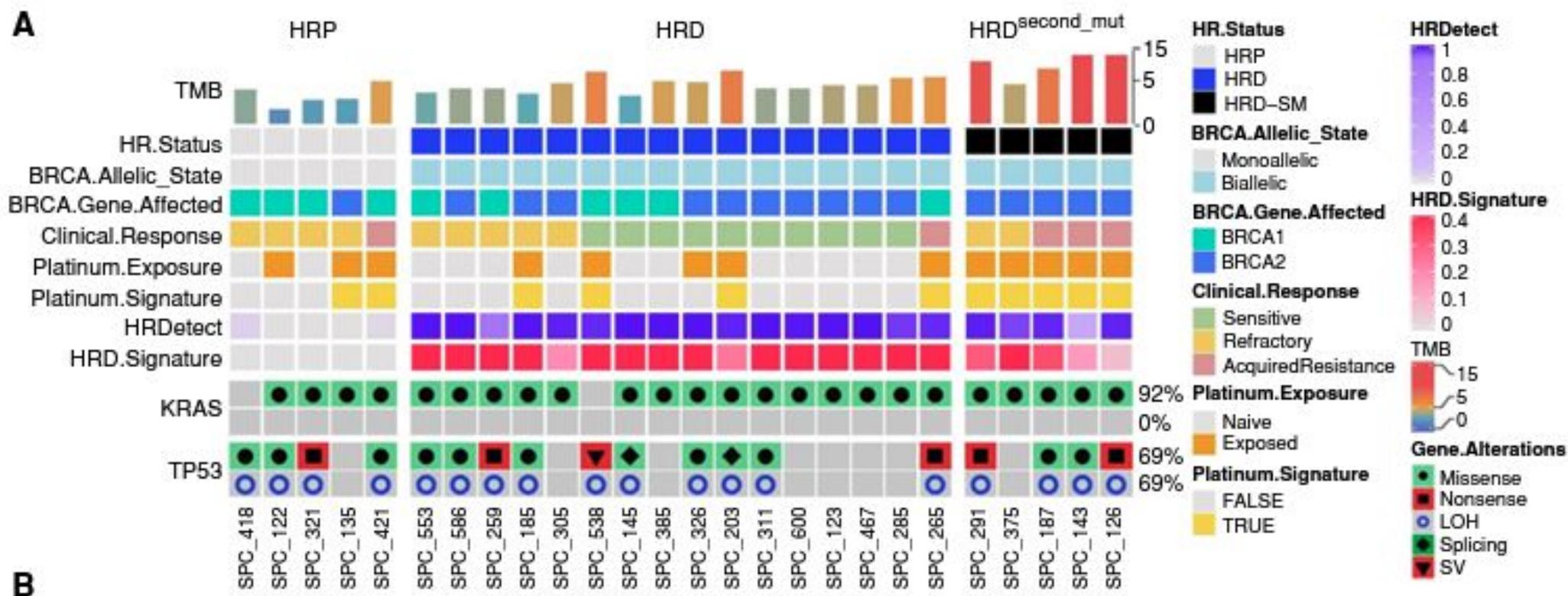
synthetic lethality



Spectrum of Response to Platinum and PARP Inhibitors in Germline *BRCA*-Associated Pancreatic Cancer in the Clinical and Preclinical Setting

Chani Stossel ; Maria Raitses-Gurevich ; Dikla Atlas ; Tamar Beller ; Yulia Glick Gorman ; Sharon Halperin ; Eyal Peer ; Robert E. Denroche ; Amy Zhang ; Faiyaz Notta ; Julie M. Wilson ; Grainne M. O'Kane ; Elina Haimov Talmoud ; Nora Amison ; Michael Schvimer ; Seth J. Salpeter ; Vered Bar ; Adi Zundeleovich ; Itay Tirosh ; Rotem Tal ; Gal Dinstag ; Yaron Kinar ; Yonatan Eliezer ; Uri Ben-David ; Nancy S. Gavert ; Ravid Straussman ; Steven J. Gallinger ; Raanan Berger ; Talia Golan 

 Check for updates



Evento responsable de la tumorigénesis

Consecuencias

Mutaciones en genes involucrados en el MMR (Mismatch repair) dejan una “marca” en el genoma tumoral



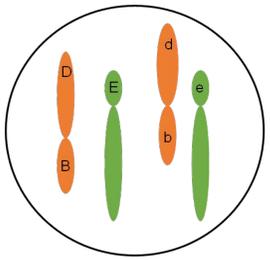
MSI – IHQ MMR –
Mutational Signatures

Mutaciones en genes involucrados en el HRR (homologous recombination repair) dejan una “marca” en el genoma tumoral

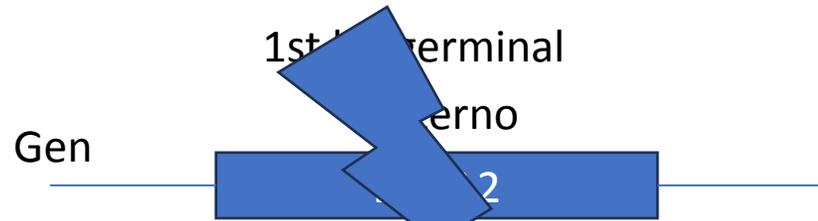


HRD (que se puede medir por : LOH, tAI, LGR) Mutational Signatures

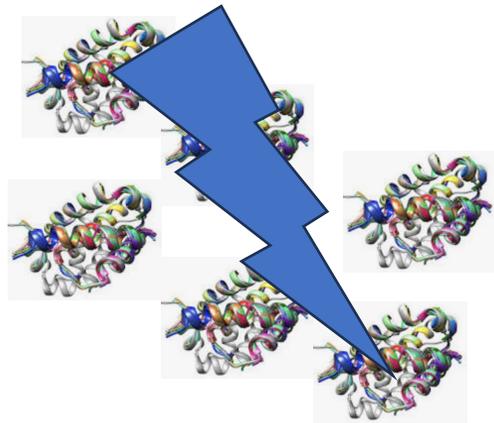
podríamos medir por IHQ las proteínas del sistema de reparación homólogo?



Caso 1 BRCA 2 mutado germinal

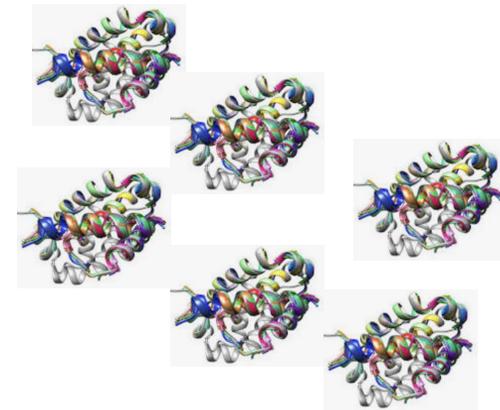


Protein



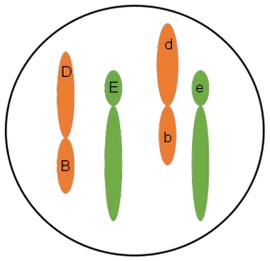
HRD(-)

2nd hit somatic
Paterno

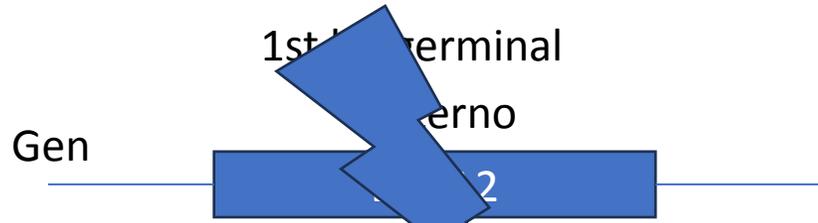


Test genético
muestra de SE

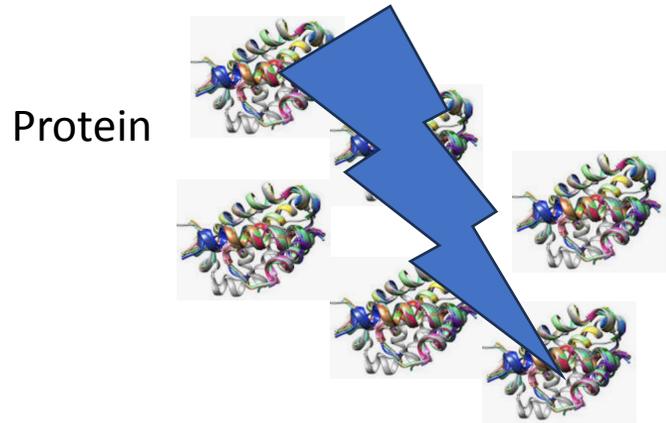




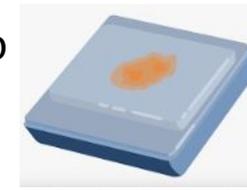
Caso 2 BRCA 2 mutado germinal + somatico



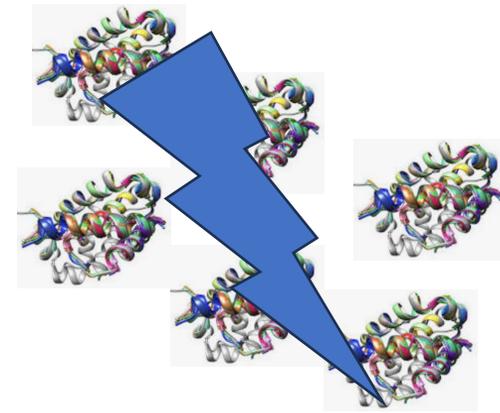
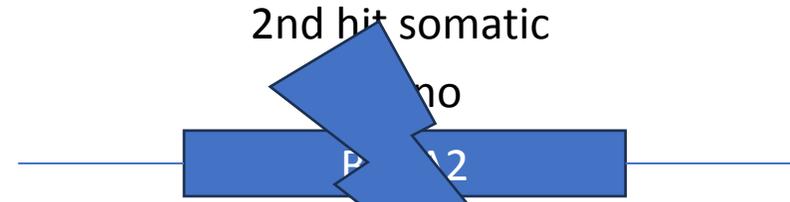
HRD (+)



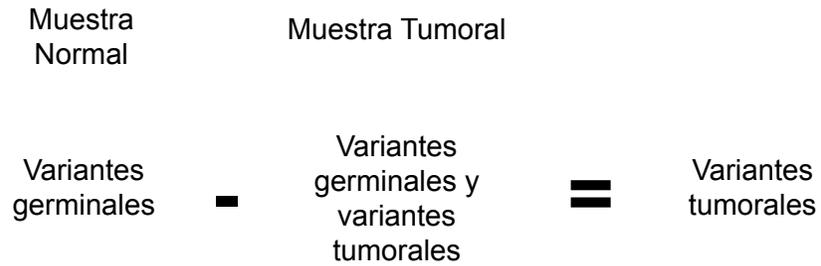
Test somatico



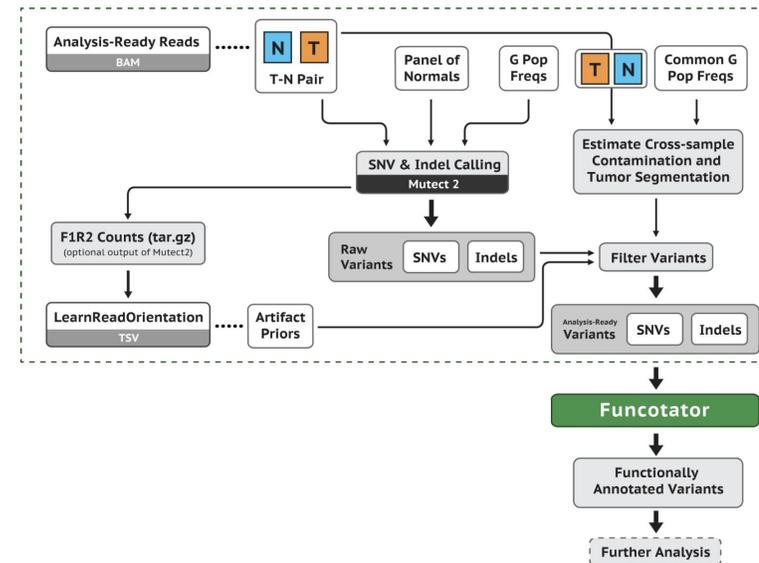
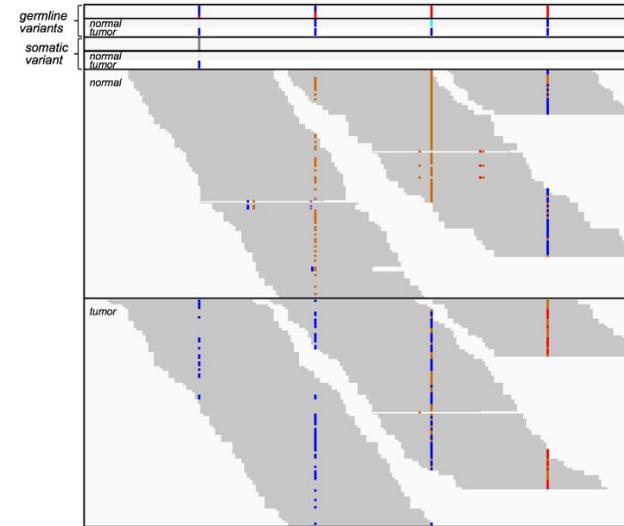
Test genetico muestra de SE



Muestra “normal” para extracción de variantes germinales sobre WES somático Calling – GATK mutect2 (varscan, strelka, deepomatic)

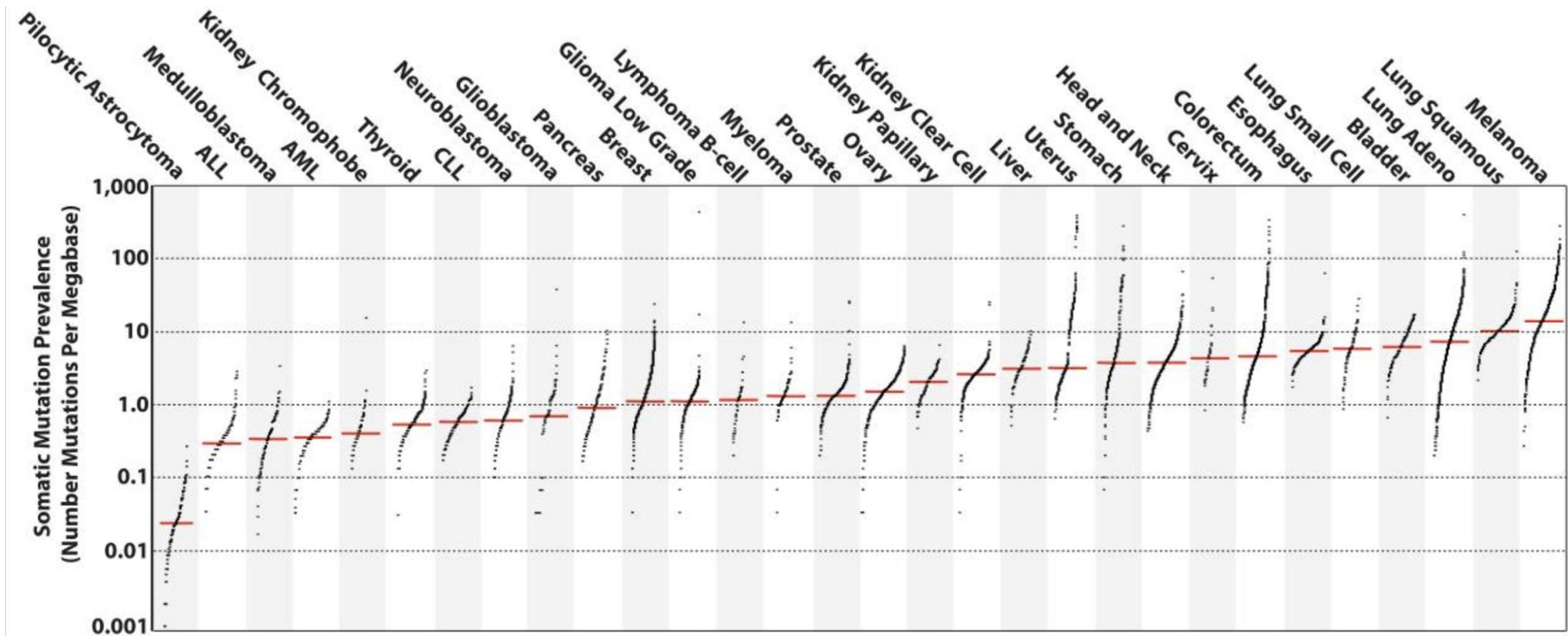


Usar una muestra normal para el calling somático, mejora drásticamente la calidad de las mutaciones somáticas

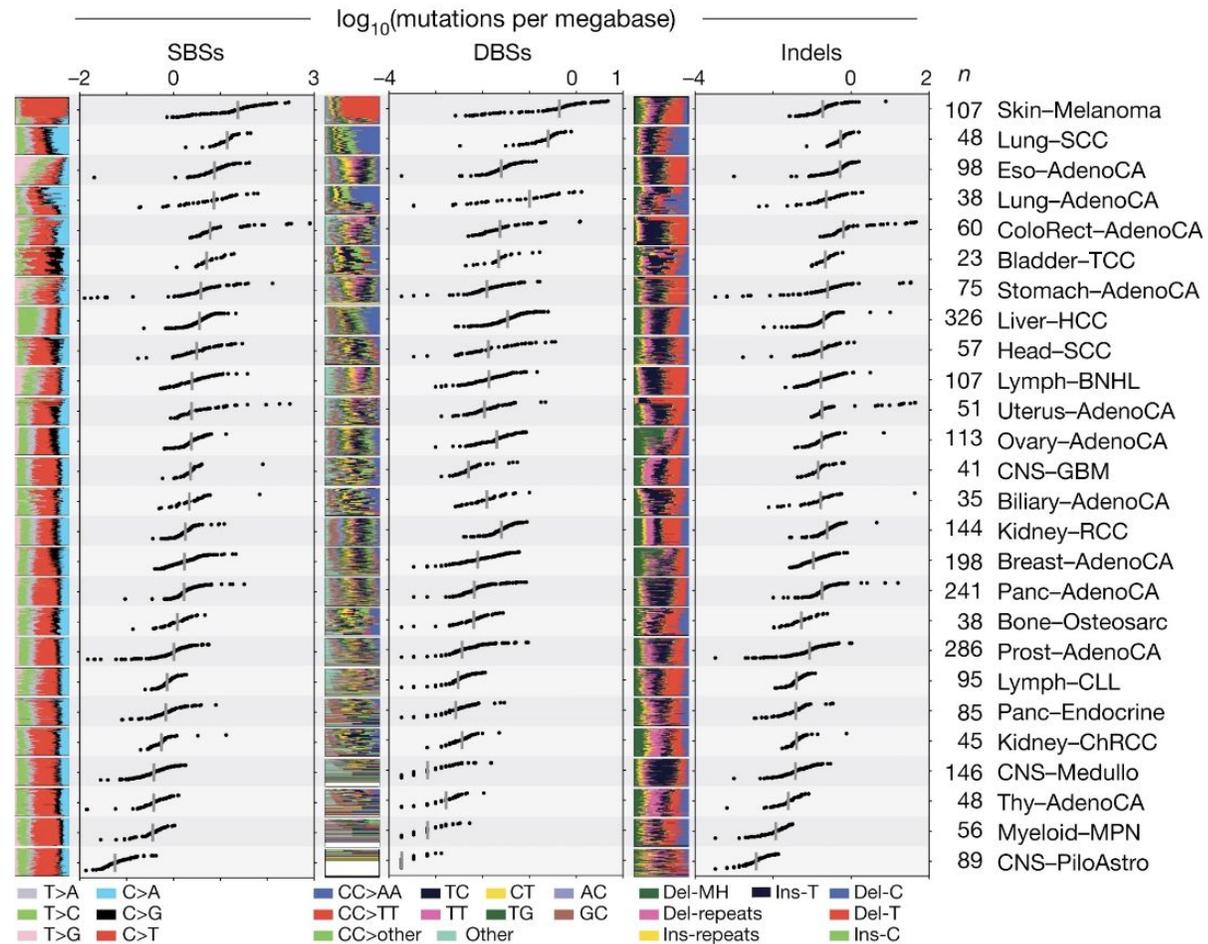


Mutaciones somáticas en cáncer. La carga de las mismas es muy variables entre tipos tumorales

Alexandrov LB. Nature 2013

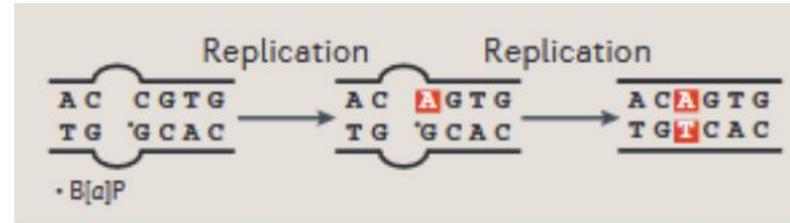


No solo la cantidad es variable
sino que también la calidad

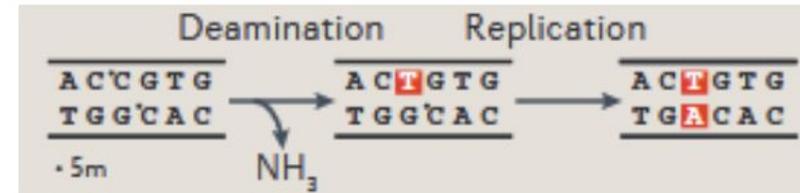


Diferentes patrones de mutaciones son asociados con diferentes fuentes de daño al DNA

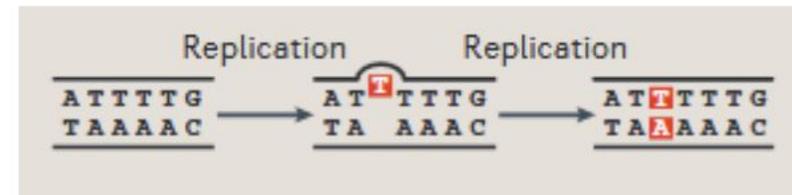
Exposiciones del ambiente (tabaco)



Actividades celulares normales
Deaminación



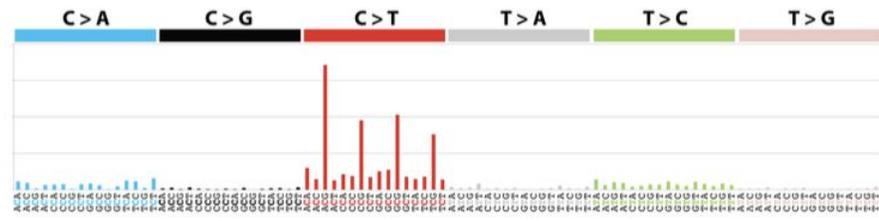
Fallas en la replicación del DNA



Mutational Signature Analysis Reveals NTHL1 Deficiency to Cause a Multi-tumor Phenotype

Judith E. Grolleman,^{1,36} Richarda M. de Voer,^{1,36,38,*} Fadwa A. Elsayed,^{2,36} Maartje Nielsen,^{3,36} Robbert D.A. Weren,^{1,36} Claire Palles,⁴ Marjolijn J.L. Ligtenberg,^{1,5} Janet R. Vos,⁶ Sanne W. ten Broeke,³ Noel F.C.C. de Miranda,² Renske A. Kuiper,¹ Eveline J. Kamping,¹ Erik A.M. Jansen,¹ M. Elisa Vink-Börger,⁵ Isabell Popp,⁷ Alois Lang,⁸ Isabel Spier,^{9,10} Robert Hüneburg,^{10,11} Paul A. James,¹² Na Li,^{13,14} Marija Staninova,¹⁵ Helen Lindsay,¹⁶

nature
medicine



HRDetect is a predictor of *BRCA1* and *BRCA2* deficiency based on mutational signatures

Helen Davies^{1,32}, Dominik Glodzik^{1,32}, Sandro Morganella¹, Lucy R Yates^{1,2}, Johan Staaf³, Xueqing Zou¹, Manasa Ramakrishna^{1,4}, Sancha Martin¹, Sandrine Boyault⁵, Anieta M Sieuwerts⁶, Peter T Simpson⁷, Tari A King⁸, Keiran Raine¹, Jorunn E Eyfjord⁹, Gu Kong¹⁰, Åke Borg³, Ewan Birney¹¹, Hendrik G Stunnenberg¹², Marc J van de Vijver¹³, Anne-Lise Børresen-Dale^{14,15}, John W M Martens⁶, Paul N Span^{16,17}, Sunil R Lakhani^{7,18}, Anne Vincent-Salomon^{19,20}, Christos Sotiriou²¹, Andrew Tutt^{22,23}, Alastair M Thompson²⁴, Steven Van Laere^{25,26}, Andrea L Richardson^{27,28}, Alain Viari^{29,30}, Peter J Campbell¹, Michael R Stratton¹ & Serena Nik-Zainal^{1,31}

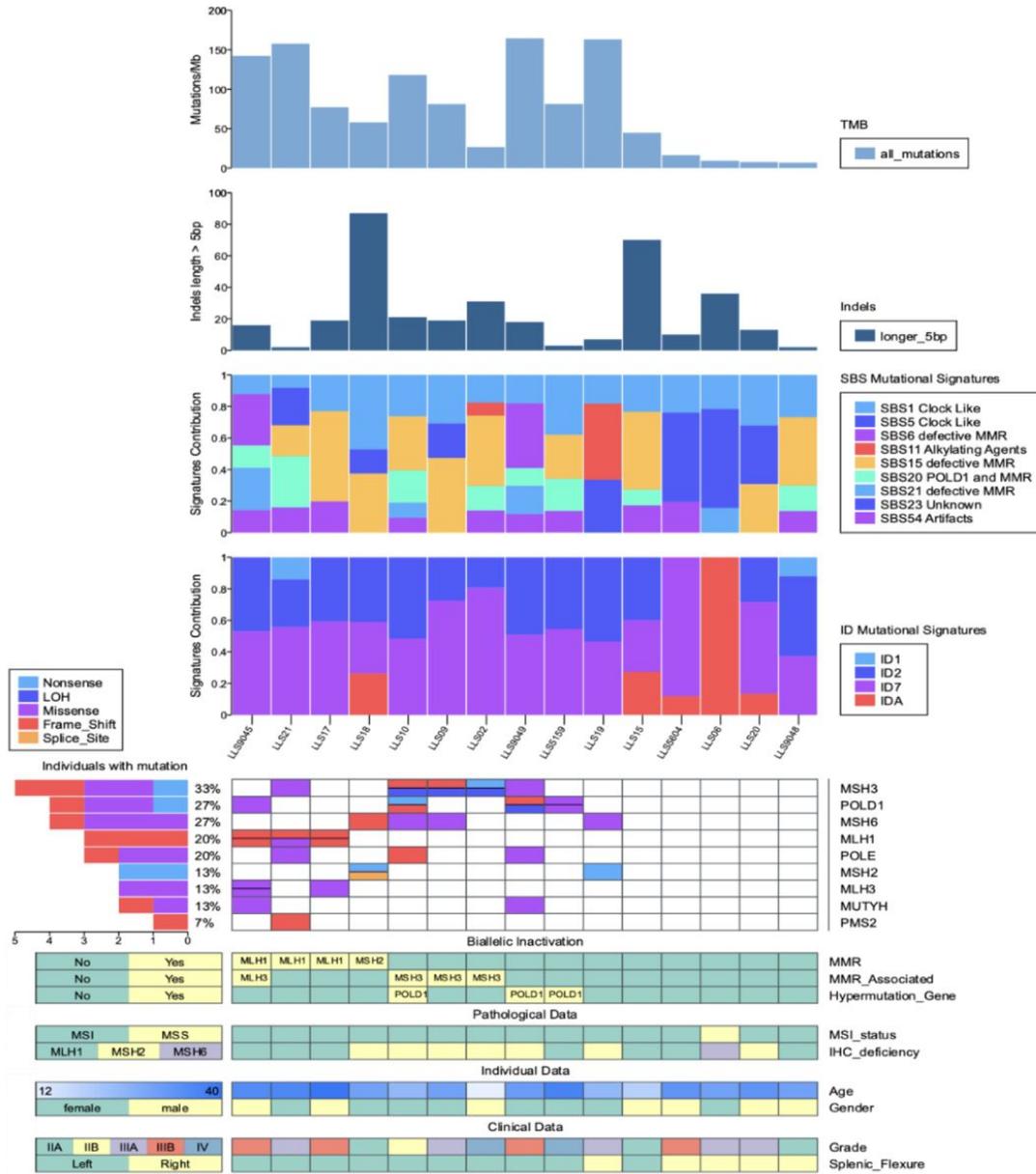
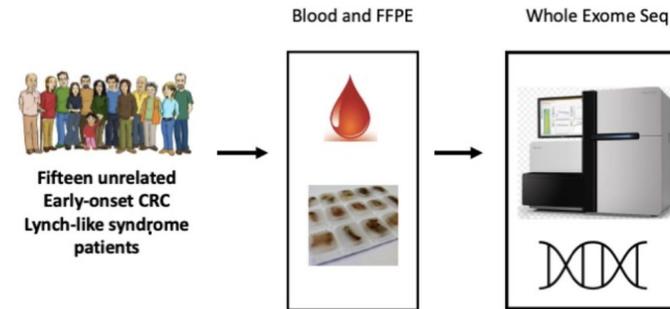
Comprehensive Genomic Characterization of Fifteen Early-Onset Lynch-Like Syndrome Colorectal Cancers

Mariano Golubicki ^{1 2}, Marcos Díaz-Gay ^{3 4}, Laia Bonjoch ³, Sebastià Franch-Expósito ³, Jenifer Muñoz ³, Miriam Cuatrecasas ⁵, Teresa Ocaña ³, Soledad Iseas ¹, Guillermo Mendez ¹, Marcela Carballido ¹, Juan Robbio ^{1 2}, Daniel Cisterna ², Enrique Roca ¹, Antoni Castells ³, Francesc Balaguer ³, Sergi Castellví-Bel ³, Marina Antelo ¹

Affiliations + expand

PMID: 33809179 PMCID: PMC7999079 DOI: 10.3390/cancers13061259 [Sign in](#)

[Free PMC article](#)



Germline WES analysis	
Nine Germline DNA Repair Candidate Genes	
Somatic Biallelic inactivation	No Somatic Biallelic inactivation
PALB2	ERCC6
UVRAG	POLE
RAD54L	EXO5
MCM2	RECQL4
	RAD52

FFPE

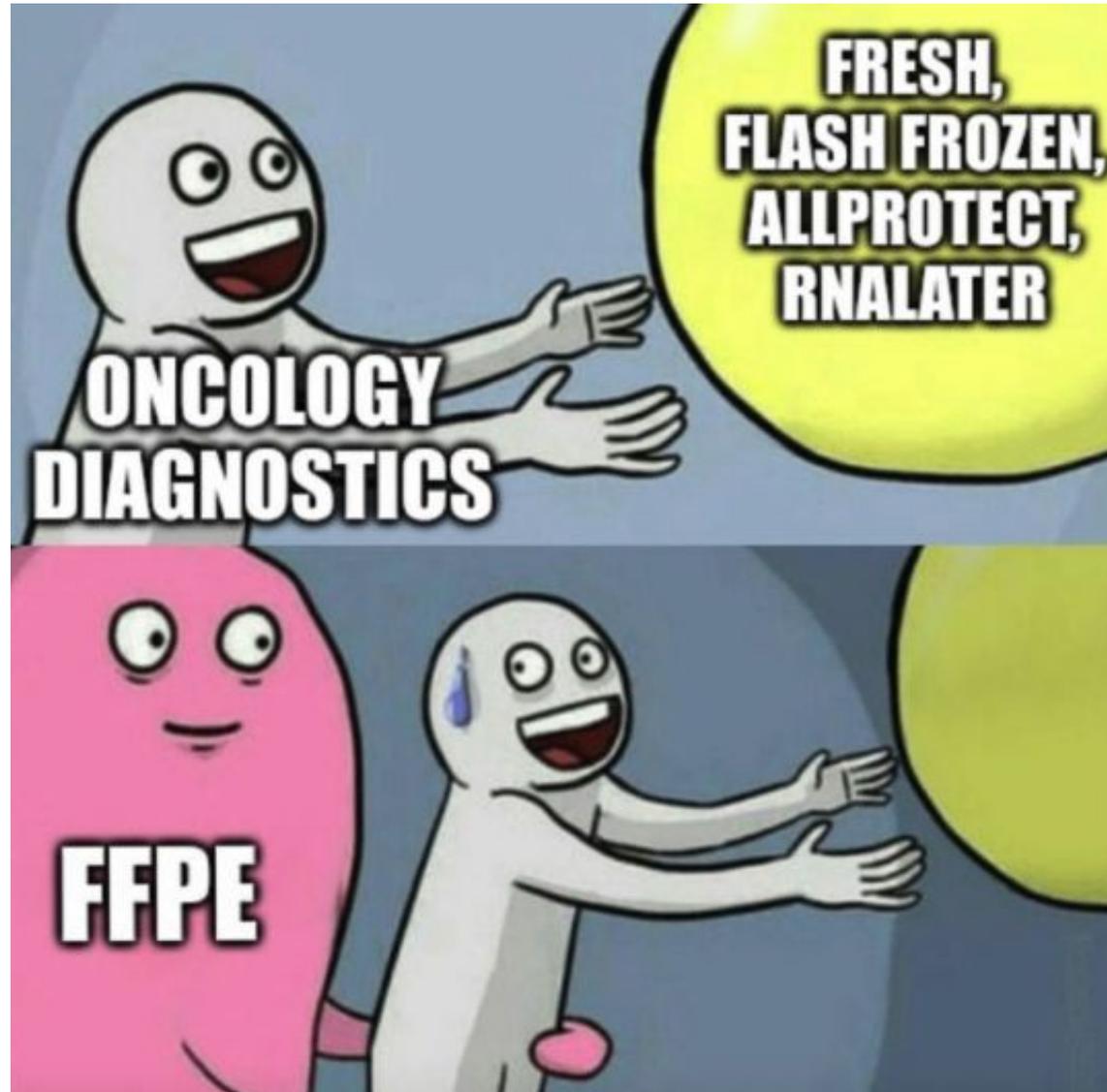
Problema 1: Tiempos de fijacion en formol.

Problema 2: La toma de la muestra está pensado para el diagnóstico histopatológico. No para el diagnóstico molecular.

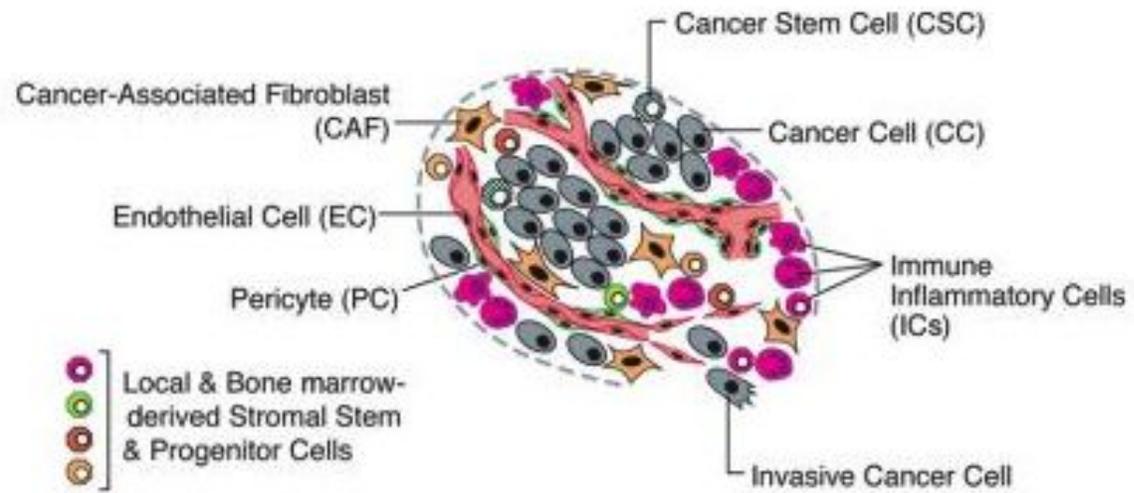
Queda mucho camino por recorrer para entrenar los que toman las muestras:

Endoscopistas
Imagenólogos
Cirujanos

Hoy se toman muestras como hace mas 40 años antes del descubrimiento de la PCR



FFPE

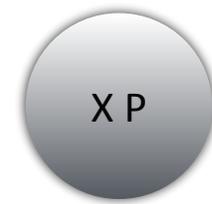
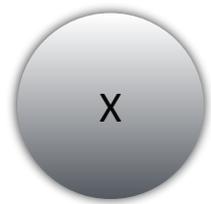


VAF - somático

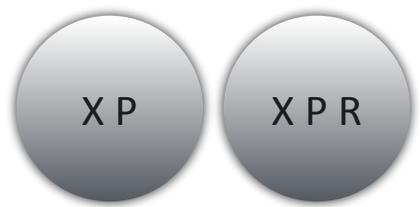
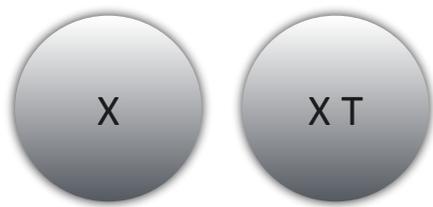
Gen	AF	Total	AA
X	0,5	2	1



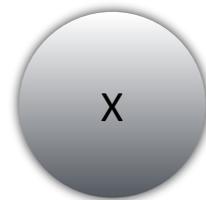
Gen	AF	Total	AA
X	0,5	4	2
P	0,25	4	1



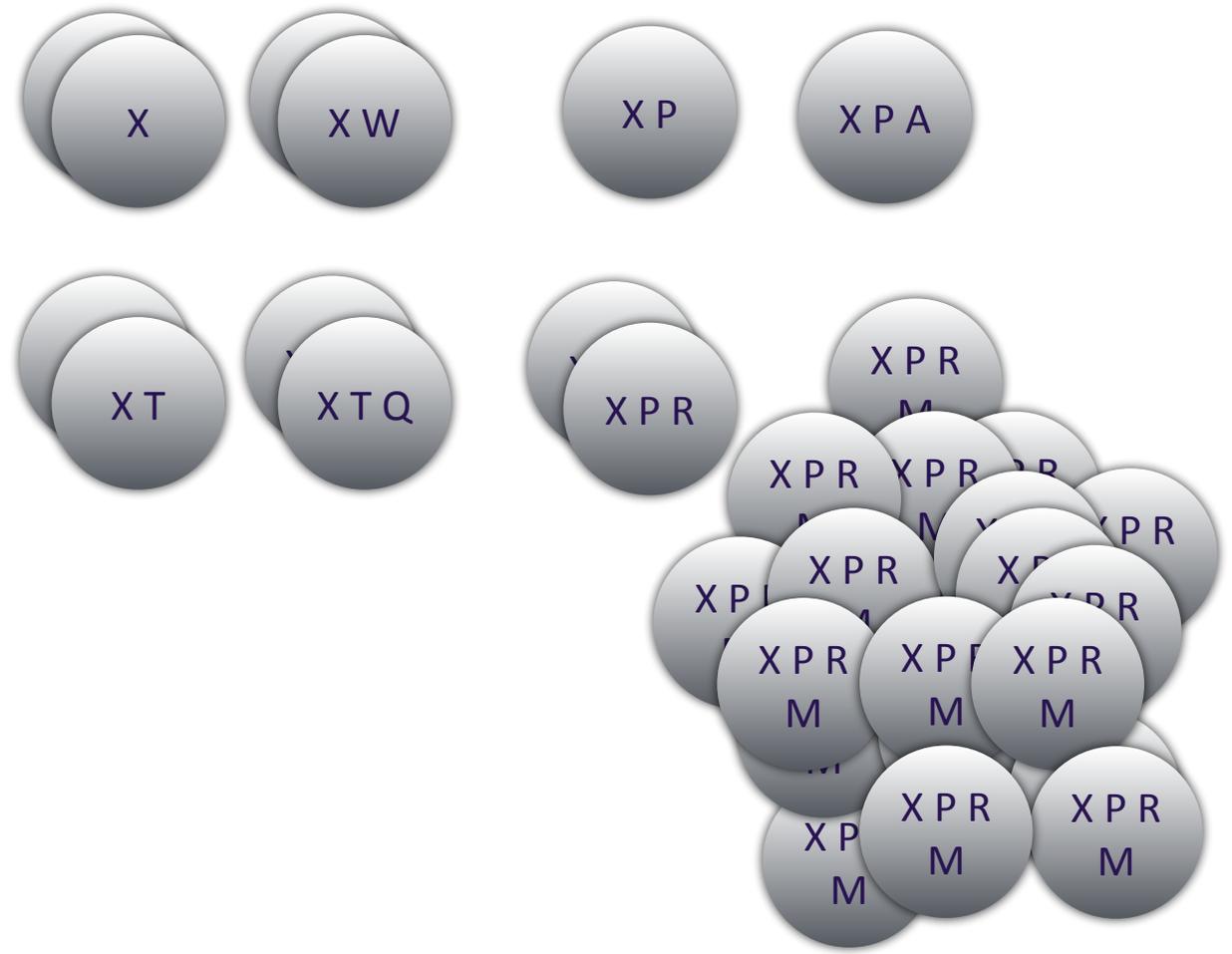
Gen	AF	Total	AA
X	0,5	8	4
P	0,25	8	2
T	0,125	8	1
R	0,125	8	1



Gen	AF	Total	AA
X	0,5	16	8
P	0,25	16	4
T	0,125	16	2
R	0,125	16	2
W	0,063	16	1
Q	0,063	16	1
A	0,063	16	1
M	0,063	16	1



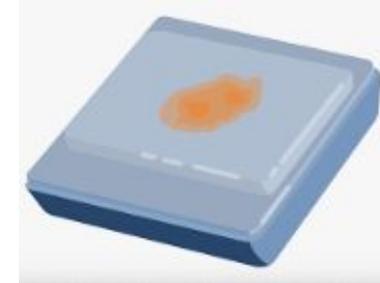
Gen	AF	Total	AA
X	0,5	68	34
P	0,38	68	26
T	0,06	68	4
R	0,324	68	22
W	0,03	68	2
Q	0,03	68	2
A	0,03	68	2
M	0,294	68	20



Reads Alelo alternativo

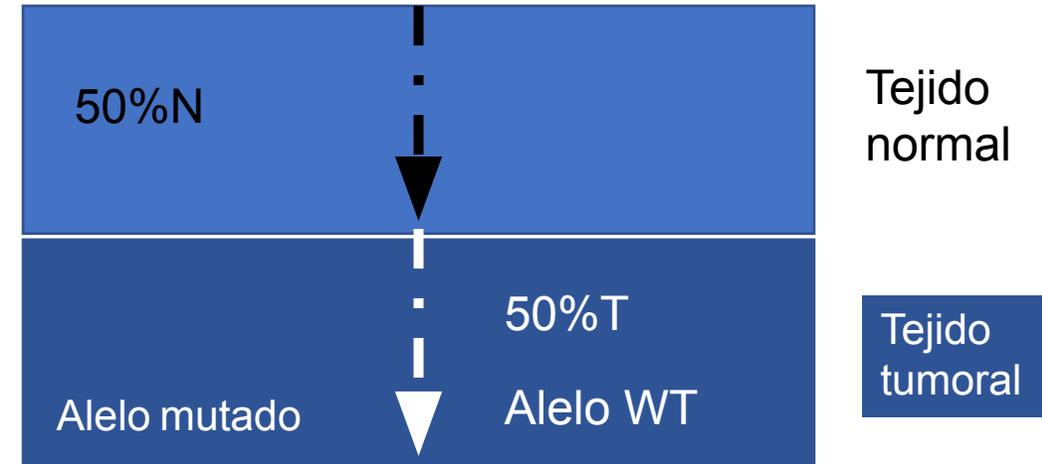
= VF o AF

Reads Alelo alternativo + Reads Alelo referencia



En tejido somático los límites se ponen difusos sobre la ploidía de las variantes

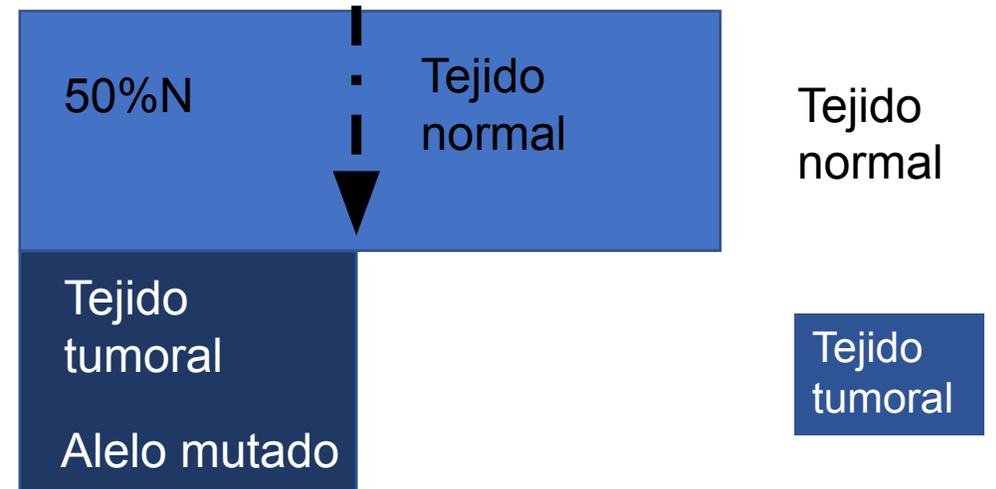
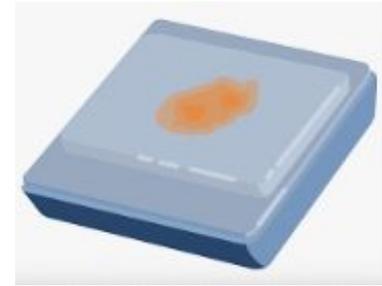
en un mundo ideal una variante heterocigota en tumor no tendría 0.5 de VF, sino que 0.25 con un porcentaje de células tumorales 50%



LOH = pérdida de heterocigosidad

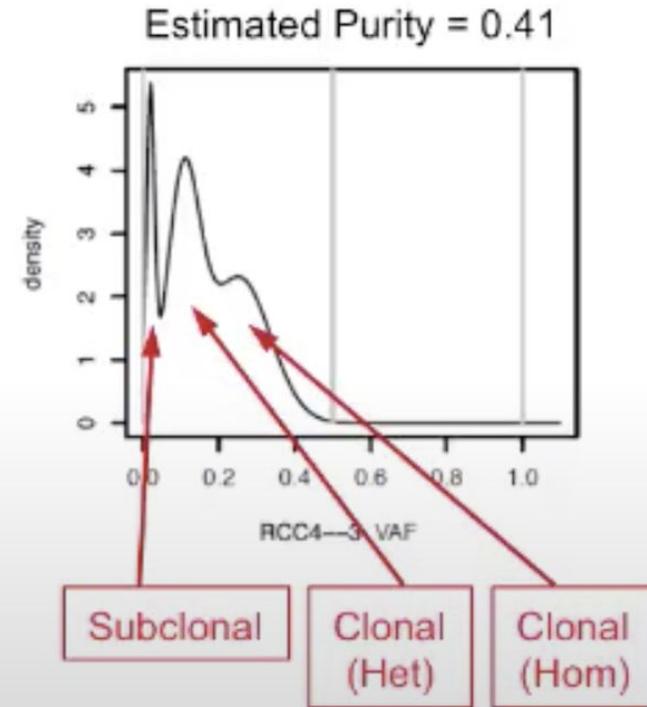
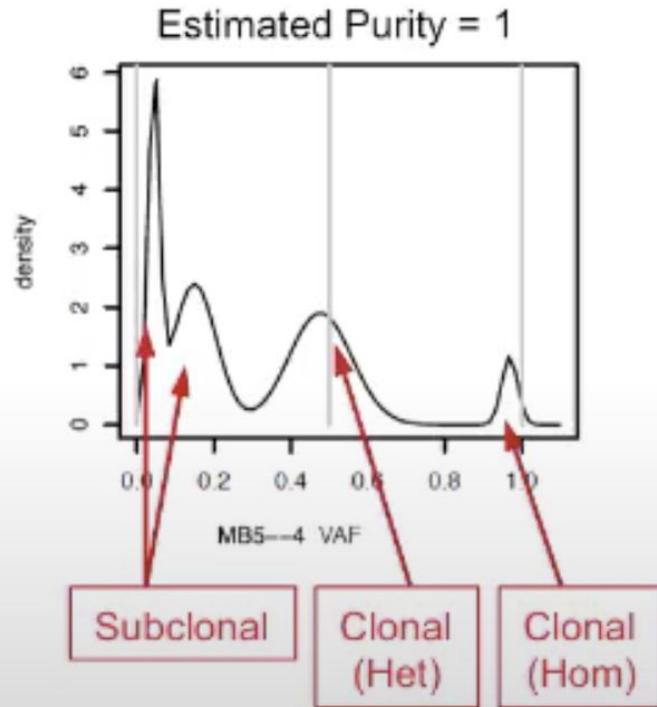
el alelo mutado va a aparecer con una VF mayor a 0.25 (0.33) por la pérdida del alelo normal

Esta predicción de pérdida de heterocigosidad se puede aplicar para estimar si esta ocurriendo la perdida del segun alelo si ocurre la pérdida se puede postular la variante como candidata

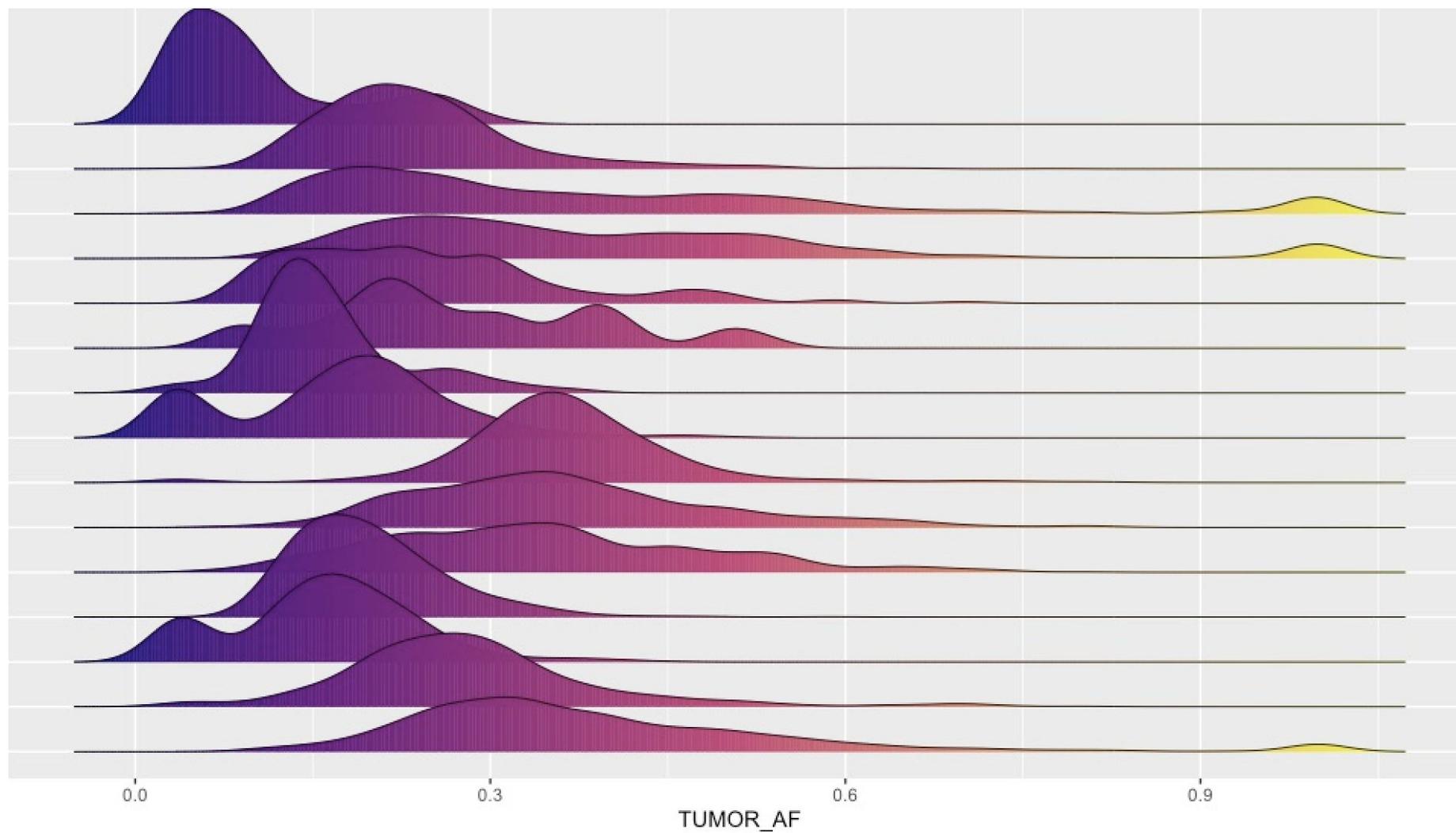


Pierdo Alelo Normal

baja pureza (bajo % de células tumorales) empuja a AF hacia la izquierda



Variant allele frequency global – Todas las variantes

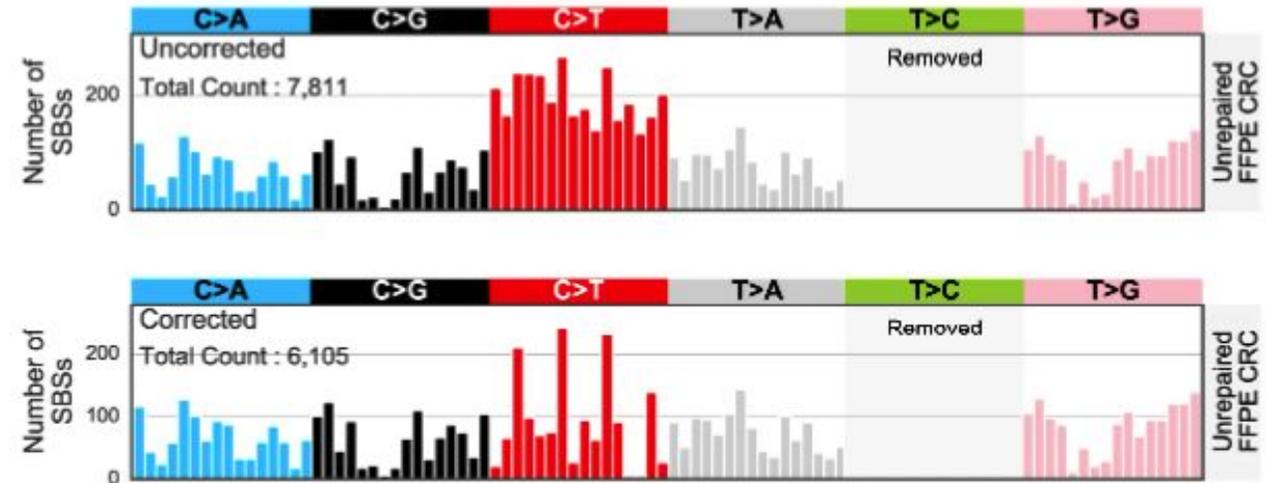
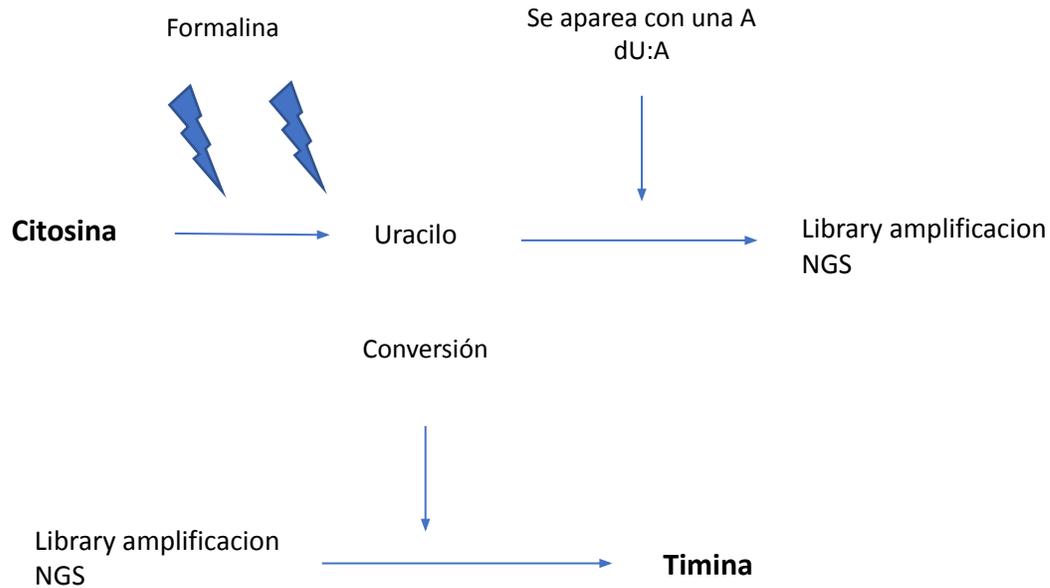


Zona de mutaciones pasajeras

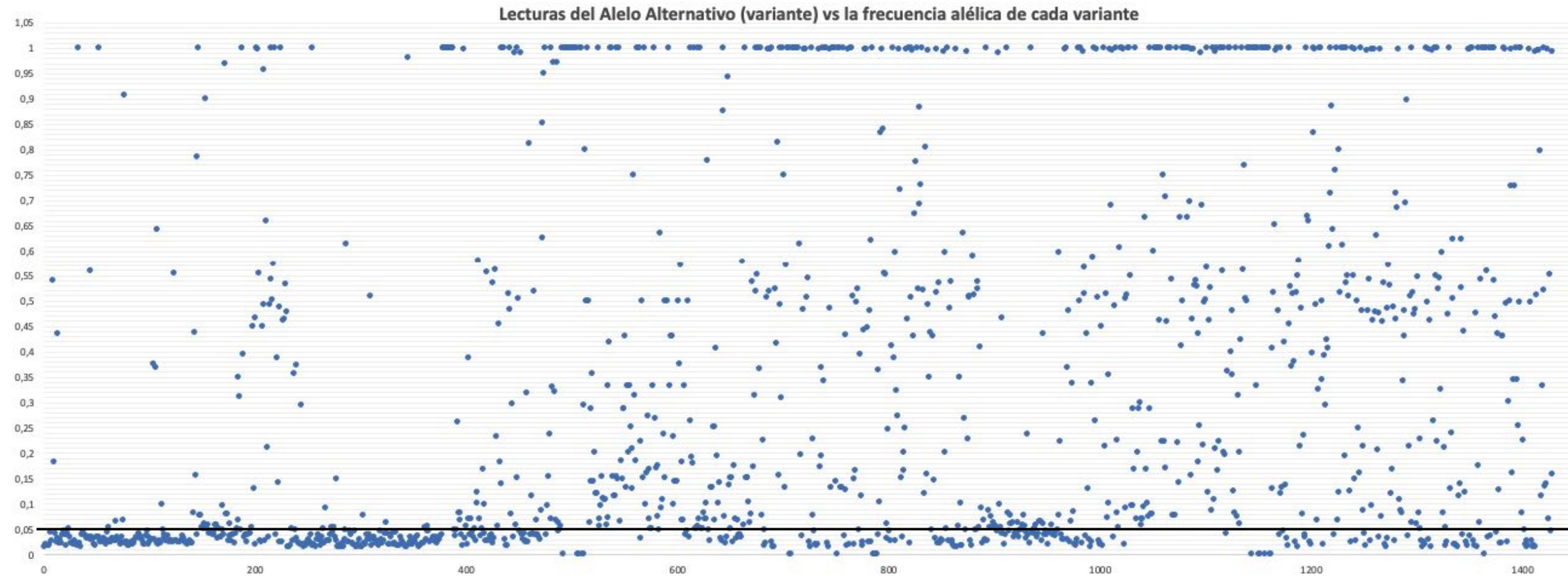
Zona de mutaciones drivers

The mutational signatures of formalin fixation on the human genome

[Qingli Guo](#), [Eszter Lakatos](#), [Ibrahim Al Bakir](#), [Kit Curtius](#), [Trevor A. Graham](#) ✉ & [Ville Mustonen](#) ✉

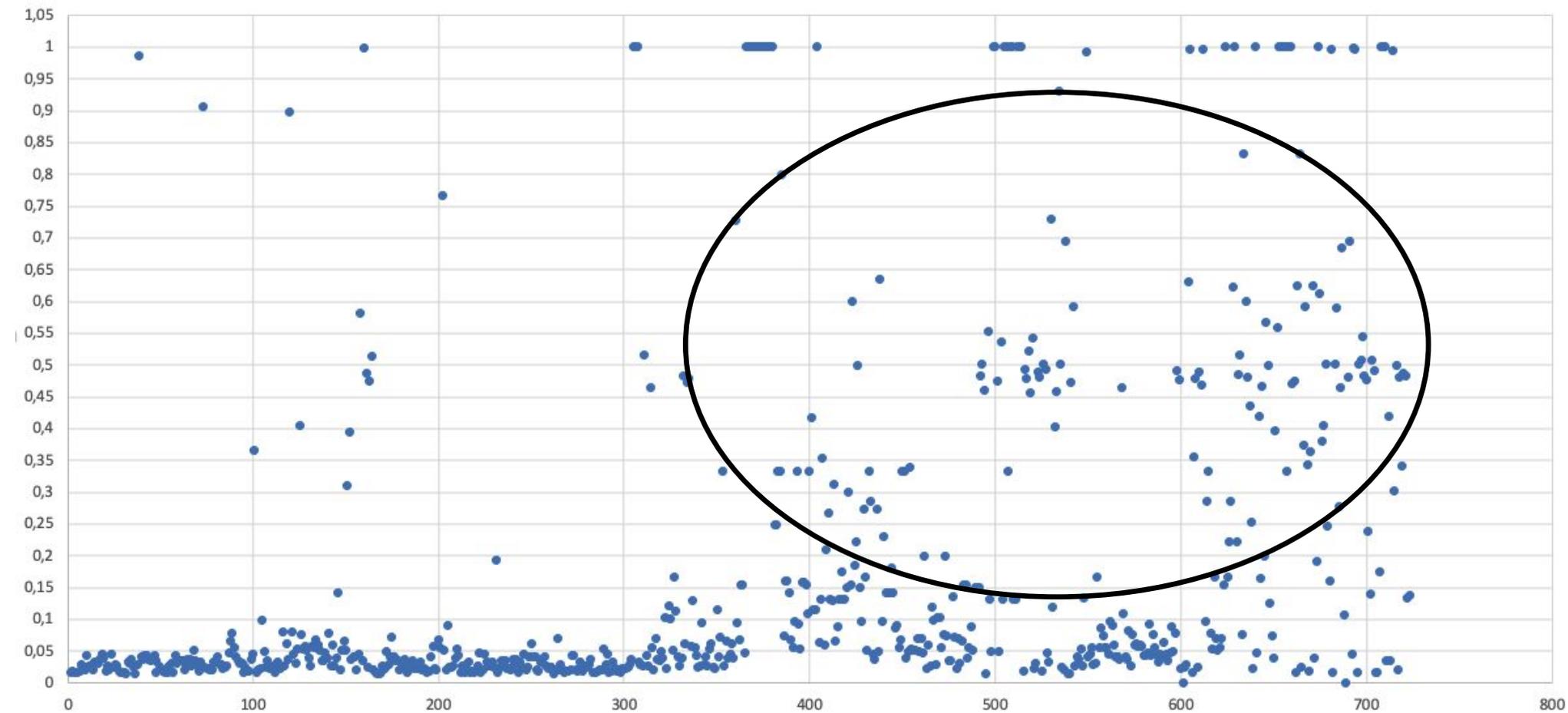


Cómo medir la calidad de lecturas



Cómo medir la calidad de lecturas

Lecturas del alelo alternativo (solo C>T) vs frecuencia alélica



30% C>T

KRAS
G12A
G12S

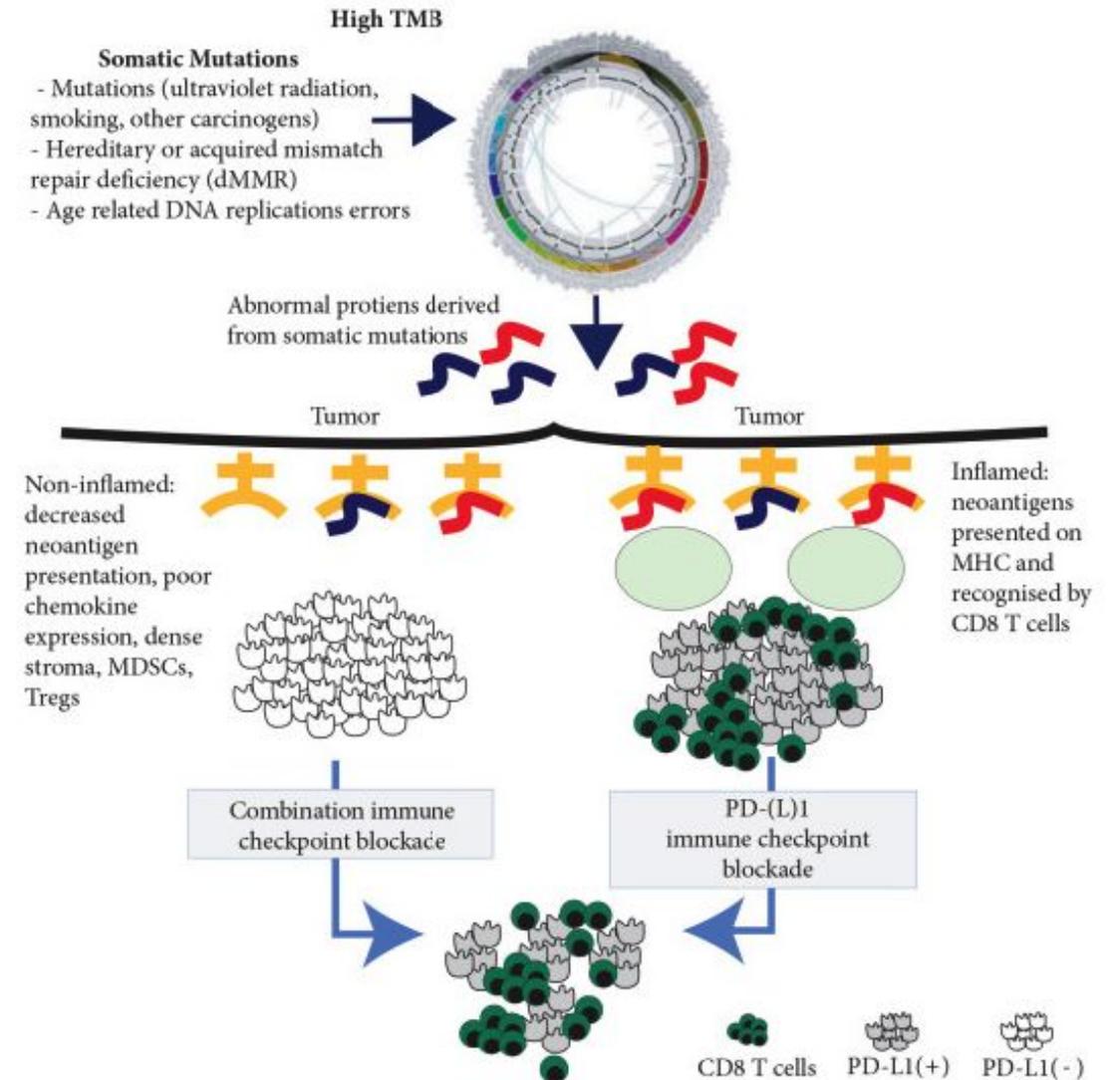
implica un
cambio
C>T

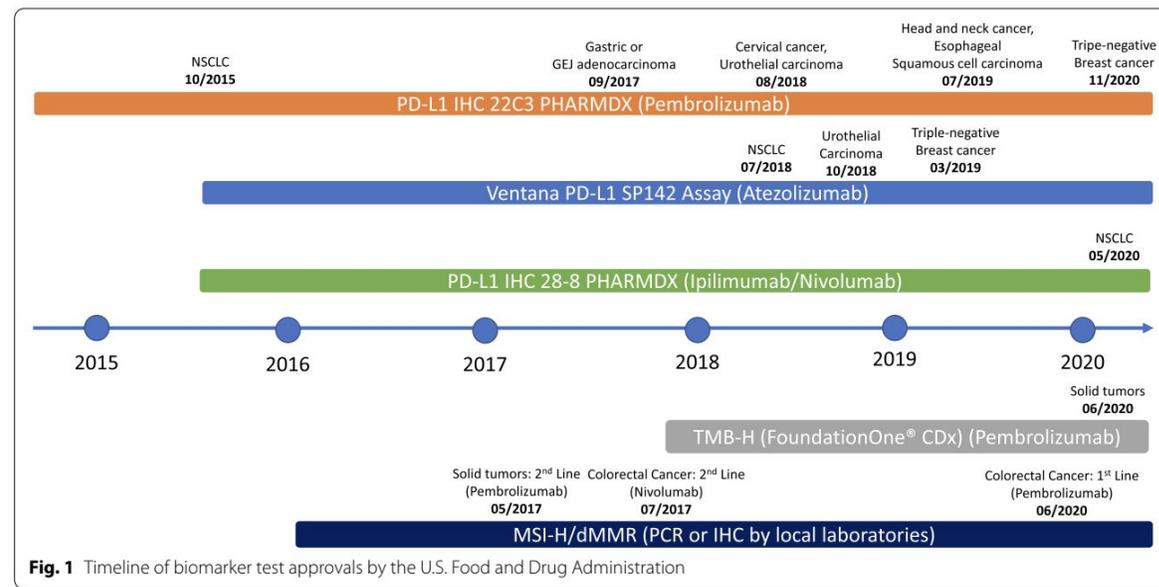
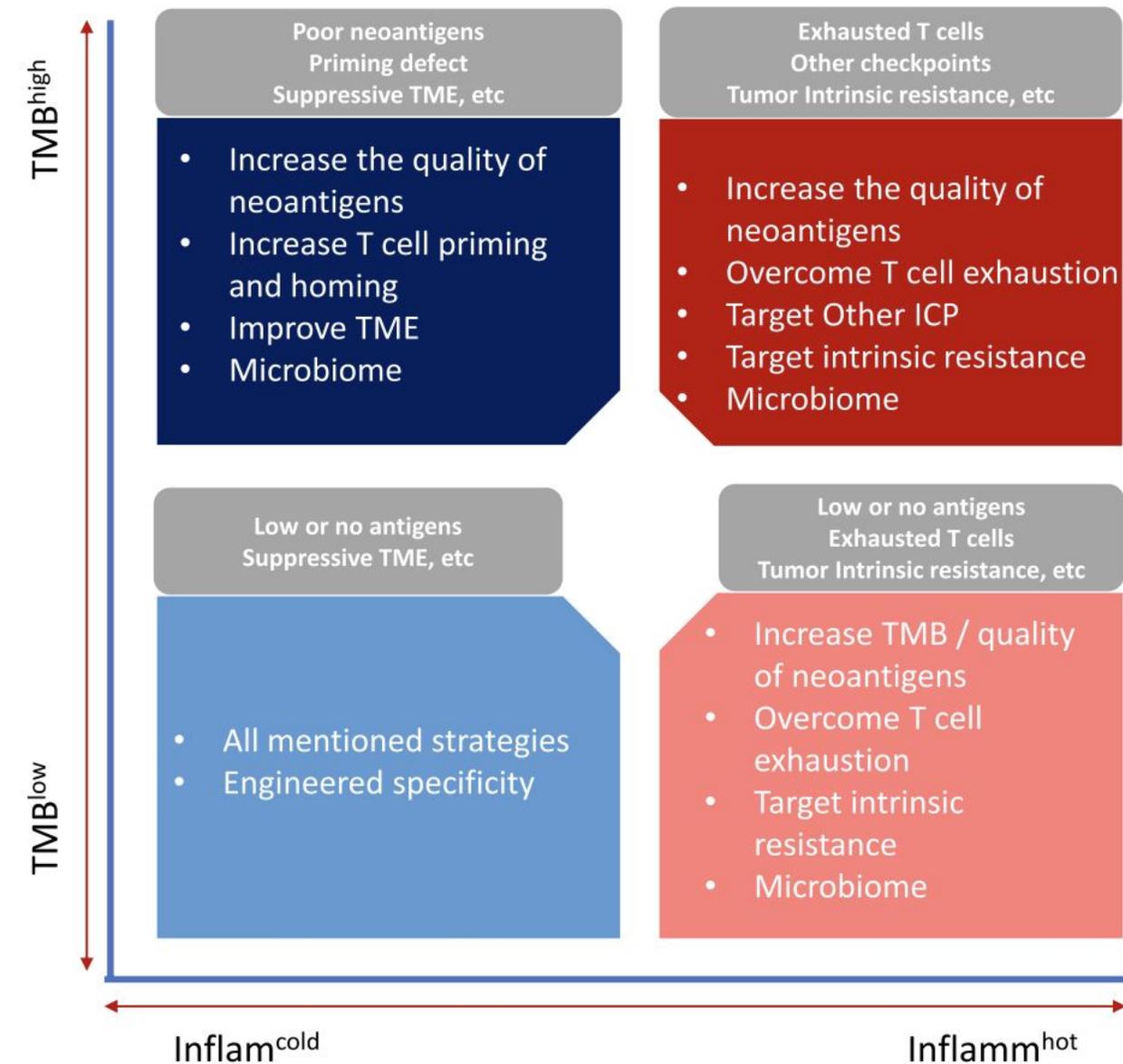
La cantidad de mutaciones que hay en el tumor como biomarcador predictivo de respuesta a la inmunoterapia

Cuanto más mutaciones tenga ese tumor, es más probable de que tenga neoantígenos

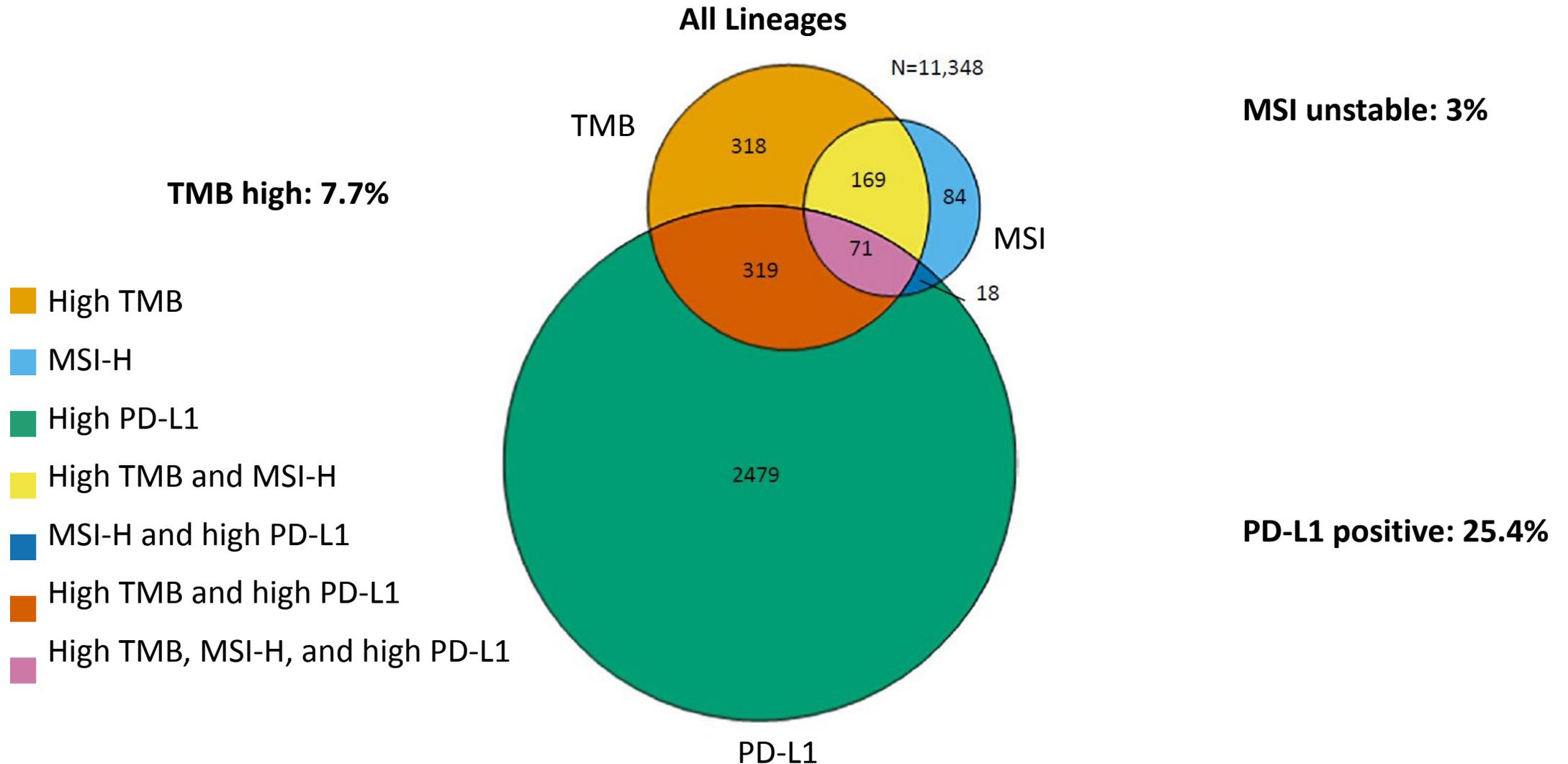
El TMB puede representar una estimación útil de la carga de neoantígenos tumorales.

No todos los inmunopéptidos en la superficie son inmunogénicos





MSI, TMB, and PD-L1



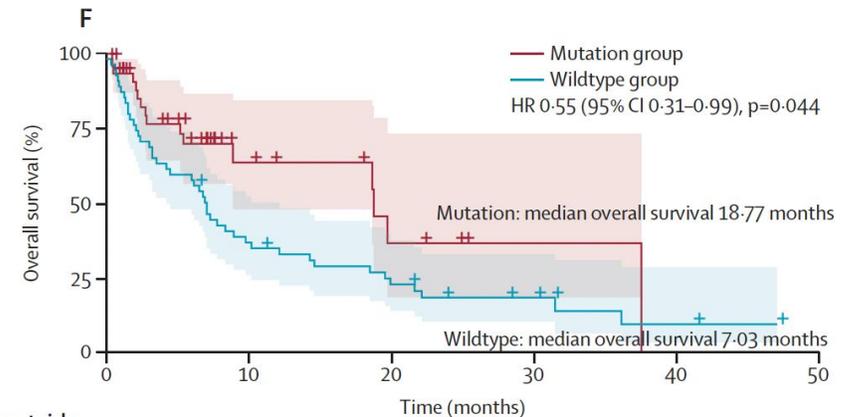
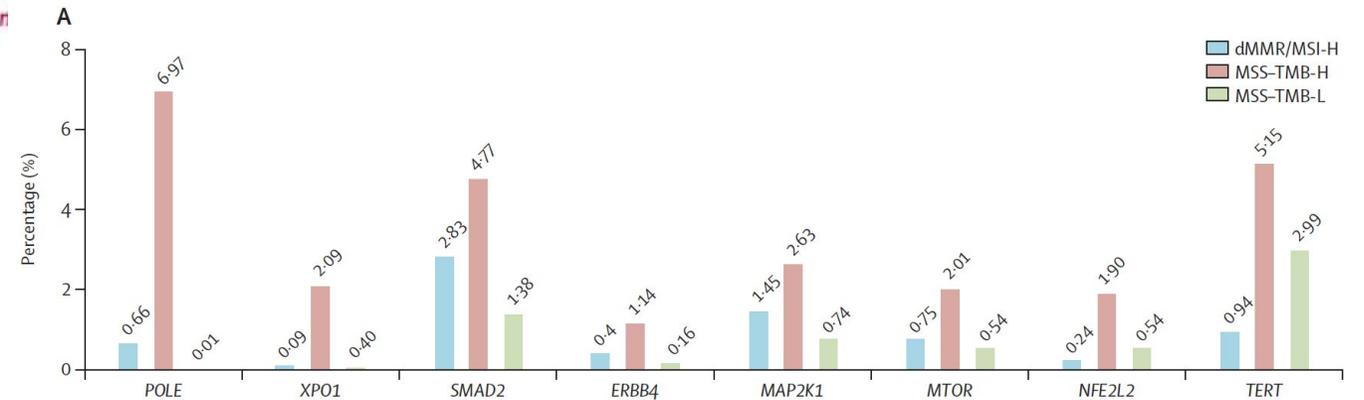
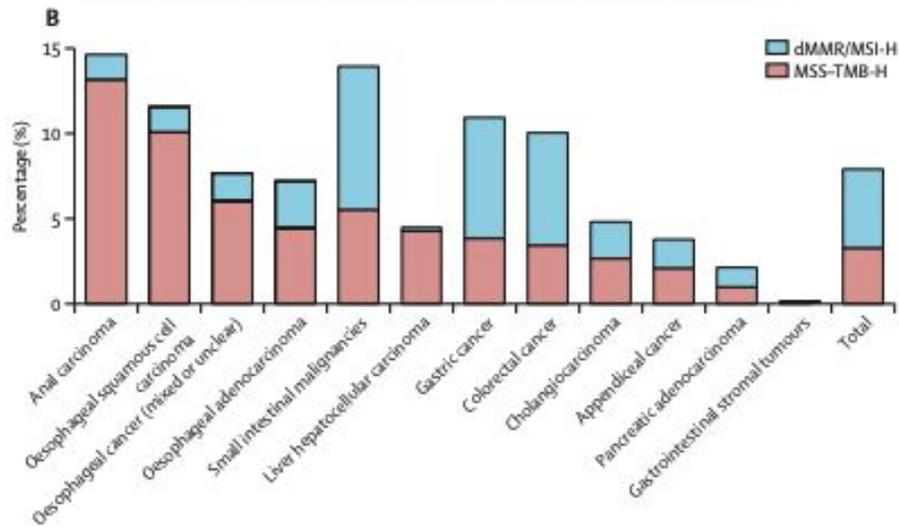
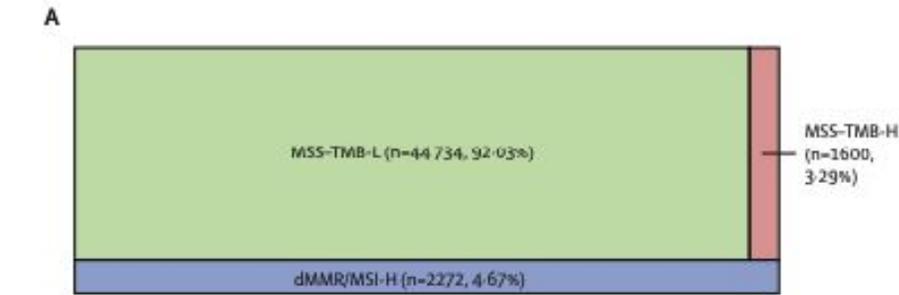
Key genomic features across 6,004 colorectal cancer cases highlighting identification of MSS cases with elevated tumor mutational burden

Variables	MSI-H (%)	MSS (%)	MSS/TMB-high (≥ 12 mut/Mb) (%)	MSS/TMB-low (< 12 mut/Mb) (%)
Total	302	5,702	164	5,538
Median age (years)	63	59	58	59
No. male	154 (51.0)	3,033 (53.2)	90 (54.9)	2,941 (53.1)
No. female	148 (49.0)	2,669 (46.8)	74 (45.1)	2,597 (46.9)
Genomic alterations				
No. <i>BRAF</i>	109 (36.1)***	453 (7.9)	20 (12.2)	433 (7.8)
No. <i>KRAS</i>	88 (29.1)***	2,987 (52.4)	76 (46.3)	2911 (52.6)
No. <i>NRAS</i>	6 (2.0)	262 (4.6)	6 (3.7)	256 (4.6)
No. <i>PIK3CA</i>	85 (28.1)***	1,008 (17.7)	53 (32.3)	955 (17.2)
No. <i>MLH1</i>	56 (18.5)***	10 (0.2)	4 (2.4)	6 (0.1)
No. <i>MSH2</i>	47 (15.6)***	20 (0.4)	15 (9.1)###	5 (0.1)
No. <i>MSH6</i>	85 (28.1)***	28 (0.5)	12 (7.3)###	16 (0.3)
No. <i>PMS2</i>	16 (5.3)***	14 (0.2)	3 (1.8)	11 (0.2)
No. <i>POLE</i>	1 (0.3)	48 (0.8)	34 (20.7)####	13 (0.2)
No. <i>POLD1</i>	4 (1.3)	5 (0.1)	0 (0.0)	5 (0.1)
No. <i>TP53</i>	100 (33.1)***	4,414 (77.4)	117 (71.3)	4,297 (77.6)
No. <i>APC</i>	133 (44.0)***	4,414 (77.4)	122 (74.4)	4,292 (77.5)
No. <i>ERBB2</i>	17 (5.6)	266 (4.7)	7 (4.3)	259 (4.7)
No. <i>EGFR</i>	11 (3.6)	119 (2.1)	8 (4.9)	111 (2.0)

Mutational analysis of microsatellite-stable gastrointestinal cancer with high tumour mutational burden: a retrospective cohort study



Jingyuan Wang, Joanne Xiu, Alex Farrell, Yasmine Baca, Hiroyuki Arai, Francesca Battaglin, Natsuko Kawanishi, Shivani Soni, Wu Zhang, Joshua Millstein, Anthony F Shields, Axel Grothey, Benjamin A Weinberg, John L Marshall, Emil Lou, Moh'd Khushman, Davendra P S Sohal, Michael J Hall, Tianshu Liu, Matthew Oberley, David Spetzler, W Michael Korn, Lin Shen, Heinz-Josef Len



	0	10	20	30	40	50
Number at risk (number censored)						
Mutation group	42 (27)	10 (6)	4 (3)	1 (0)	0 (0)	0 (0)
Wildtype group	53 (9)	19 (8)	11 (7)	6 (4)	2 (2)	0 (0)

MLH1/PMS2 MSH2/MSH6

POLE or POLD1 exonuclease domain

Sporadic MSI

Lynch

Sporadic High TMB
MSS

PPAP



1st Hit Somatic
2nd Hit Somatic

1st Hit Germline
2nd Hit Somatic

1st Hit Somatic
2nd Hit Somatic

1st Hit Germline
2nd Hit Somatic



dMMR/MSI

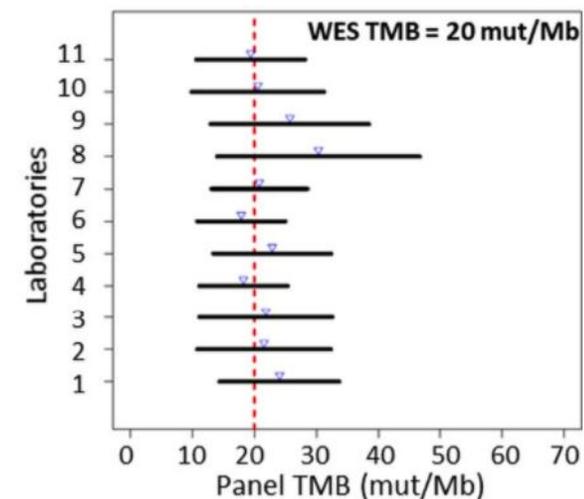
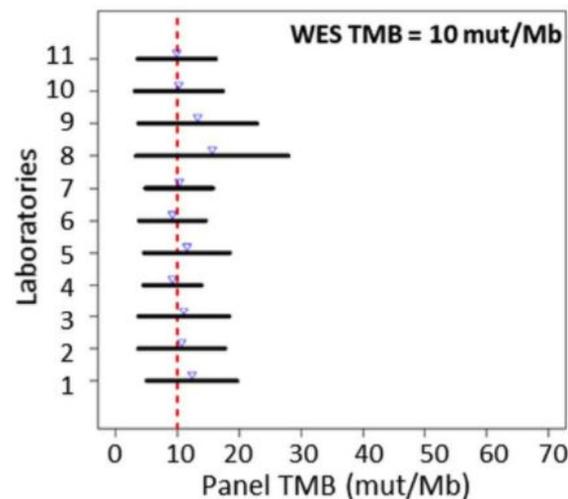
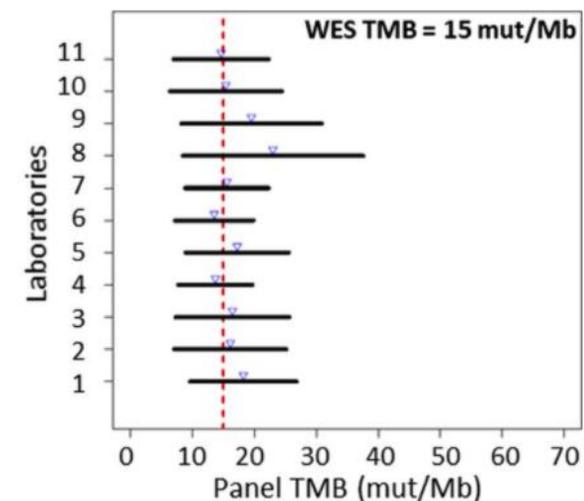
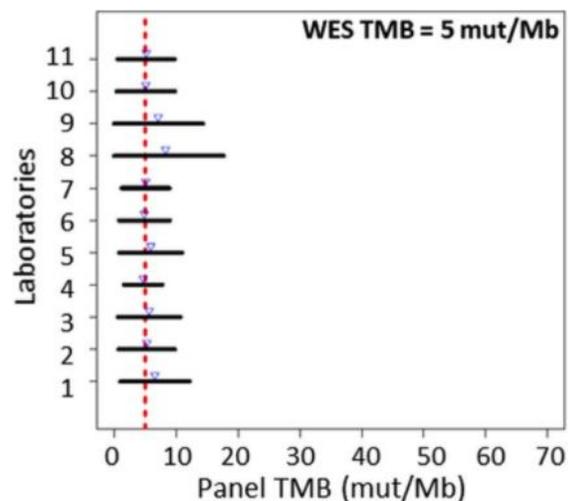
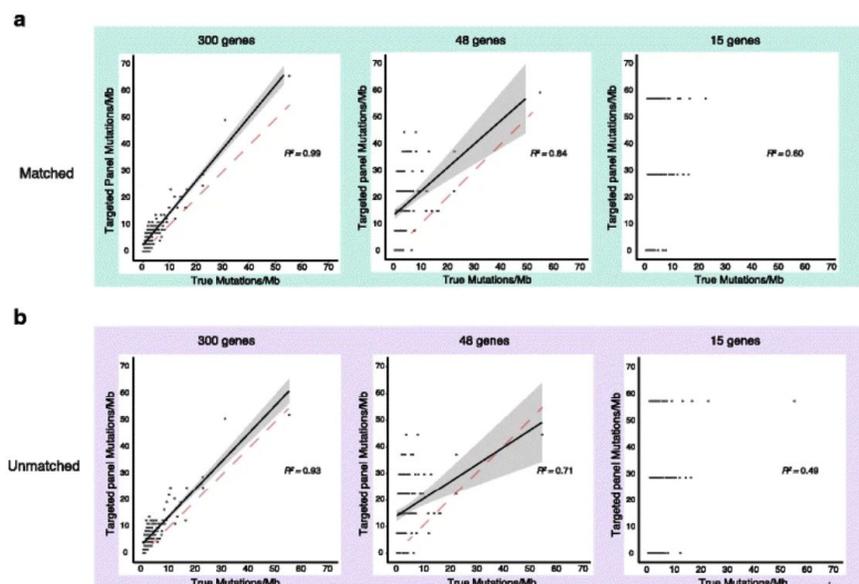
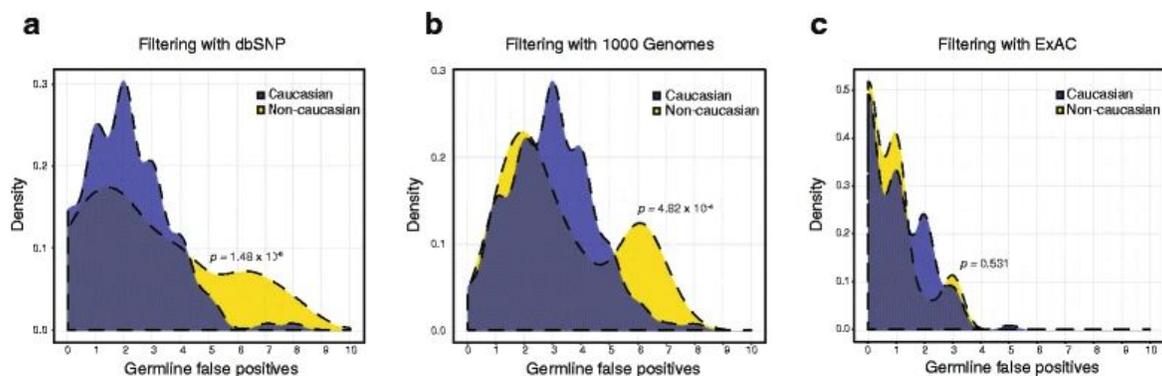
dMMR/MSI

pMMR/MSS or dMMR/MSI

High TMB



Establishing guidelines to harmonize tumor mutational burden (TMB): in silico assessment of variation in TMB quantification across diagnostic platforms: phase I of the Friends of Cancer Research TMB Harmonization Project



Factor type	ACT	AZ	BWH	Caris	FMI	ILLUM	IPG	JHU	MSKCC	NeoGenomics	OmniSeq	PGDx	Q2	QIAGEN	Thermo_OCA	Thermo_OTMLA
Panel assay characteristics																
Name of panel assay	ACTOnco+	AZ650	OncoPanel v3.1	SureSelectXT	F1 CDx	TSO500	TheraMap Solid Tumor (TSO500)	JHOP2	MSK-IMPACT	NeoTYPE Discovery Profile for Solid Tumors	Ion AmpliSeq Comprehensive Cancer Panel	PGDx elio tissue complete	TSO500	Q(Aseq TMB panel	Oncomine Comprehensive Assay Plus (OCA Plus)	Oncomine Tumor Mutation Load Assay (OTMLA)
Number of genes	440	649	447	592	324	523	523	432	468	372	409	505	523	486	517	409
TMB region covered	1.1 Mb	1.65 Mb	1.94 Mb	1.40 Mb	0.8 Mb	1.33 Mb	1.27 Mb	1.14 Mb	1.14 Mb	0.935 Mb	1.17 Mb	1.3 Mb	1.2 Mb	1.33 Mb	1.06 Mb	1.2 Mb
Processing																
Minimum DNA input	40 ng	100 ng	50 ng	50 ng	50 ng	40 ng	40 ng	50 ng	150 ng	20 ng	30 ng	50 ng	40 ng	40 ng	20 ng	20 ng
Quantification method	Fluorescence	Fluorescence	Fluorescence	Electrophoresis	Fluorescence	Fluorescence	Fluorescence	Electrophoresis	Fluorescence	Fluorescence	Fluorescence	Fluorescence	Fluorescence	Fluorescence	Fluorescence	Fluorescence
Technology uses UMIs	No	Yes	No	No	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	No	No
Deduplication	No	Yes, UMI based	Yes, not UMI based	Yes, not UMI based	Yes, UMI based	Yes, UMI based	Yes, UMI based	Yes, not UMI based	Yes, not UMI based	Yes, UMI based	No	Yes, UMI based	Yes, UMI based	Yes, UMI based	No	No
Sequencing																
Seq platform	Ion Torrent	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina	Illumina	Ion Torrent	Illumina	Illumina	Illumina	Ion Torrent	Ion Torrent
Library prep/target enrichment	Amplicon	Hybrid	Hybrid	Hybrid	Hybrid	Hybrid	Hybrid	Hybrid	Hybrid	Amplicon	Amplicon	Hybrid	Hybrid	Amplicon (single primer extension)	Amplicon	Amplicon
Sample-level minimum coverage threshold	800x	NA	30x	300x	250x	150x	300x	300x	50x	500x	125x	100x	50x	100x	500x	500x
Sample-level avg coverage for cell line exercise	1400x	1060.5x	394x	750x	982x	549x	800x	>400x	753x	>500x	314x	1517x	100x	500x	2000x	1300x
Variant-level minimum coverage	20x	50x	50x	100x	100x	50x	50x	50x	20x	100x	20x	Position-specific threshold. Determined by ML	150x	100x	60x	60x
Variant-level minimum read (ALT depth)	20	5	5	10	5	2 ^a	3	3	8	10	4	6	2	4	10	10
Variant calling																
Type of variant	Non-synonymous and synonymous	Non-synonymous and synonymous	Non-synonymous only	Non-synonymous only	Non-synonymous and synonymous	Non-synonymous and synonymous	Non-synonymous and synonymous	Non-synonymous and synonymous	Non-synonymous only	Non-synonymous and synonymous	Non-synonymous only	Non-synonymous and synonymous	Non-synonymous and synonymous	Non-synonymous only	Non-synonymous only	Non-synonymous only
Germline variant filtration approach	Tumor only	Normal tissue	Tumor only	Tumor only	Tumor only	Tumor only	Tumor only	Tumor only	Normal tissue	Tumor only	Tumor only	Tumor only	Tumor only	Tumor only	Tumor only	Tumor only
Removes variants from known cancer genes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	No	No
Published performance characteristics			30,31	32	9,20,33,34				9,35-37			38				39-42

Conclusiones:

Es momento de implementar en la rutina los datos de exomas germinales y tumorales para mejorar las decisiones clínicas

Los datos de WES germinal sirven para identificar variantes germinales que predisponen al cáncer y así poder implementar medidas de vigilancia preventiva en familiares portadores sanos y además, para predecir la sensibilidad a algunas terapias dirigidas.

Mejora la calidad del llamado de variantes en muestras somáticas.

Permite ayudar a predecir la pérdida de heterocigosidad (LOH) valorando la frecuencia alélica. Y a su vez la identificación del segundo hit somático.

Los datos de WES somático permiten evaluar el panorama global de mutaciones a través de patrones o firmas de mutaciones más allá de los grupos de genes interesados.

Permite la identificación de biomarcadores agnósticos como la carga mutacional tumoral.

TMB y MSI a través de NGS en muestras somáticas son biomarcadores agnósticos para indicar inmunoterapia.

Ambos tipos de muestras se complementan. El WES somático mejora el resultado del WES germinal y viceversa.

Unidad de Investigación Traslacional



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