DoCiència

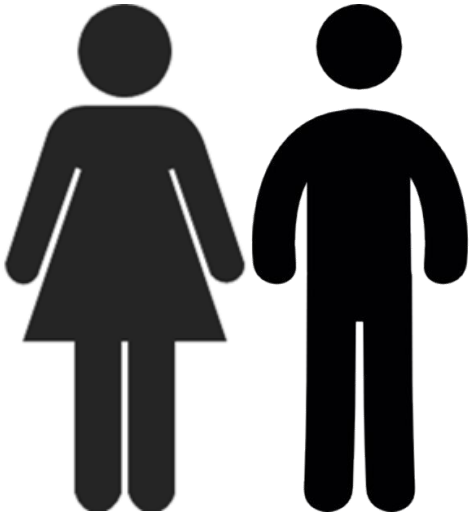
Escola de Primavera

GLORIA RIBAS - Oncología Médica

INCLIVA

COMIDAS PROCESADAS

CONTAMINACIÓN



IRRADIACIÓN SOLAR

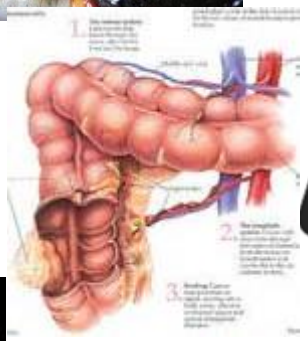
TABACO

FACTORES ENDOCRINOS

ALCOHOL

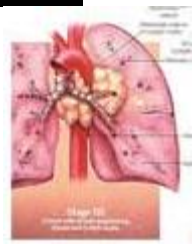
COMIDAS PROCESADAS

CONTAMINACIÓN

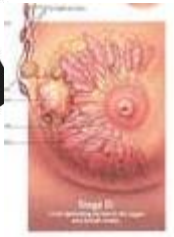


IRRADIACIÓN SOLAR

TABACO

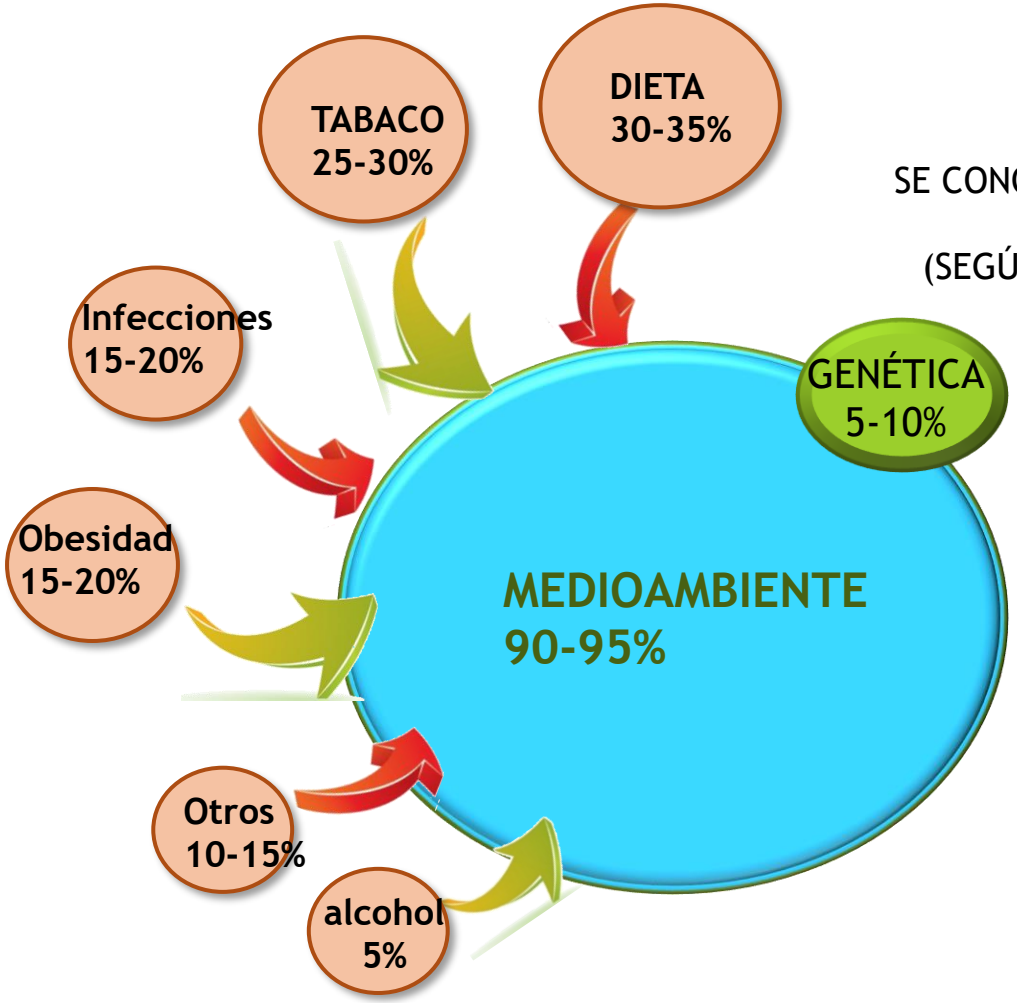


FACTORES ENDOCRINOS



ALCOHOL

CÁNCER ESPORÁDICO



SE CONOCEN MAS DE 200 TIPOS
(SEGÚN EL TEJIDO DE ORIGEN):

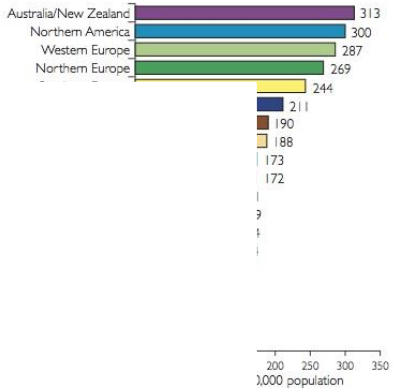
CANCER RESEARCH UK

International Agency for Research on Cancer

World Health Organization

Cancer Incidence Worldwide

Breakdown of the estimated 12.7 million new cases, World-age standardised incidence rates and the most commonly diagnosed cancers by the different regions of the world, 2008.



Northern America
Numbers 1,603,870
Lung 15%
Prostate 13%
Breast 13%
Colorectum 11%

Western Europe
Numbers 1,029,993
Prostate 16%
Breast 14%
Colorectum 13%
Lung 11%

Northern Europe
Numbers 482,080
Breast 15%
Prostate 13%
Colorectum 13%
Lung 12%

Central and Eastern Europe
Numbers 983,408
Lung 14%
Colorectum 13%
Breast 12%
Stomach 7%

Southern Europe
Numbers 713,401
Colorectum 14%
Breast 13%
Lung 12%
Prostate 11%

Eastern Asia
Numbers 3,720,658
Lung 17%
Stomach 16%
Liver 13%
Colorectum 10%

Northern Africa
Numbers 164,350
Breast 17%
Lung 7%
Bladder 7%
Non-Hodgkin lymphoma 7%

Caribbean
Numbers 79,347
Prostate 20%
Breast 11%
Lung 11%
Colorectum 9%

South-Eastern Asia
Numbers 725,446
Lung 14%
Breast 12%
Liver 10%
Colorectum 9%

Western Africa
Numbers 184,071
Breast 16%
Cervix uteri 16%
Liver 11%
Prostate 7%

Western Asia
Numbers 223,042
Breast 13%
Lung 12%
Colorectum 8%
Stomach 7%

Central America
Numbers 176,564
Prostate 12%
Breast 10%
Cervix uteri 9%
Stomach 8%

South-Central Asia
Numbers 1,423,213
Cervix uteri 12%
Breast 12%
Lung 7%
Lip, oral cavity 7%

Melanesia
Numbers 7,028
Lip, oral cavity 12%
Cervix uteri 10%
Breast 9%
Liver 7%

Middle Africa
Numbers 66,895
Liver 16%
Breast 12%
Cervix uteri 12%
Prostate 6%

South America
Numbers 650,097
Breast 14%
Prostate 13%
Lung 8%
Colorectum 7%

Southern Africa
Numbers 79,179
Breast 11%
Prostate 10%
Oesophagus 9%
Cervix uteri 8%

Eastern Africa
Numbers 221,076
Cervix uteri 14%
Kaposi sarcoma 11%
Breast 8%
Oesophagus 7%

Australia/New Zealand
Numbers 127,022
Prostate 17%
Colorectum 14%
Breast 13%
Melanoma of skin 11%

Source: GLOBOCAN 2008, v. 1.2, Cancer Incidence and Mortality Worldwide. IARC, 2010 (http://globocan.iarc.fr)
Map updated February 2011

http://info.cancerresearchuk.org/cancerstats/

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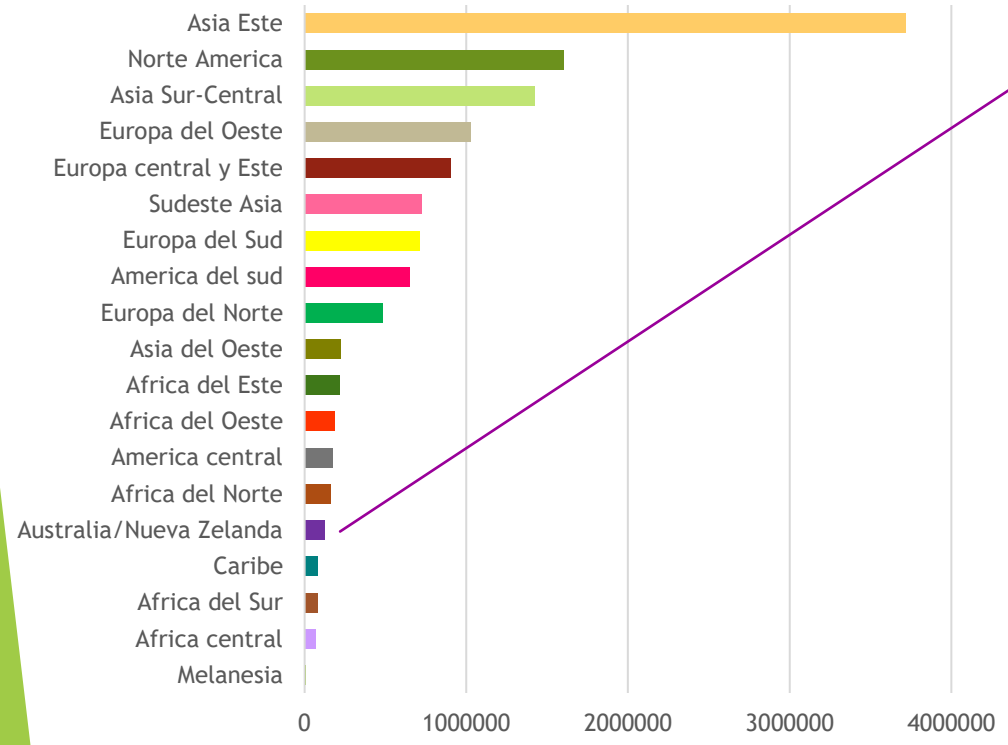
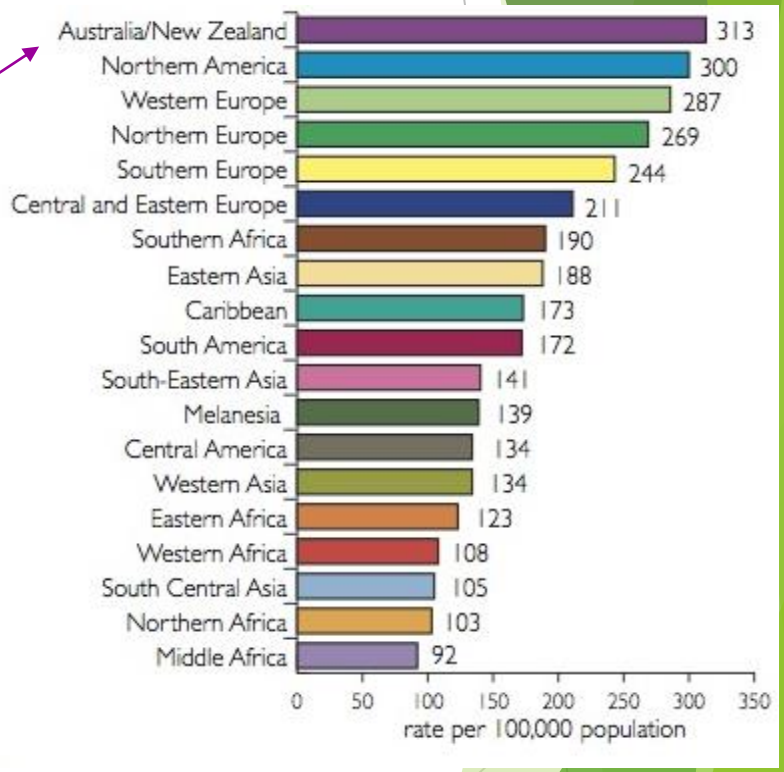
Registered charity no.1089464 (England & Wales) & SC041666 (Scotland)

INCIDENCIA DE CÁNCER MUNDIAL

Número casos por regiones



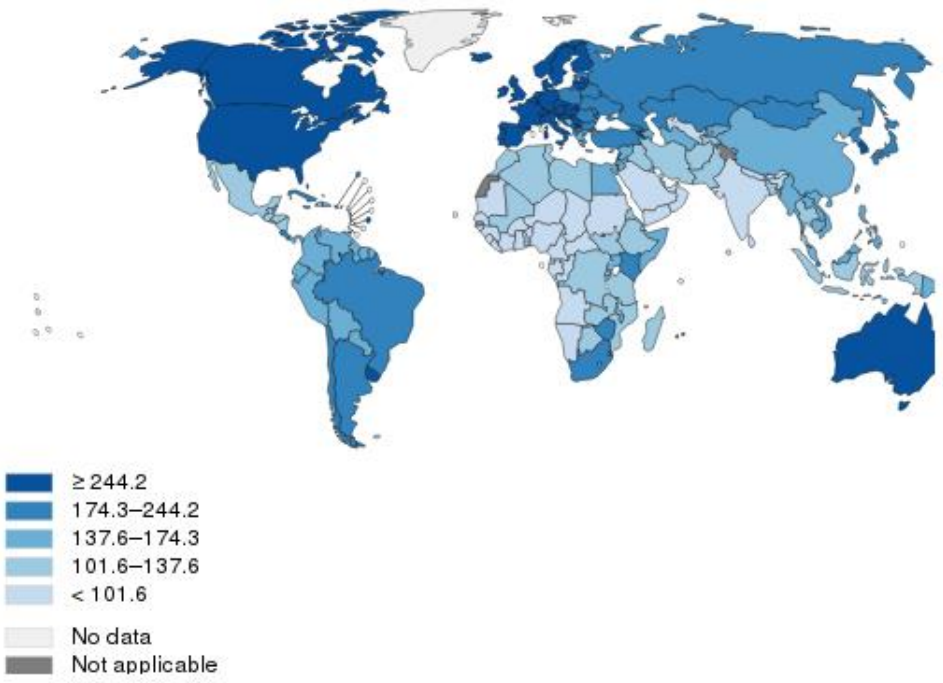
Proporción por 100000 habitantes



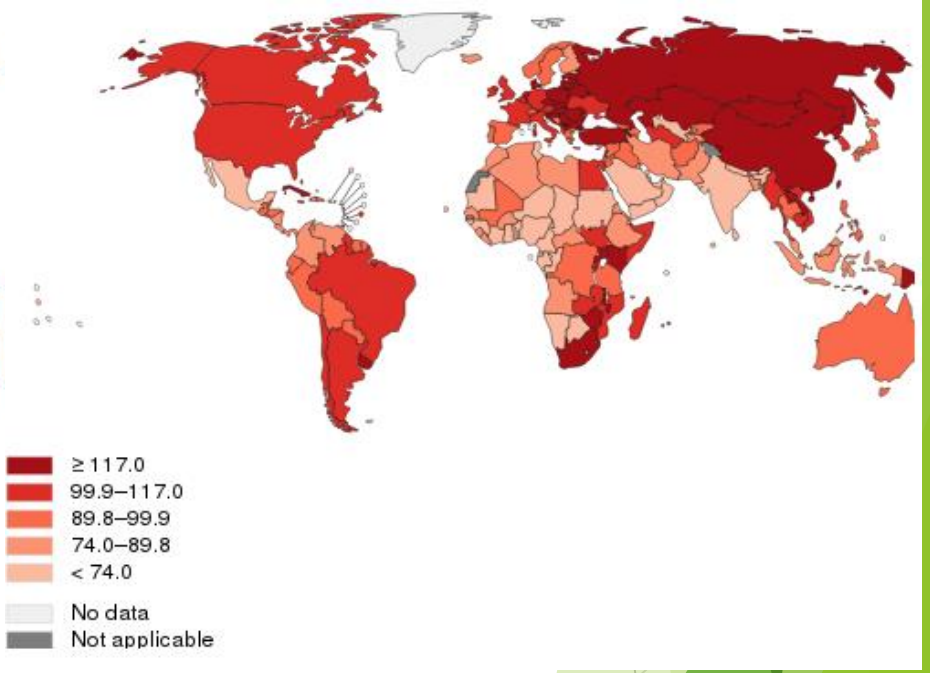
NORTEAMERICA 1,6 M	ASIA > 6M
LATINOAMERICA < 1M	AFRICA 700K
EUROPA > 3M	OCEANIA 135K

Estimated age-standardized rates (World) of….. both sexes, all cancers excluding non-melanoma skin, worldwide in 2012

Incidence cases,



Deaths



Data source: GLOBOCAN 2012
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization

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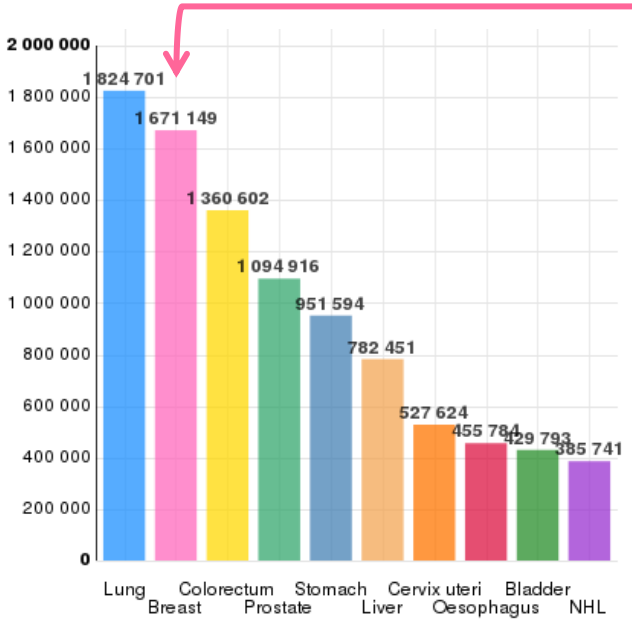
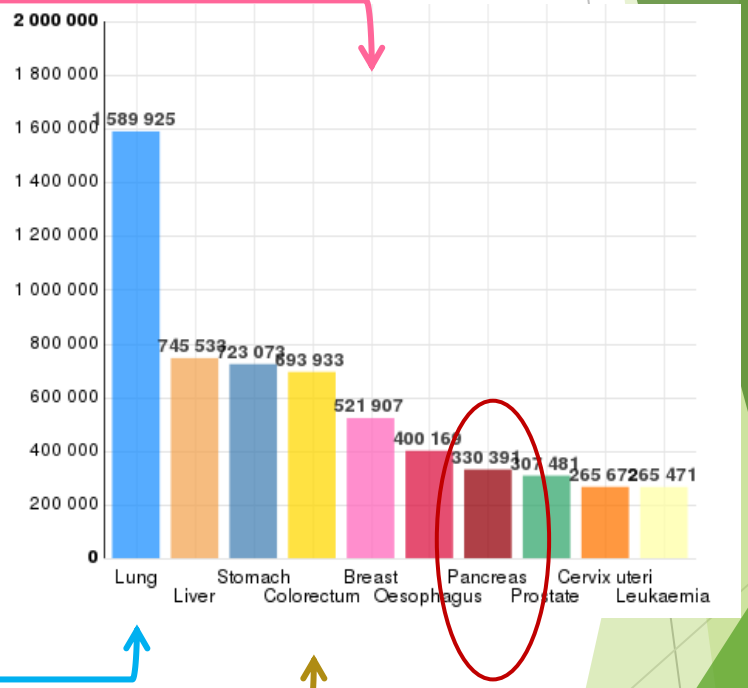
Incidencia y Mortalidad en ambos sexos, Todos los tipos de cancer exceptuando el cancer de piel no melanoma 2012

Incidence cases,



Deaths



Data source: GLOBOCAN 2012
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(http://gco.iarc.fr/today)
World Health Organization

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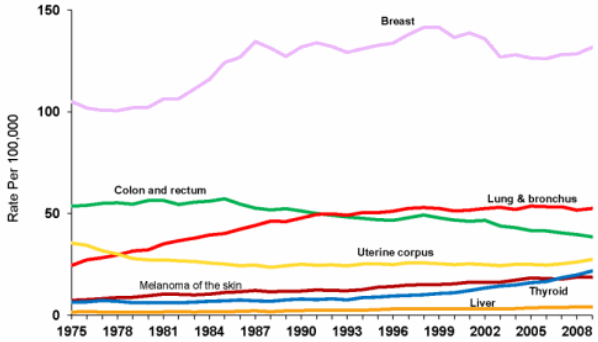
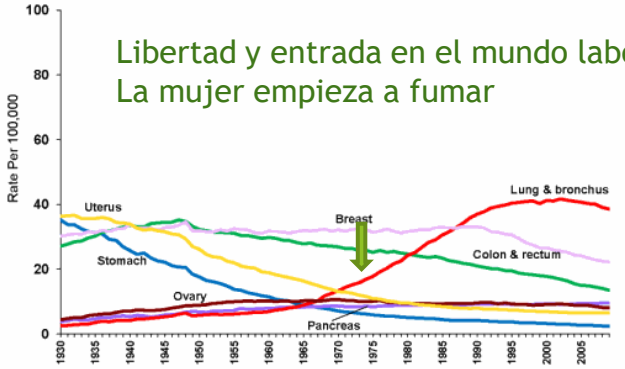
EVOLUCIÓN INCIDENCIA Y MUERTES CÁNCER

Cancer Incidence Rates* Among Women, US, 1975-2009



*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database: SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2009, National Cancer Institute, 2012.

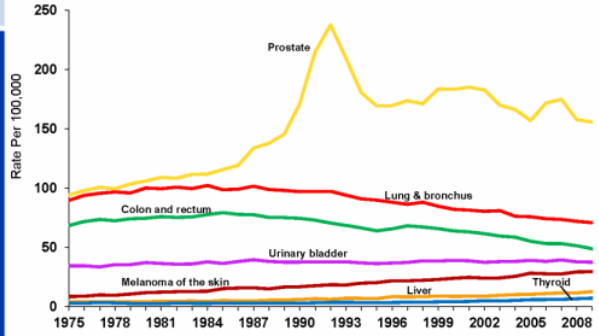
Cancer Death Rates* Among Women, US,1930-2009



Libertad y entrada en el mundo laboral,
La mujer empieza a fumar

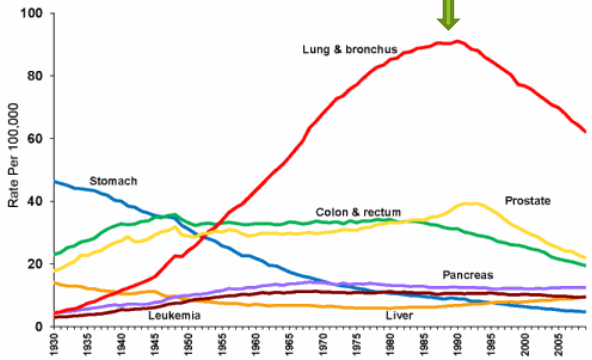
*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer Incidence Rates* Among Men, US, 1975-2009



*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database: SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2009, National Cancer Institute, 2012.

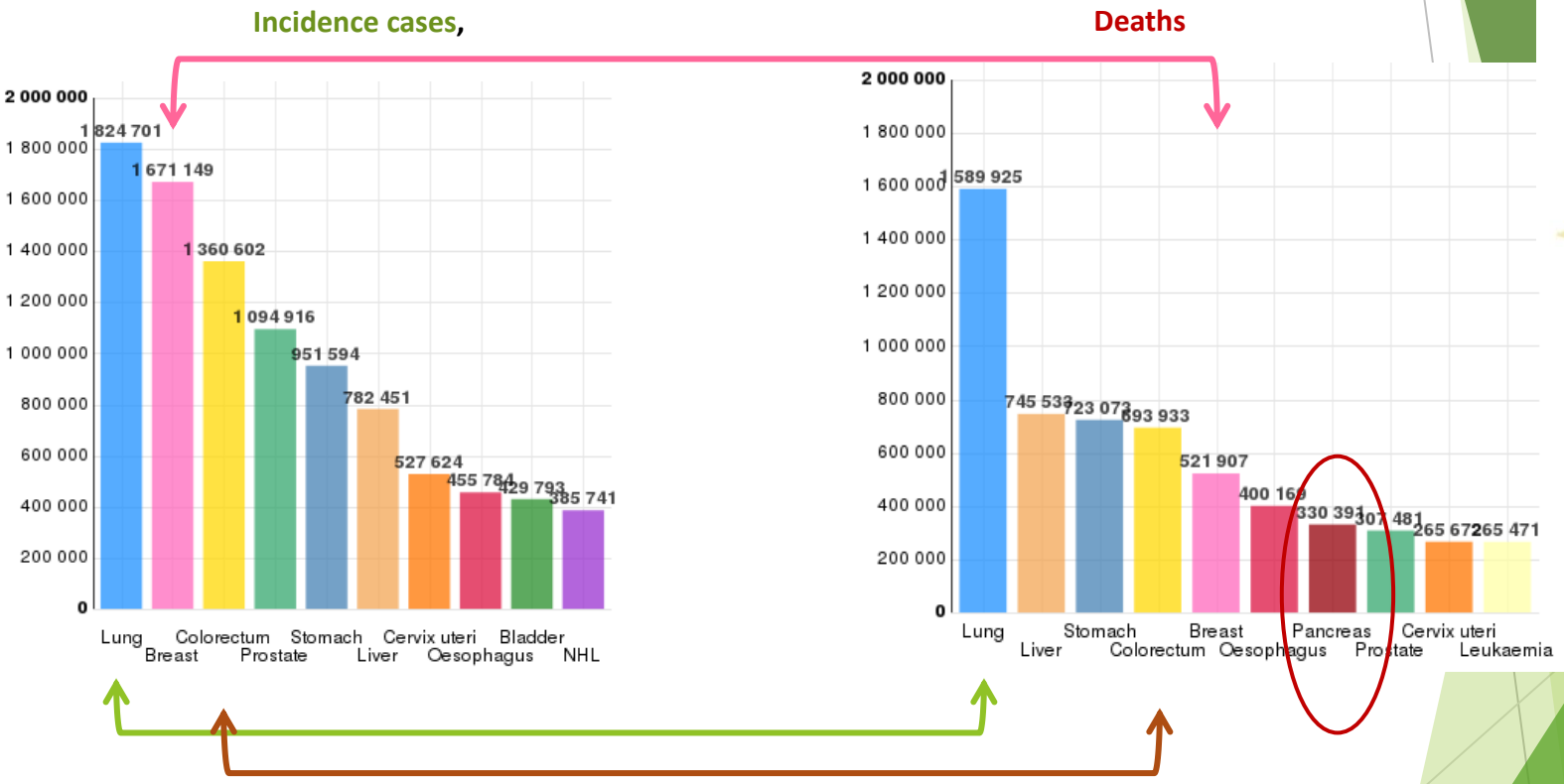
Cancer Death Rates* Among Men, US,1930-2009



Campañas en contra de fumar

*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Estimated age-standardized rates (World) of….. both sexes, all cancers excluding non-melanoma skin, worldv



Data source: GLOBOCAN 2012
Graph production: IARC
(http://gco.iarc.fr/today)
World Health Organization

World Health Organization

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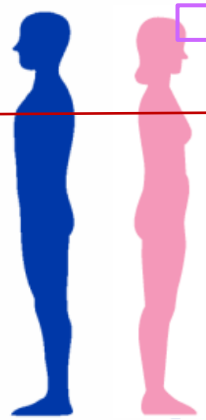
¿INCIDENCIA/MUERTES POR SEXO?

Estimated New Cancer Cases* in the US in 2013

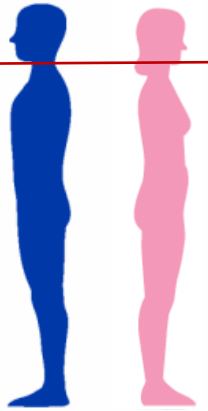
Men 854,790		Women 805,500	
Prostate	28%	29%	Breast
Lung & bronchus	14%	14%	Lung & bronchus
Colon & rectum	9%	9%	Colon & rectum
Urinary bladder	6%	6%	Uterine corpus
Melanoma of skin	5%	6%	Thyroid
Kidney & renal pelvis	5%	4%	Non-Hodgkin lymphoma
Non-Hodgkin lymphoma	4%	4%	Melanoma of skin
Oral cavity	3%	3%	Kidney & renal pelvis
Leukemia	3%	3%	Pancreas
Pancreas	3%	3%	Ovary
All Other Sites	20%	19%	All Other Sites



*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Estimated Cancer Deaths in the US in 2013

Men 306,920		Women 273,430	
Lung & bronchus	28%	26%	Lung & bronchus
Prostate	10%	14%	Breast
Colon & rectum	9%	9%	Colon & rectum
Pancreas	6%	7%	Pancreas
Liver & intrahepatic bile duct	5%	5%	Ovary
Leukemia	4%	4%	Leukemia
Esophagus	4%	3%	Non-Hodgkin lymphoma
Urinary bladder	4%	3%	Uterine corpus
Non-Hodgkin lymphoma	3%	2%	Liver & intrahepatic bile duct
Kidney & renal pelvis	3%	2%	Brain/other nervous system
All other sites	24%	25%	All other sites

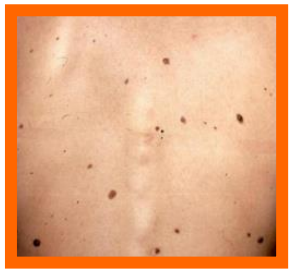


CÁNCER ESPORÁDICO: MELANOMA

FACTORES DE RIESGO

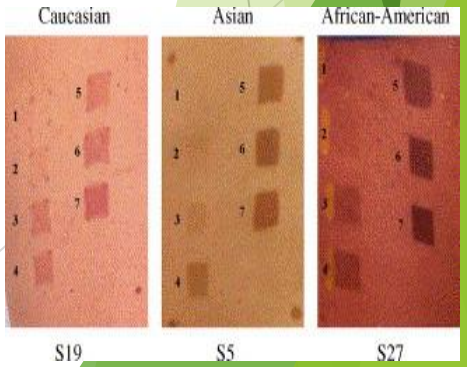
ENFERMEDAD Disease multifactorial. Familiar and sporadic cases are influenced by:

Endogenous Factors: **Phototipo**



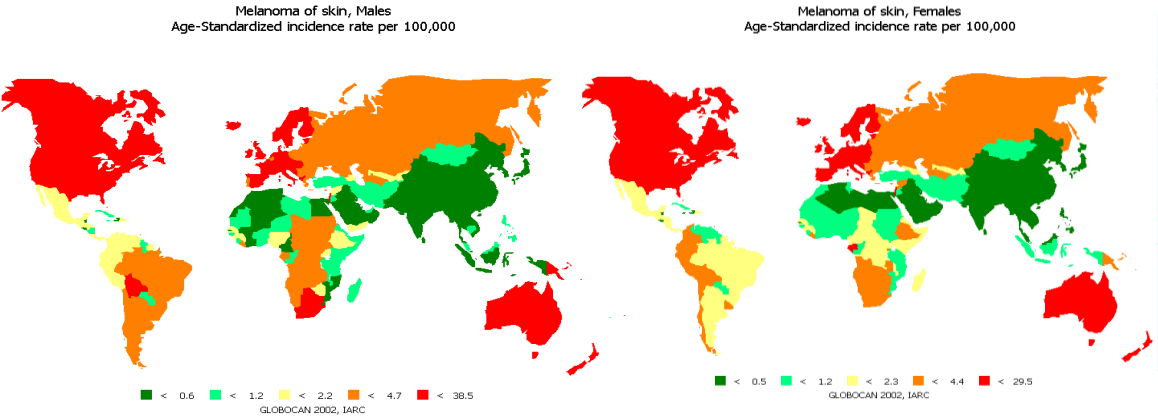
FOTOTIPO FITZPATRICK

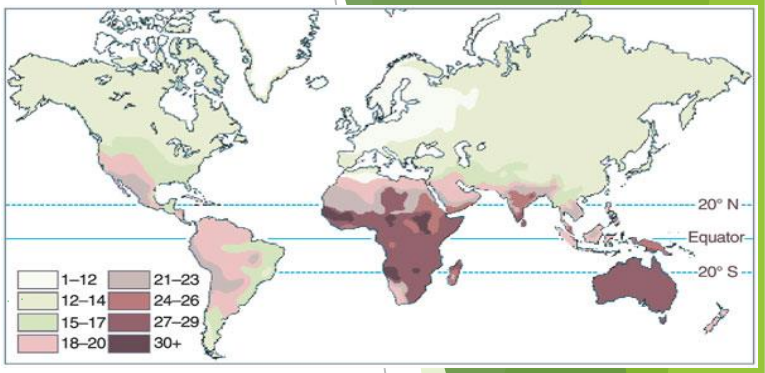
Skin type	Susceptibility to sunburn	Constitutive skin colour	Facultative tanning ability	Susceptibility to skin cancer
I	High	White	Very poor	High
II	High	White	Poor	High
III	Moderate	White	Good	Moderate
IV	Low	Olive	Very good	Low
V	Very low	Brown	Very good	Very low
VI	Very low	Black	Very good	Very low



INTRODUCTION

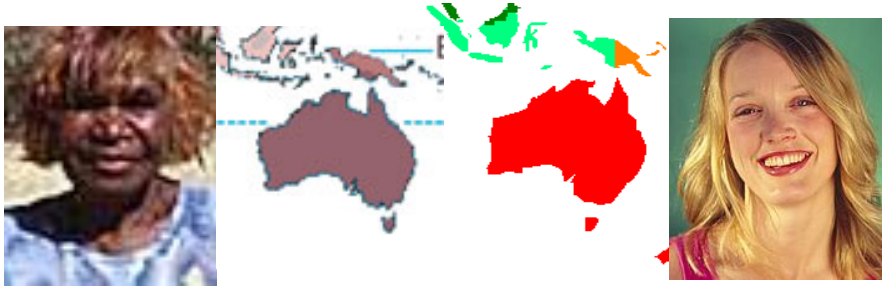
MELANOMA SUSCEPTIBILITY



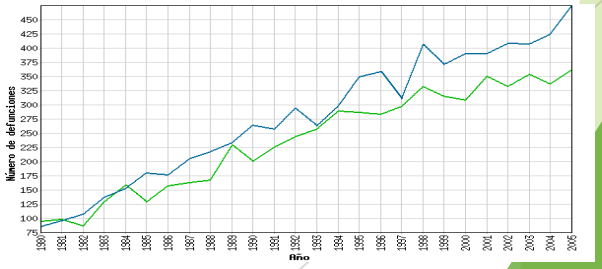


INCIDENCIA MELANOMA

PIGMENTATION DE LA PIEL DE POBLACIÓN INDIGENA (MELANIN INDEX)

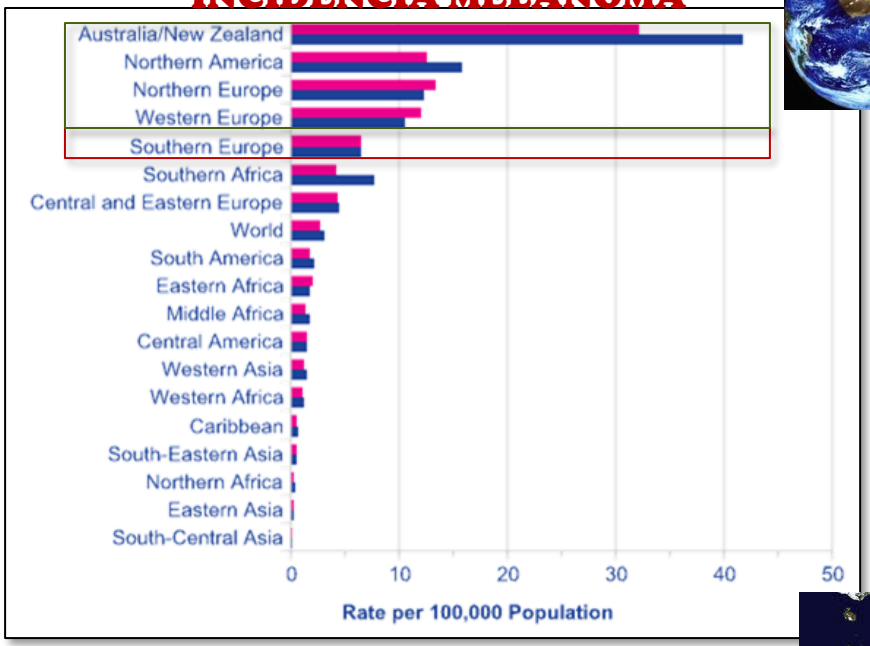


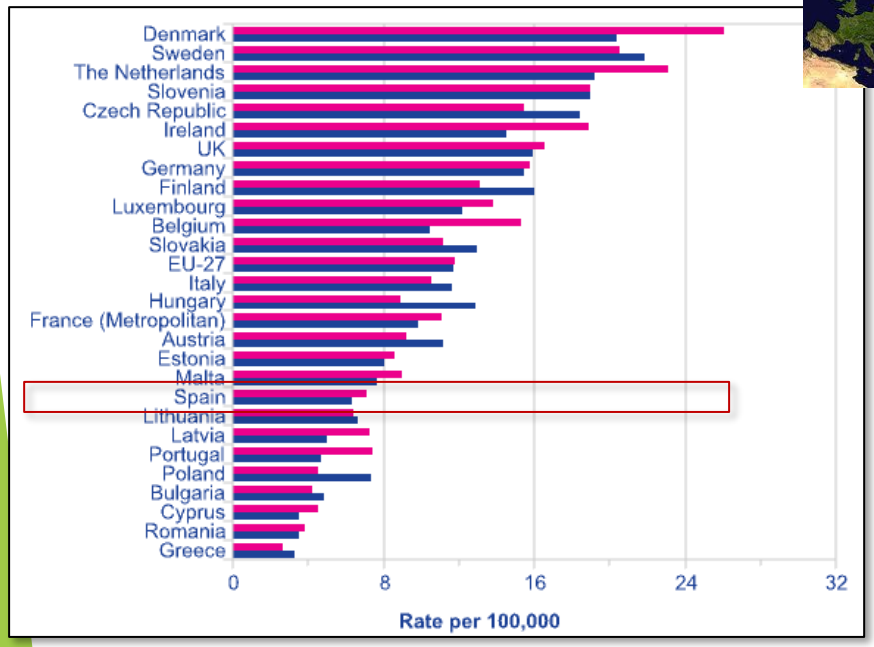
Spain has some of Europe's lowest MM incidence, however this incidence is increasing faster than that of any other malignancy.



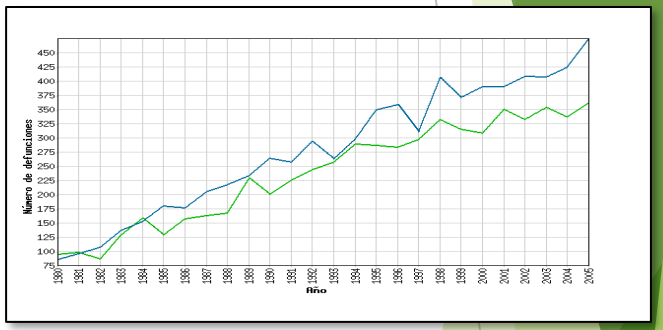
Epidemiologia:

INCIDENCIA MELANOMA





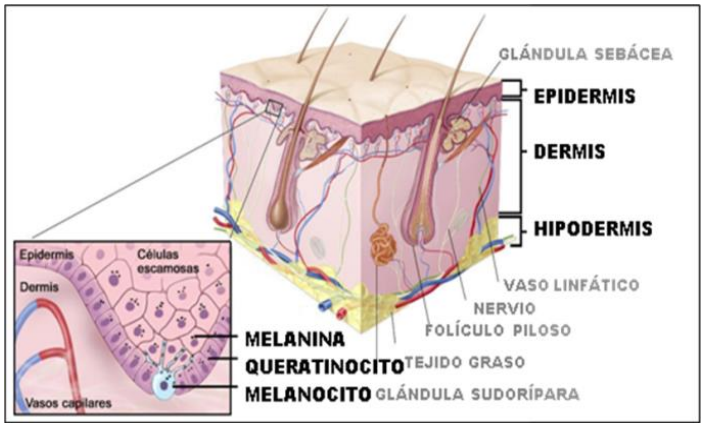
La característica más relevante del MM es su incidencia creciente en poblaciones "caucásicas" : USA, Australia y Europe



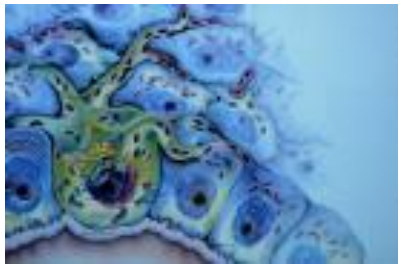
España tendría una de las incidencias mas bajas en Europa, sin embargo ésta esta experimentado un rápido aumento mas rápido que otras enfermedades.

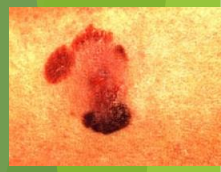
INTRODUCTION

MELANOMA SUSCEPTIBILITY

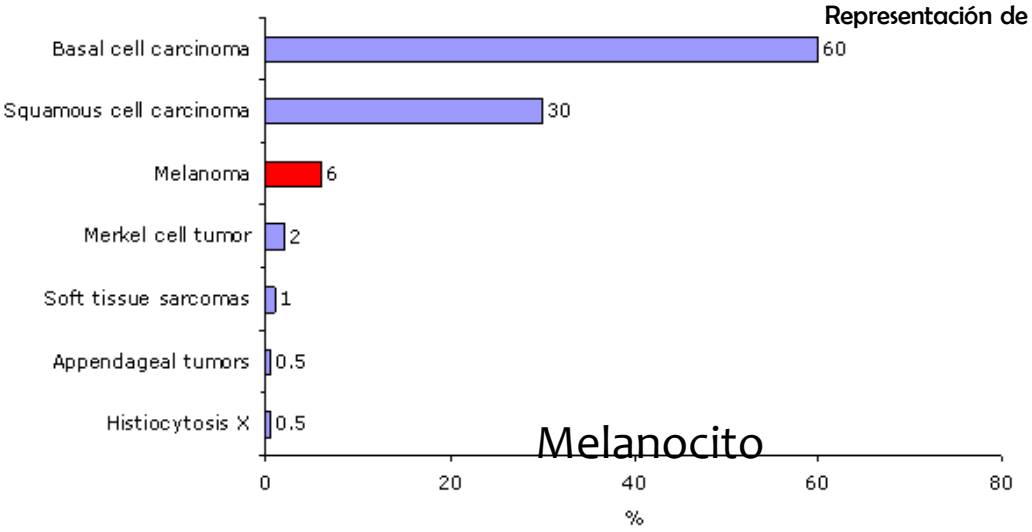


Malignant Melanoma (MM) is a cancer of melanocytes.

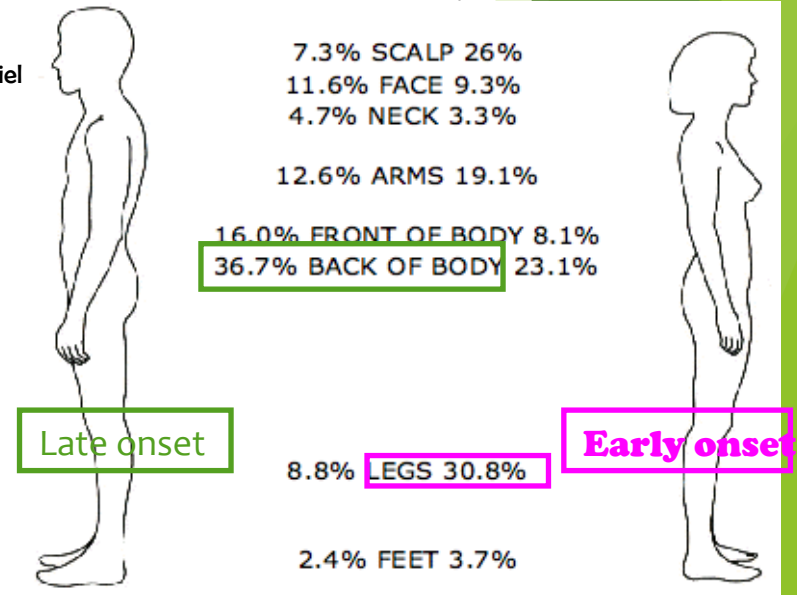




Types of skin cancer:



Typical areas



Cutaneous melanoma is the most frequent type of melanoma.

It represents approximately 5% to 7% of all skin malignancies.

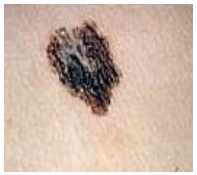
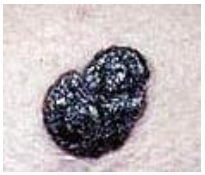
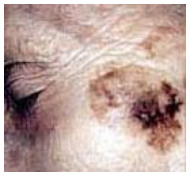
- Average of onset: 45 years, rare prior puberty
- No sex predilection
- Responsible of nearly 90% of deads of skin cancer

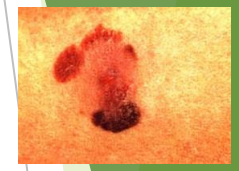
INTRODUCCION

CLASIFICACIÓN CLÍNICA DE LOS MELANOMAS

Melanoma Maligno (MM) tiene su origen en los melanocitos.

SUBTIPOS

Extensión Superficial	Nodular	Lentigo Maligno	Lentiginoso Acral	OTROS
MES	MN	MLM	MLA	mucosas, melanoma amelanótico, demoplástico, nevoide y verrucoso.
				
70%	10-15%	4-15%	5-10%	< 5%

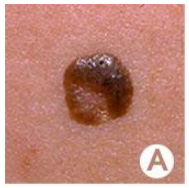


- no tiene predilección por sexos
- La media de aparición esta sobre los 57 años (es raro que aparezca antes de la pubertad)

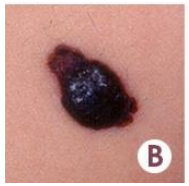
- Responsable del 75% de las muertes por cáncer de piel
- Mortalidad estabilizada por campañas de prevención y detección precoz

DIAGNÓSTICO, PRONÓSTICO Y TRATAMIENTO DE LA ENFERMEDAD

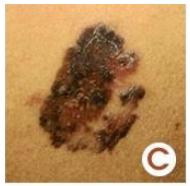
- Detección precoz y extirpación completa del tumor es el mejor tratamiento
- Ipilimumab y vemurafenib para melanomas metastáticos *BRAF*^{Val600}
- Regla ABCDE



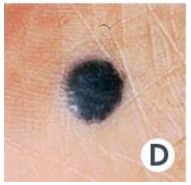
ASIMETRÍA



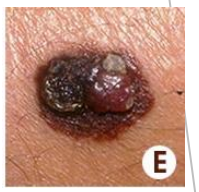
BORDES IRREGULARES



COLOR IRREGULAR

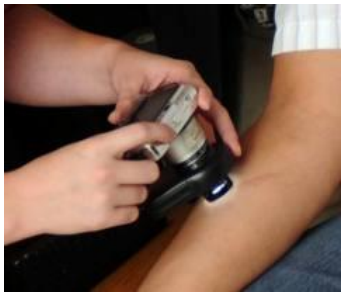


DIÁMETRO >6 mm



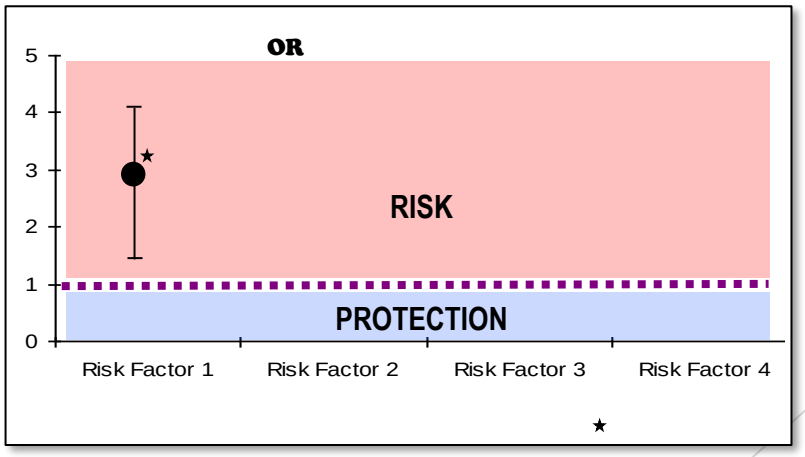
EVOLUCIÓN

- Test clínico sensible pero poco específico
- Dermoscopios y escáneres de luz visible, IR y UV

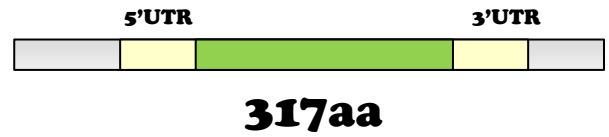


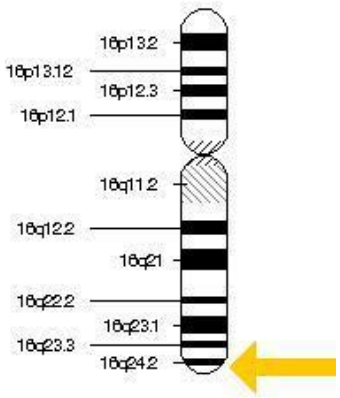
- Factor pronóstico más fiable: Índice de Breslow profundidad en mm medida verticalmente
- Supervivencia 80-90% si el tumor se detecta en los estadios iniciales

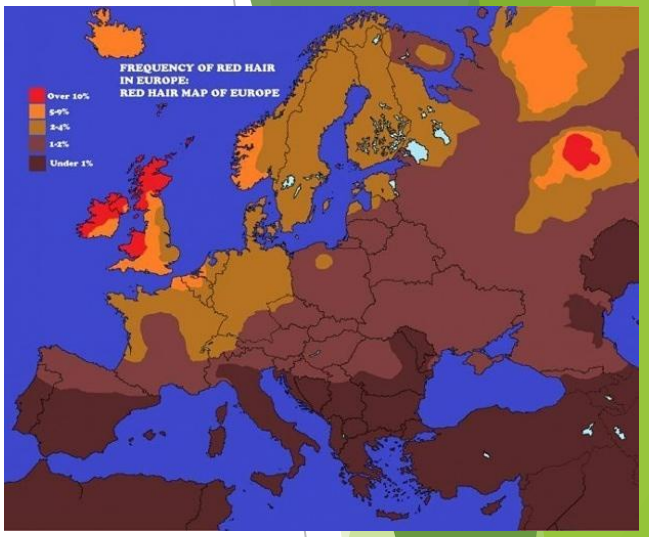
ESTUDIOS CASO - CONTROL

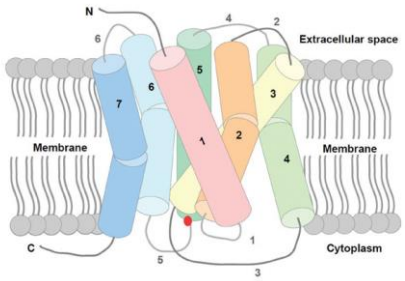


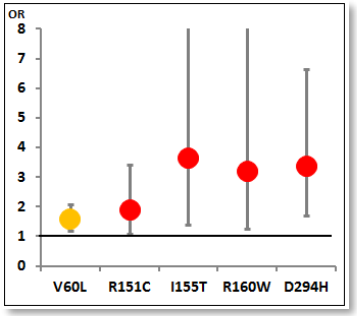
- **85-97 % del MELANOMA ES ESPORÁDICO**
- ***MUTACIONES/SNPs en EL GEN MC1R***

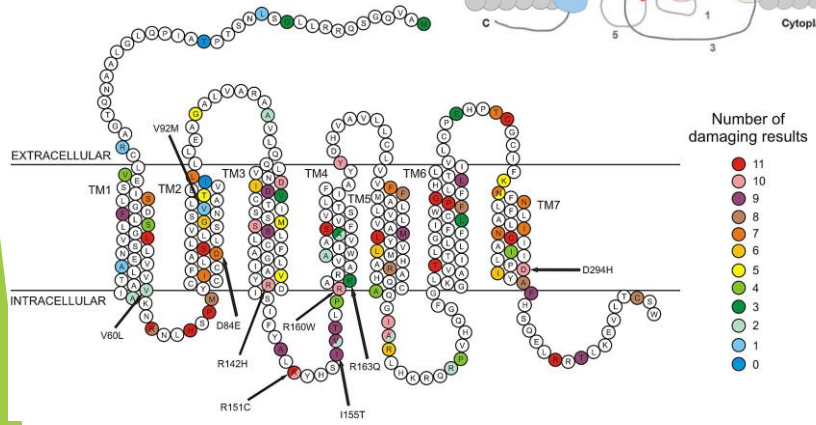


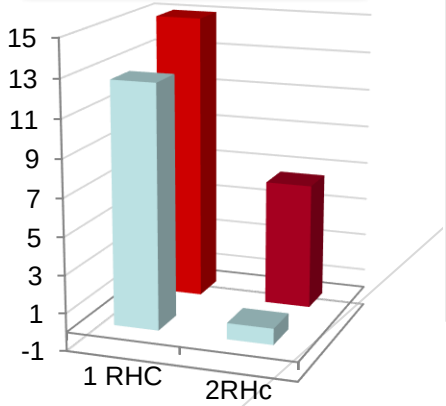


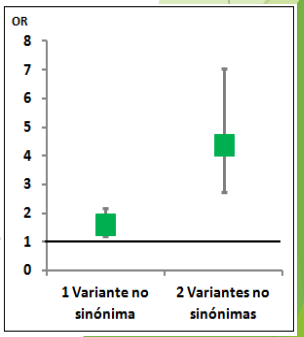




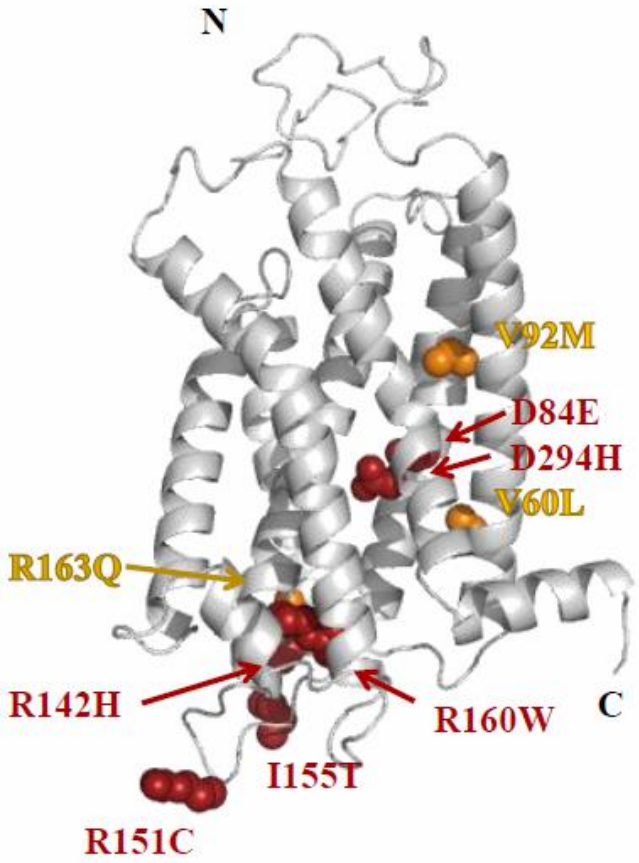




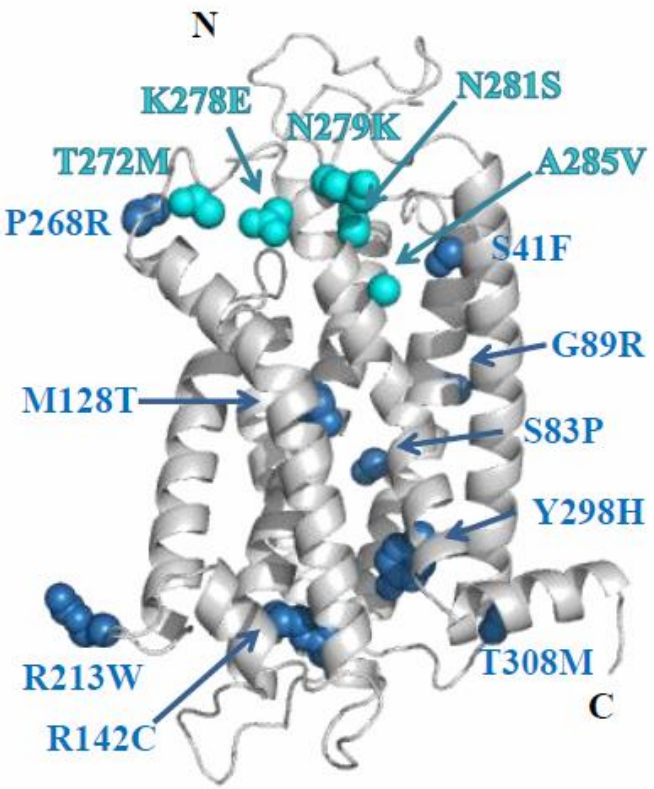




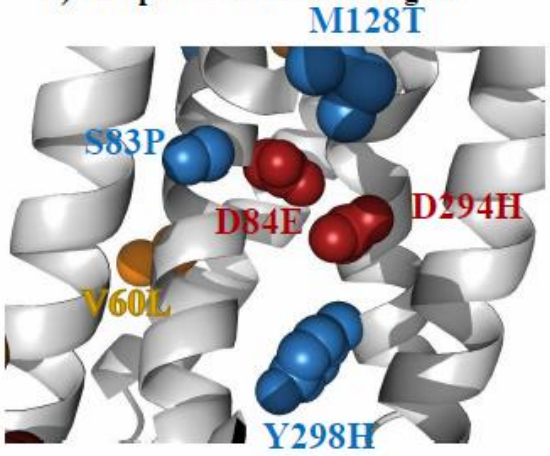
a) Position of Red hair colour (RHC) and non red hair colour (NRHC) variants



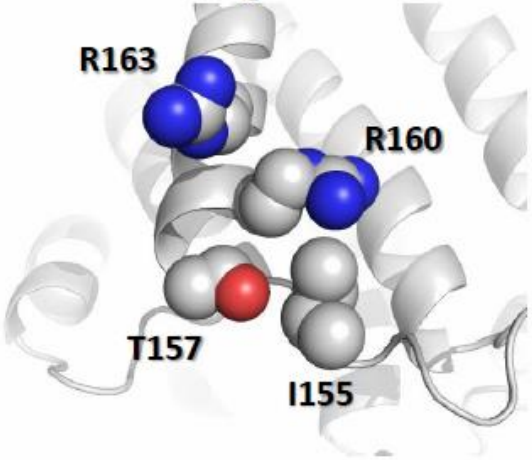
b) Position of potentially functional rare variants according to MC1R structure



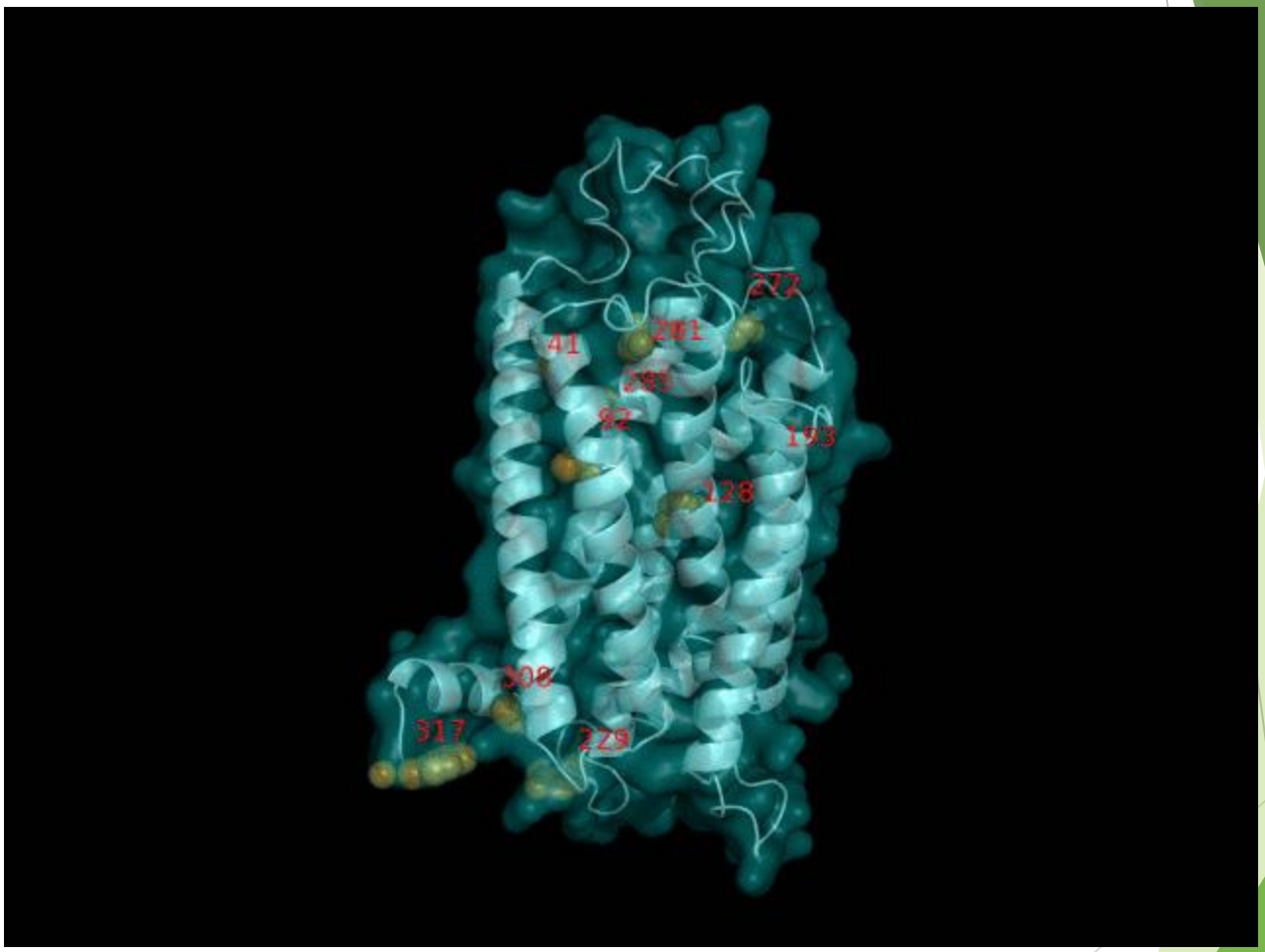
c) Receptor's core central region



d) Important residues in PKC MC1R interacting domain

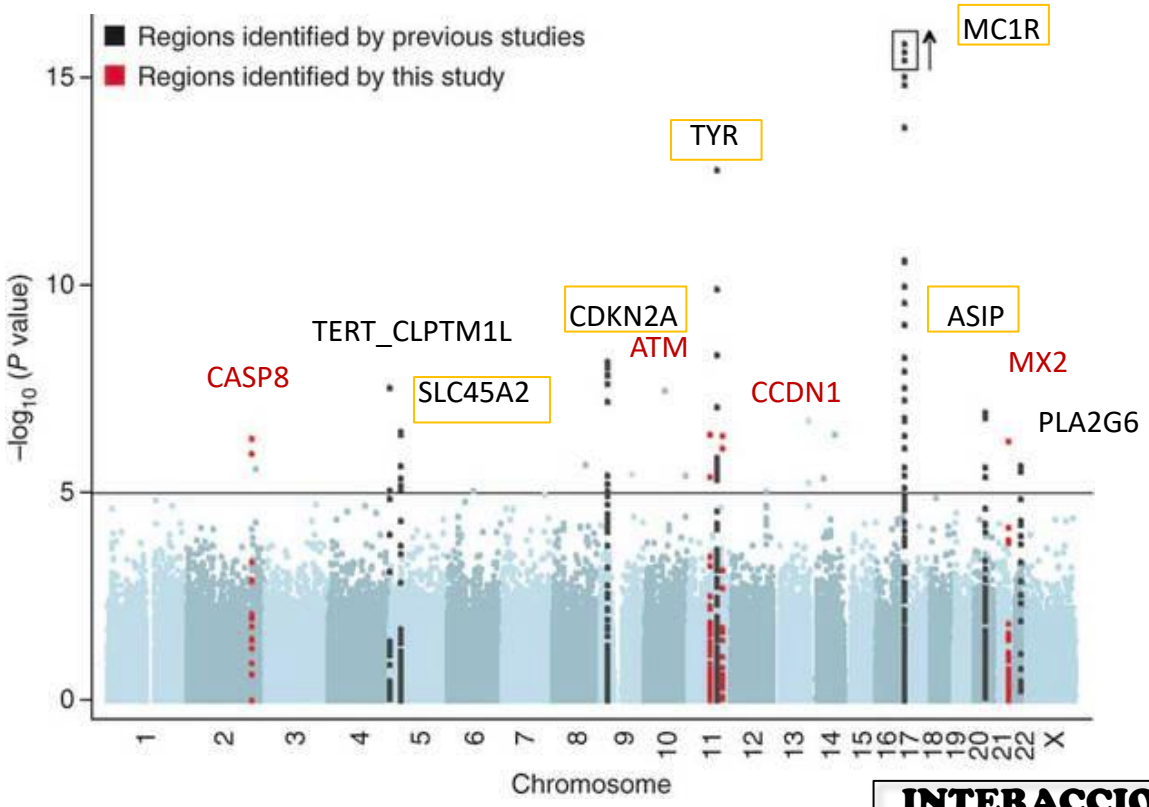


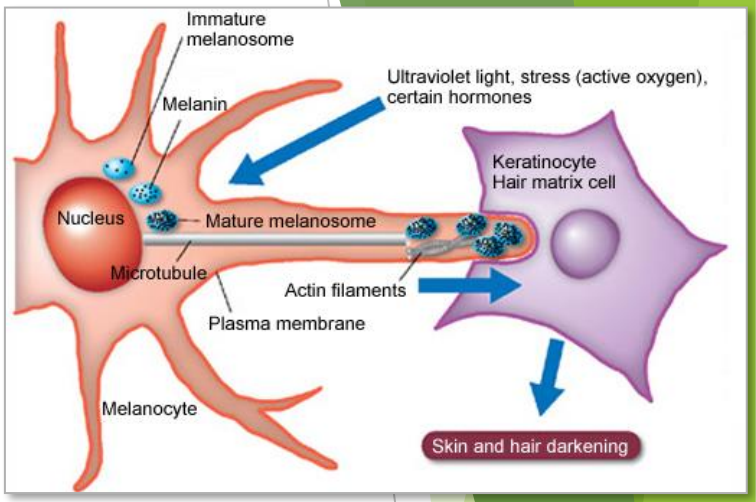
Modelado 3D MC1R con variaciones nuevas detectadas en población española



Basado en PDB 2IQR

Cortesia Dr. J. Bravo (IBV)





SNPs EN GENES:

- MC1R
- SLC45A2
- HERC2-OCA2
- GSTP1
- NOS1

INTERACCIONES:

COOPERAN EN EL RIESGO:

- DOS O/+ VARIANTES EN MC1R
- ADAMTS20 + TYR
- GSTP1 + MC1R

COOPERAN EN LA PROTECCION:

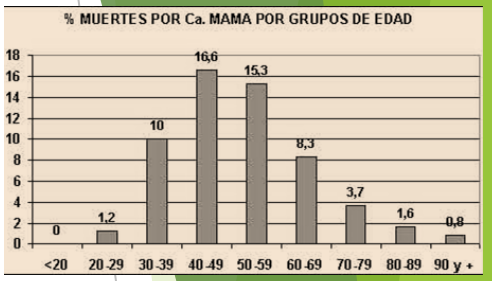
- SLC45A2 + SILV

NEUTRALIZAN EFECTOS:

- MC1R – SLC45A2

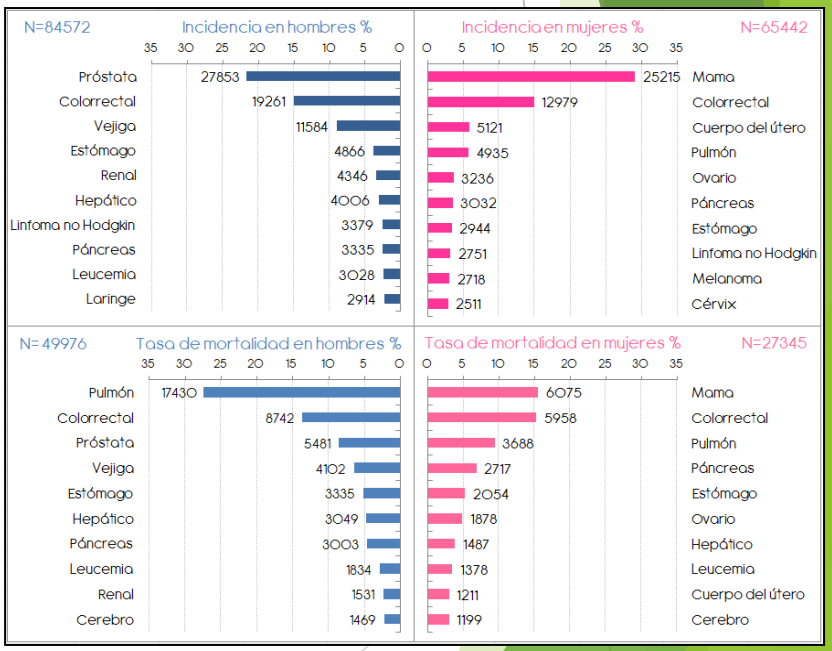
CÁNCER DE MAMA

El cáncer de mama es el **tumor más frecuente en la mujer**, ésta neoplasia empieza a presentarse en torno a los 30 años, aumentando de forma progresiva su incidencia, hasta afectar al 9% de la población femenina a los 70 años de edad.



Incidencia En España la enfermedad presenta una tasa de 66.8 pacientes por 100.000 mujeres/año, con un incremento anual del 2.5%.

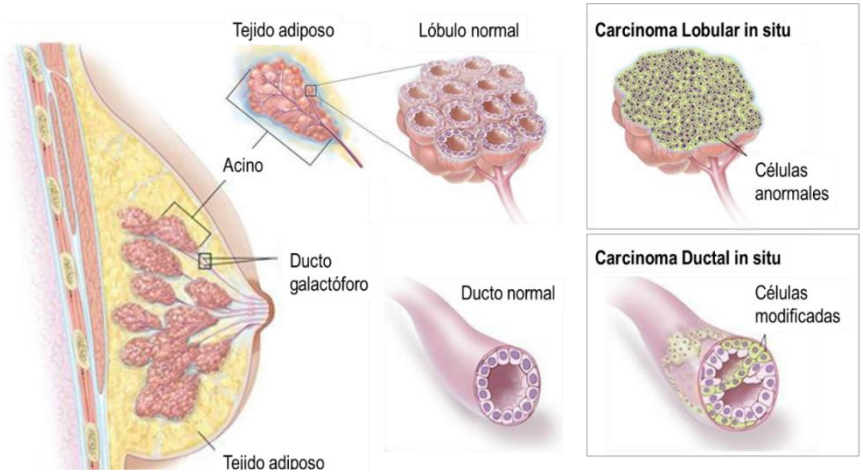
Esta incidencia se correlaciona con la **mortalidad**, que en España y ajustada por edad, mostró en el año 2000 una tasa de 20.87/100.000 mujeres (5.663 casos), representando el 16.7% de los fallecimientos por tumor maligno y el 3.3% del total de las defunciones.

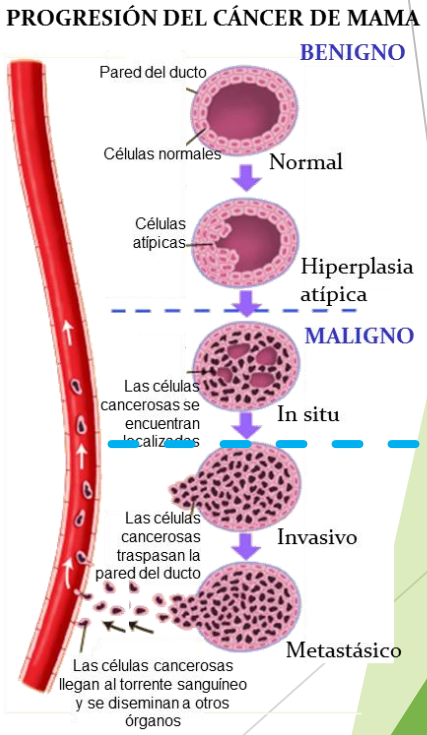


Por todo esto, el cáncer de mama supone en nuestro medio la cuarta causa de muerte y la primera causa de años potenciales de vida perdidos.

CÁNCER DE MAMA

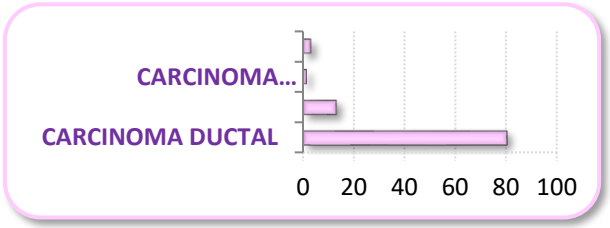
- ✓ EL CÁNCER DE MAMA ES EL DE MAYOR INCIDENCIA EN LA POBLACION FEMENINA
  - ✓13.44% DEL TOTAL DE CANCER EN MUJERES
- ✓ 1 DE CADA 8-10 MUJERES DESARROLLARÁ UN CANCER DE MAMA A LO LARGO DE SU VIDA

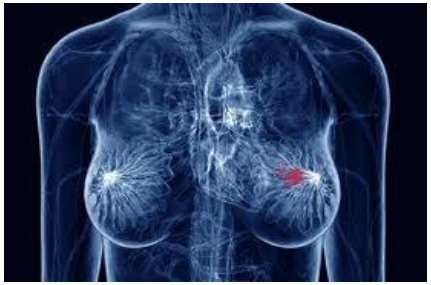




TIPOS TUMORALES:

- ✓ DIAGNÓSTICO ANATOMO-PATOLÓGICO

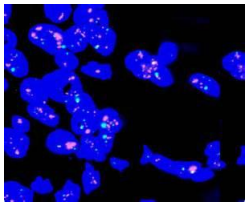


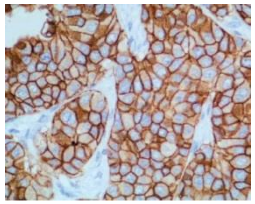


CÁNCER DE MAMA

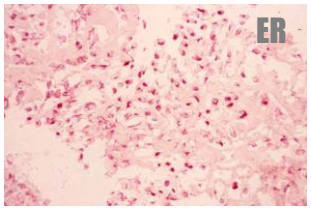
IHC : INMUNOHISTOQUIMICA

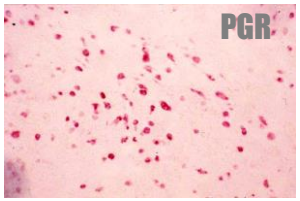
SOBRE – EXPRESIÓN HER2



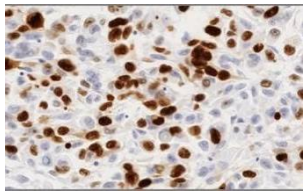


SOBRE – EXPRESIÓN RECEPTORES ENDOCRINOS





KI67 PROLIFERACIÓN



LUMINALES A

62%

- EXPRESAN RECEPTORES HORMONALES
- EXPRESAN QUERATINAS (CK7, CK8, CK18)
- BUEN PRONÓSTICO

HORMONOTERAPIA: Tamoxifeno o Aromatasa

LUMINALES B

18%

HORMONOTERAPIA + QMT

LUMINALES C

Bevacizumab (antiVEGF)

ENRIQUECIDAS CON HER2+

10%

- % ALTA MUTACIONES P53
- ALTO GRADO
- TENIAN MAL PRONÓSTICO

TERAPIA DIRIGIDA: ANTI-HER2:
Trastuzumab
Pertuzumab
lapatinib

RESISTENCIAS

TRIPLES NEGATIVAS

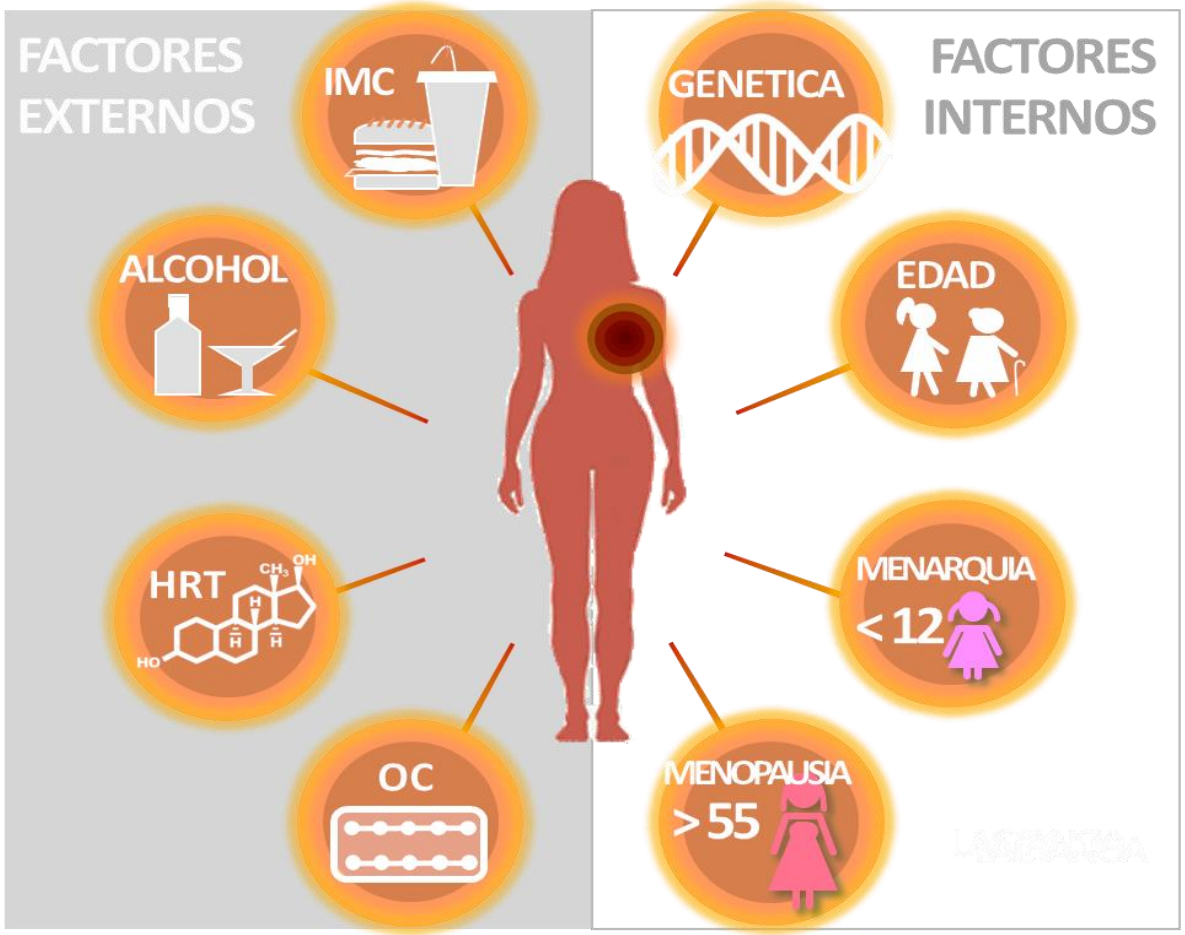
10%

- NO EXPRESAN RH
- EXPRESAN QUERATINAS (CK5/6, CK14, P63)
- PEOR PRONÓSTICO

TERAPIA DIRIGIDA: Inhibidores PARP
No funcionan!

NO HAY DIANAS VALIDAS

FACTORES DE RIESGO EN EL CANCER DE MAMA



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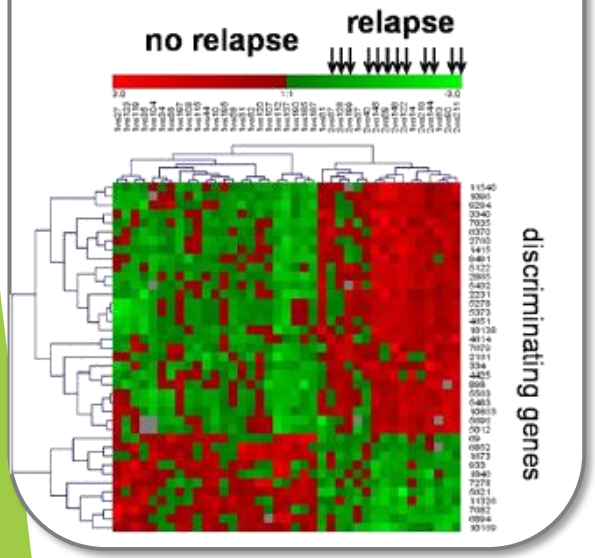
Pruebas diagnósticas en cáncer de mama

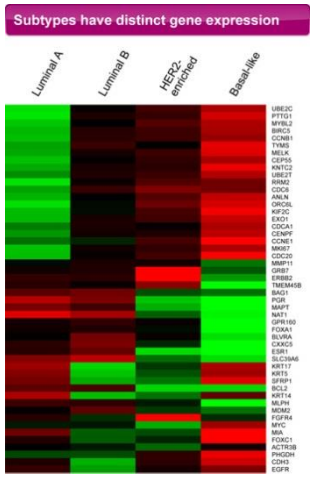
Pruebas multigénicas:
pruebas en las que se estudian muestras de tejidos para observar la actividad de varios genes a la vez.
se utiliza para estimar el **riesgo de recurrencia** de cáncer de mama con receptores de hormonas positivos en estadio temprano, así como **el beneficio de la quimioterapia** después de una cirugía de cáncer de mama

Oncotype DX:
esta prueba ayuda a predecir si el cáncer de mama en estadio I o el cáncer de mama en estadio II que tienen receptores de estrógeno positivos y ganglios linfáticos negativos se diseminarán hasta otras partes del cuerpo.

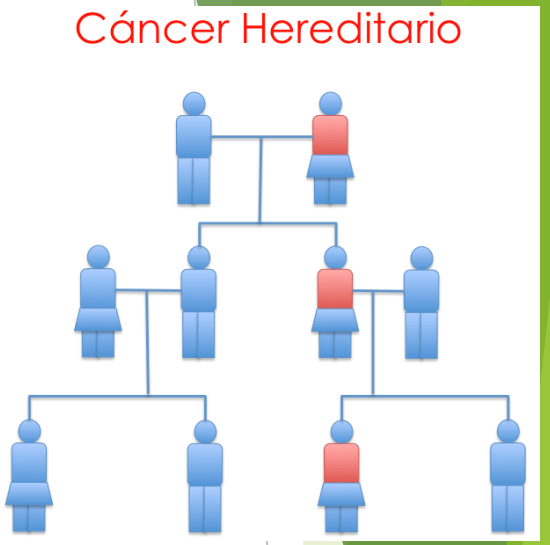


MammaPrint:
esta prueba ayuda a predecir si un cáncer de mama en estadio I o en estadio II con ganglios negativos, se diseminará hasta otras partes del cuerpo.
Si el riesgo de diseminación es alto, se puede administrar quimioterapia para reducir el riesgo.

PAM50
PREDICTOR SUBTIPOS INTRINSECOS DE CANCER MAMA:
Luminales A
Luminales B
Her2+
Basal like



CÁNCER HEREDITARIO:



- El **5-10% de los cánceres tienen un factor hereditario.**

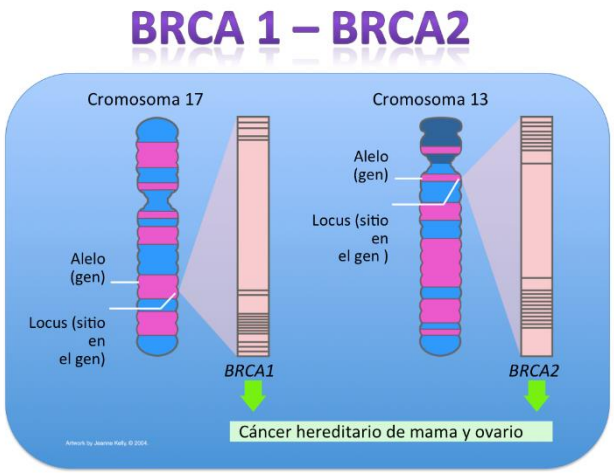
- **AGREGACIÓN FAMILIAR** (sin conocerse un gen responsable)

- HEREDITARIO : **algunos**, se conoce el gen (con la **mutación germinal**) responsable de la enfermedad, con un patrón de herencia conocido: autosómico dominante o recesivo.

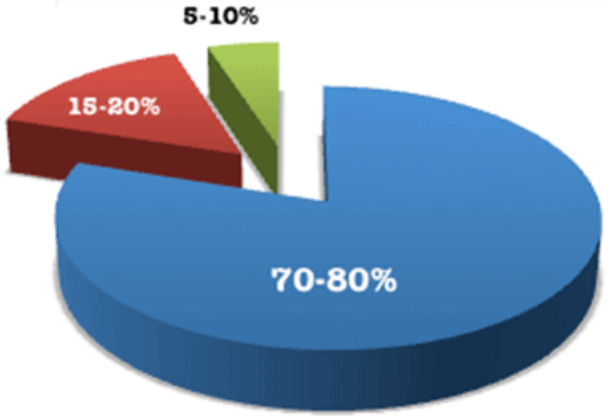
-Se han identificado alrededor de 50 genes implicados en otros tantos síndromes de predisposición hereditaria al cáncer

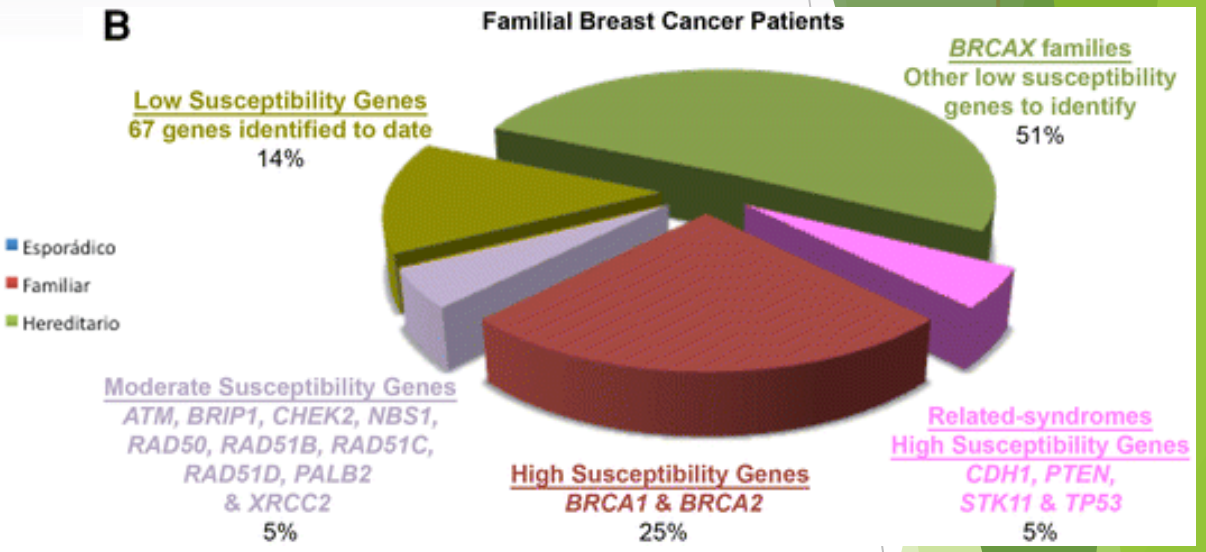
CONSEJO GENÉTICO

Cáncer de mama / ovario hereditario (CMOH)	1/500-2.500	*BRCA1/BRCA2*	17q21.113q12.3/13q

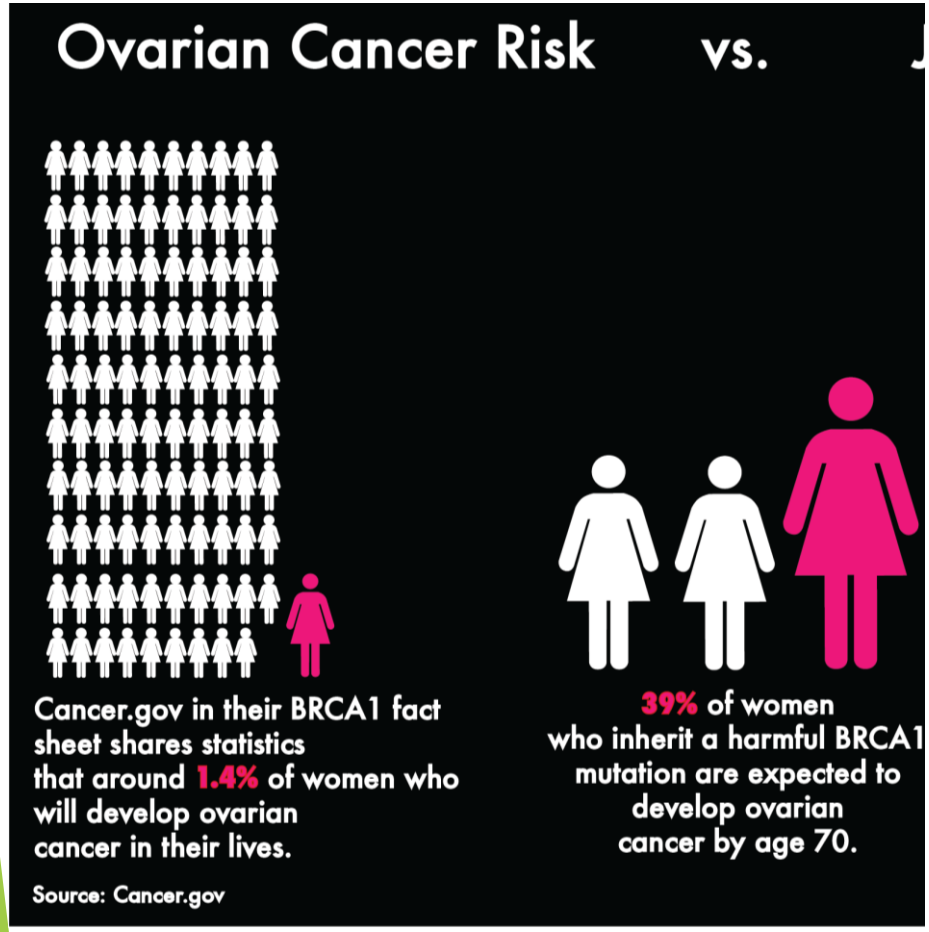


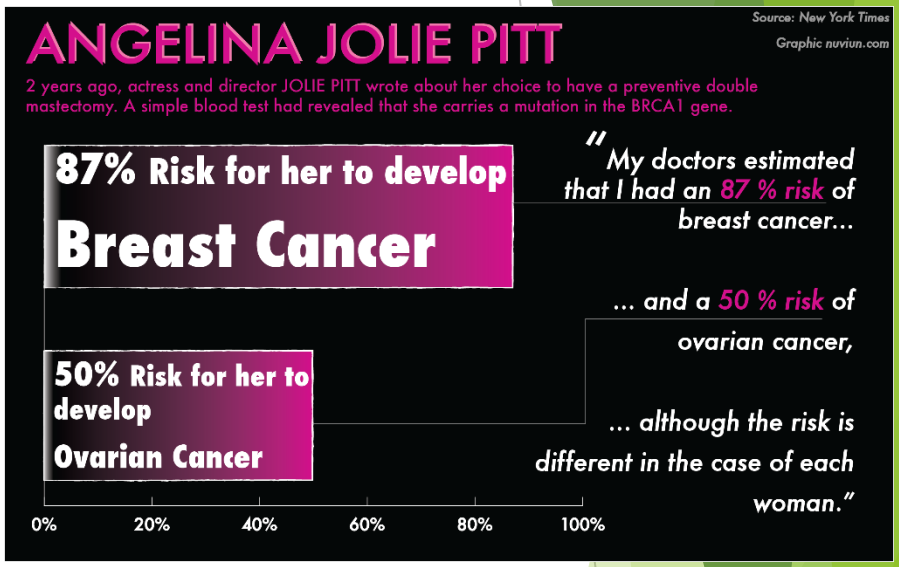
FACTORES DE RIESGO GENÉTICOS : CANCER DE MAMA





CONSEJO GENÉTICO


Ovarian Cancer Risk vs.
Cancer.gov in their BRCA1 fact sheet shares statistics that around 1.4% of women who will develop ovarian cancer in their lives.
39% of women who inherit a harmful BRCA1 mutation are expected to develop ovarian cancer by age 70.
Source: Cancer.gov

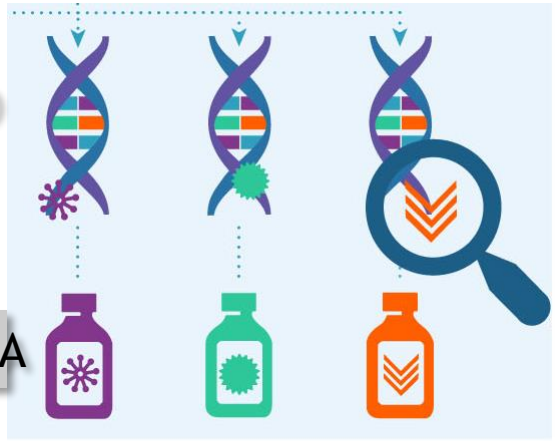

ANGELINA JOLIE PITT
Source: New York Times
Graphic nuvun.com
2 years ago, actress and director JOLIE PITT wrote about her choice to have a preventive double mastectomy. A simple blood test had revealed that she carries a mutation in the BRCA1 gene.
87% Risk for her to develop Breast Cancer
50% Risk for her to develop Ovarian Cancer
0%
20%
40%
60%
80%
100%
"My doctors estimated that I had an 87 % risk of breast cancer...
... and a 50 % risk of ovarian cancer,
... although the risk is different in the case of each woman."

- **OBJETIVO: IMPLANTAR UNA ESTRATEGIA DE MEDICINA DE PRECISIÓN BASADA EN PERFILES MOLECULARES DE LOS TUMORES**
- **TUMORES SÓLIDOS – AQUELLOS QUE NO RESPONDAN A TRATAMIENTO ESTANDAR**

PACIENTES DE CANCER SERÁN CRIBADOS MEDIANTE UNA BIOPSIA TUMORAL

BÚSQUEDA DE ALTERACIONES

DESARROLLO TECNOLÓGICO



DESARROLLO INDÚSTRIA FARMACÉUTICA

BENEFICIO AL PACIENTE/SOCIEDAD

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modificado de www.cancer.gov/nci-match

- **OBJETIVO: IMPLANTAR UNA ESTRATEGIA DE MEDICINA DE PRECISIÓN BASADA EN PERFILES MOLECULARES DE LOS TUMORES**
- **TUMORES SÓLIDOS – AQUELLOS QUE NO RESPONDAN A TRATAMIENTO ESTANDAR**

PACIENTES DE CANCER SERÁN CRIBADOS MEDIANTE UNA BIOPSIA TUMORAL

SELECCIÓN PLATAFORMA
SELECCIÓN GENES/MUTACIONES A ESTUDIA

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modificado de www.cancer.gov/nci-mat

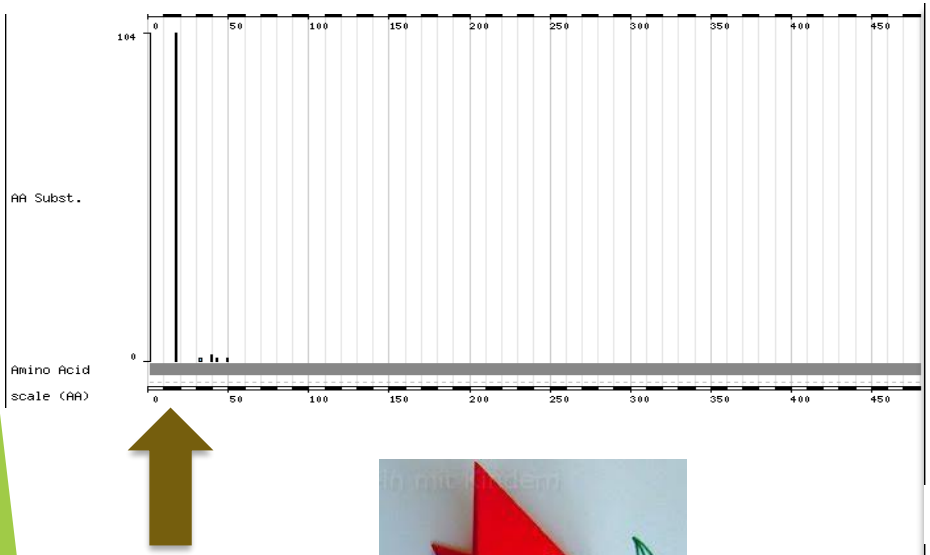
TYPE OF FUNCIONAL GENES – IMPORTANCE TO DESIGN ASSAYS

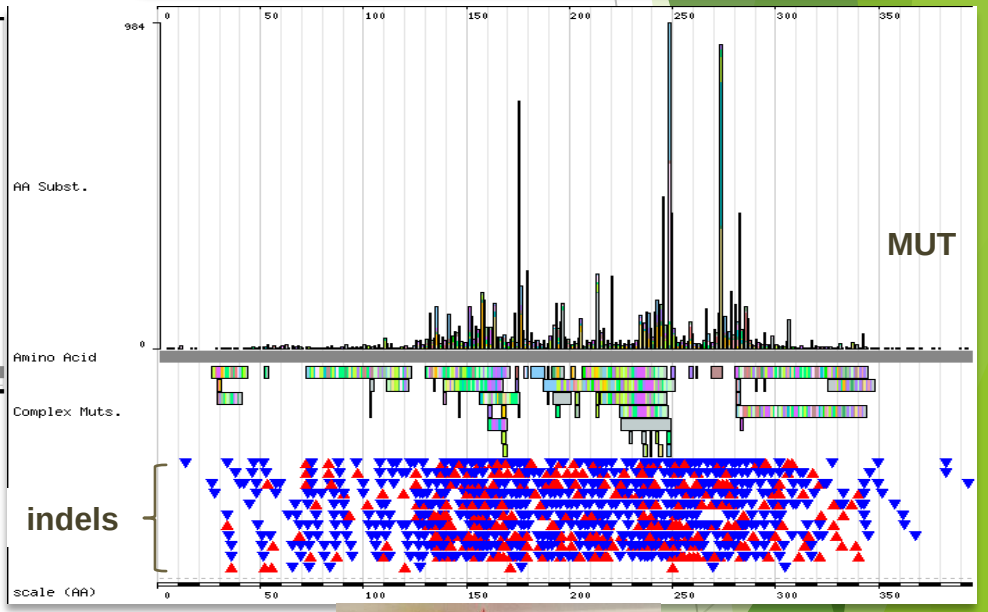
ONCOGENES: Hostspots

AKT1, BRAF, KRAS, PIK3CA, NRAS, HRAS . . .

SUPPRESORES DE TUMORES: great diversity of alterations

TP53, PTEN, P53, NF1, VHL . . .





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- **OBJETIVO: IMPLANTAR UNA ESTRATEGIA DE MEDICINA DE PRECISIÓN BASADA EN PERFILES MOLECULARES DE LOS TUMORES**
- **TUMORES SÓLIDOS – AQUELLOS QUE NO RESPONDAN A TRATAMIENTO ESTANDAR**

PACIENTES DE CANCER SERÁN CRIBADOS MEDIANTE UNA BIOPSIA TUMORAL

SELECCIÓN PLATAFORMA
SELECCIÓN GENES/MUTACIONES A ESTUDIAR

PANEL 6 GENES

PANEL 25 GENES

PANEL 14 GENES

PANEL (22-220)
- COMERCIALES
- CUSTOMIZADOS

KRAS/HRAS/NRAS

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www.cancer.gov/nci-matc

TRATAMIENTO PERSONALIZADO

NO TODAS LAS ALTERACIONES SE RELACIONAN CON UNA TERAPIA

SI SE DETECTA UNA ALTERACIÓN DIANA PARA ALGUNA TERAPIA, EL PACIENTE PUEDE SER SELECCIONADO PARA ENTRAR EN ALGÚN ENSAYO CLÍNICO

NECESIDAD DE UN COMITÉ TRASLACIONAL

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www.cancer.gov/nci-match

TRATAMIENTO PERSONALIZADO

Table 2.1 Examples of Clinically Relevant Cancer Biomarkers, 2016

Biomarker	Tumor Type	Year of CDx approval	Drug
BCR-ABL Translocation	CML	2005	Imatinib, Dasatinib, Nilotinib
KRAS Mutation	Colorectal	2006	Cetuximab
HER2 Amplification	Breast Cancer	2008	Trastuzumab
BRAF V600E Mutation	Melanoma	2011	Vemurafenib
ALK Fusion	NSCLC	2011	Crizotinib
KRAS Mutation	Colorectal	2012	Panitumumab
c-kit protein/CD 117 antigen expression	GIST	2012	Imatinib Mesylate
BRAF V600E & V600K Mutation	Melanoma	2013	Tramatenib, Dabratenic
EGFR Mutation	NSCLC	2013	Erlotinib
exon 19 deletions and exon 21 (L858R) mutation	NSCLC	2013	Afatinib
BRCA1/2 gene defect	Ovarian Cancer	2015	Olaparib
ALK Fusion	NSCLC	2015	Crizotinib

www.cancer.gov/nci-match

ROUTINE SCREENING PROGRAM AT OUR HOSPITAL

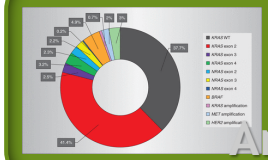
CLINICIAN requests
For somatic mutation profiling

MOLECULAR PATHOLOGY LAB
selects FFPE blocks
Evaluates tumor content and cuts slices

Min 3-4 days
(max 1 week)

CANCER FX GENOMICS LAB
Extracts DNA
Quantifies and QCs
Performs mutation detection

1 week
x patients



Results are curated

And are sent back to the clinician

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Total prescreening Program
Turnaround time 2 weeks

NGS FIRST GENERATION


BARATO


RAPIDO

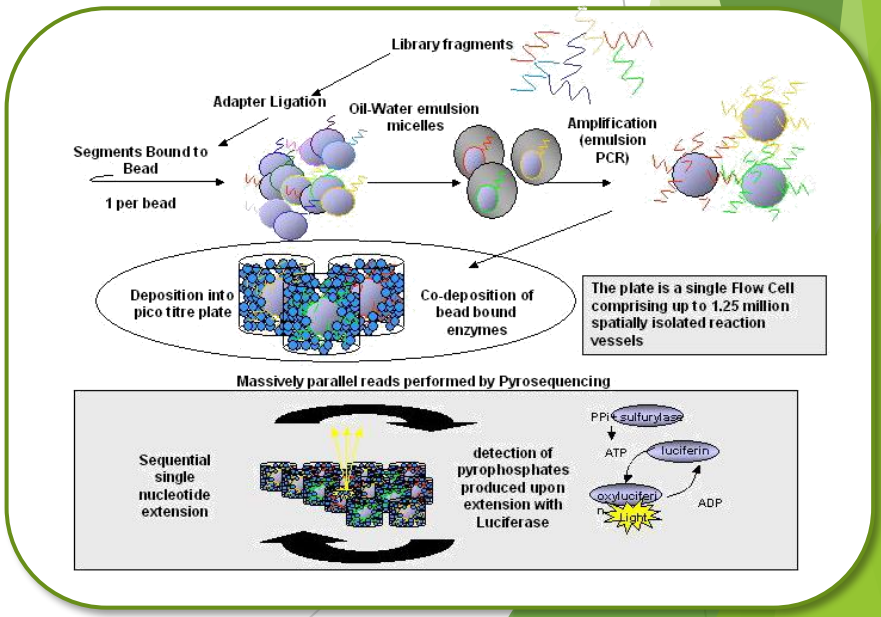

SENCILLO


HOT-SPOTS

NEXT GENERATION SEQUENCING: NGS JUNIOR (ROCHE)

GENOTING Y GENETIC DIAGNOSTIC (UCIM, UV-INCLIVA
6 GENES (AKT1, BRAF, KRAS, PIK3CA, NRAS and EGFR
15 HOTSPOTS

Nº	GENE	CHR	EXON	LONG	MUT
1	AKT1	14	E3	125	p.E17K
2	BRAF	7	E15	119	p.V600F
3	KRAS	12	E2	122	p.G12+/p.G13+
4	KRAS	13	E3	179	p.Q61+
5	PIK3CA	3	E2*	428	p.E110K
6	PIK3CA	3	E10*	125	p.e542+/p.E545+
7	PIK3CA	3	E21*	6000	p.T1025+/p.H1047+
8	NRAS	1	E2	128	p.G12+/p.G13+
9	EGFR	7	E19	99	p.E747del
10	EGFR	7	E20	186	p.T790M
11	EGFR	7	E21	156	p.L858R



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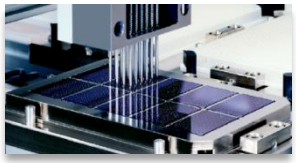
MASSARRAY – AGENA:


BARATO


RAPIDO


SENCILLO


HOT-SPOTS

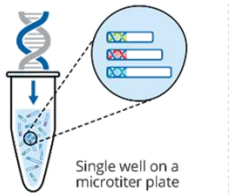


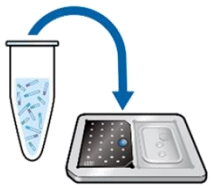
OncoCarta Panelv1:
19 Oncogenes/238 hostspots

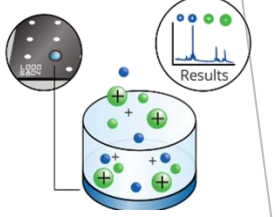
Gene	No. Mutations	Gene	No. Mutations
ABL1	14	JAK2	1
AKT1	7	KIT	27
AKT2	2	MET	5
BRAF	24	HRAS	6
CDK	2	KRAS	12
EGFR	43	NRAS	8
ERBB2	7	PDGFR	11
FGFR1	2	PIK3CA	13
FGFR3	5	RET	6
FLT3	2		

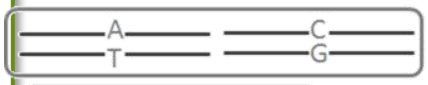
Clia-Vall D'Hebron Panel:
5 additional oncogenes, 8 genes

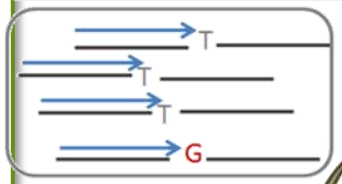
Incliva Panel:
ERBB2,ERBB3,ERBB4

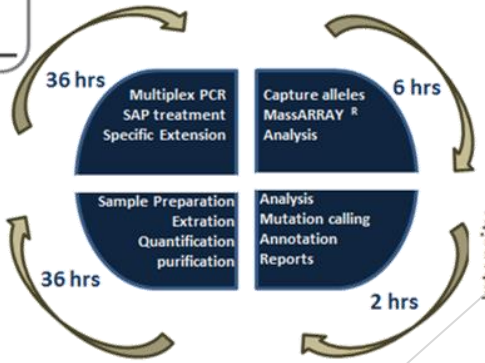


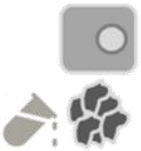


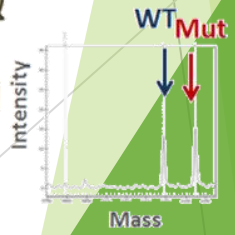












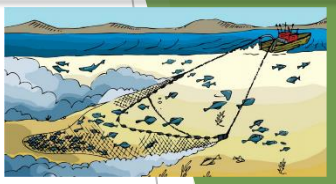
Multiplex up to 40 SNPs/reaction, 150,000 genotypes/day courtesy of Dr Charles Cantor, Sequenom **iPlex Gold from Sequenom**

GENOMIC PLATFORMS TO SCREEN A PANEL OF CANDIDATE GENES

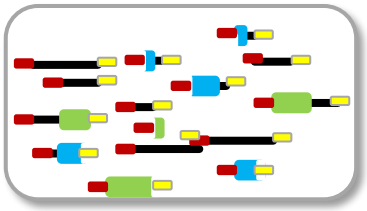

CARO


DIFICULTAD

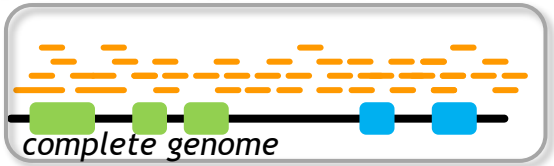

DIFICULTAD

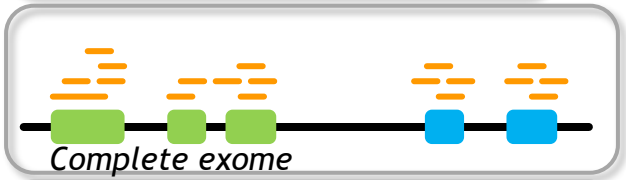

TODO

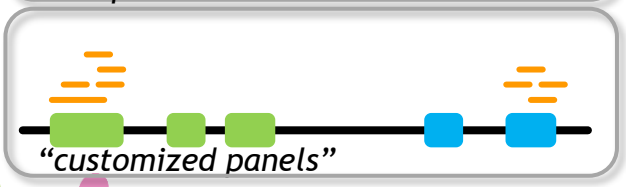

NGS

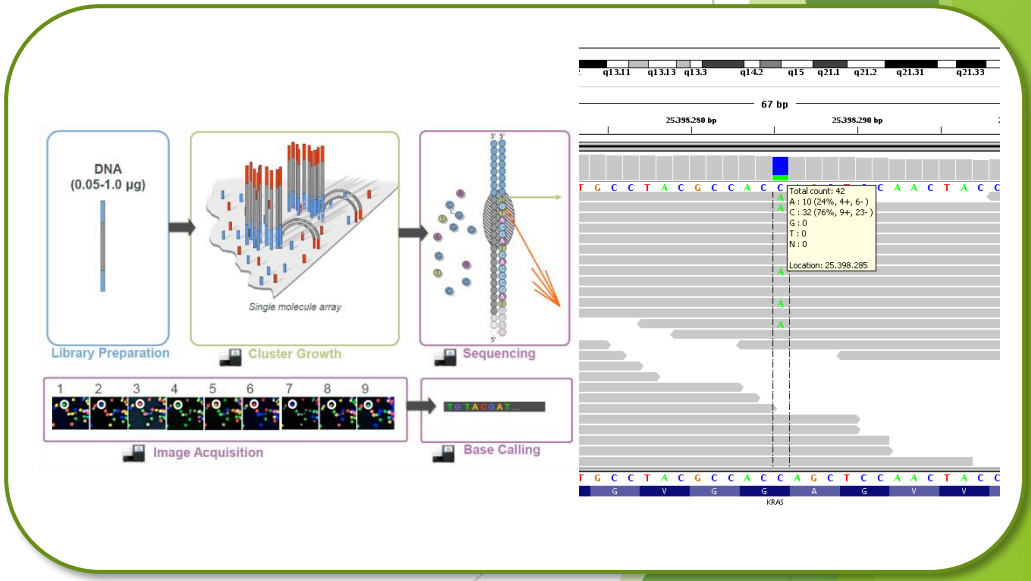


AMPLIFICACIÓN LIBRERIAS:
TrueSight –Illumina
Qiaseq Targeted panels – Qiagen









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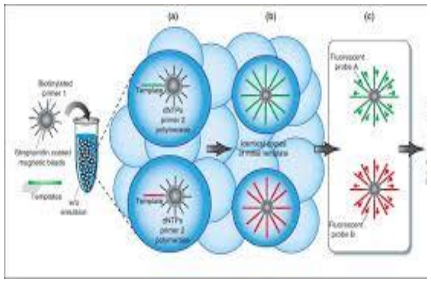
GENOMIC PLATFORMS to SCREEN IN LIQUID BIOPSY: Digital PCR/ NGS


VARIABLE

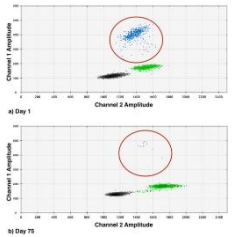

CIERTA DIFICULTAD

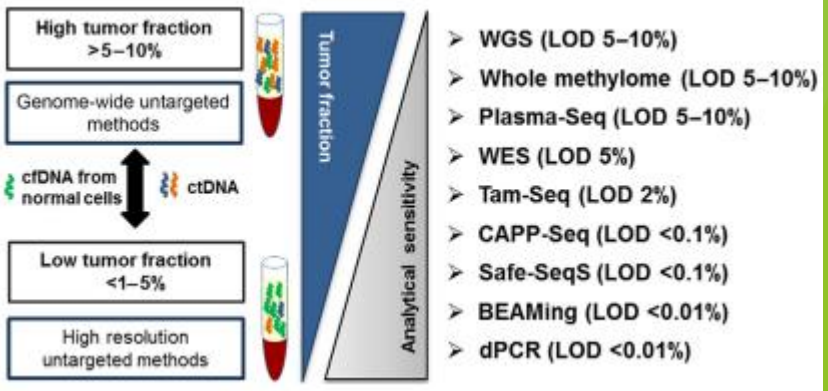

SENCILLO/DIFICIL


ÚNICO/VARIOS

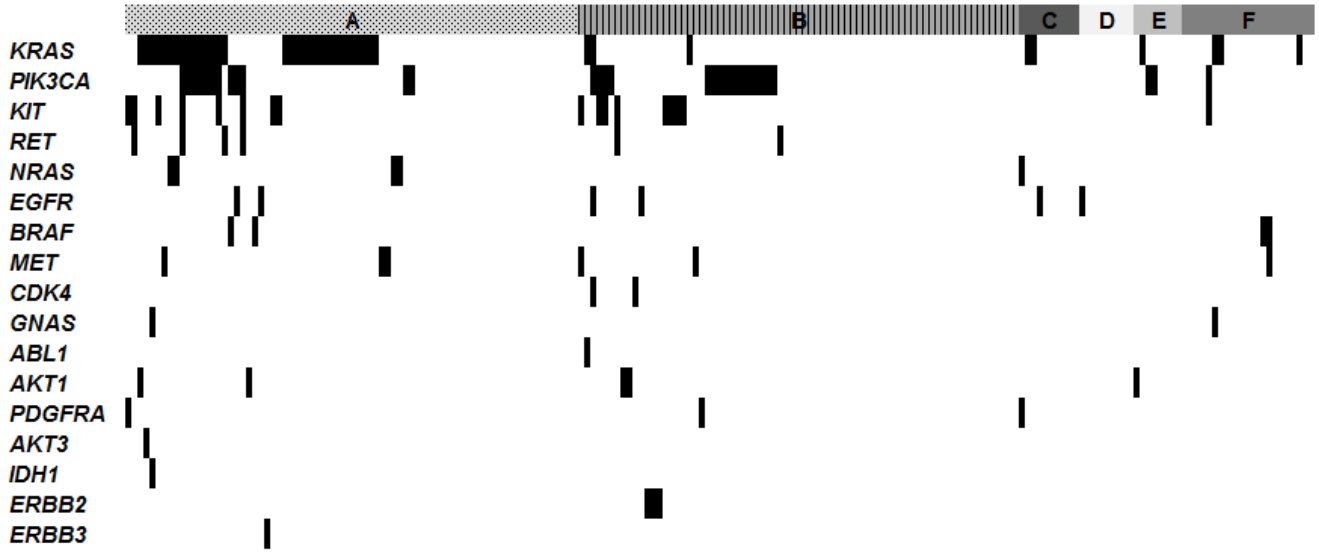


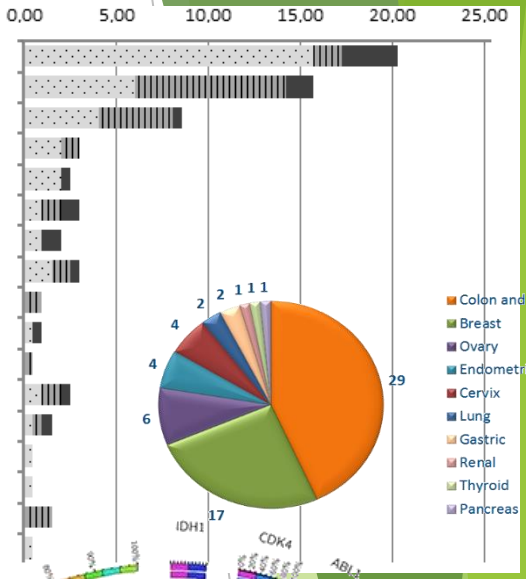
"customized panels"

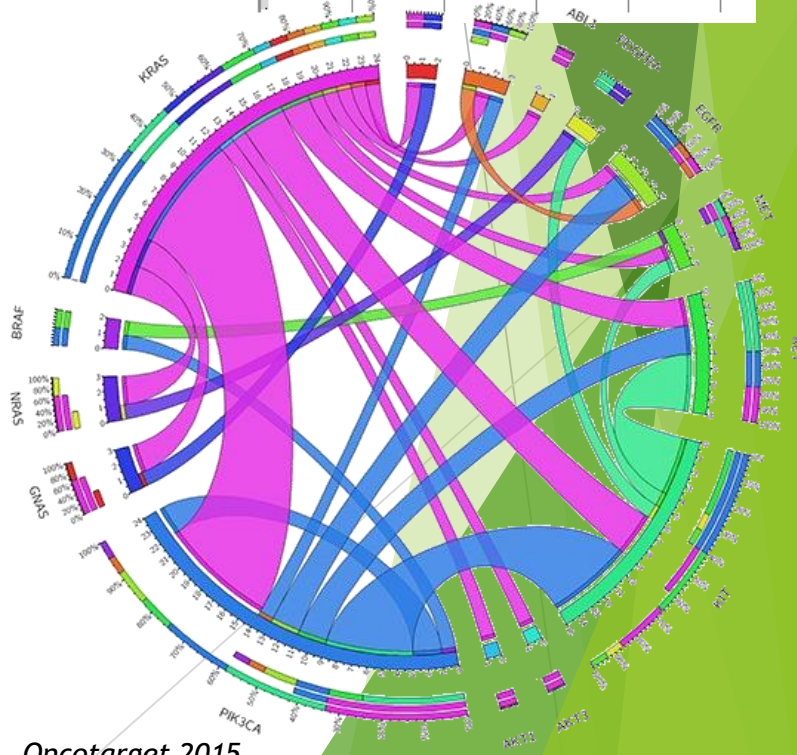




MUTATIONS FOUND ACROSS TUMOR SAMPLES







197 samples analysed (49% HAD 1 MUTATION IN 16 DIFFERENT GENES 38% CRC, 37% Breast)

-Mutations in **KRAS** and **PIK3CA** were detected in 40/97 (**41.2%**) and 30/97 (**30.9%**) patients respectively.

-Thirty-one patients (32.0%) had mutations in two genes,

-20 of them (64.5%) initially diagnosed with colorectal cancer

- co-occurrence of mutation involved mainly KRAS, PIK3CA,
- KIT and RET

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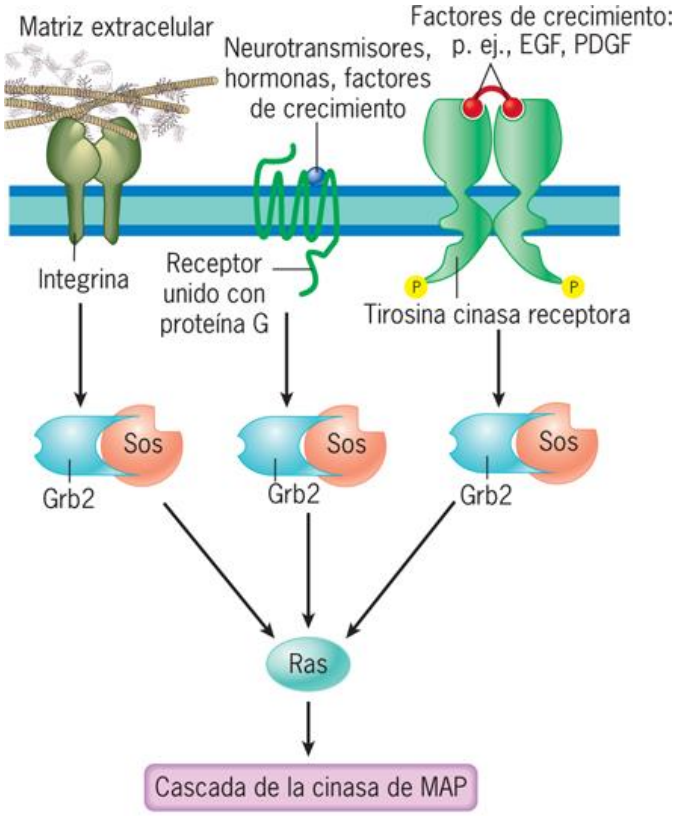
Ibarrola-Villava et al., Oncotarget 2015



Fuente: Gerald Karp: *Biología celular y molecular. Conceptos y experimentos*, 7e: www.accessmedicina.com
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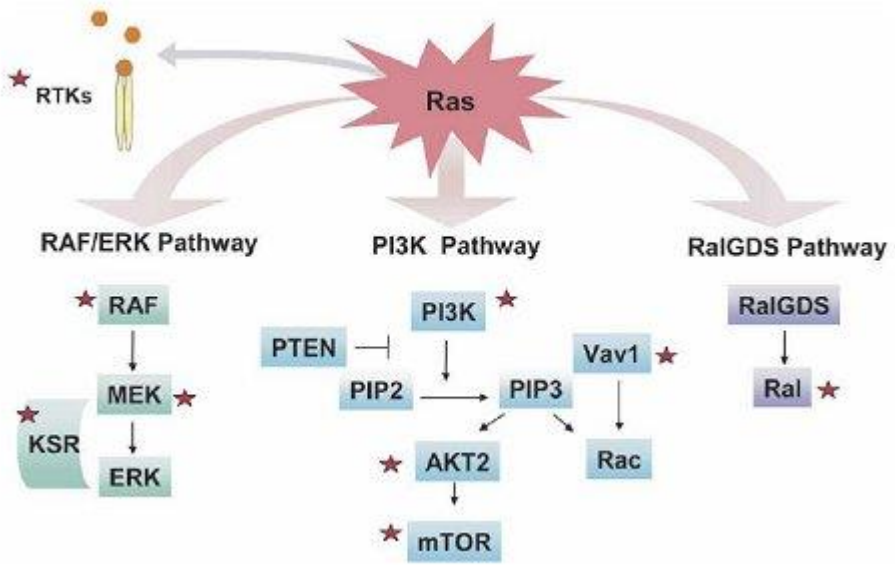


OPTIONS OF TARGETED THERAPIES

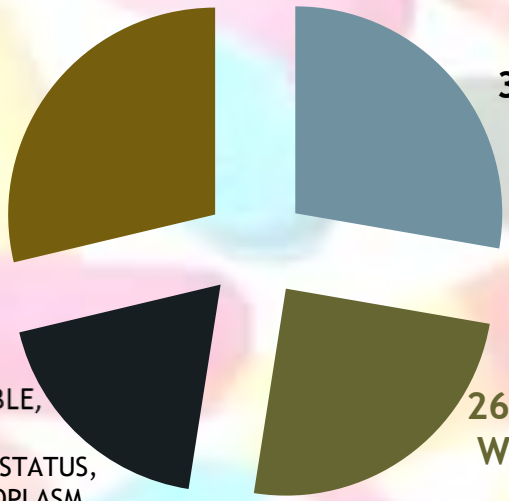
101 PATIENTS WERE CANDIDATES TO BENEFIT FROM TARGETED THERAPIES

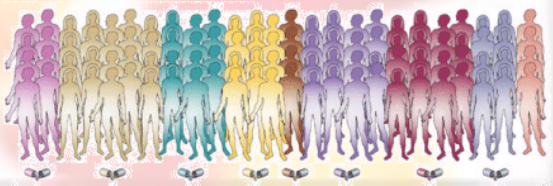
75 had actionable mutations

26 were KRASwt and could have possible be treated with anti-EGFR agents

5 anti-EGFR
15 OTHER THERAPIES
8 were selected for clinical trials
5 got PI3K/AKT inhibitors
1 anti-IGF1,
2 anti ERBB3

28% ACTUALLY BENEFITED FROM TARGETED THERAPIES





Ibarrola-Villava et al., Oncotarget 2015

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MEMBERSHIPS

AACR American Association for Cancer Research

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

EATRIS European Infrastructure for Translational Medicine

WIN Worldwide innovative networking in personalized cancer medicine

ciberonc Centro de Investigación Biomédica en Red Cáncer

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FUNDING

MOTRICOLOR

Horizon 2020 European Union funding for Research & Innovation

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Proyectos PROMETEO Generalitat Valenciana

aecc Contra el Cáncer