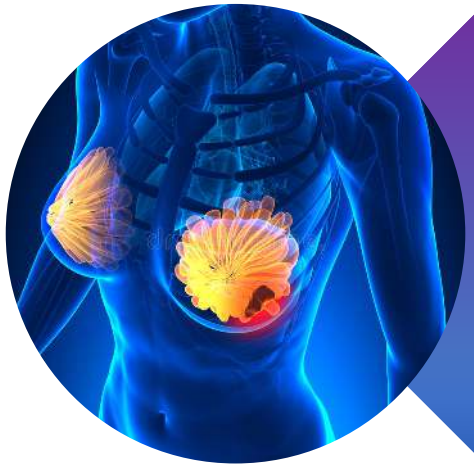
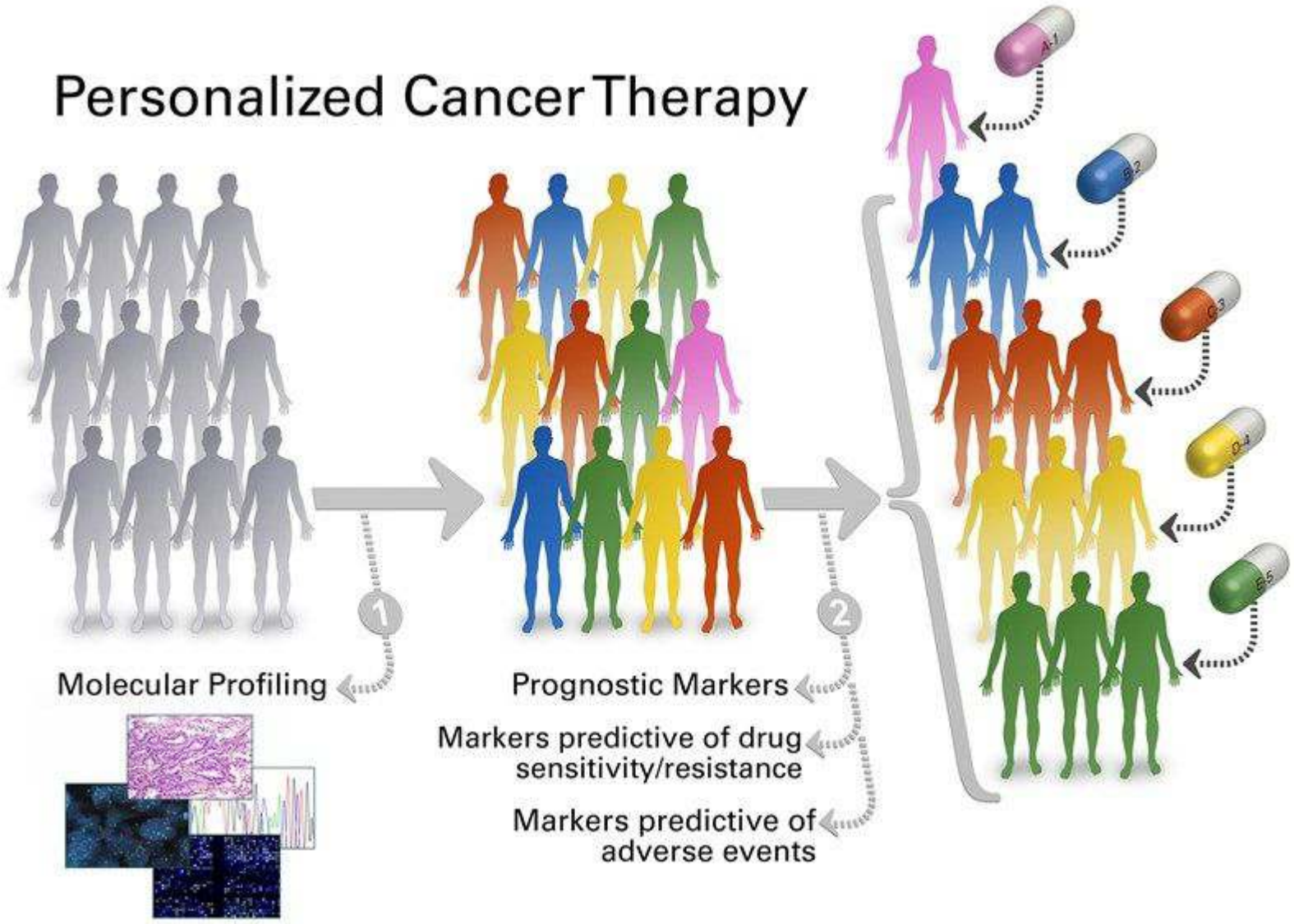
Héritas
Medicina de precisión
CIBIC + INDEAR



Oncología de Precisión

Dr. Martín Vázquez
Director Científico
Héritas


Personalized Cancer Therapy
Molecular Profiling
Prognostic Markers
Markers predictive of drug sensitivity/resistance
Markers predictive of adverse events
1
2
A-1
B-2
C-3
D-4
E-5

Sally Davis
2017
Directora Médica
Servicio Nacional de Salud (NHS), Inglaterra

A todo paciente de Cancer se le debería ensayar el perfil tumoral de su ADN para acelerar diagnóstico y salvar más vidas

Introduction

Tumor profiling

A todo paciente de Cancer se le debería ensayar el perfil tumoral de su ADN para acelerar diagnóstico y salvar más vidas

Sally Davis
2017
Directora Médica
Servicio Nacional de Salud (NHS), Inglaterra

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NHS at 70

Routine DNA tests will put NHS at the 'forefront of medicine'

From 1 October new cancer patients will have tumours screened for key mutations

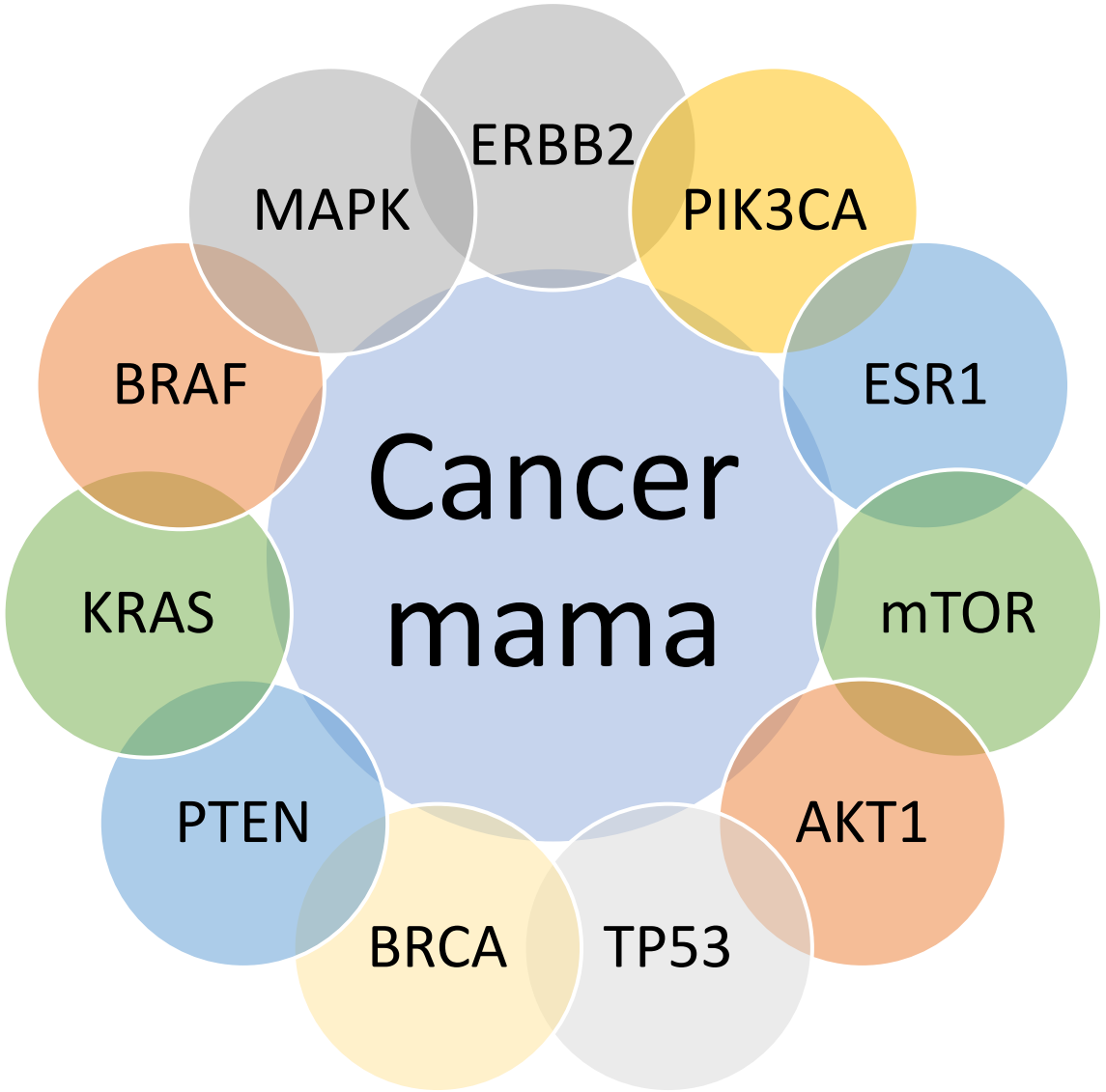
Héritas
Medicina de precisión
CIBIC + INDEAR

Enrolamiento

Oncología de Precisión

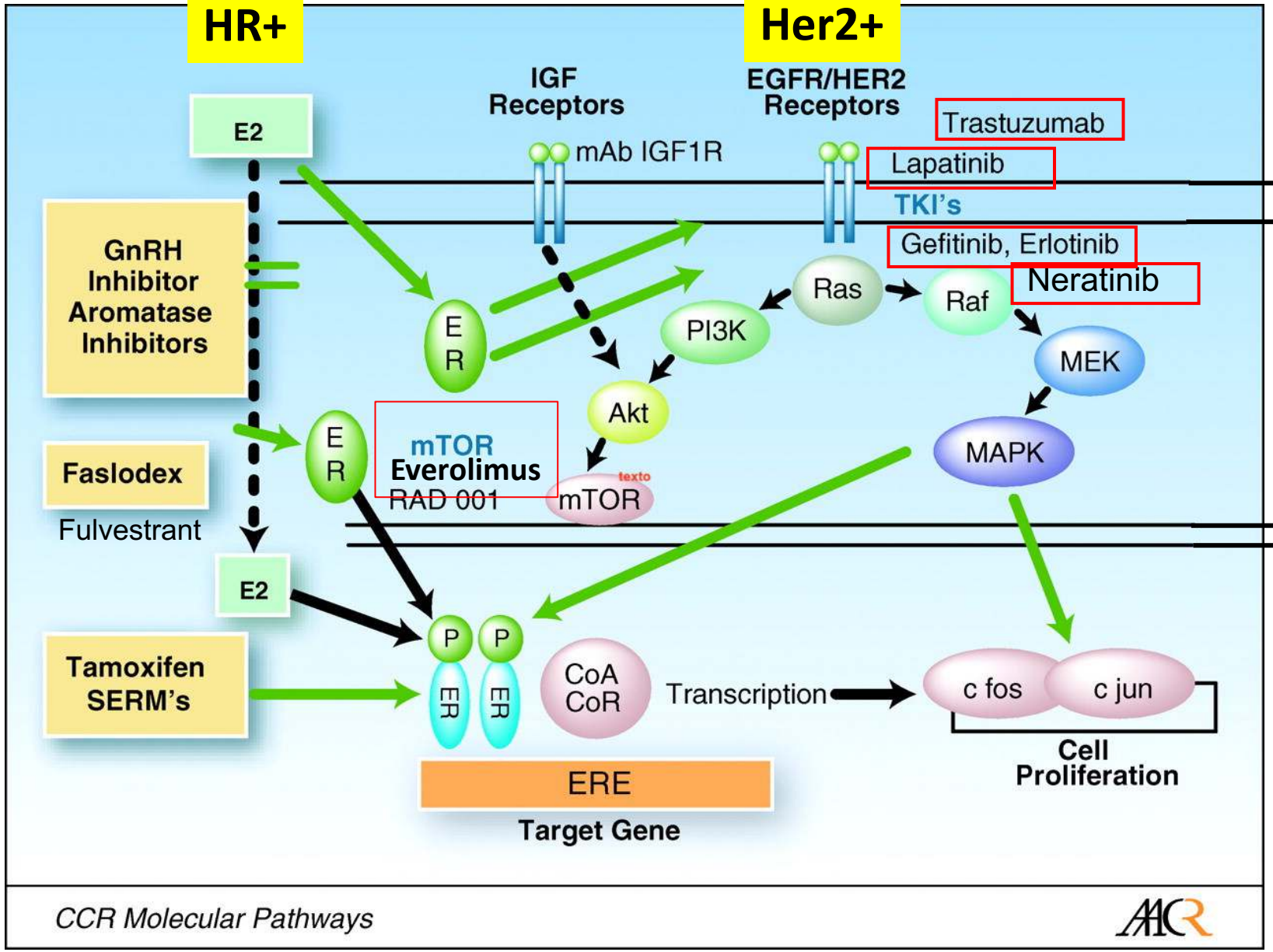
Todas tienen Cancer de Mama: todos son diferentes

- 70% HR+/Her2-
- 10% HR+/Her2+
- 5% HR-/Her2+
- 15% TNBC



Introduction

Oncología de Precisión en Cancer Mama



Triple Neg Her2 -

New indication 2018

Olaparib

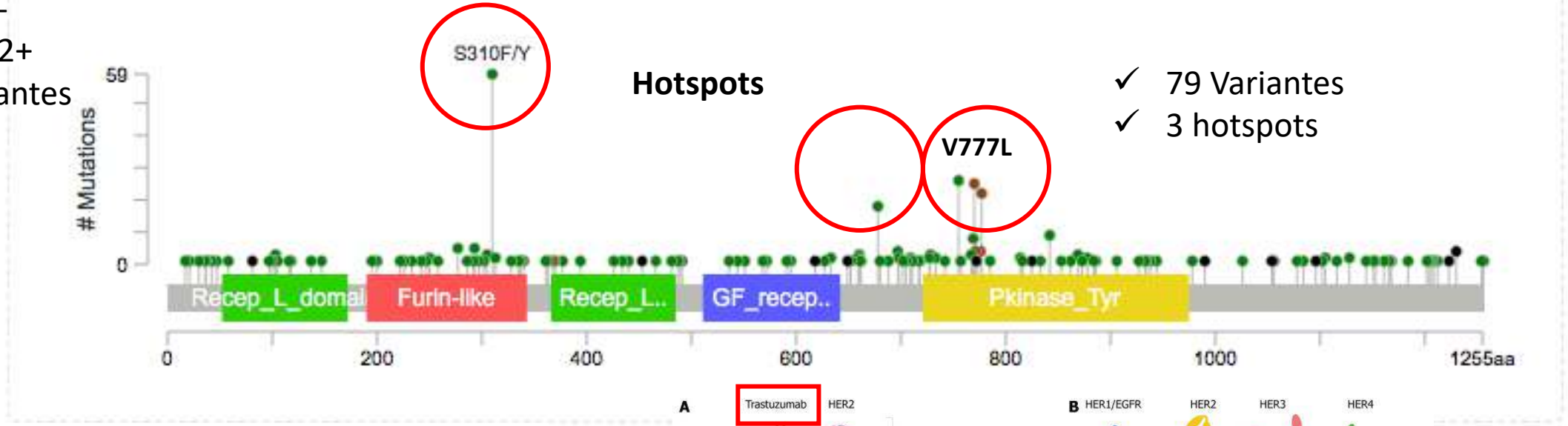
gBRCA1m

gBRCA2m

ERBB2 - Biomarkers Cancer Mama

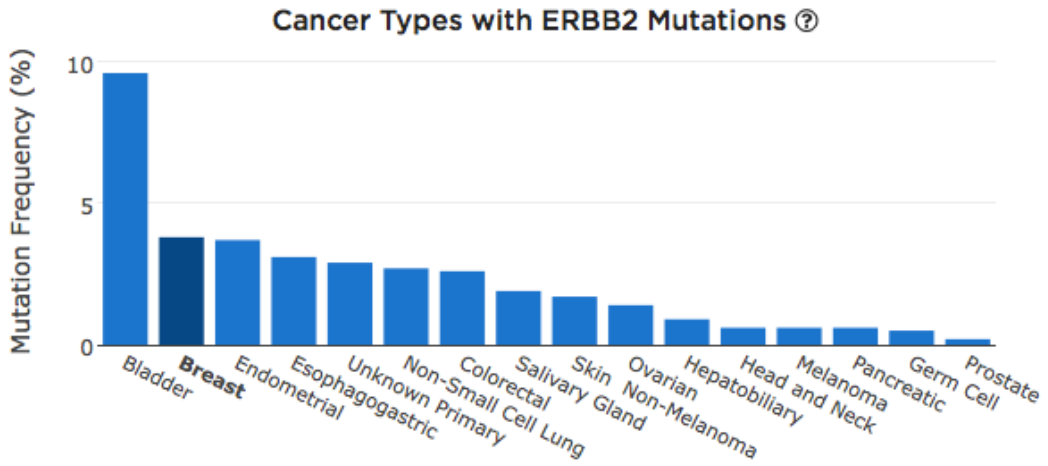
ERBB2 mut predice resistencia a Trastuzumab/Pertuzumab y sensibilidad a Neratinib/Lapatinib

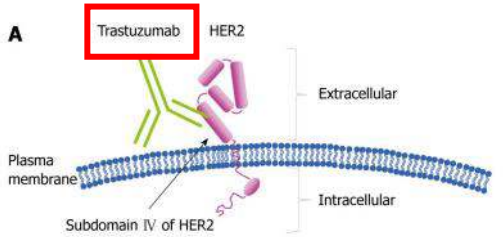
- 3% en HR+, HER2-
- 36% en HR+, HER2+
- Mutaciones activantes

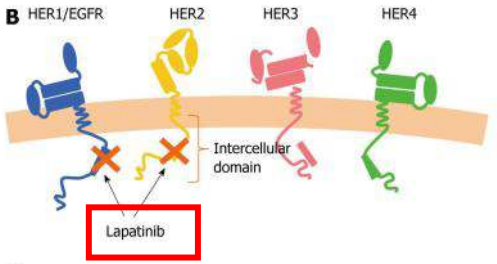


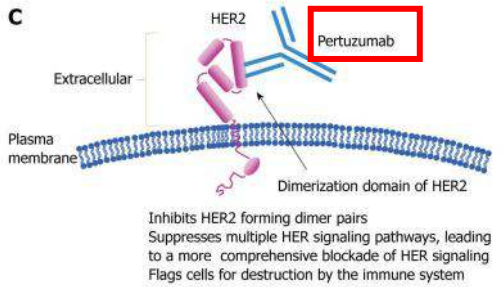
Hotspots

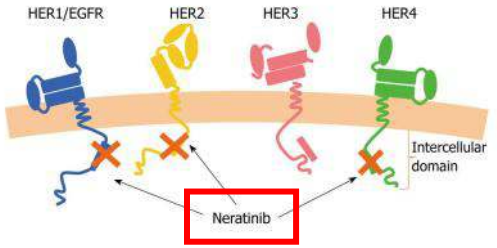
- ✓ 79 Variantes
- ✓ 3 hotspots











Héritas
Medicina de precisión
CIBIC + INDEAR

Oncología de Precisión Gastrointestinal

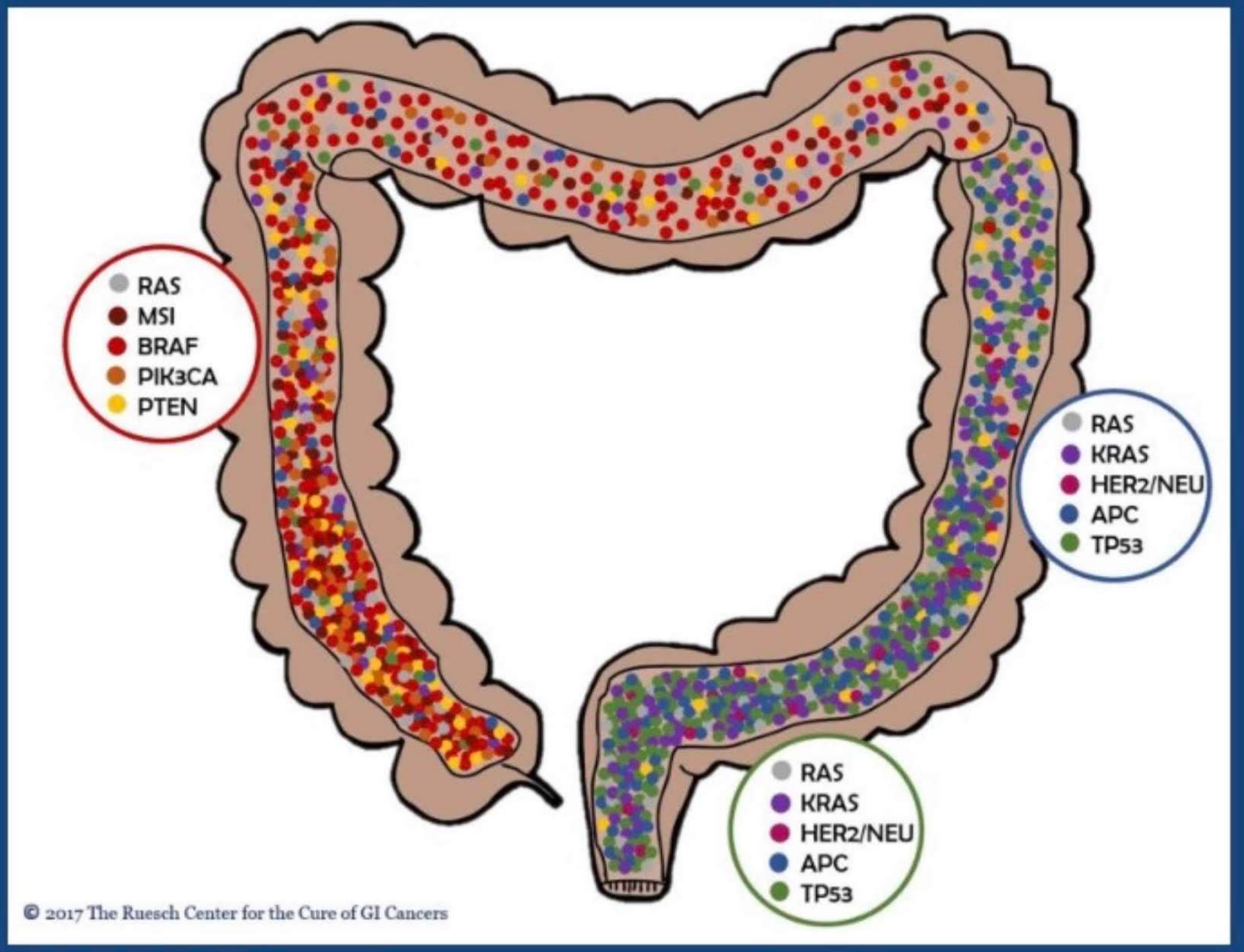
Mutation Rates

RIGHT:

- *APC* = 64%
- *TP53* = 56%
- *KRAS* = 51%
- *BRAF* = 25%
- HER2 = 1%

- MSI-H = 22%

↓*EREG/AREG*



Mutation Rates

LEFT:

- *APC* = 82%
- *TP53* = 67%
- *KRAS* = 42%
- *BRAF* = 7%
- HER2 = 5%

- MSI-H = 5%

↑*EREG/AREG*

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

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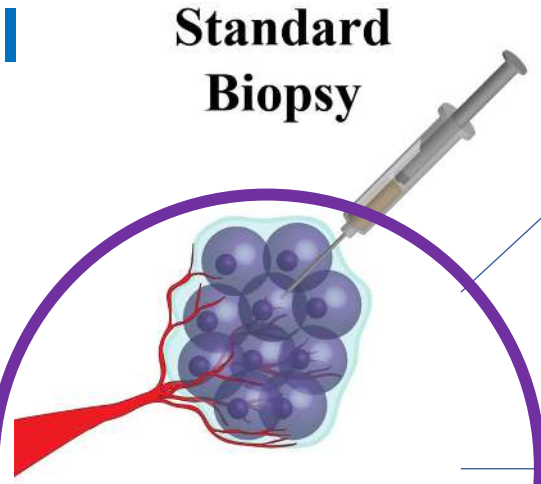
PRESENTED BY:

Salem ME, et al. *Oncotarget* 2017;8(49):86356-86368.

Why NGS for tumour profiling?

All in One vs Sequential



Scarce Material
Difficult to obtain

NGS

- SNVs, INDELs
- FUSIONS
- Amplifications
- TMB
- MSI
- Tens to hundreds of genes

ddPCR

- COBAS/ddPCR
- SNVs, INDELs

EGFR 35%

IHQ

- Biomarkers
- Amplif

FISH

- Fusions
- Amplif

RET 1%
ROS 1%
ALK 5%

MET 3%
ERBB2 x%

Héritas
Medicina de precisión
CIBIC + INDEAR

Why NGS for tumour profiling?

All in One vs Sequential

Economic Impact of Next-Generation Sequencing Versus Single-Gene Testing to Detect Genomic Alterations in Metastatic Non–Small-Cell Lung Cancer Using a Decision Analytic Model

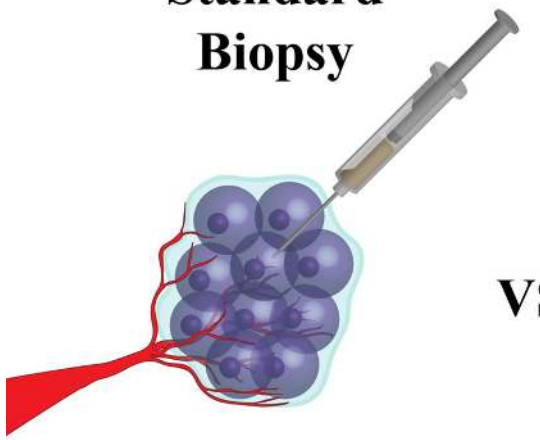
Nathan A. Pennell, MD, PhD[1] ✉; Alex Mutebi, PhD[2]; Zheng-Yi Zhou, PhD[3]; Marie Louise Ricculli, MSc[3]; Wenxi Tang, MS[3]; Helen Wang[3]; ...

Show More

Introduction

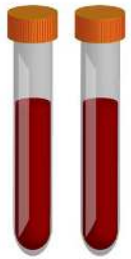
Tumor profiling

Standard Biopsy



VS.

Liquid Biopsy

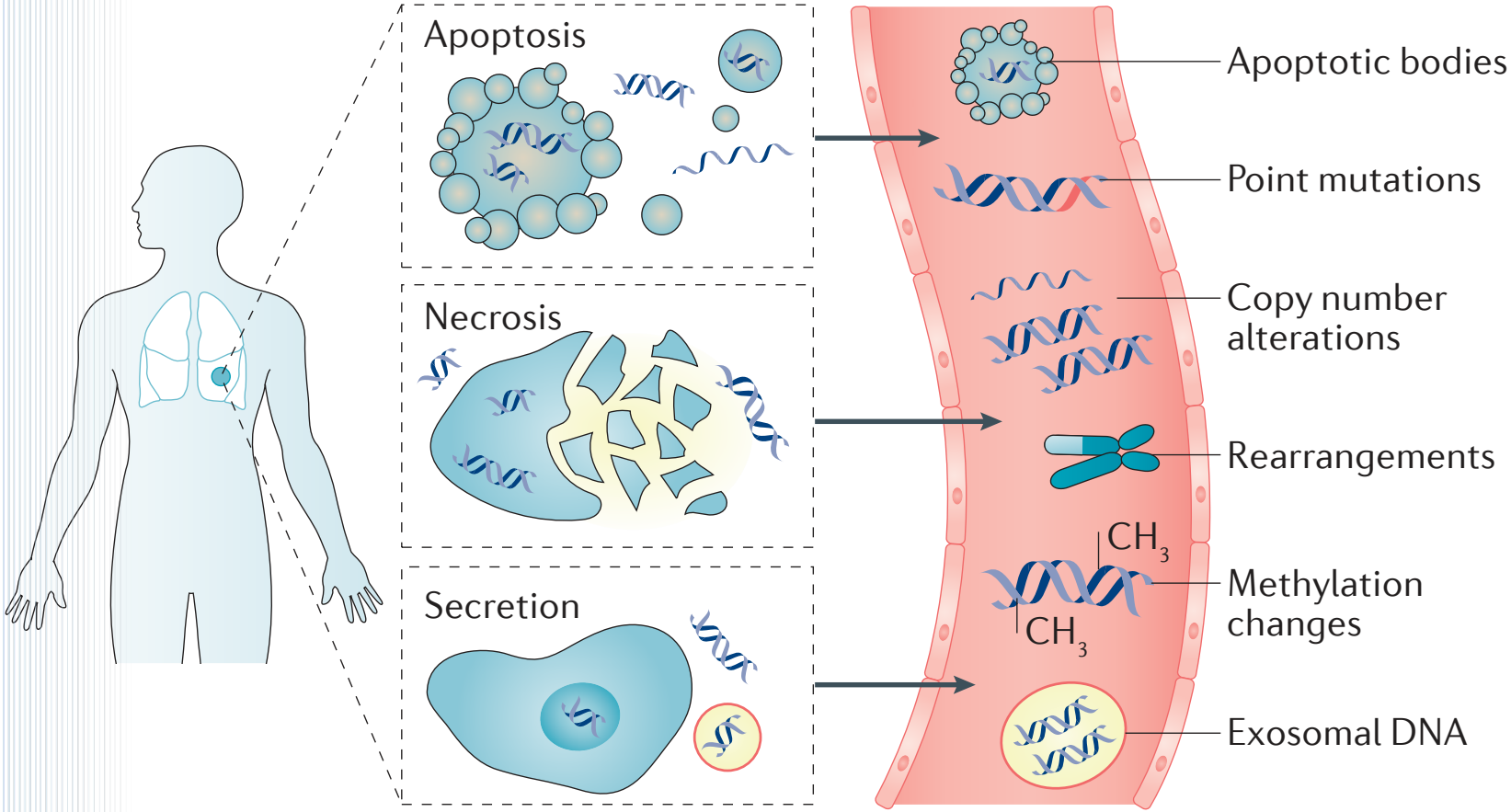


- ✓ Heterogeneo
- ✓ Escaso material
- ✓ invasivo
- ✓ Gold standard

- ✓ Mas homogeneo
- ✓ Facil re-biopsia
- ✓ No invasivo
- ✓ En desarrollo

Introducción

ctDNA



ctDNA vida media:
16 min a 2.5hs

Ventajas:

- Foto a tiempo real
- Monitoreo en tiempo = película
- No invasivo
- Menos heterogéneo que tejido

Desventajas:

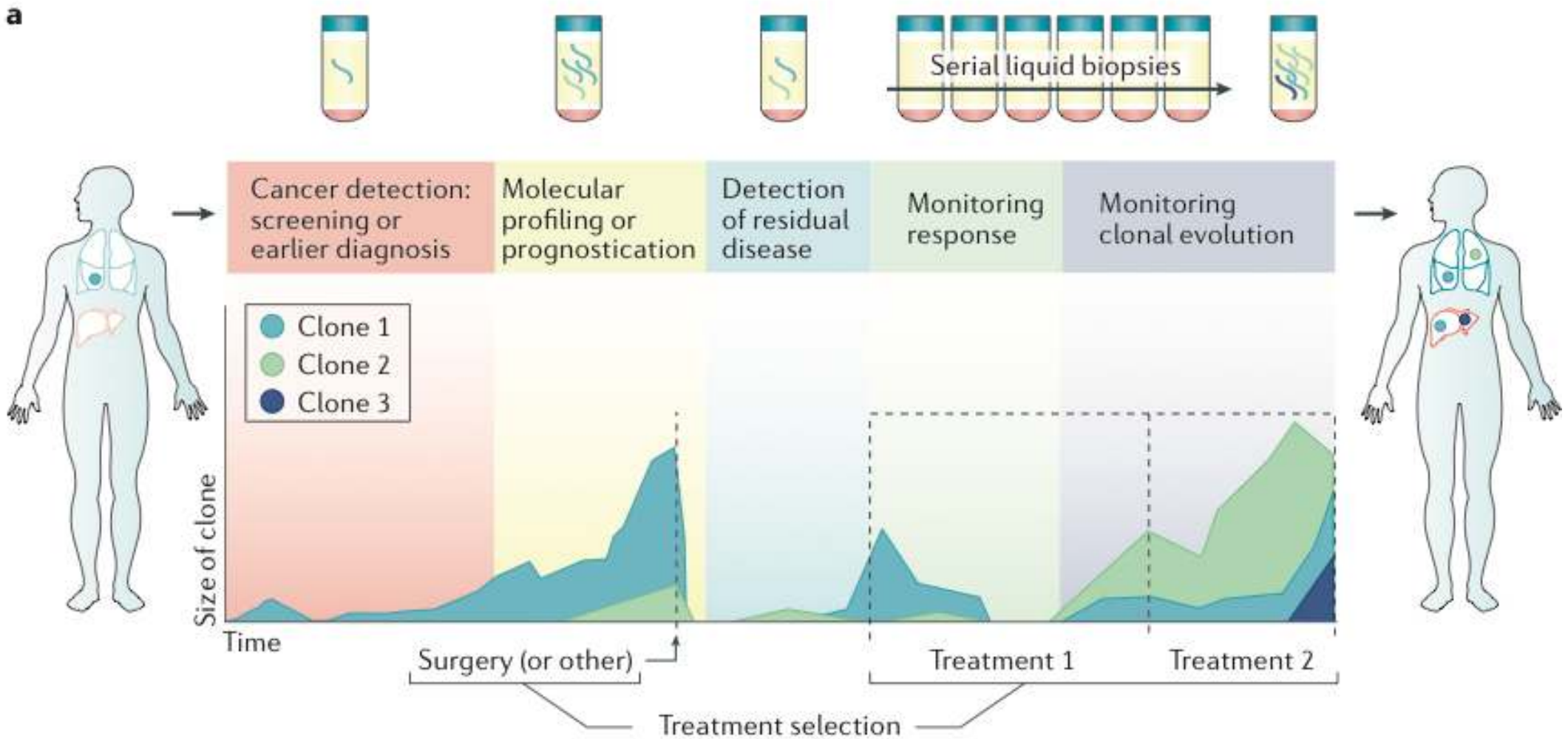
- Escaso material en plasma

Introduction

ctDNA definition

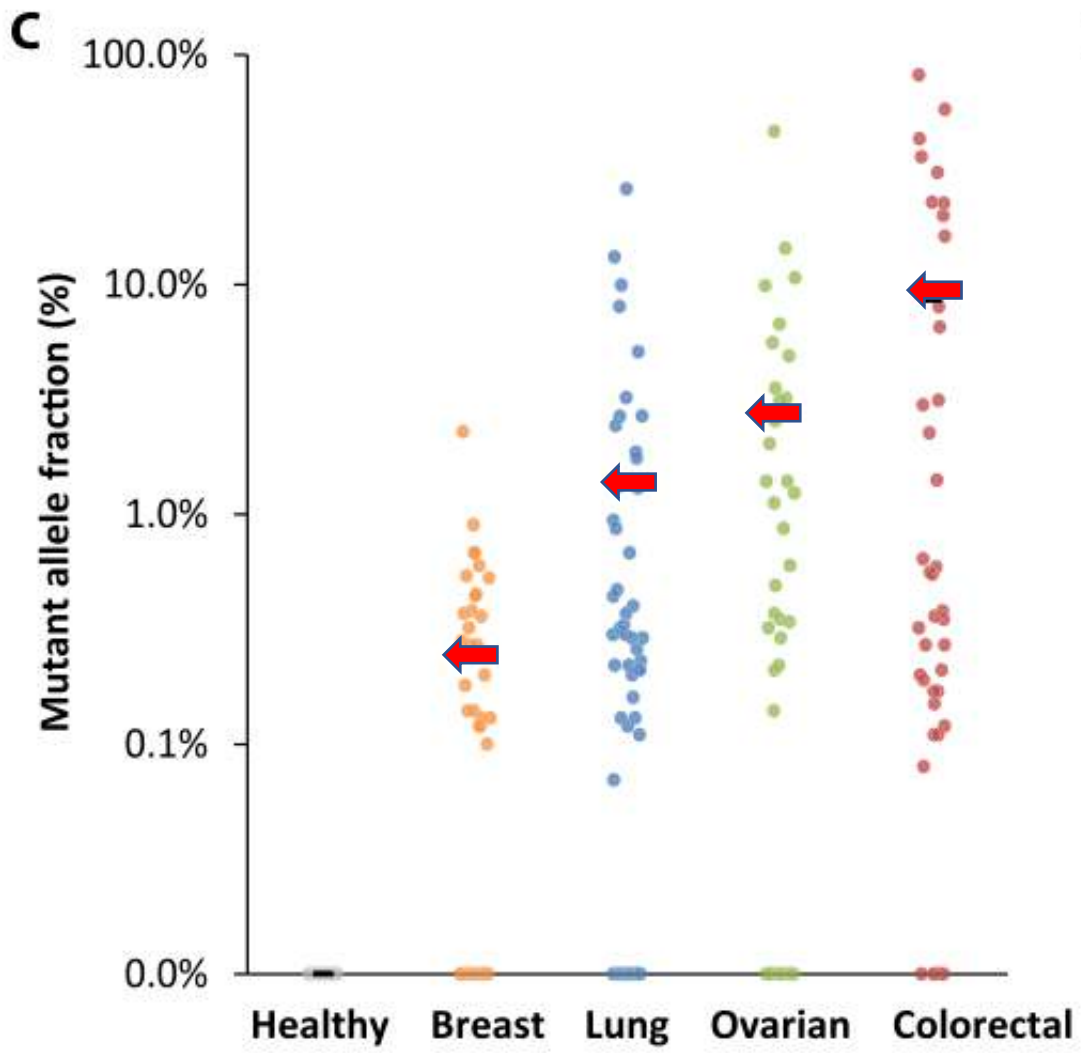
- **Diagnóstico**
- **Pronóstico**
- **Predicción**

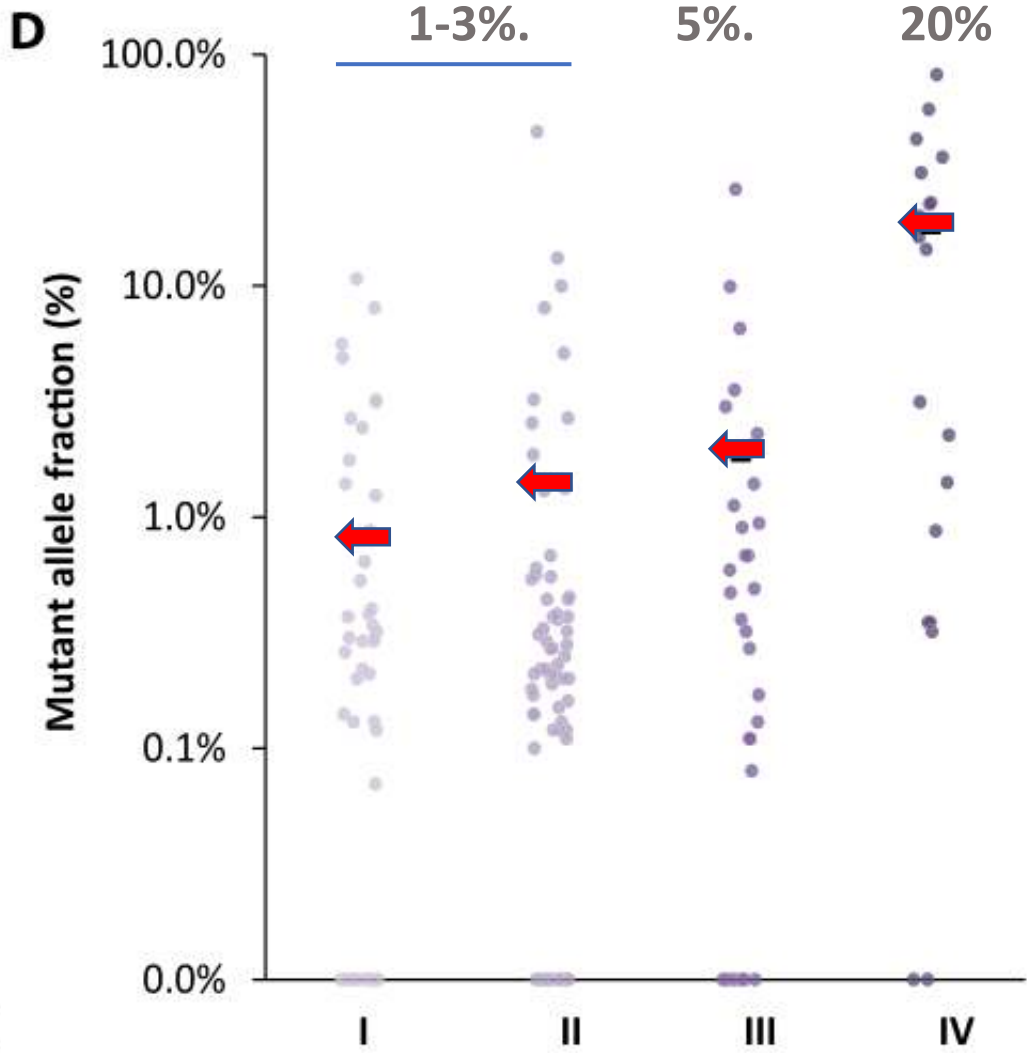
6 weeks earlier than CT scan



Introduction

ctDNA Challenges

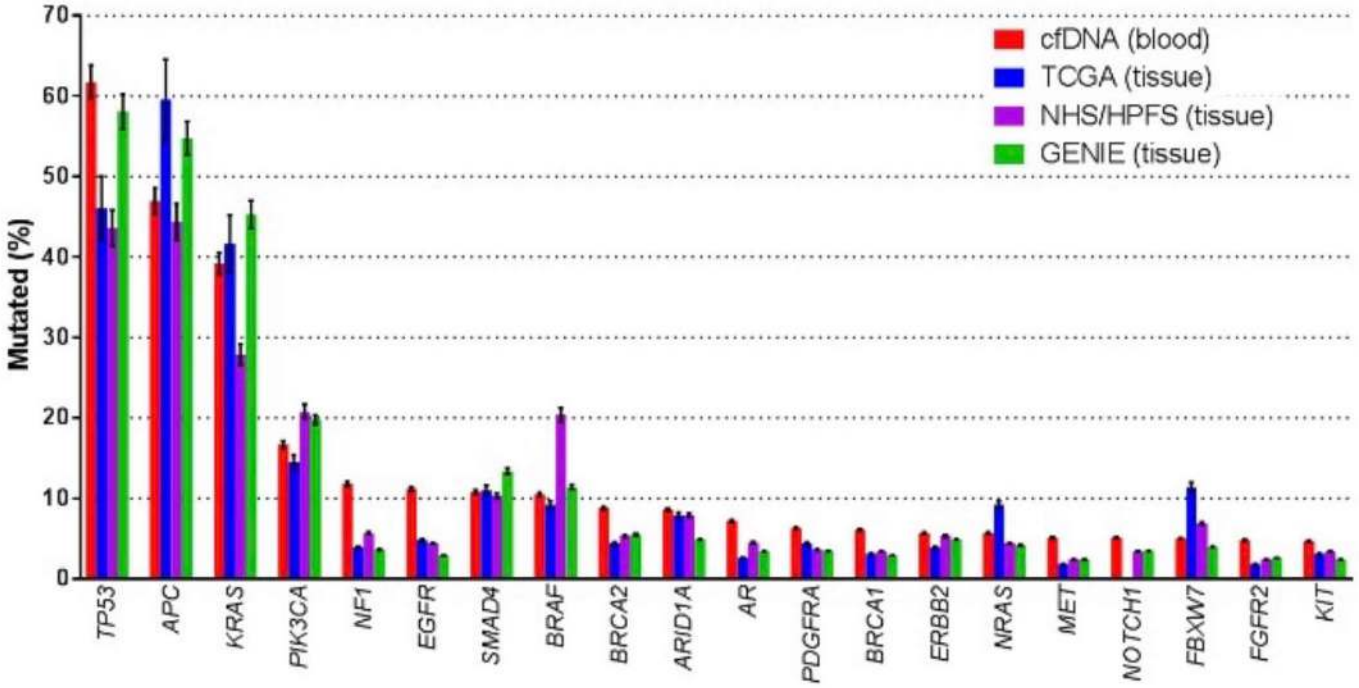


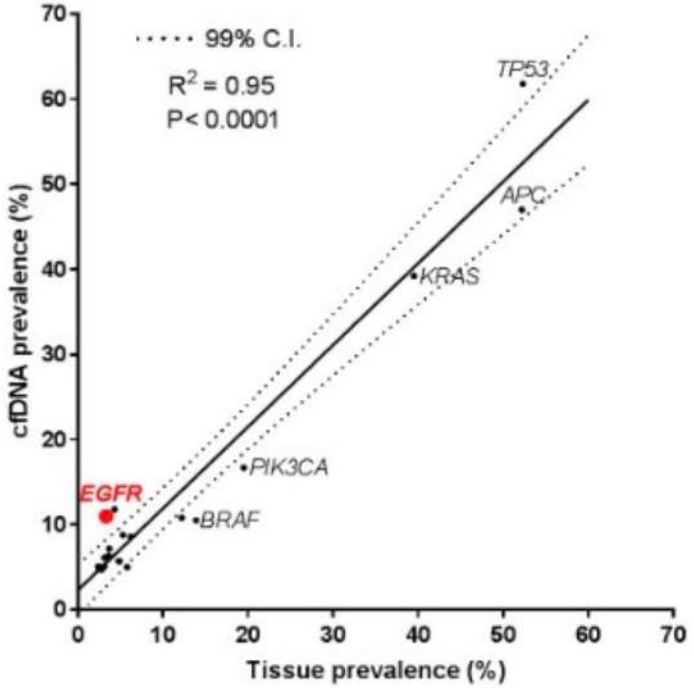


Phallen *et al.*, *Sci. Transl. Med.* **9**, eaan2415 (2017) 16 August 2017

GI Cancers - ASCO 2019

Tissue and plasma concordance in GI cancers





MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

Strickler et al, Cancer Discovery 2018

GI Cancers - ASCO 2019

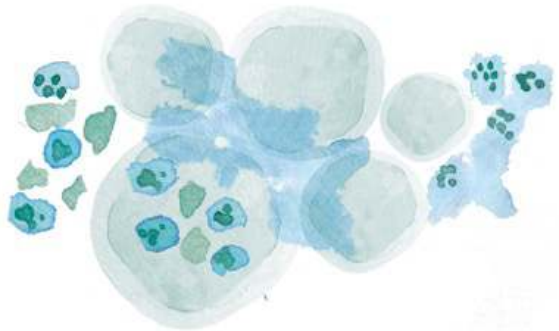
Applications

Identifying actionable alterations	Ready for prime time
Predicting treatment response	Soon, more trials needed
Monitoring therapeutic resistance	Ready for prime time
Detection of residual disease post-surgery	Soon, more trials needed

MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

oncoSens

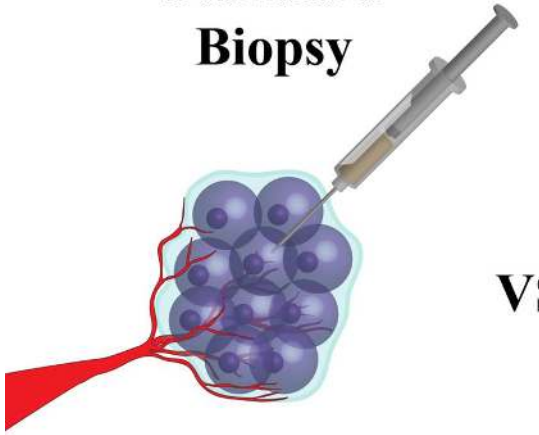
HÉRITAS BIOPSIA LÍQUIDA



Introduction

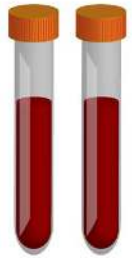
OncoSens - Hospital Aleman BA

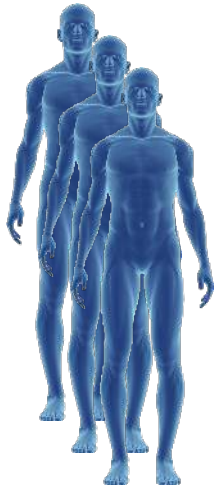
Standard Biopsy



VS.

Liquid Biopsy





Estadio IV

- ✓ Breast
- ✓ NSCLC
- ✓ CRC

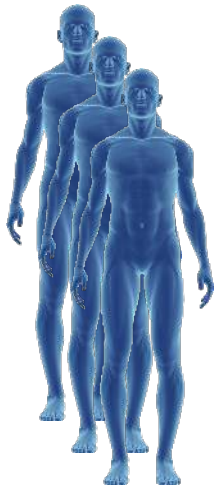
Dr. Carlos bas
Dr. Gonzalo Gomez Abuin
Dra. Mercedes Tamburelli
Lab Central

T0

Introduction

OncoSens - Hospital Aleman BA

T0

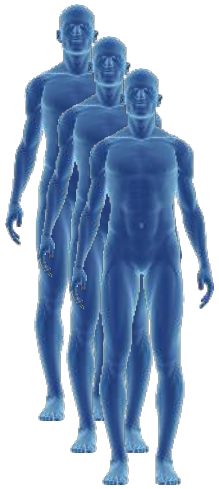


Estadio IV
- ✓ Breast
- ✓ NSCLC
- ✓ CRC

Tratamiento

3 MESES

T1



Evolución ctDNA
Monitoreo

Introduction

OncoSens - Hospital Aleman BA

Version 1

Tipo de tumor	Gen	Region target
mama	AKT1	E17K
colon, pulmón	BRAF	EXON 11,12,7,15,16
pulmón	EGFR	Focal amplification, exon 12 (partial), 18, 19, 20, 21 (partial)- insertions, deletions and indels G719/A/C/S, L858R, L861Q, S7681, T790M
mama, pulmón	ERBB2	full CDS
colon, pulmón	KRAS	exon 2 (partial), 3 (partial), 4 - codons 12,13,19,59,61,117,146
colon, pulmón	MET	EXON 19
colon	NRAS	exon 2 (partial) 3 (partial) 4 - codons 12,13,59,61,117,146
pulmón, mama	PIK3CA	full CDS
pulmón	RET	exon 16 - M918T
pulmón, colon	TP53	full CDS
pulmón	ALK	hotspots (exons 5,8,15,18,19,20,22,23,24,25,29)
pulmón	CTNNB1	hotspots (exon 3)
mama	ERBB3	hotspots (exons 2,3,7,8,9,12,23,27)
mama	ESR1	hotspots (exons 2,5,9) intron 7
pulmón, colon	RAF1	hotspots (exon 7)

FCLPA 04071977

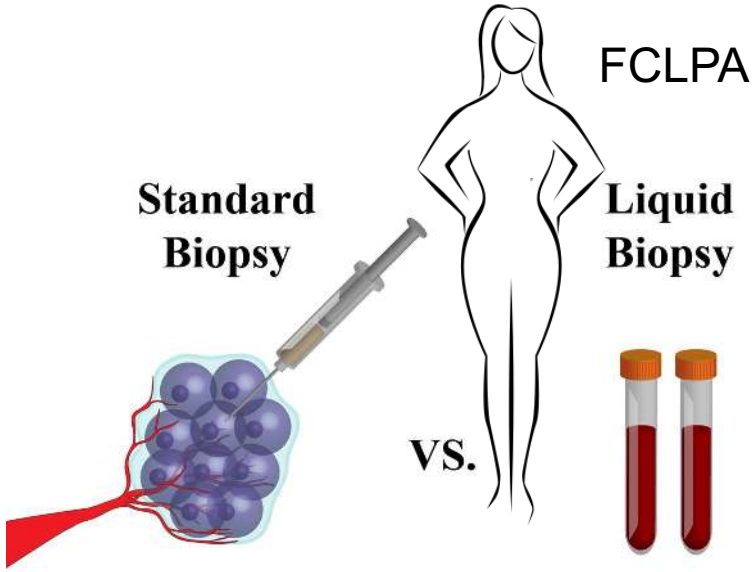
Case report 1- Hospital Alemán

FCLPA 04071977

Hospital Alemán
Deutsches Hospital

40 años, Dx 2015
Estadio IV
Cancer mama metastasis (Her2+)
Metastasis Pulmón (biopsia)

Match
Biopsia Tejido
Vs
Biopsia Líquida



TP53 W91* 57%
9158X
(21500X)

ERBB2 3-4X

Trastuzumab

ERBB2 3-12X

TP53 W91* 3.7%
5800X
(157800X)

- Pobre pronóstico
- Beneficio: Alta dosis de quimio (epirubicin)

ERBB2 V777L 4.7%
6500X
(137000X)

Trastuzumab resistencia

Neratinib sensibilidad

ERBB2 V777L 1.7%
10800X
(640000X)

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