



NÚCLEO DE QUITO

Programa de Certificación Oncológica para Médicos Residentes

Biología y Genética del Cáncer



Paola E. Leone, PhD, Acad



Coordinadora, Laboratorio de Genética – SOLCA Núcleo de Quito



Presidente, Sociedad Ecuatoriana de Biología



Ex Presidente, Sociedad Ecuatoriana de Genética Humana



Ex Presidente, Academia de Ciencias del Ecuador



Coordinadora General y de Nodo de Redes Iberoamericanas de Mieloma y Linfomas



90 artículos Scopus, 50 artículos Latindex, 11 libros, 19 capítulos libros (Ecuador, España)

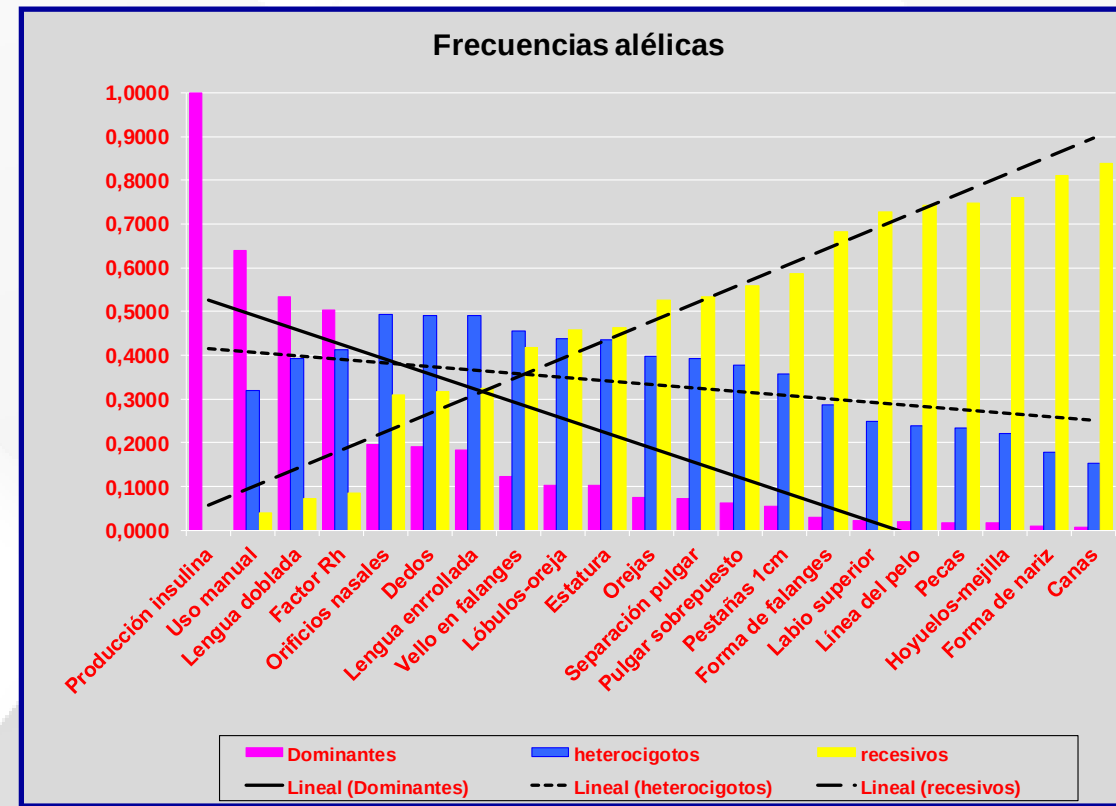
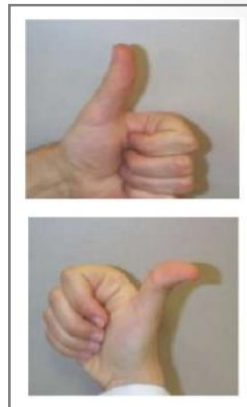
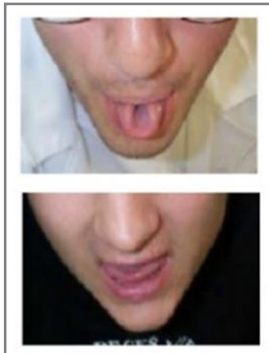
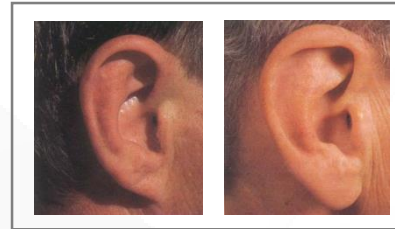


No hay conflictos de interés por declarar



Características físicas de la población ecuatoriana

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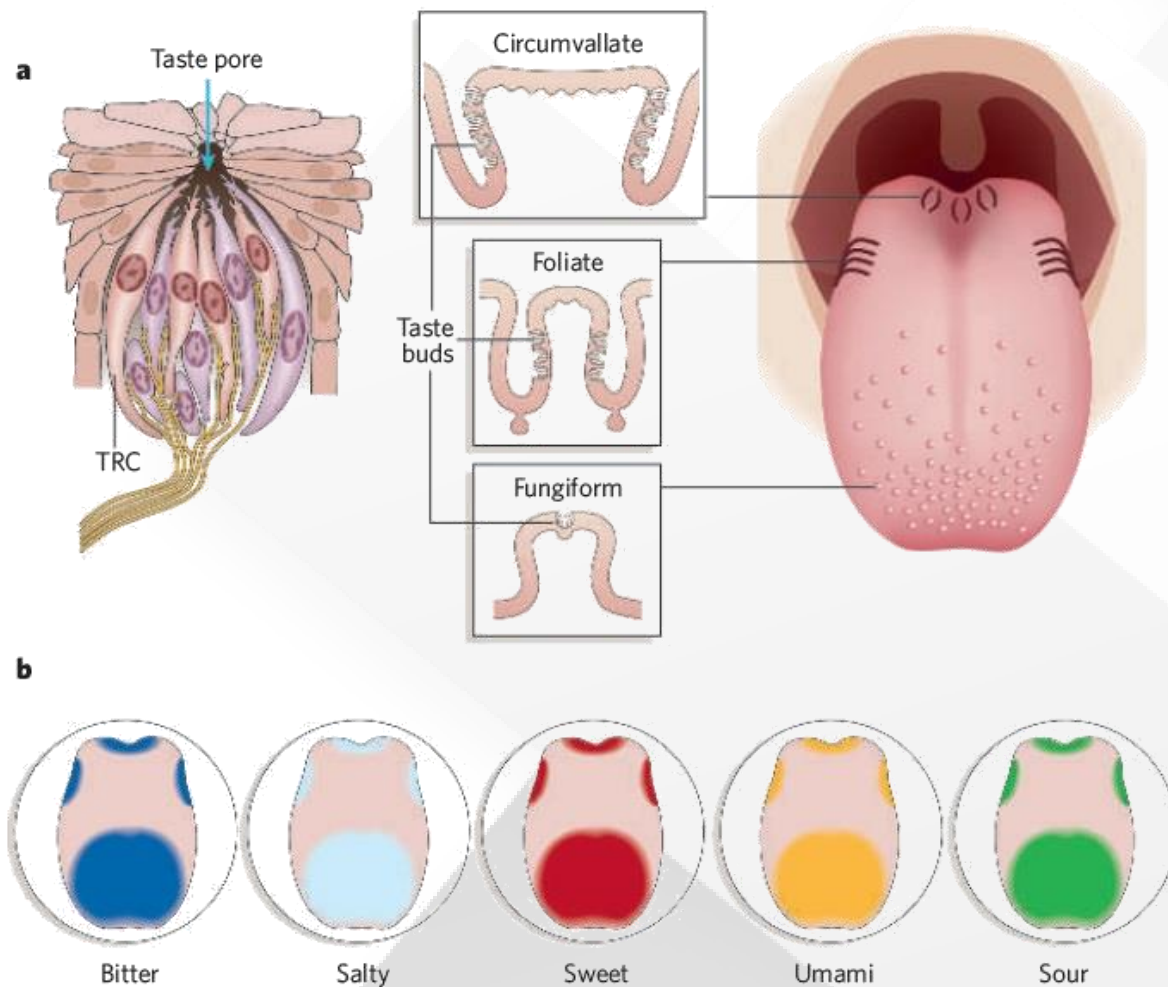
Rev. Facultad de Ciencias Médicas, UCE. 2000; 25(2):23-26

EDUCA - <https://www.facebook.com/EducaTele/videos/1383376915184229/>



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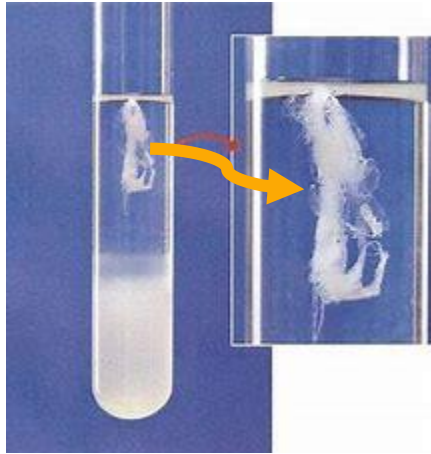
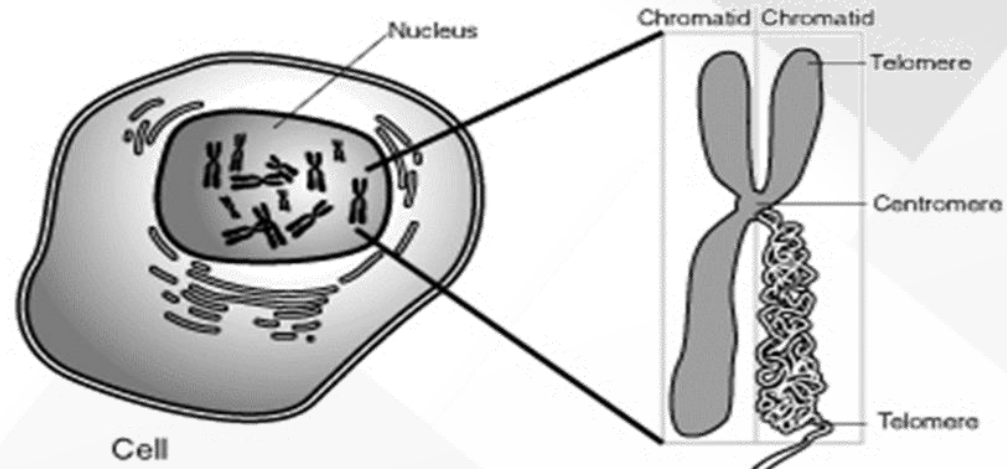
Tipos de sabores



*Genes determinantes de la percepción de los sabores ecuatorianos
En: El sabor de mi Ecuador, 22-24 (2013)*



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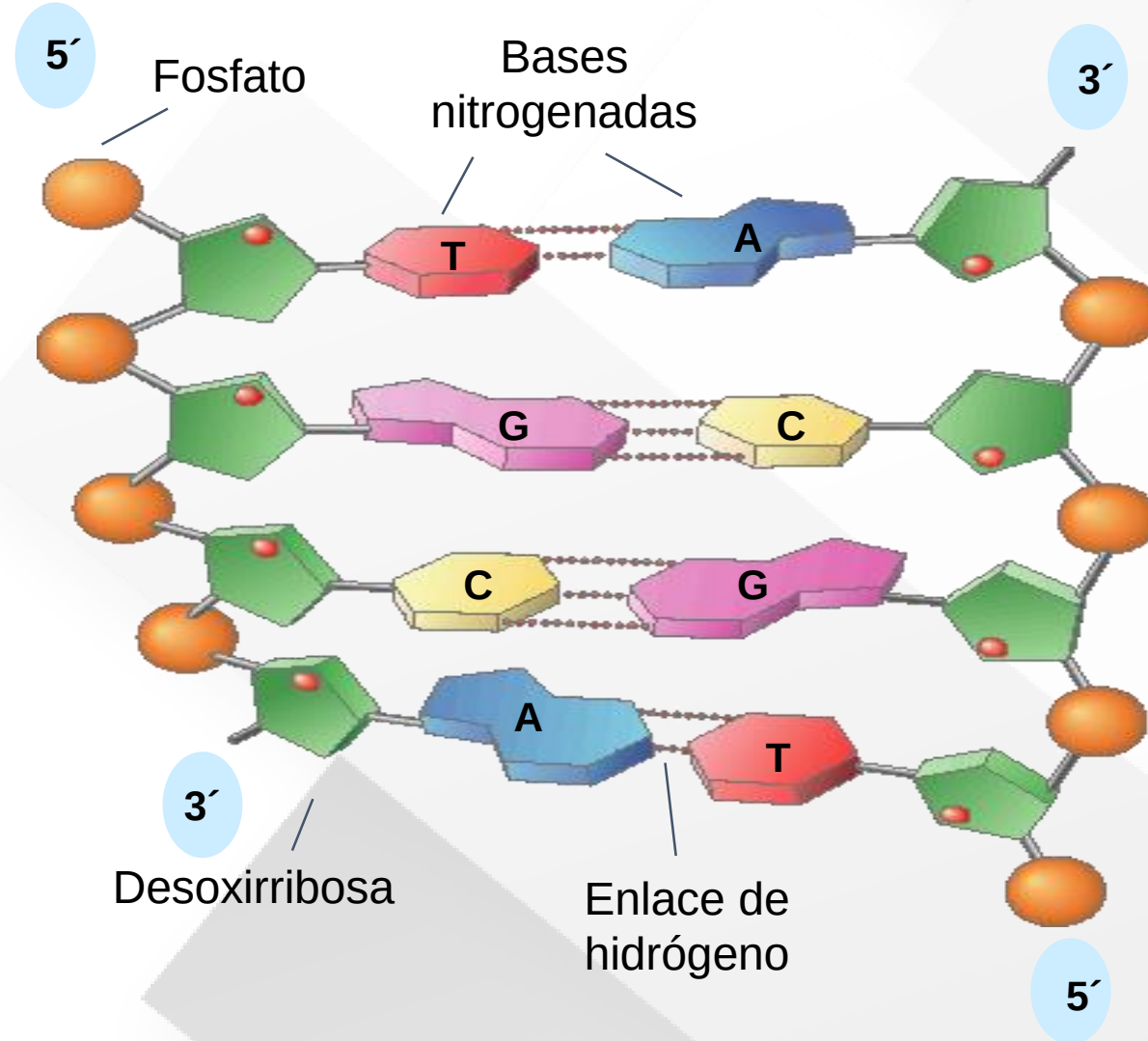
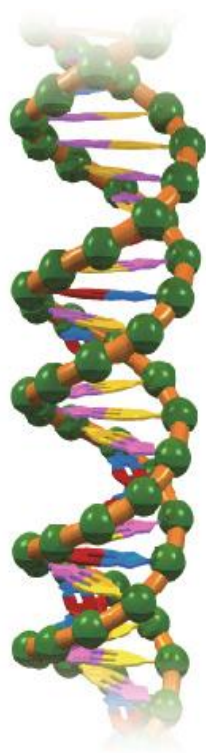




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Estructura del ADN

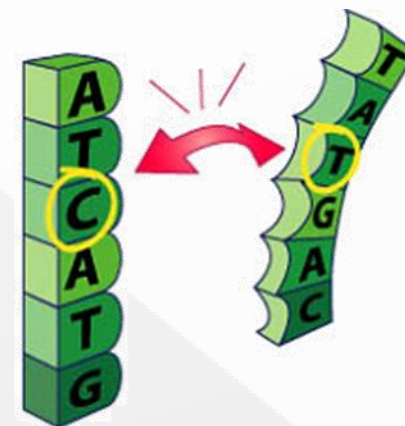
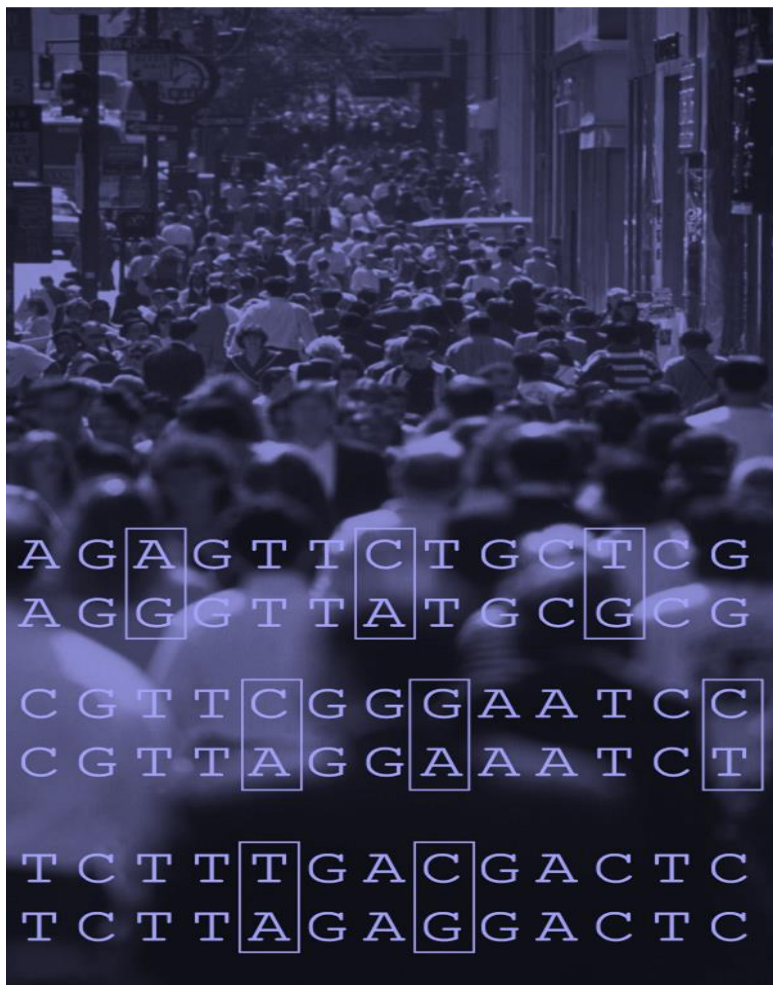
Doble
hélice de
ADN





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Variabilidad genética





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Gen *XRCC1*: mutación nueva

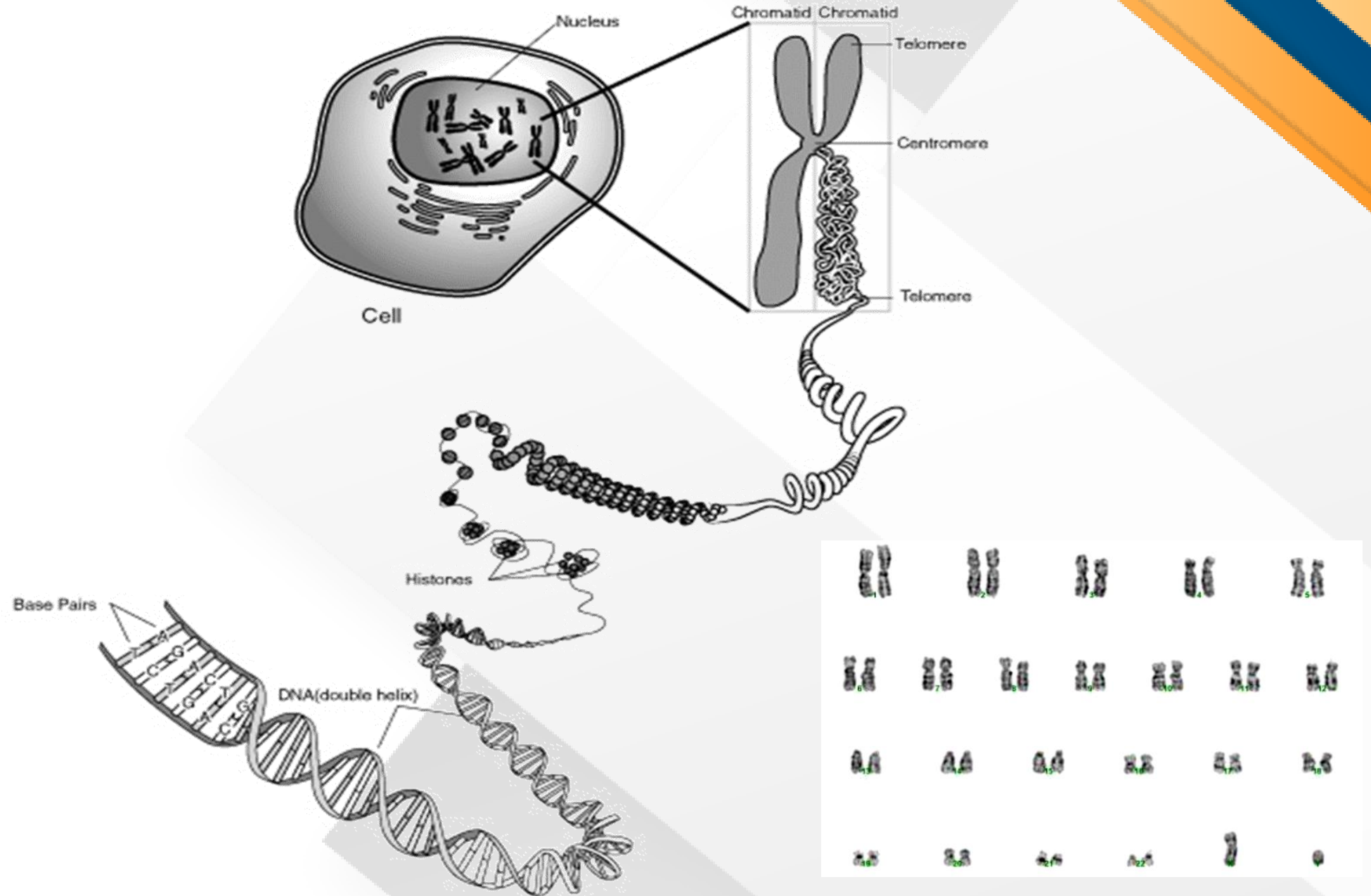
43.551.656



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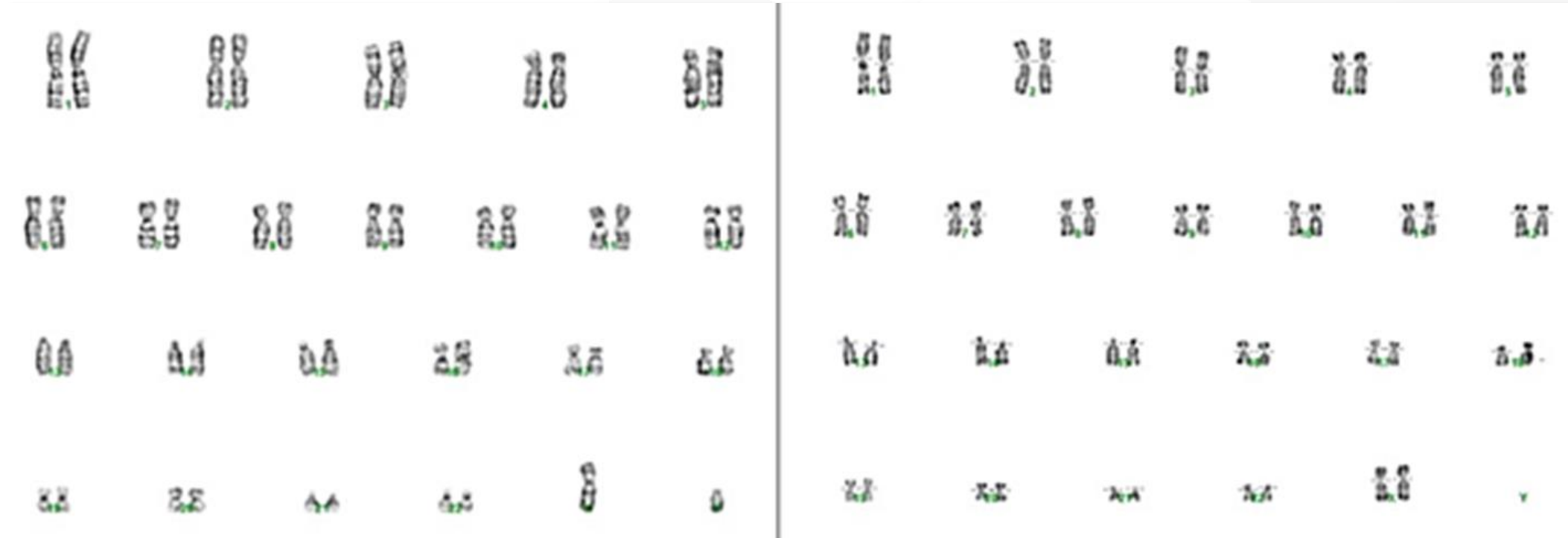
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Cromosomas humanos



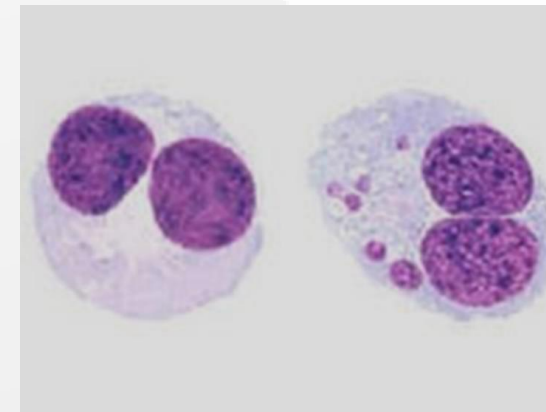
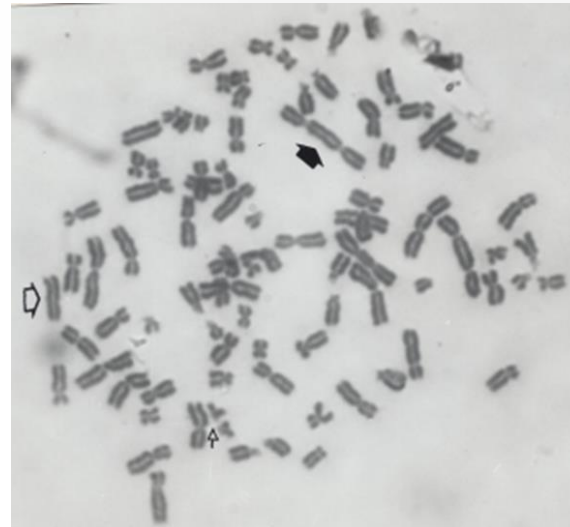
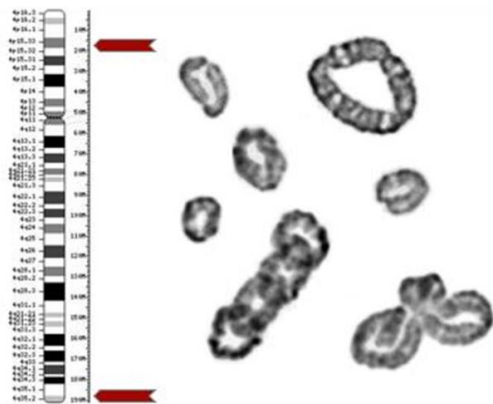
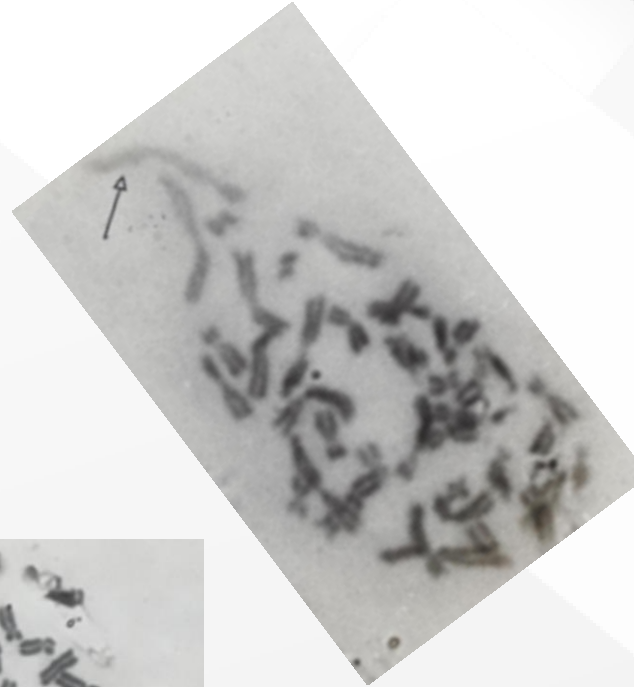
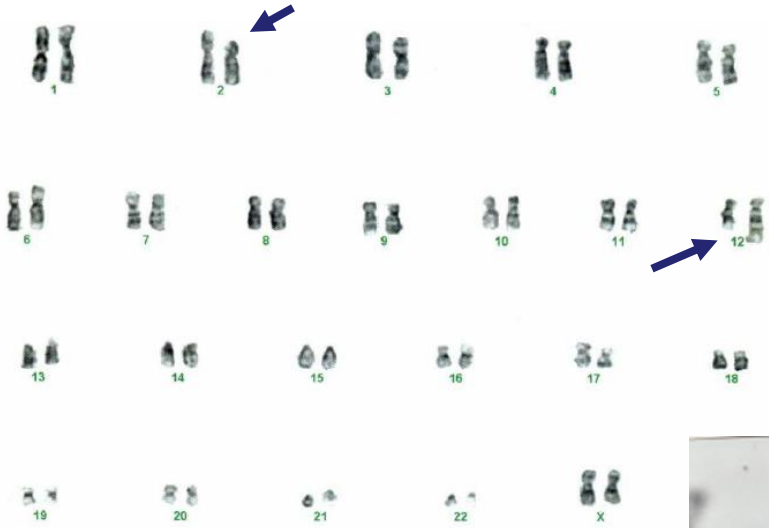
46,XY

46,XX



NÚCLEO DE QUITO

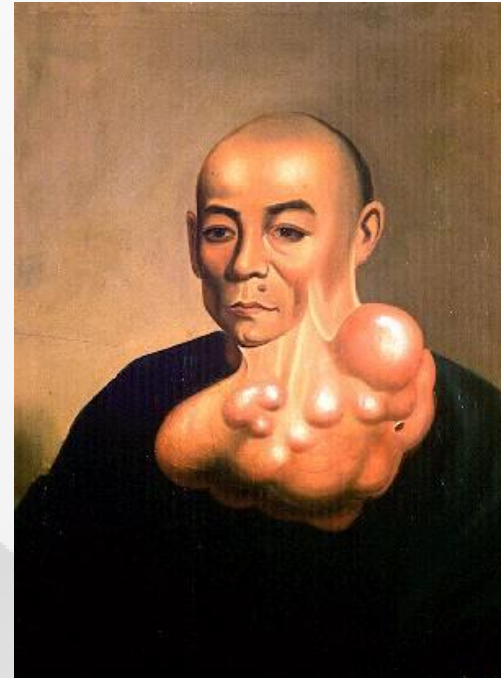
Alteraciones cromosómicas





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Cáncer en la pintura



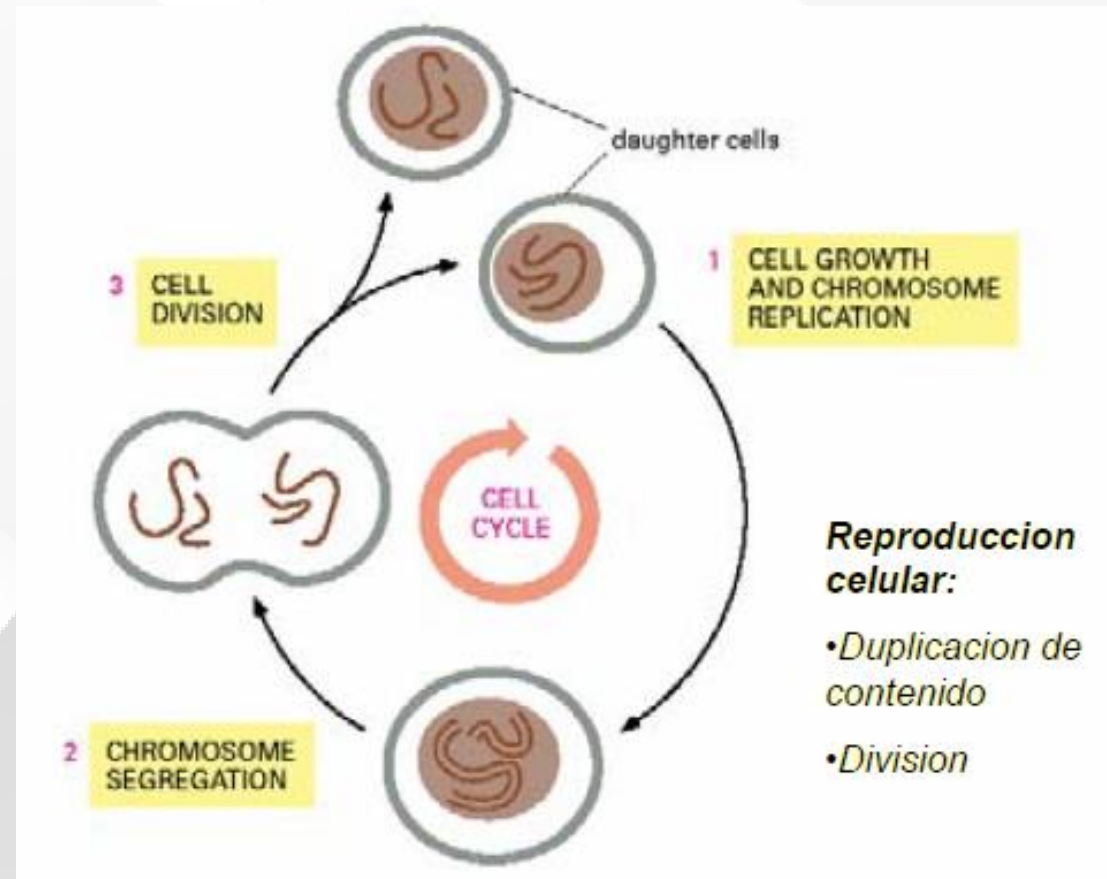
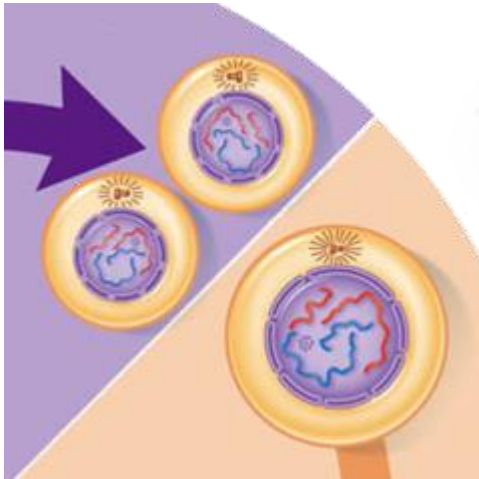
Lam Qua, 1801-1860



NÚCLEO DE QUITO

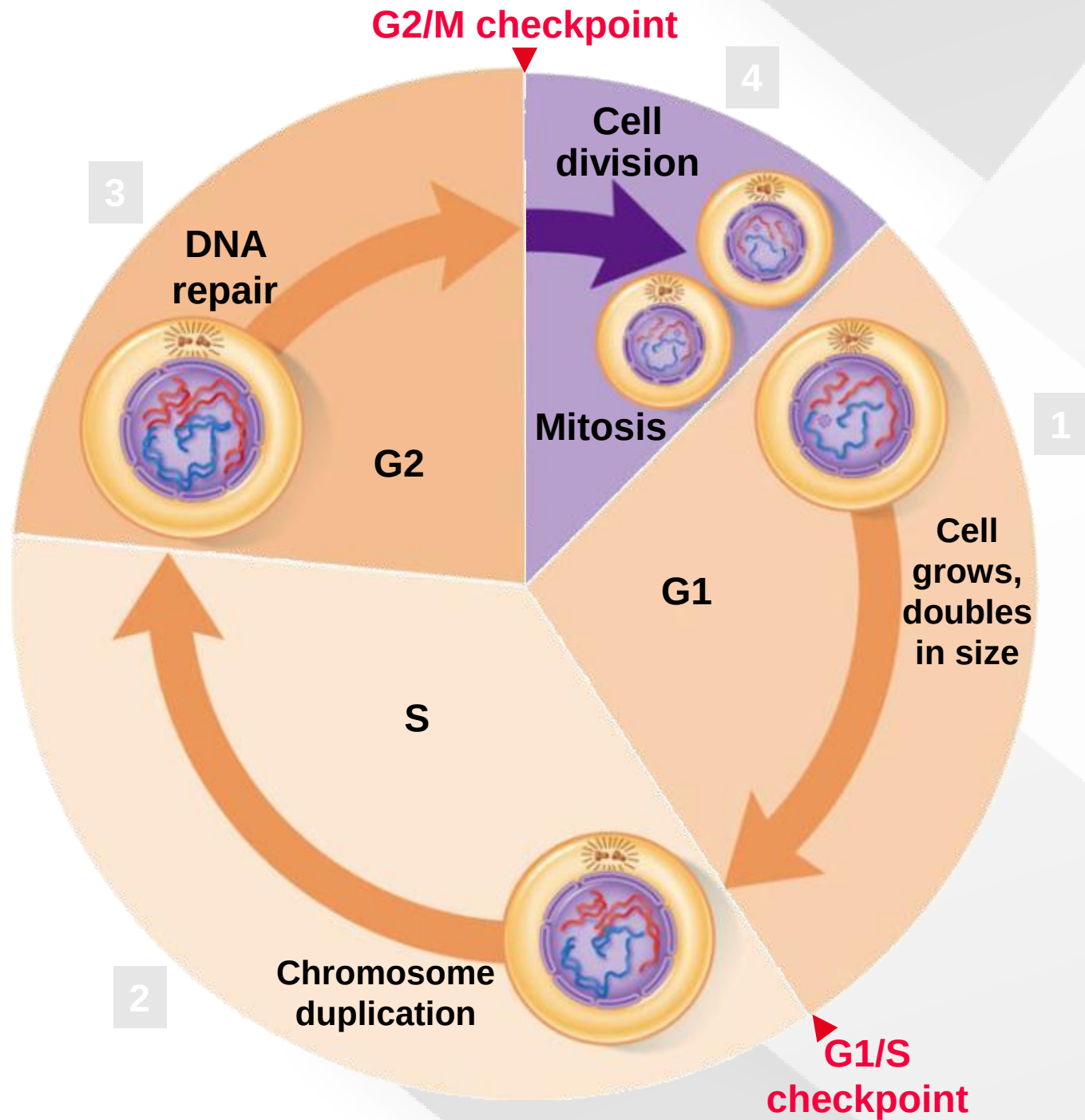
Ciclo celular

Conjunto ordenado de sucesos que conducen al crecimiento de la célula y la división en dos células hijas.





NÚCLEO DE QUITO

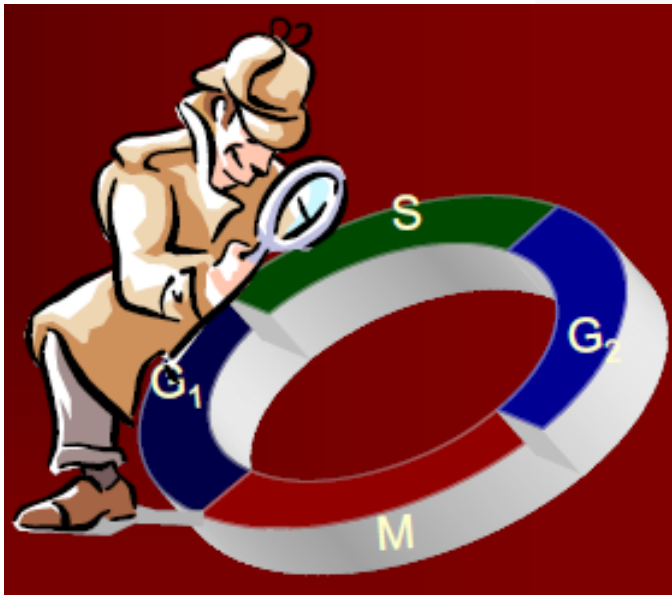




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Checkpoint: Puntos de control

Son mecanismos moleculares que verifican que se cumplen las condiciones necesarias para permitir el paso de una fase del ciclo celular a otra.



Vista al este

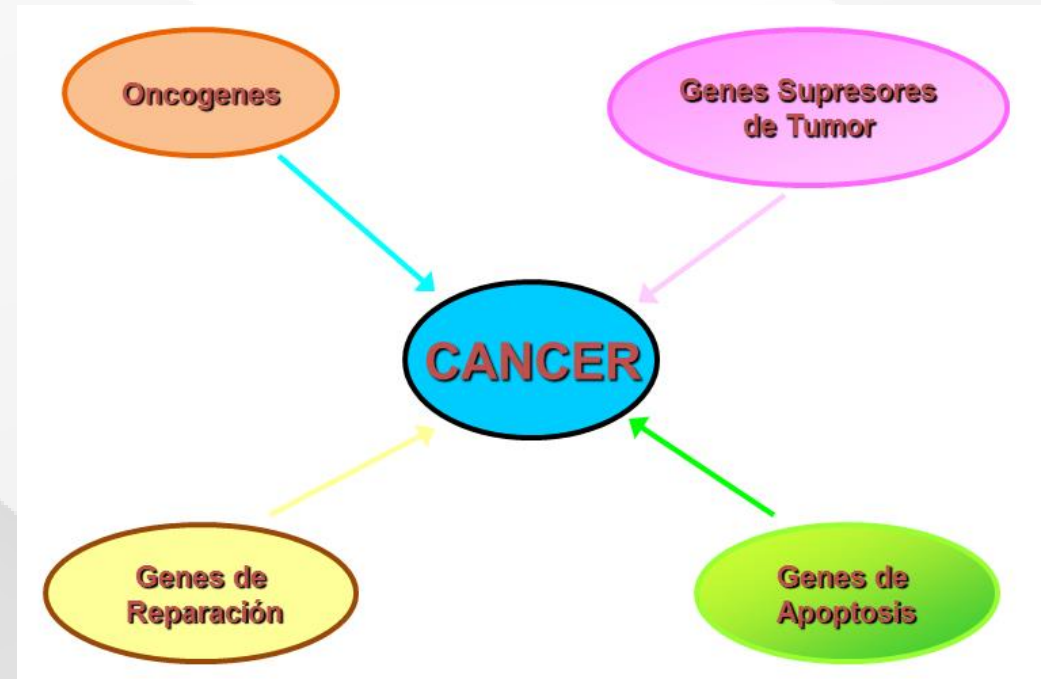


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Componentes reguladores

Genes asociados a cáncer controlan estos checkpoints:

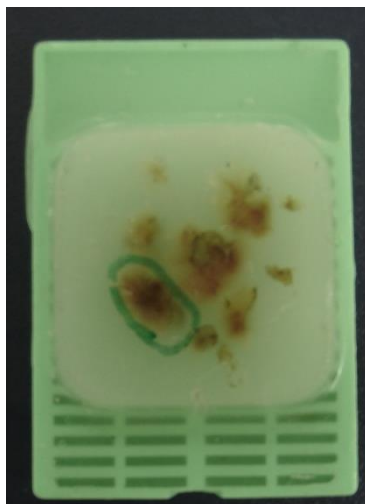
- Genes supresores de tumor reducen la tasa de división celular
- Proto-oncogenes aumentan la división celular
- Genes reparación
- Genes de apoptosis





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Muestras de estudio



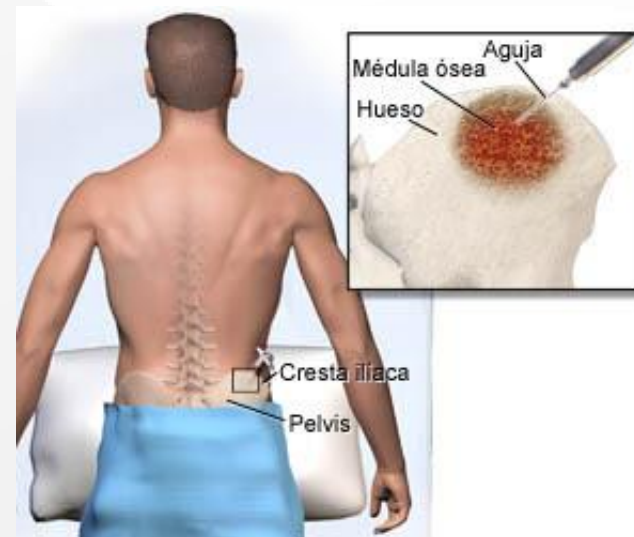
Tumor
fresco o
parafina



Raspado
bucal, saliva
o pelo



Sangre periférica



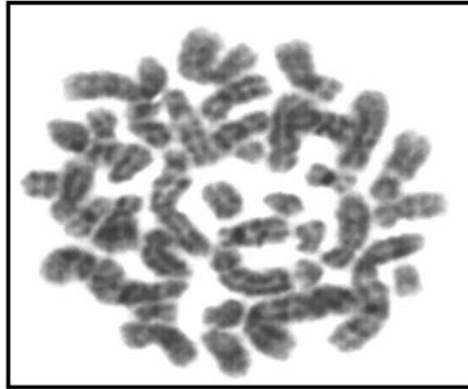
Médula ósea



NÚCLEO DE QUITO

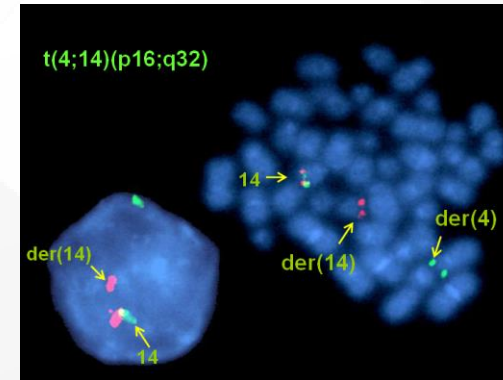
Detección de alteraciones cromosómicas

Citogenética convencional



Resolución **20 Mb**

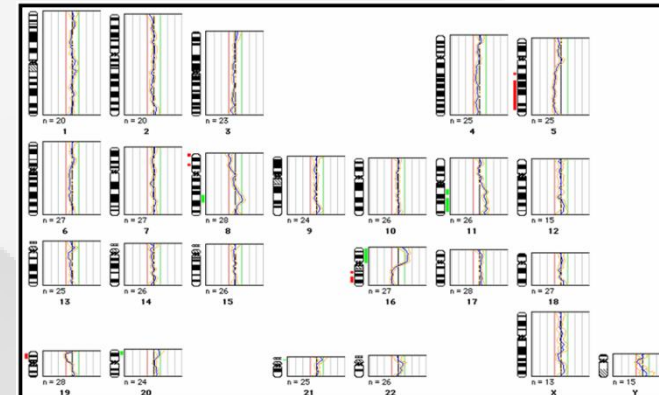
Hibridación *in situ* fluorescente (FISH)



Cariotipo espectral (SKY)



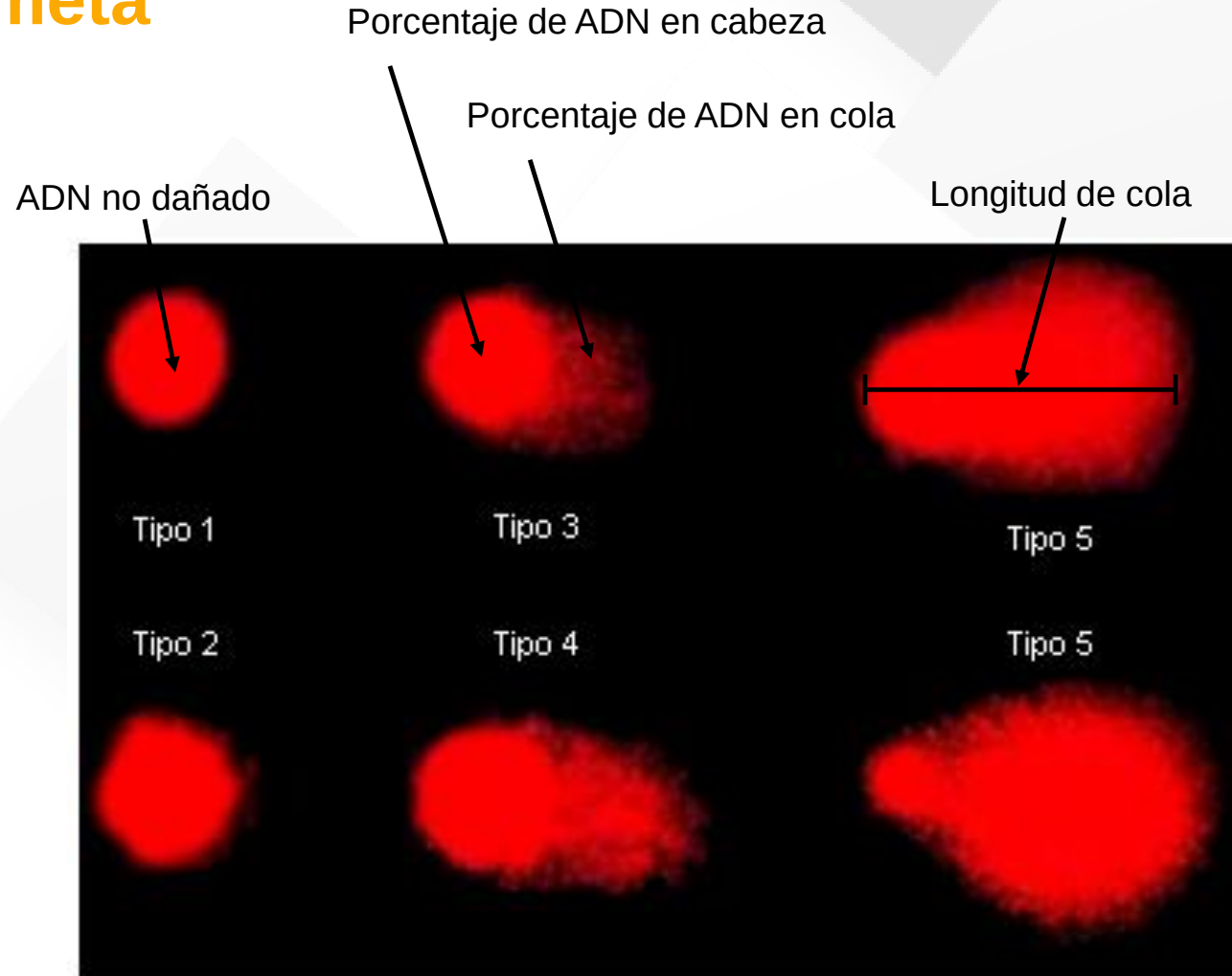
Hibridación genómica comparada (CGH)





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Ensayo Cometa



Momento de cola = longitud de cola / porcentaje de ADN en cola



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Chip/array en la vida diaria



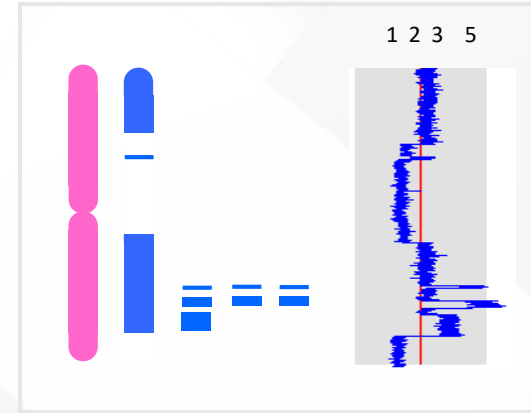
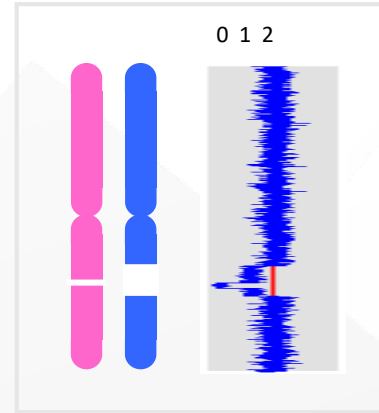


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Cambios en el número de copias cromosómicas



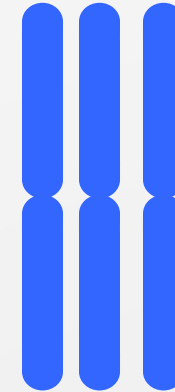
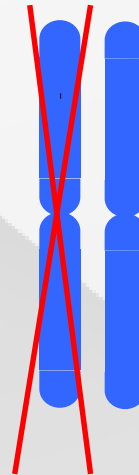
500K SNP GeneChip
Mapping arrays



Resolución **Submegabase**



tumour
suppressor
genes

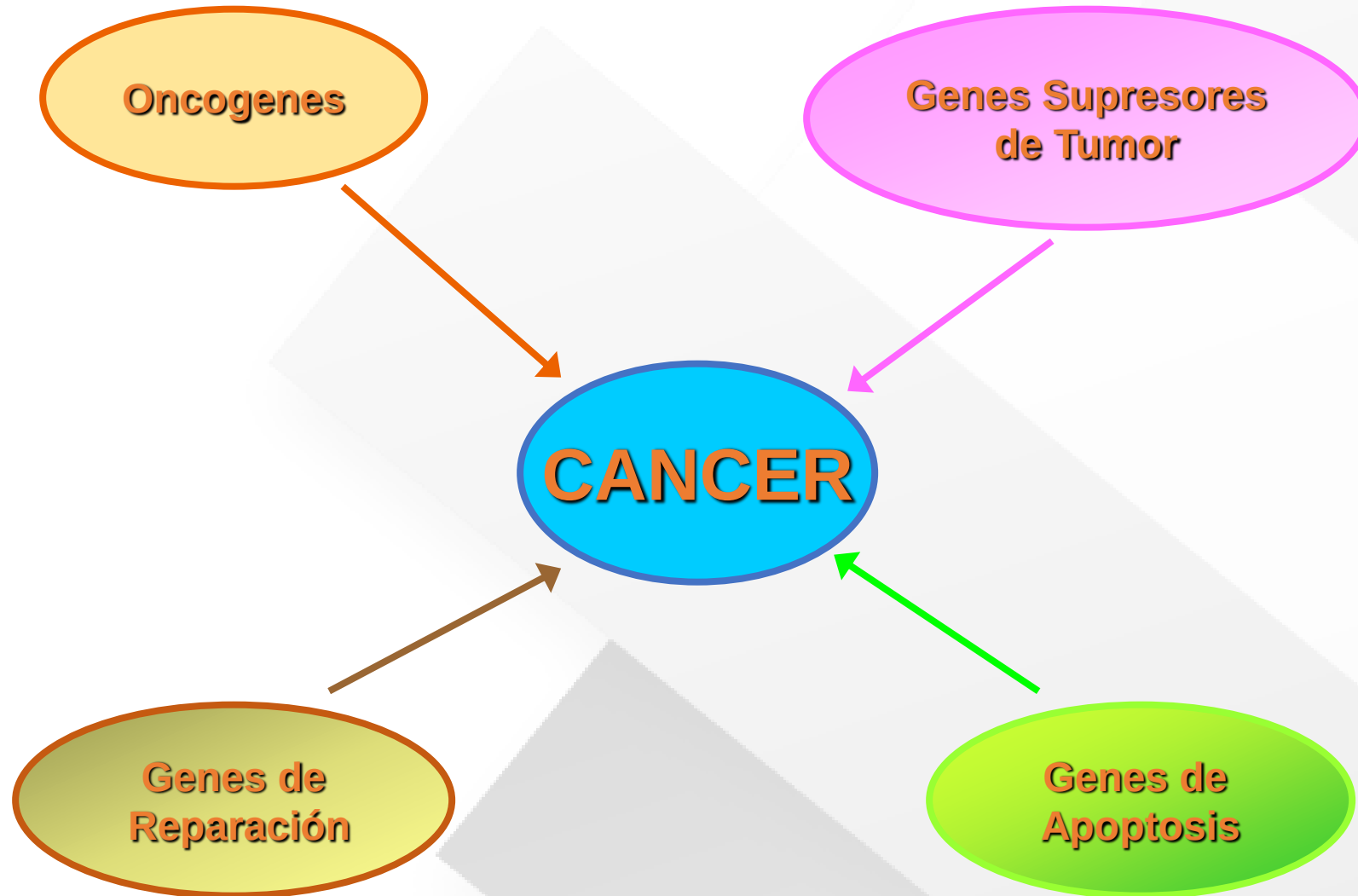


oncogenes



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Genes de cáncer: Oncogenes

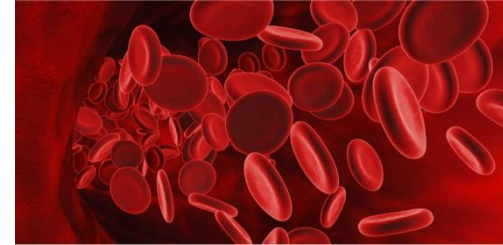




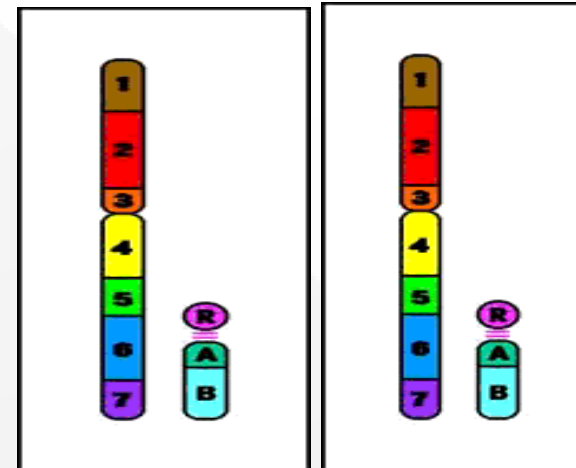
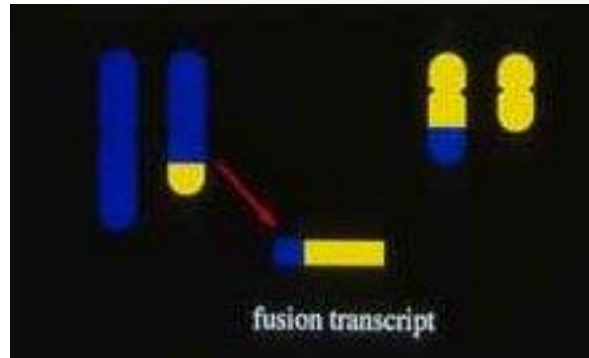
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Oncogenes en cáncer

Oncogenes



Rearreglos cromosómicos y moleculares:



Translocaciones cromosómicas & mutaciones:

Protooncogen



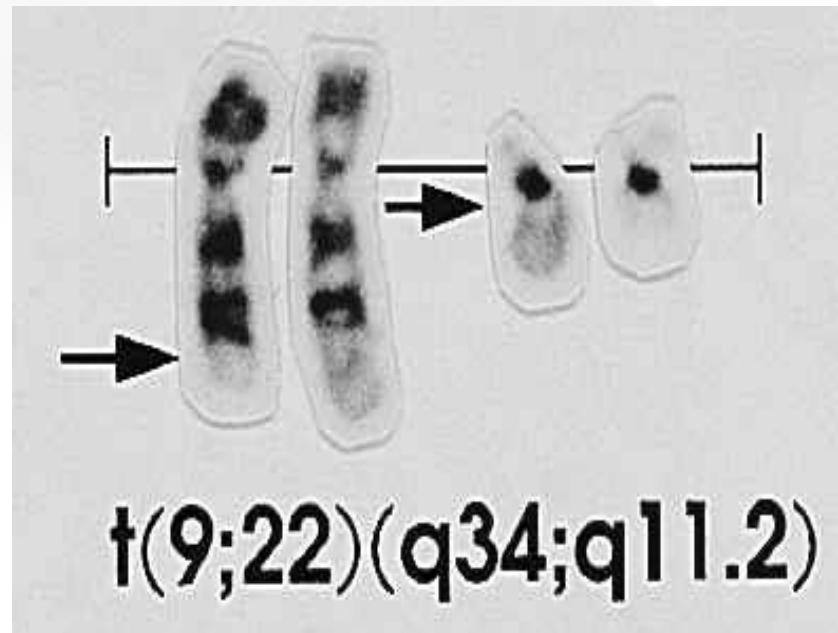
Oncogen



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t(9;22)(q34;q11)

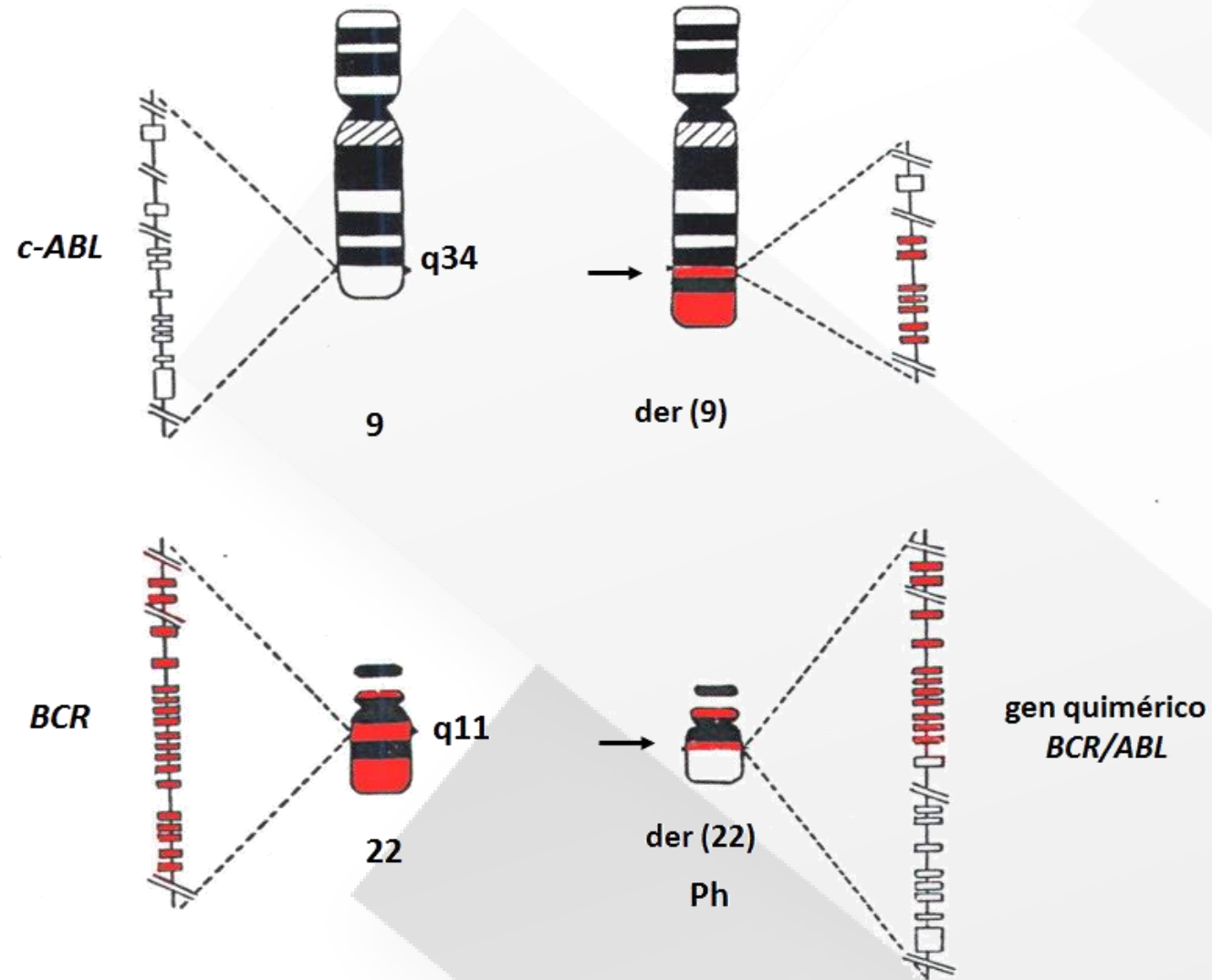
**Cromosoma Philadelphia (Ph) es marcador
para LMC y para LLA**





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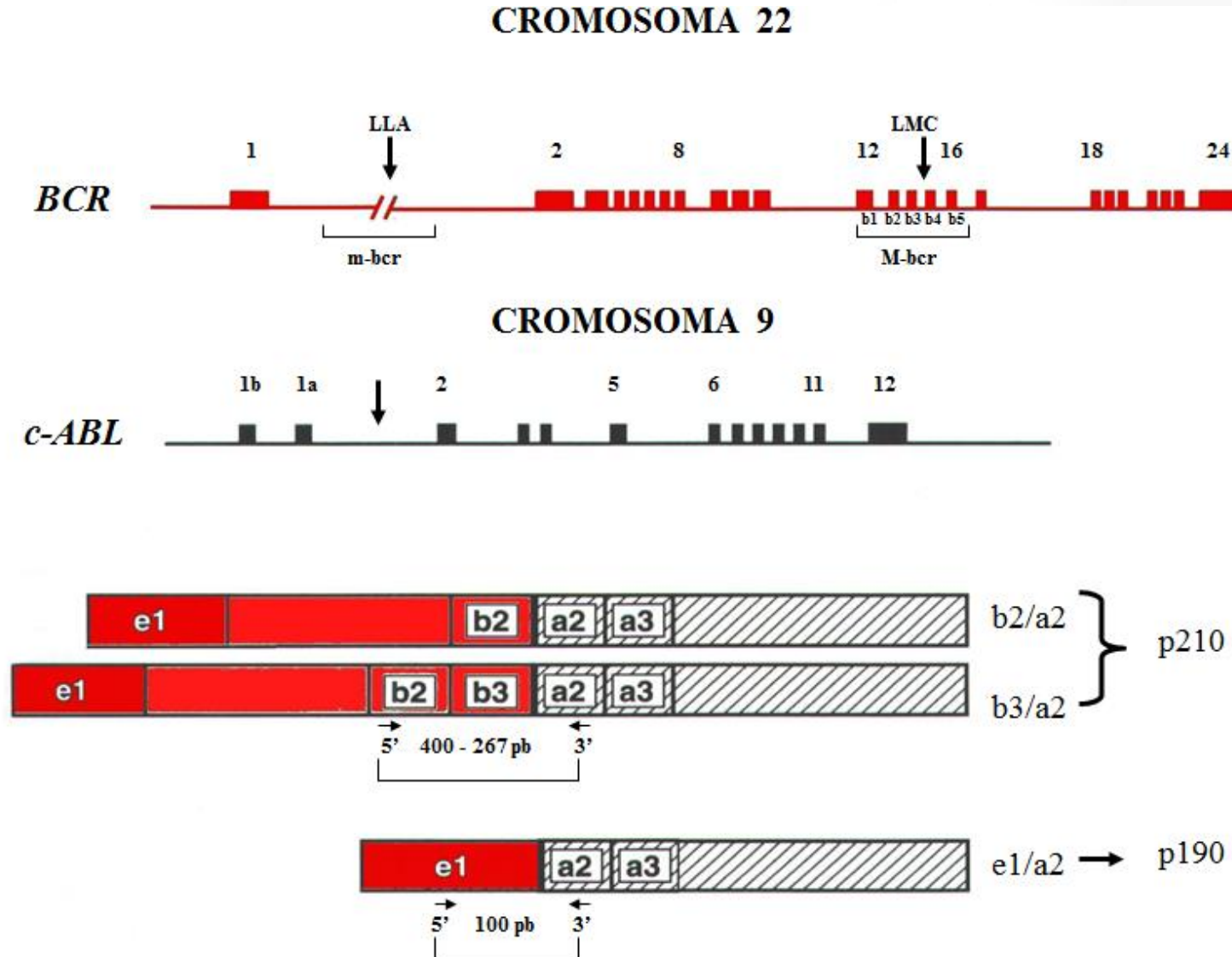
Oncogen: *BCR-ABL*





NÚCLEO DE QUITO

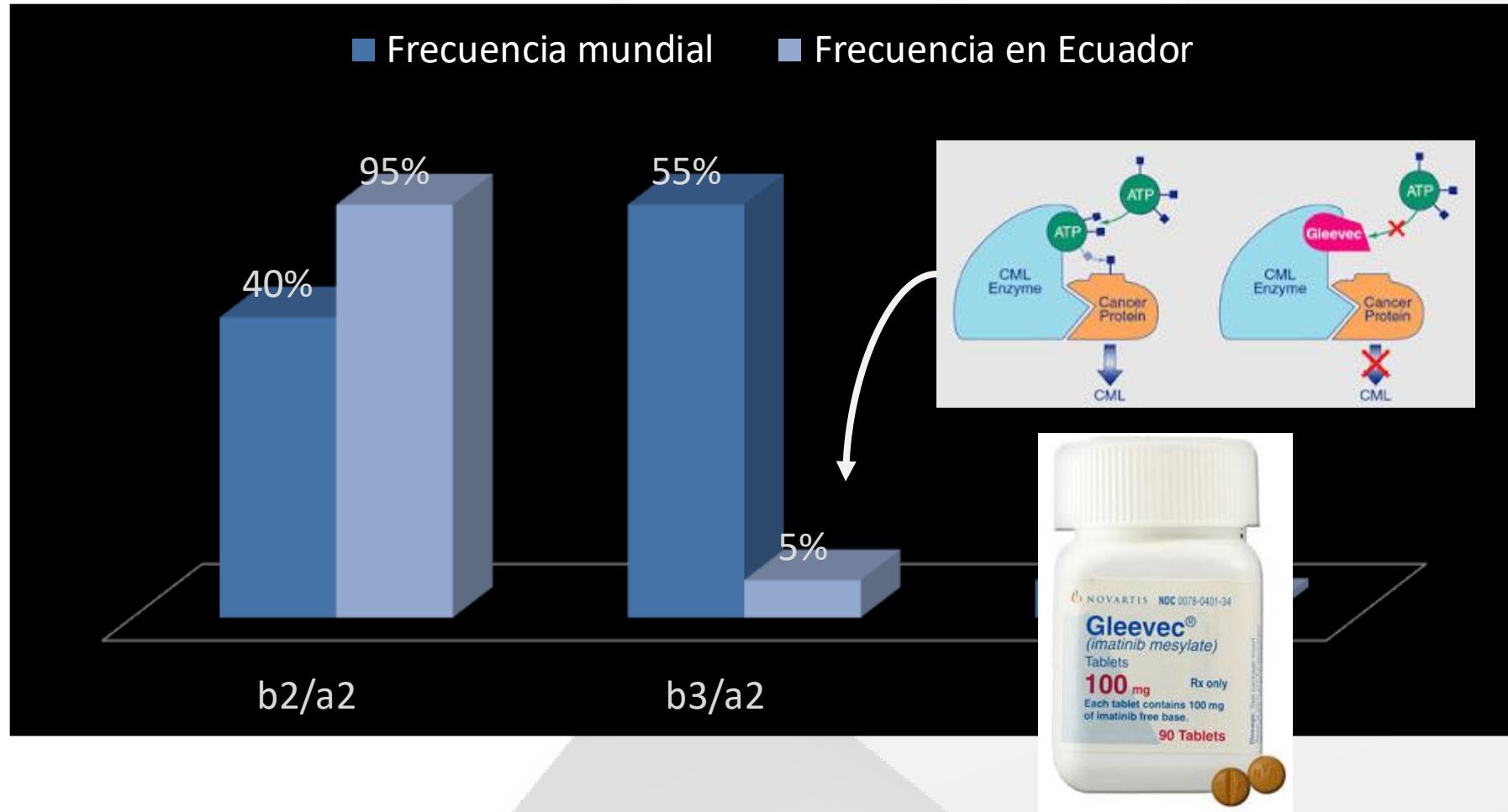
BCR-ABL: gen quimérico





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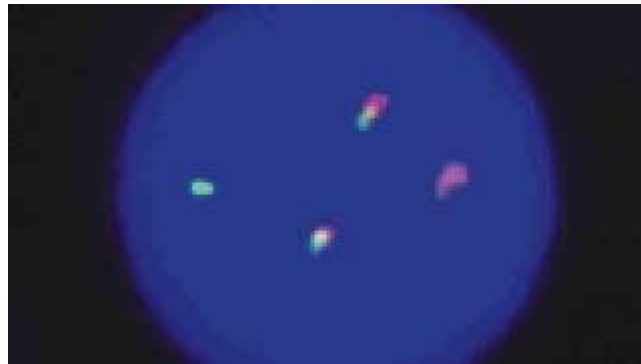
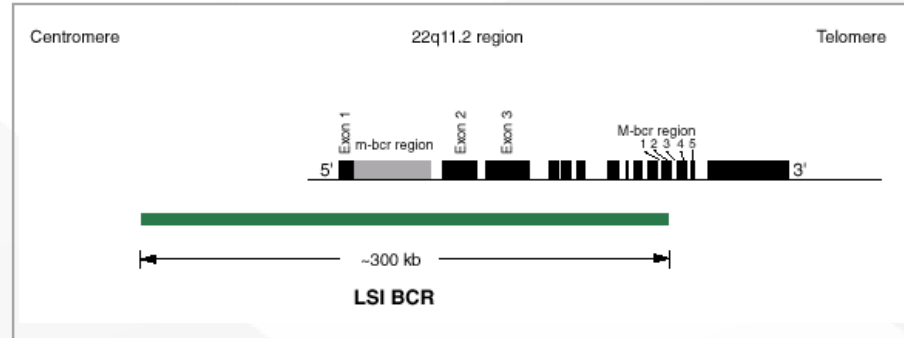
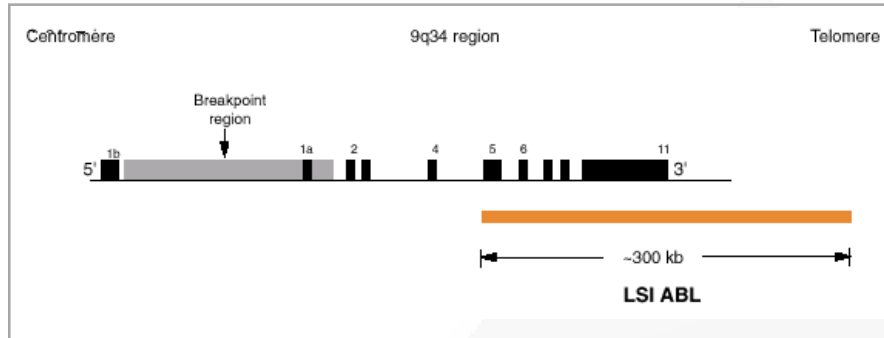
Rearreglos del gen influyen en respuesta a tratamiento



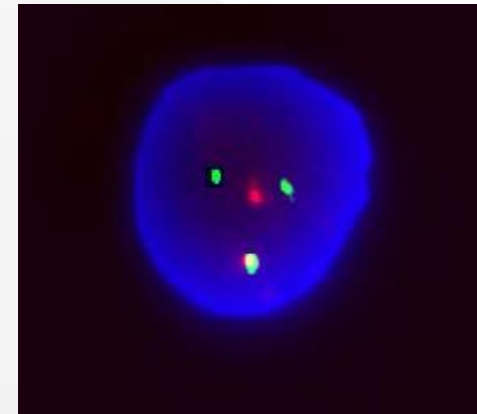


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t(9;22) *BCR/ABL*: Delección de 9q



LSI BCR/ABL Dual Color,
Dual Fusion Translocation Probe

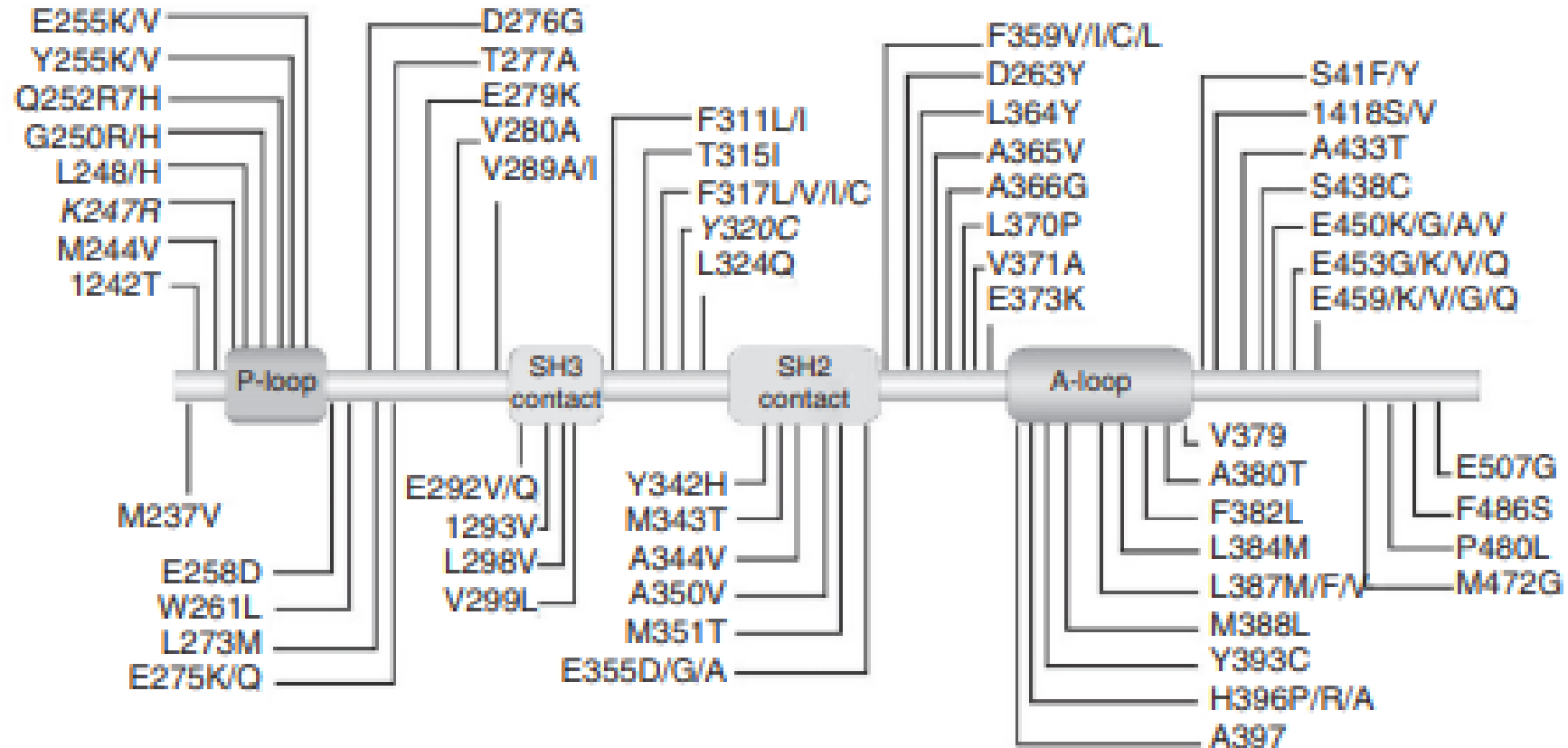


10% del(9q34) → pacientes
refractarios a Glivec™



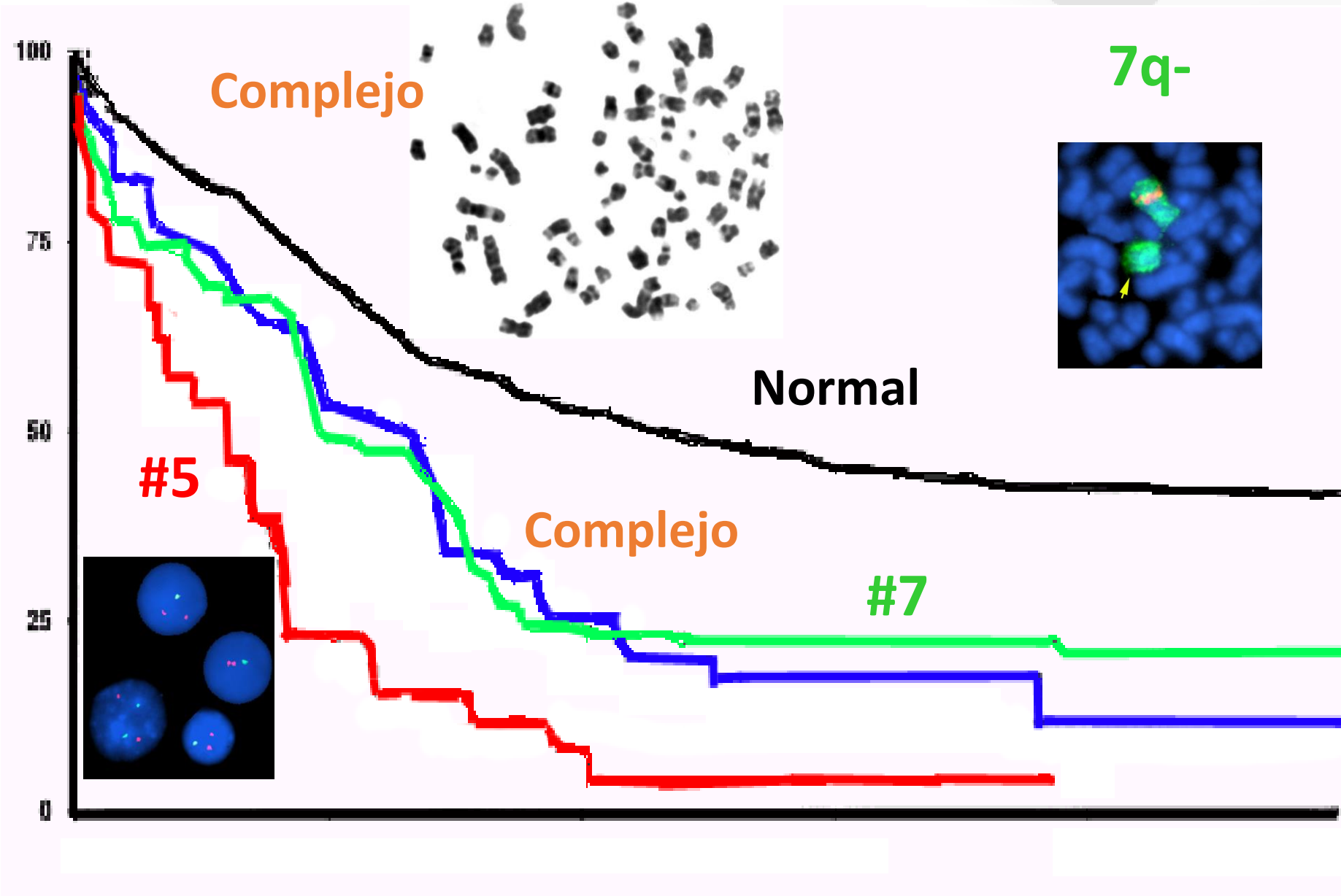
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Mutaciones asociadas a resistencia a Imatinib



100 mutaciones

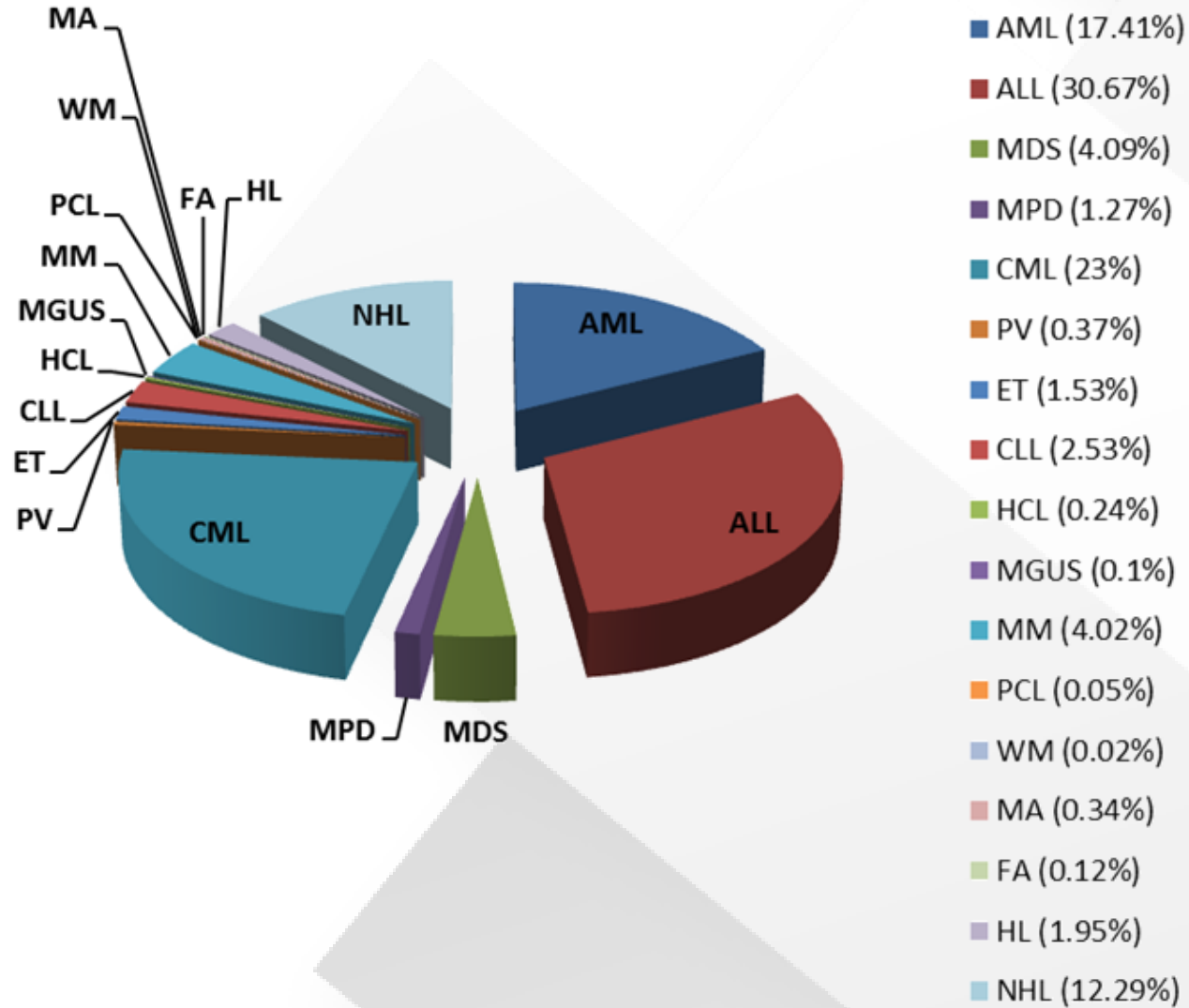
Leucemias: Pronóstico





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Hemopatías en Ecuador 1984-2012





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Citogenética en hemopatías de Ecuador

Hematological diseases ^a	Cases (n)	Normal Karyotype		Altered Karyotype								No methaphases	
				Hyperdiploid		Hypodiploid		Translocation		Complex			
		n	%	n	%	n	%	n	%	n	%	n	%
AML	715	259	36.2	66	9.2	57	8.0	68	9.5	110	15.4	155	21.7
ALL	1260	419	33.3	102	8.1	92	7.3	99	7.9	191	15.2	357	28.3
MDS	168	75	44.6	15	8.9	9	5.4	4	2.4	20	11.9	45	26.8
MPD	52	26	50.0	8	15.4	3	5.8	3	5.8	8	15.4	4	7.7
CML	945	100	10.6	6	0.6	6	0.6	756	80.0	10	1.1	67	7.1
PV	15	9	60.0	1	6.7	1	6.7	0	0	0	0	4	26.7
ET	63	35	55.6	0	0	1	1.6	1	1.6	4	6.3	22	34.9
CLL	104	46	44.2	7	6.7	5	4.8	2	1.9	15	14.4	29	27.9
HCL	10	5	50.0	1	10.0	0	0	0	0	0	0	4	40.0
MGUS	4	3	75.0	0	0	0	0	0	0	0	0	1	25.0
MM	165	63	38.2	14	8.5	7	4.2	8	4.8	30	18.2	43	26.1
PCL	2	1	50.0	0	0	0	0	0	0	0	0	1	50.0
WM	1	1	100.0	0	0	0	0	0	0	0	0	0	0
MA	14	5	35.7	0	0	0	0	0	0	2	14.3	7	50.0
FA	5	2	40.0	0	0	0	0	0	0	3	60.0	0	0
HL	80	56	70.0	3	3.8	2	2.5	0	0	9	11.3	10	12.5
NHL	505	300	59.4	30	5.9	27	5.3	14	2.8	66	13.1	68	13.5
Total	4108												





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FISH & RT-PCR en casos sin metafases

FISH		RT-PCR		
AML				
probe	No. Cases	fusion gene	No. Cases	transcripts
t(8;21)	4	<i>AML1-ETO</i>	4	
t(15;17)	5	<i>PML-RARA</i>	11	4 (bcr2) & 7 (bcr3)
inv(16)	1	<i>CBFB-MYH11</i>	7	7 (type F)
(v 11q23)	3			
ALL				
probe	No. Cases	fusion gene	No. Cases	transcripts
t(9;22)	9	<i>BCR-ABL</i>	18	18 (e1a2)
(v 11q23)	10	<i>MLL-AF4</i>	4	4 (e8-e7)
t(1;19)	1	<i>E2A-PBX1</i>	1	7 (type F)
t(12;21)	9			
t(8;14)	2			
CML				
probe	No. Cases	fusion gene	No. Cases	transcripts
t(9;22)	7	<i>BCR-ABL</i>	65	62 (b2-a2) & 3(b3a2)

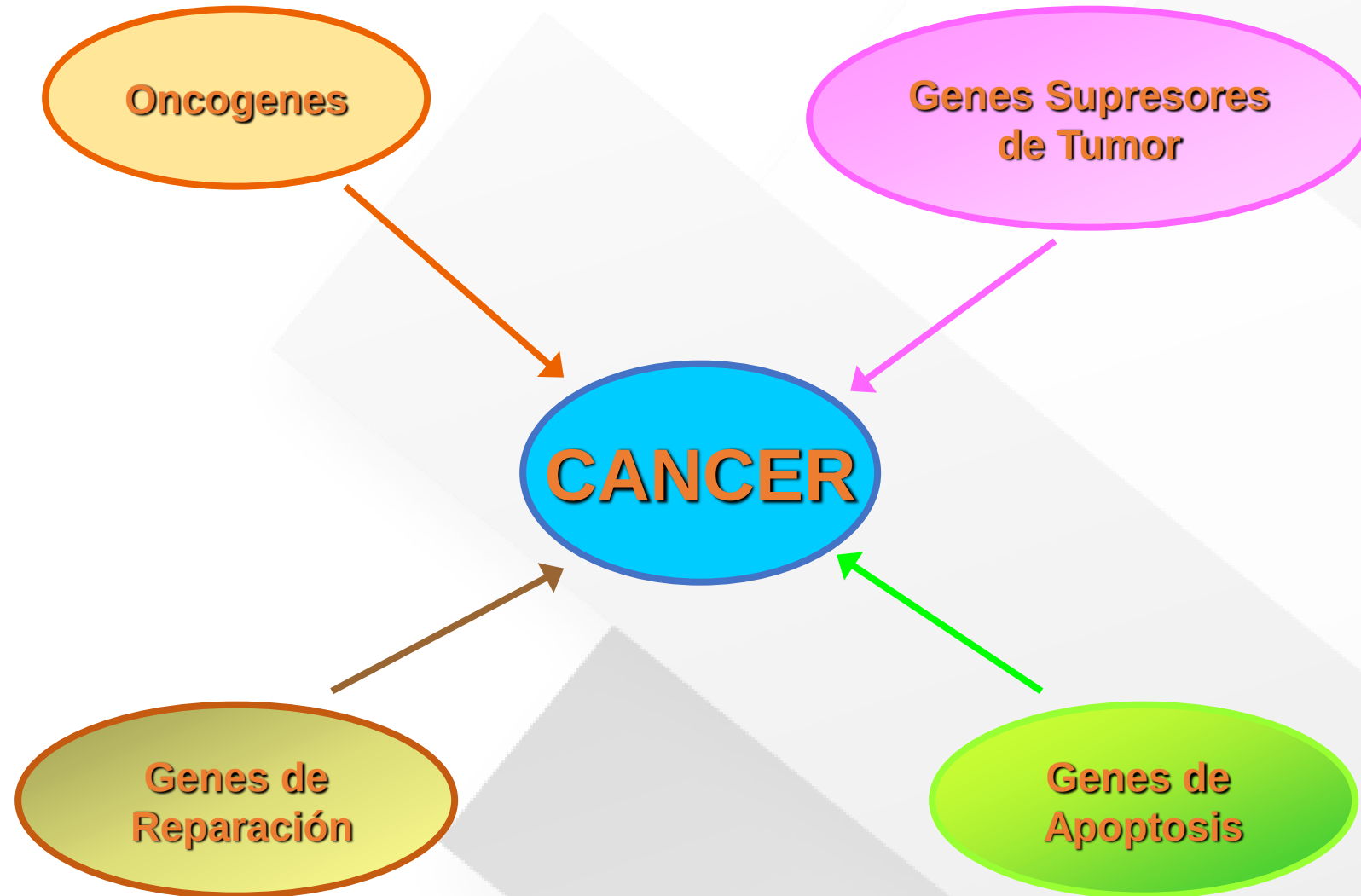
➔ 1,8%

➔ 4,1%



NÚCLEO DE QUITO

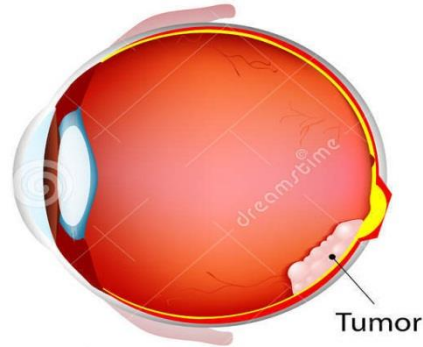
Genes de cáncer: Genes supresores de tumor



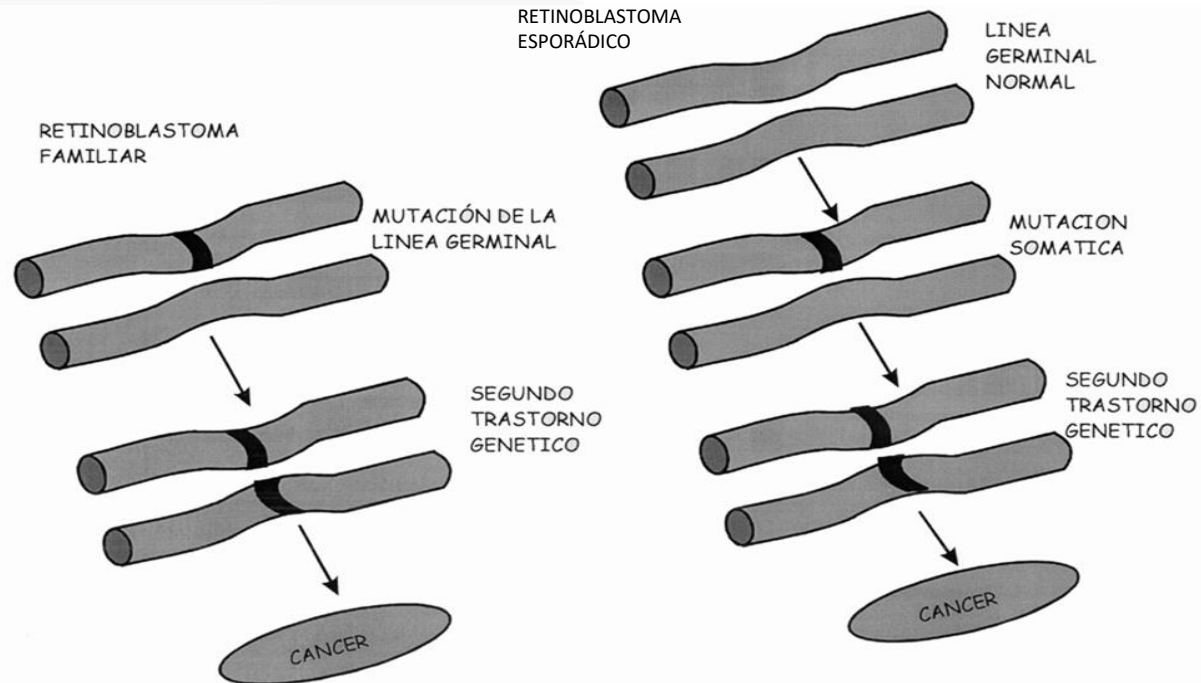
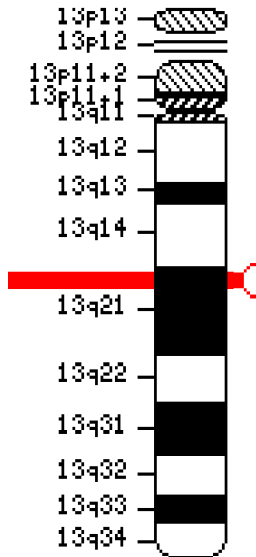


NÚCLEO DE QUITO

Gen supresor de tumor: *RB1*



Genes Supresores de Tumor



Teoría de Knudson: doble mutación



NÚCLEO DE QUITO

Gen *RB1*: Responsable de retinoblastoma

IVS3+45 T/C			
		Ecuador	España
Secuencia 1	AAATGA	0,125	0,64
Secuencia 2	AAACGA	0,875	0,36

IVS2+75 T/C			
		Ecuador	España
Secuencia 1	AAAAATTG	1	0,963
Secuencia 2	AAAACTG	0	0,037

IVS4+23 G/T			
		Ecuador	España
Secuencia 1	AGGTT	0,8	0,92
Secuencia 2	AGGTTT	0,2	0,08

IVS11-72 T/G			
		Ecuador	España
Secuencia 1	ATTGAAAA	1	0,91
Secuencia 2	ATGAAAA	0	0,09

c1770 T/C			
		Ecuador	España
Secuencia 1	TTGTCC	1	0,98
Secuencia 2	TTGCC	0	0,02

IVS19-77 A/G			
		Ecuador	España
Secuencia 1	AGCAATT	0,9	0,895
Secuencia 2	AGCGATT	0,1	0,115

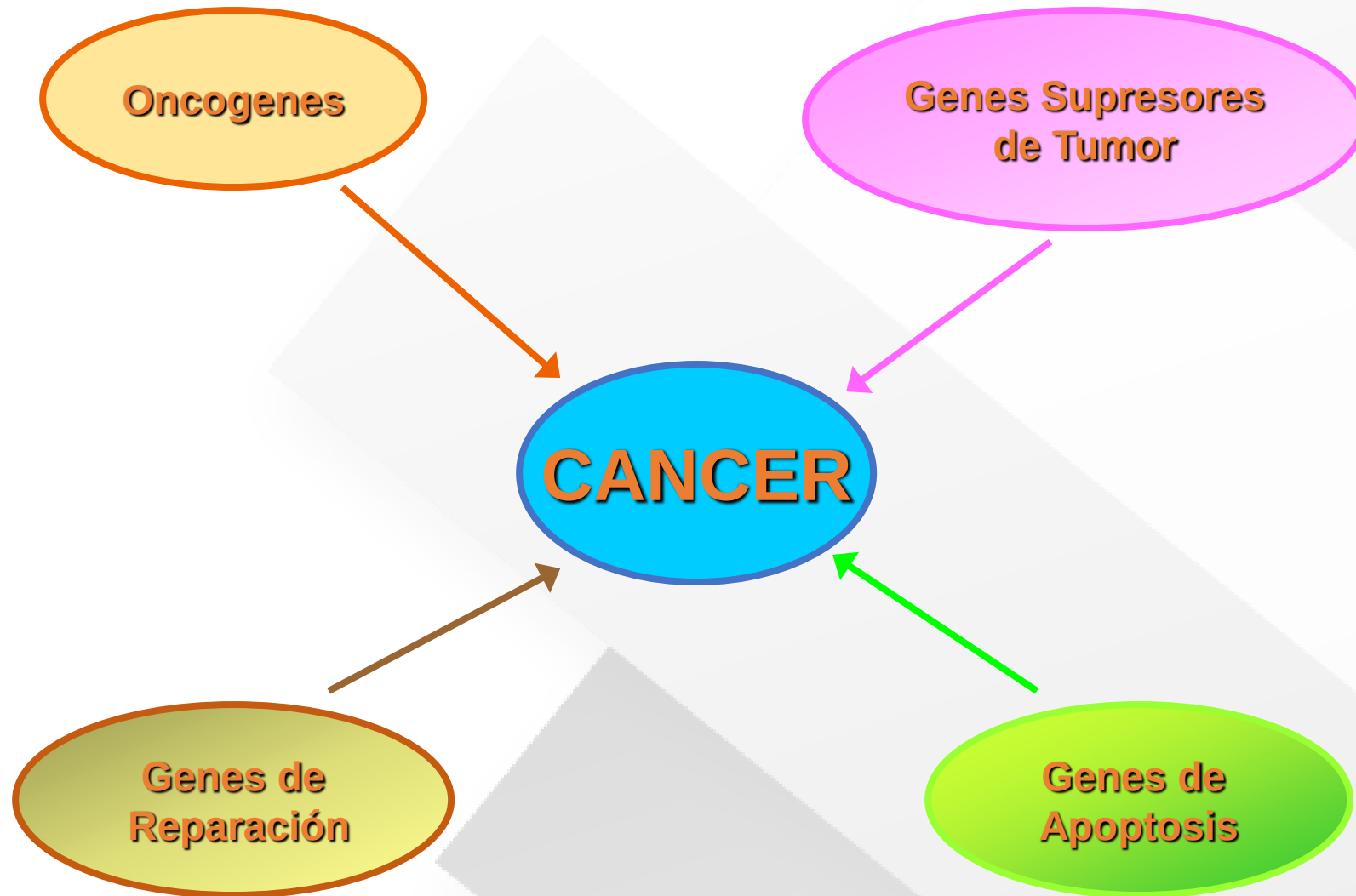
IVS16-57 A/delA			
		Ecuador	España
Secuencia 1	CAAAAAAT	0,5	0,93
Secuencia 2	CAAAAAAT	0,5	0,07

IVS25-10 T/A			
		Ecuador	España
Secuencia 1	TTTTTTTA	0,86	0,76
Secuencia 2	TTTTTTAA	0,14	0,24



NÚCLEO DE QUITO

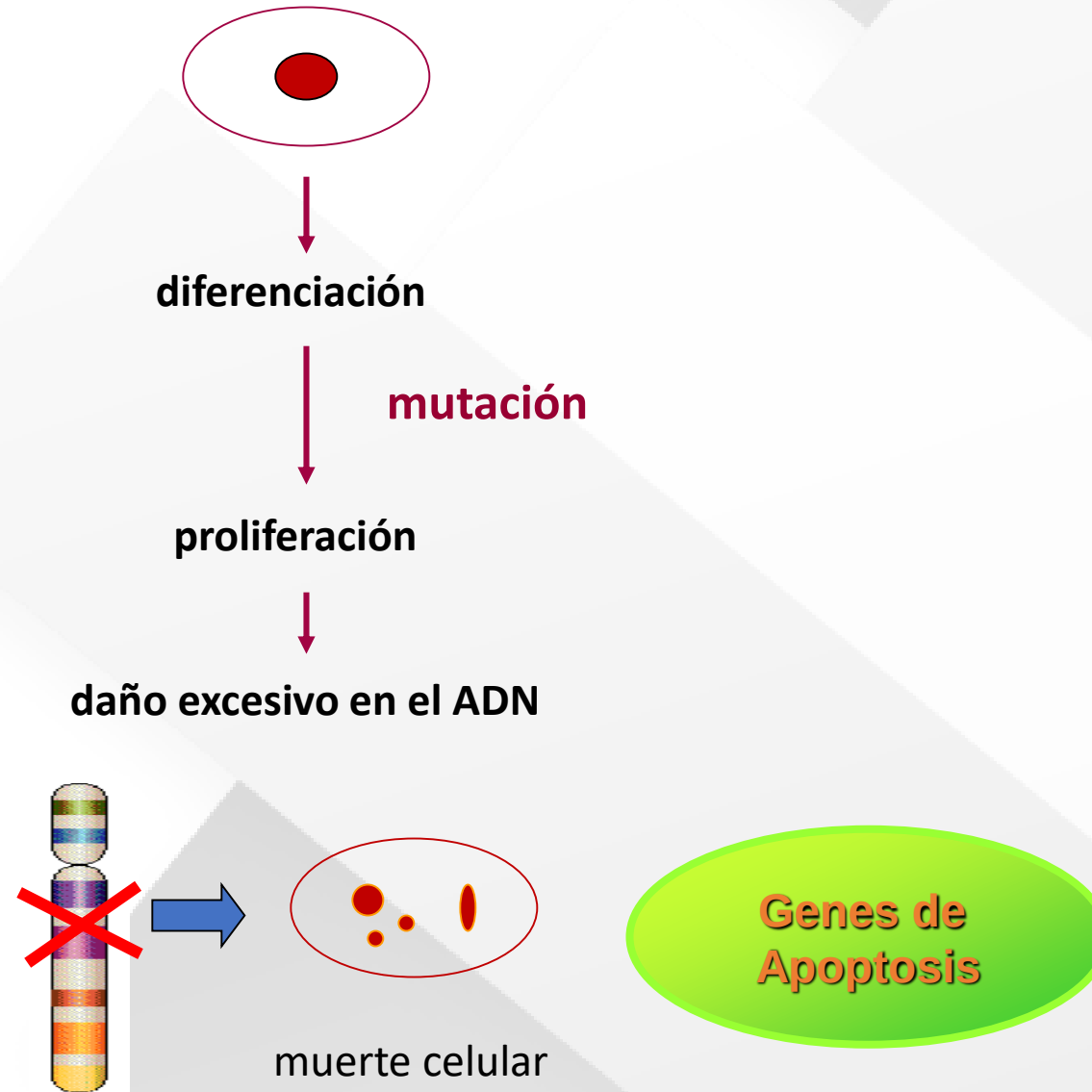
Genes de cáncer: Apoptosis





NÚCLEO DE QUITO

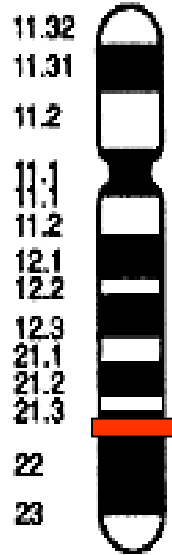
Apoptosis: muerte celular programada





NÚCLEO DE QUITO

Bcl-2 / t(14;18) es rara en Ecuador

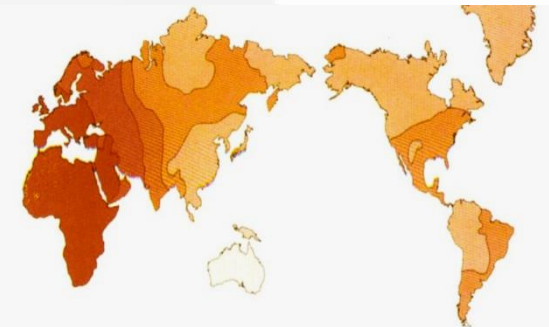
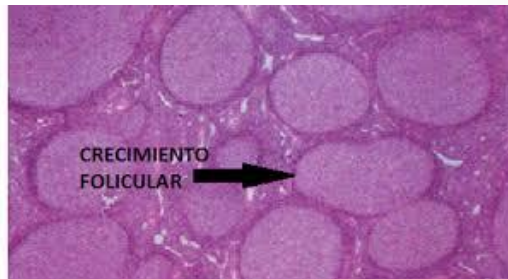


Non-Hodgkin lymphoma subtypes and frequency of MBR and mcr rearrangement of t(14;18)(q32;q21)

Non-Hodgkin lymphoma subtypes	Case no.	Incidence (%)	t(14;18)(q32;q21) rearrangements		
			MBR	mcr	Control
Follicular	5	7.7	—	—	5
Diffuse	60	92.3	—	—	60



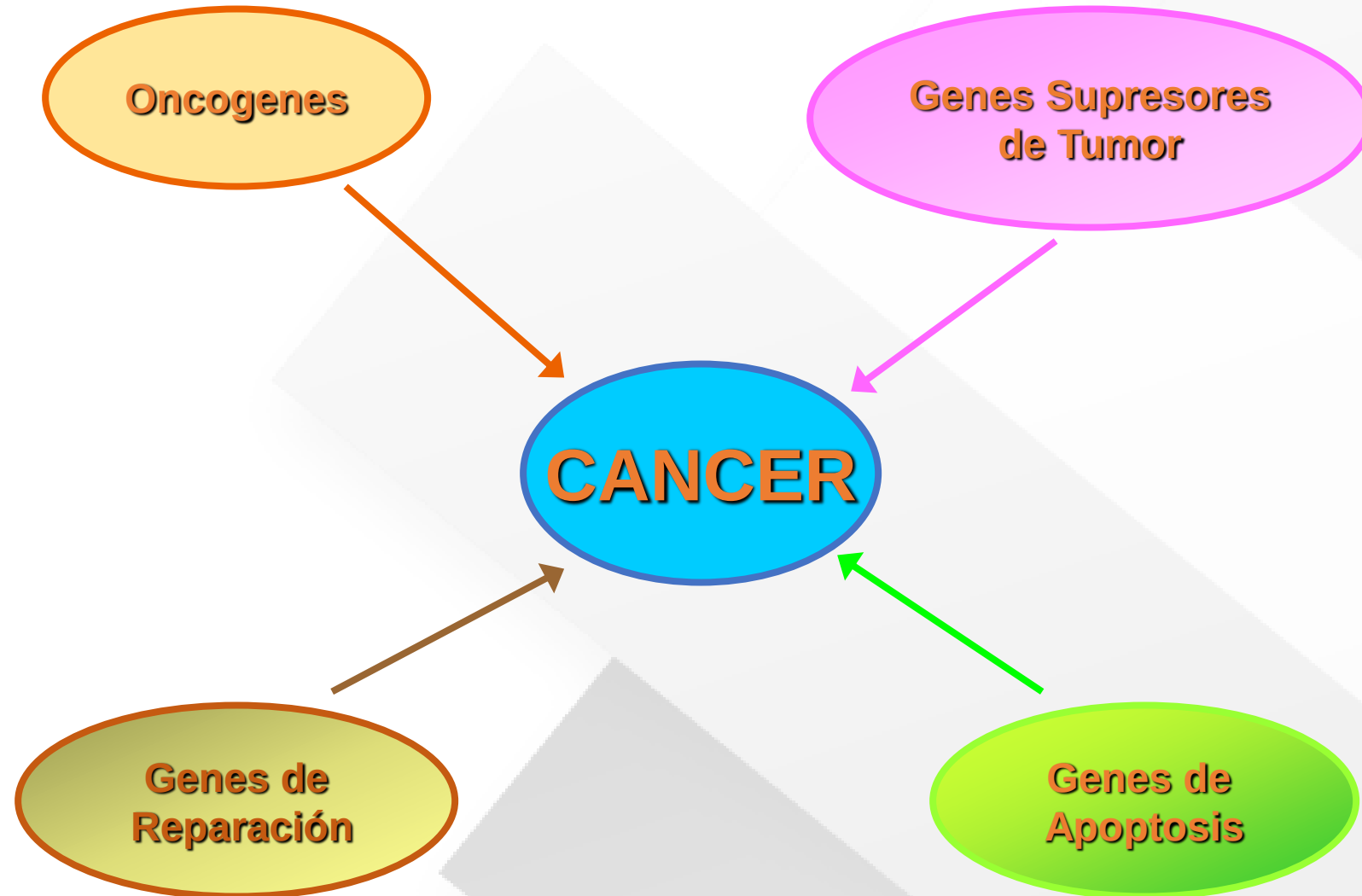
30-40% Norteamérica
20-30% Europa
10% Asia





NÚCLEO DE QUITO

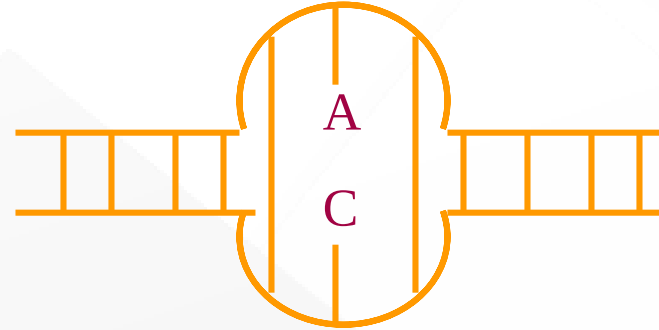
Genes de cáncer: Reparación



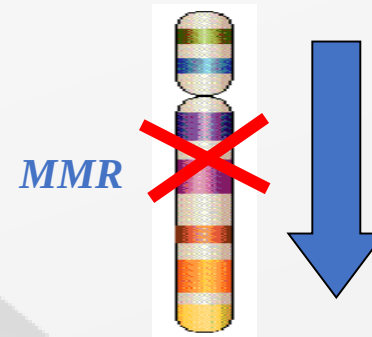


NÚCLEO DE QUITO

Reparación del ADN



mal emparejamiento



MMR

Genes de
Reparación



ADN reparado



NÚCLEO DE QUITO



2p21

Gen de reparación: MSH2

Población	No. individuos analizados	No. cromosomas analizados	No. cromosomas polimorfismo	Frecuencia de C → T
Normal	40	80	4	0,05
Linfomas	22	44	5	0,11 ^{p<0,01}
Leucemias	10	20	1	0,05
FQ	7	14	3	0,21
DMD	2	4	1	0,25



NÚCLEO DE QUITO

Genes de reparación en hemopatías

RAD54

hMSH2

Table 1
Distribution of the allele found (gIVS12-6T>C)

	Number of individuals Analyzed	Number of individuals			Polymorphism frequency	% of individuals with the polymorphism
		T/T	C/T	C/C		
Normal	50	46	3	1	0.05	7.5
NHL	22	17	5	0	0.114*	22.73*

Abbreviation: NHL, non-Hodgkin lymphoma.
*P<0.01 when compared with normal group.

Table 1 - Distribution of the 2290 C/T polymorphism in leukemia (CML, ALL) and control populations.

Group	Genotype	Individual (%)	Genotypic frequency	Allele frequency
Leukemia (n = 137)	C/C	112 (82)	0.82	0.9
	C/T	23 (17)	0.17	
	T/T	2 (1)	0.01	0.1
CML (n = 60)	C/C	45 (75)	0.75	0.86
	C/T	13 (22)	0.22	
	T/T	2 (3)	0.3	0.14
ALL (n = 61)	C/C	55 (90)	0.90	0.95
	C/T	6 (10)	0.10	
	T/T	0 (0)	0	0.05
Control (n = 102)	C/C	87 (85)	0.85	0.925
	C/T	15 (15)	0.15	
	T/T	0 (0)	0	0.075

TABLE I Distribution of the allele [gIVS12-6T > C]

Group	Number of individuals				Polymorphism Frequency
	Sample size	T/T	T/C	C/C	
Control	50	46	3	1	0.05
Lymphoma	87	70	17	0	0.09**
Leukemia	90	81	8	1	0.05
MDS	4	4	0	0	0.00

**Significant differences when compared to the control group (p < 0.01).

Genet Mol Biol. 33(4), 646-9 (2010); Leukemia & Lymphoma 44, 375-6 (2003);
Cancer Genet Cytogenet 133, 29-33 (2002)



NÚCLEO DE QUITO

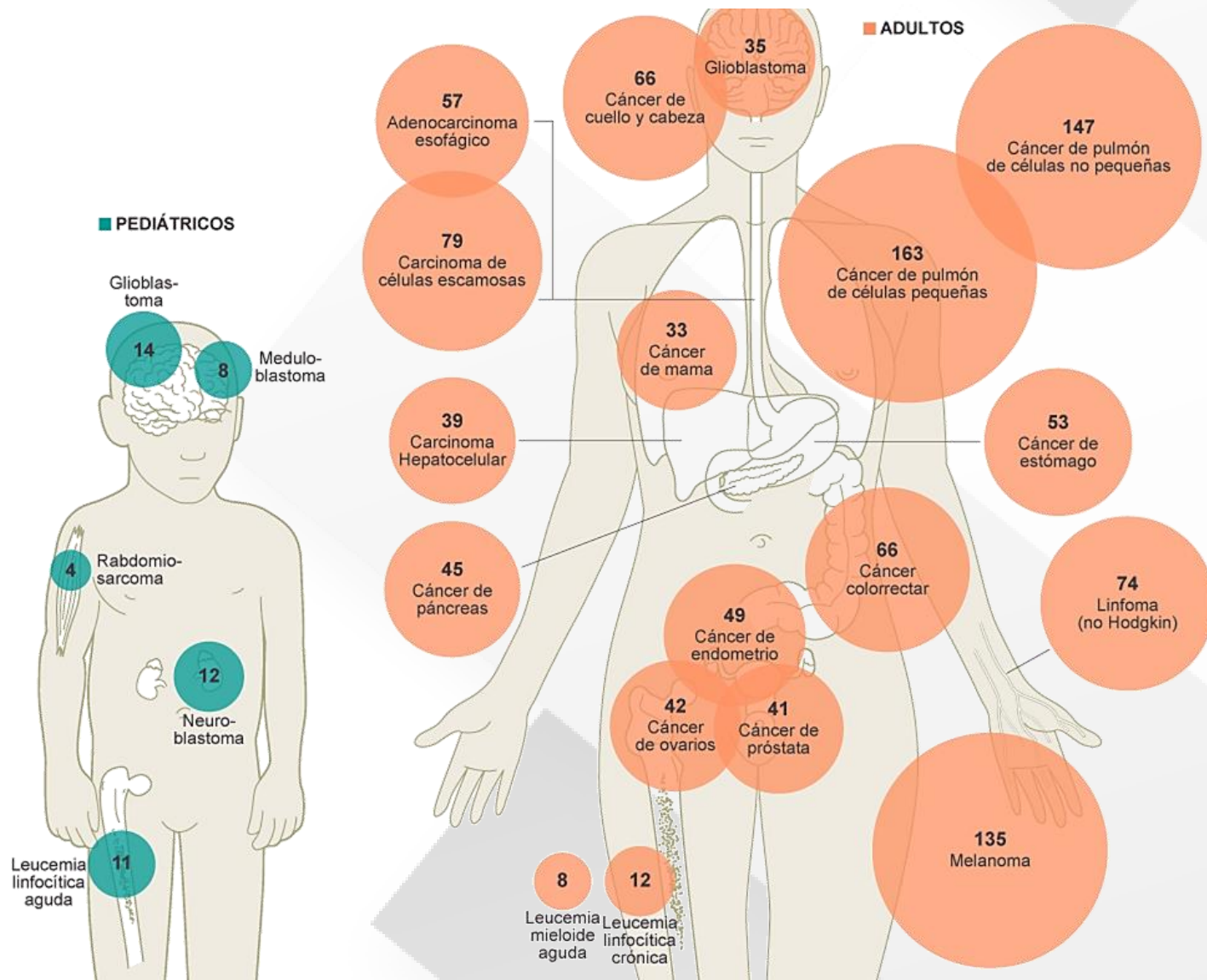
Genes de reparación en retinoblastoma

SNP	GENOTIPO	Casos (n=80), n %	Controles (n=80), n %	OR ^a	95% IC ^b	P
rs13181 ERCC2	A/A	48 (60,0)	60 (76,5)	1,0 ^R	-	-
	A/C	31 (38,75,0)	19 (23,8)	2,03	1,02 - 4,04	0,040 ^S
	C/C	1 (1,25)	1 (1,3)	1,25	0,07 - 20,5	0,69
	A/C + C/C	32 (40,0)	20 (25,0)	2	1,01 - 3,92	0,042 ^S
rs2228001 XPC	A/A	21 (26,25)	30 (37,5)	1,0 ^R		
	A/C	45 (56,25)	43 (53,8)	1,49	0,74 - 3,00	0,25
	C/C	14 (17,5)	7 (8,8)	2,86	0,99 - 8,28	0,052
	A/C + C/C	59 (73,75)	50 (62,5)	1,69	0,86 - 3,30	0,126
rs17655 XPG	G/G	23 (28,75)	14 (17,5)	1,0 ^R		
	G/C	56 (70,0)	65 (81,3)	0,52	0,24 - 1,11	0,09
	C/C	1 (1,25)	1 (1,1)	0,61	0,03 - 10,5	0,62
	G/C + C/C	57 (71,25)	66 (82,5)	0,52	0,25 - 1,12	0,09
rs25487 XRCC1	G/G	9 (11,25)	43 (53,8)	1,0 ^R		
	A/G	70 (87,6)	27 (33,8)	12,4	5,3 - 28,82	< 0,001 ^S
	A/A	1 (1,25)	10 (12,5)	0,47	0,05 - 4,2	0,44
	A/G + A/A	71 (88,75)	37 (46,25)	9,1	4,03 - 20,8	< 0,001 ^S
rs861539 XRCC3	C/C	65 (85,0)	68 (85,0)	1,0 ^R		
	C/T	14 (13,8)	11 (13,8)	1,33	0,56 - 3,14	0,51
	T/T	1 (1,3)	1 (1,3)	1,04	0,06 - 17,0	0,740
	C/T + T/T	15 (18,75)	12 (15,0)	1,31	0,57 - 3,00	0,53



NÚCLEO DE QUITO

Genes del cáncer

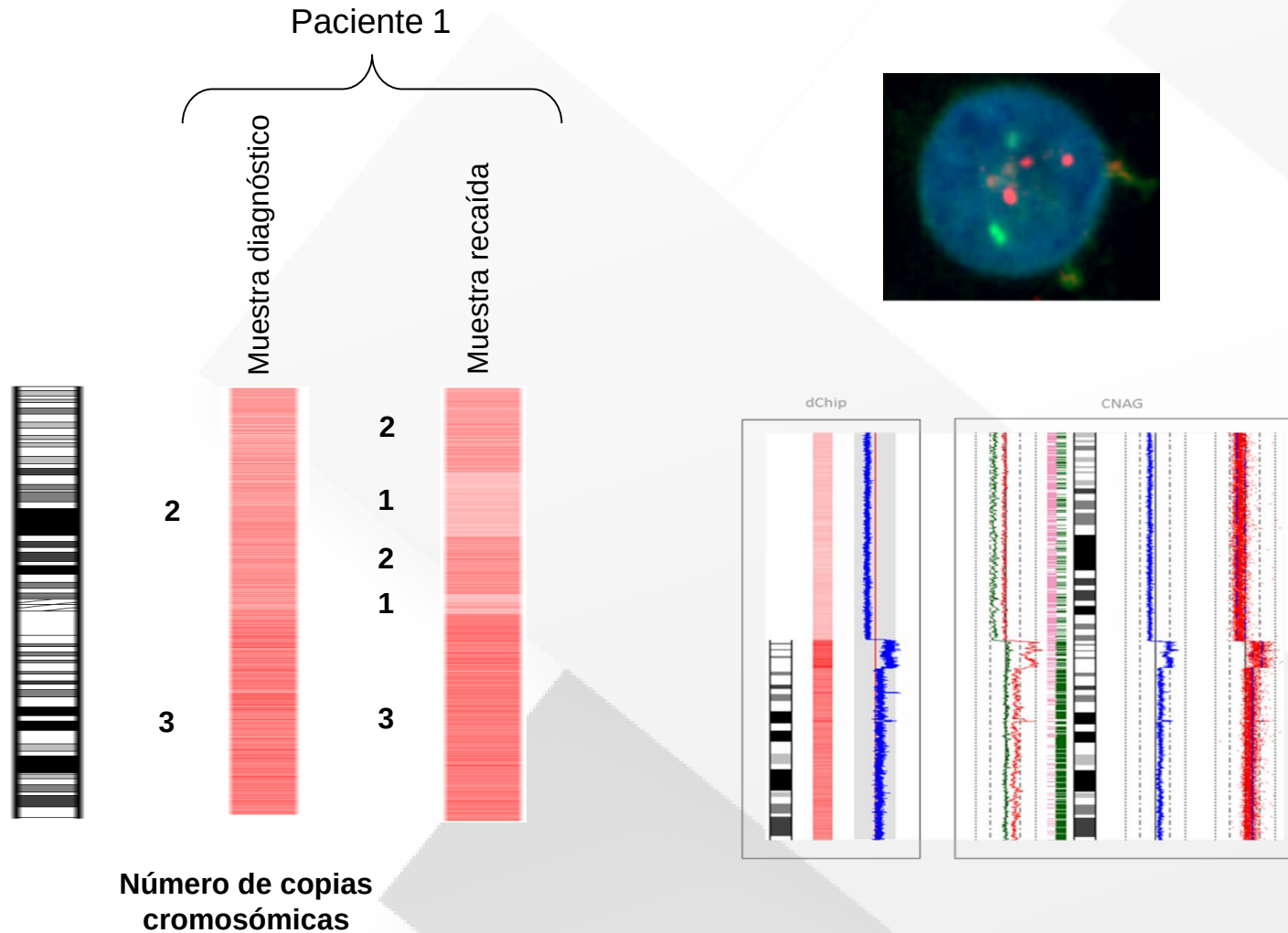


Tomado de Science, 2013



NÚCLEO DE QUITO

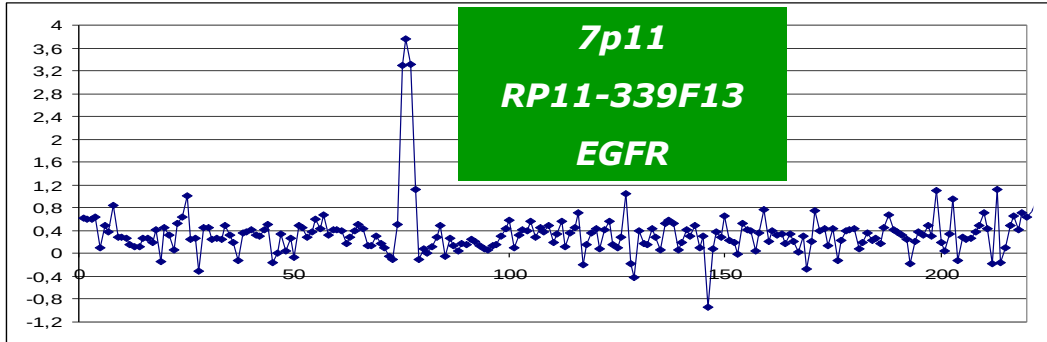
Seguimiento de pacientes con Mieloma



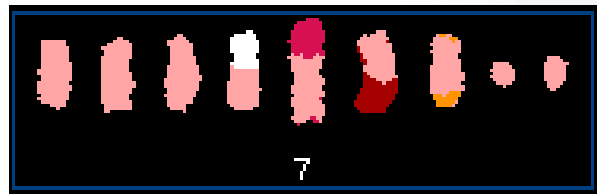
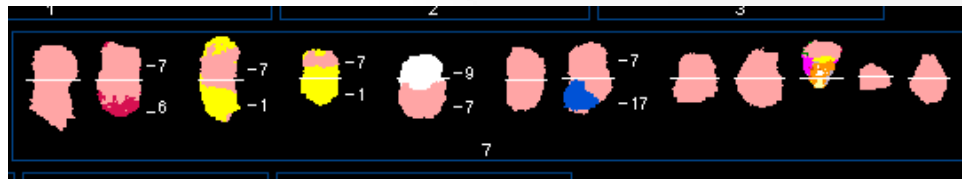


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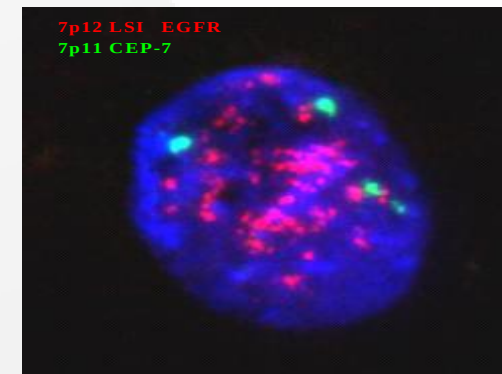
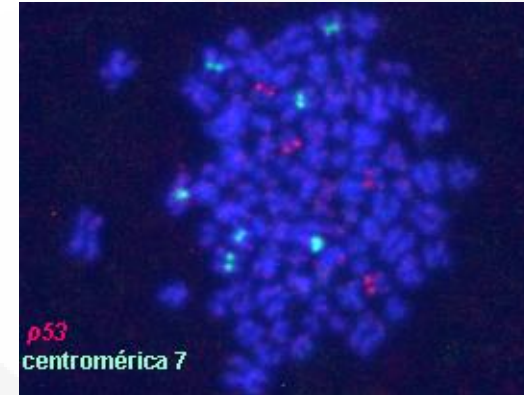
Daño de 7p11: Receptor de factor de crecimiento



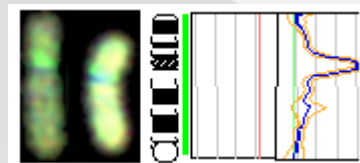
CGH array



SKY



FISH



CGH

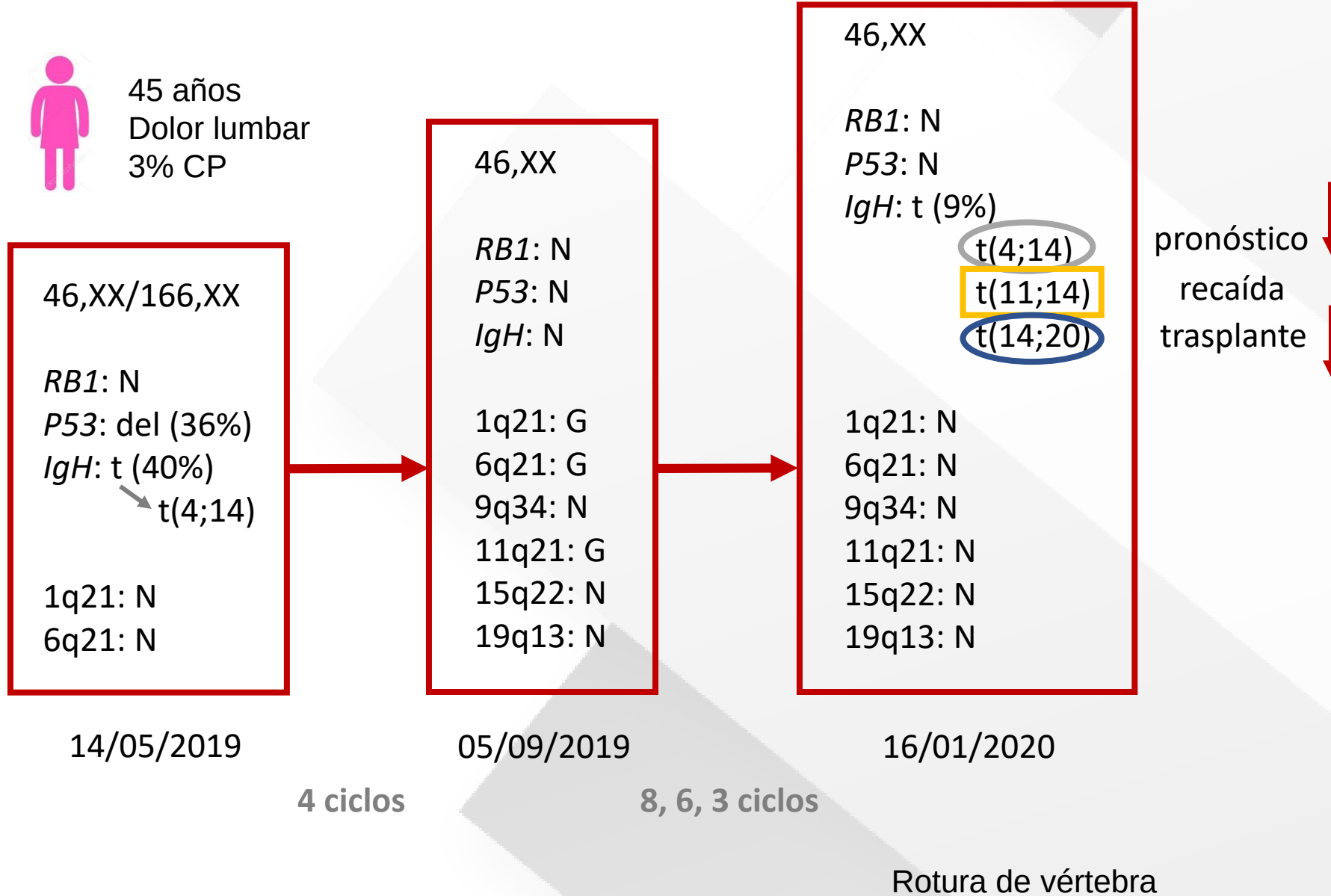


NÚCLEO DE QUITO

MM: Evolución de la enfermedad



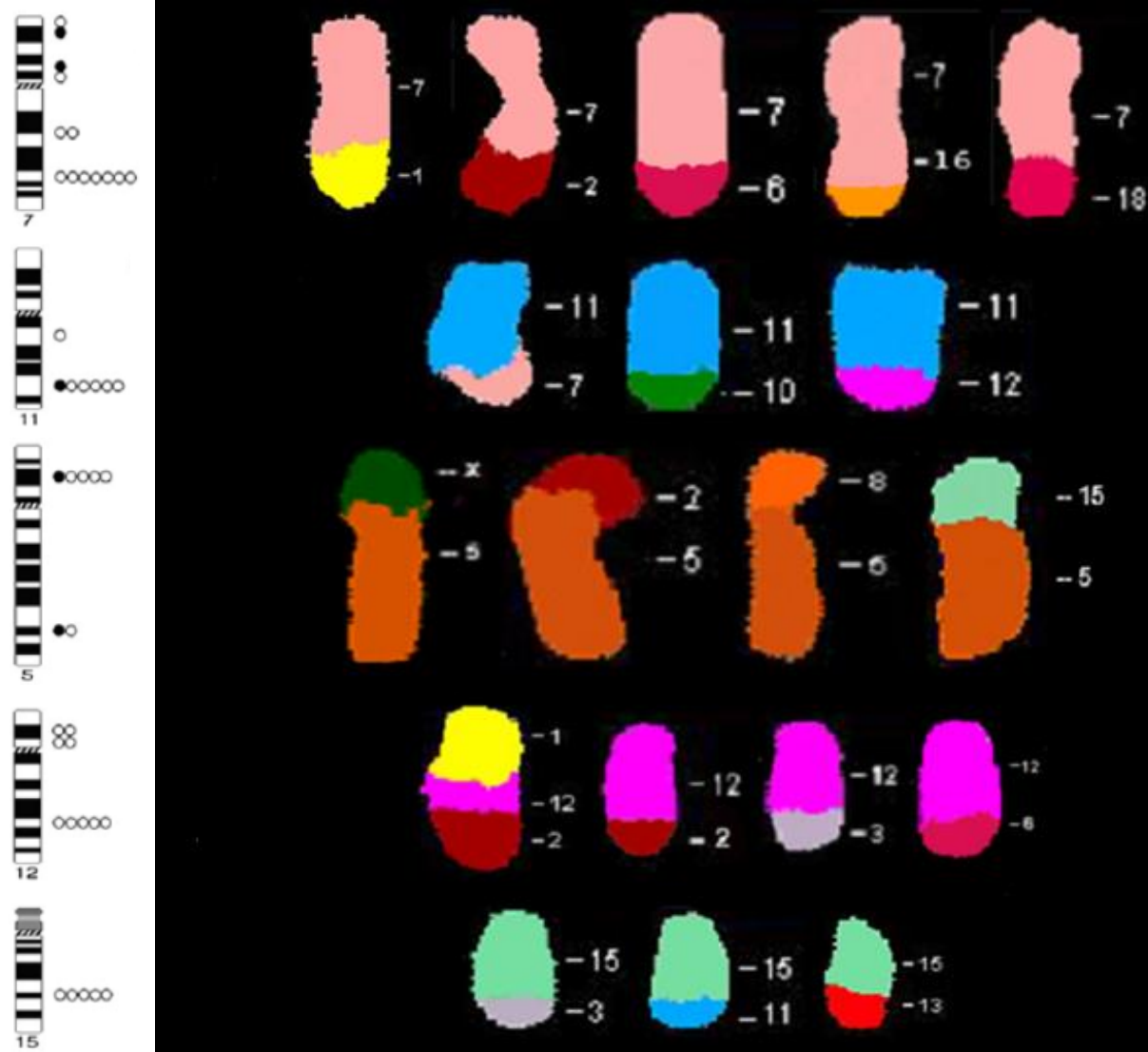
45 años
Dolor lumbar
3% CP



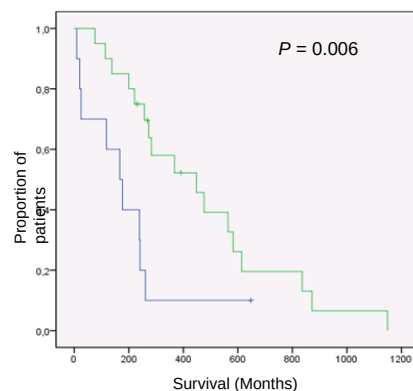


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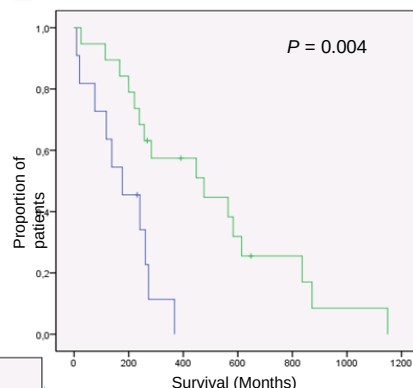
Glioblastoma: Puntos de rotura frecuentes por SKY



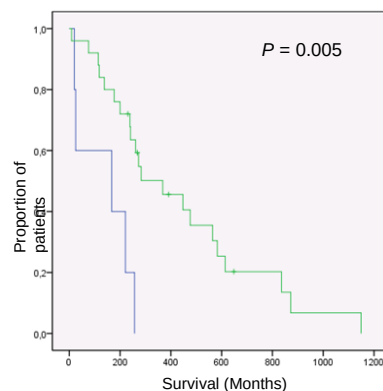
Efecto de los 406 genes en supervivencia



— CACNA2D3 low
— CACNA2D3 high



— PROM1 high
— PROM1 low



— PPP2R2B low
— PPP2R2B high

s	Fold change >2
n	(GBM vs NORMAL)
	AKR7A2, C1orf144, C1QA, C1QB, CAPZB, CLIC4, DDOST, EIF1AX, ENO1, FUSIP1, HMG2, ID3, NECAP2, NPM1, PDPN, PGD, RER1, RPL11, RPL12, RPL18A, RUNX3, SH3BGRL3, TNFRSF1B, VAMP3
	ACOT7, CAMK2N1, CAMTA1, CDC42, CHD5, CLSTN1, DVL1, EXTL1, FBXO2, GABRD, KCNAB2, KIF1B, LUZP1, NBL1, PINK1, PRDM2, PRKCZ, RAP1GAP, RERE, RP1-21018.1, STMN1, UBE4B, VPS13D
	C1orf106, CH3L1, DTL, DYRK3, IKBKE, KIF14, MAPKAPK2, PTPRC, RNPEP, TMEM189-UBE2V1
	CAMK1G, DSTYK, KIF21B, NFASC, PLXNA2, PPFIA4, TIMM17A, TMCC2
	EIF2AK2, PRKD3, RPLP0, SFRS7
	FAM98A
	ARE1, WNT5A
	CACNA2D3 , RRC2, FEZF2, MAGI1
	DAG1, GNAI2, GPX1, HYAL2, IFRD2, MAP4, NT5DC2, RHOA, SMARCC1, STAB1, TKT, ZNF167
	BSN, CAMKV, CELSR3, DOCK3, IP6K1, LZTFL1, NCKIPSD, NISCH, P4HTM, SEMA3B
	ACTL6A, BCHE, FNDC3B, FXR1, GMPS, KPNA4, MFSD1, NMD3, PLOD2, PLSCR1, RAP2B, RARRES1, SELT, SERP1, SGEF, SMC4, SOX2, WWTR1
	KCNAB1, PLCH1, SERPINI1
	FAM114A1, LAP3, MED26, NCAPG, PROM1 , RBM47
	LDB2, QDPR, SLIT2
	MSN
	AKTIP, CDH10, CDH18
	ANKHD1, CD14, CD74, CDC25C, CSF1R, CSNK1A1, DCTN4, DPYSL3, EGR1, G3BP1, GALNT10, GM2A, H2AFY, KIF20A, KIF4A, PCDHGA 1-12, PCDHGB 1-7, PCDHGC 3-4, SAR1B, SPARC, TGFBI, TXNDC15
	CAMK2A, CYFIP2, FABP6, KIF1L3, LARP1, LRRTM2, PCDHA 1-13, PCDHC 1-2, PCYOX1, PPP2R2B , PURA, SKP1, UBE2D2
	ARPC1B, CDK6, GAL3S14, GNB2, MCM7, POLR2J, SERPINE1, SLC25A13, SRI, SRRT, SYPL1, TFPI2, ZNHIT1
	ACTL6B, ASNS, DYNC1I1, GRM3, PCLO, PFTK1, PRKAR2B, RUNDC3B, SRPK2, TAC1
	CALU, EEF1G, UBE2H
	DERL1, GPR172A, MYC, RPL8, SLA, TMED10
	EFR3A, ENPP2, LY6H, PTK2

Genes con efecto en supervivencia



NÚCLEO DE QUITO

Gen *XRCC1*: mutación nueva

GeneView via analysis of contig annotation: [XRCC1](#) X-ray repair cross complementing 1

View more variation on this gene (click to hide).

☒ Clinical Source: ☐ in gene region ☒ cSNP ☐ has frequency ☐ double hit

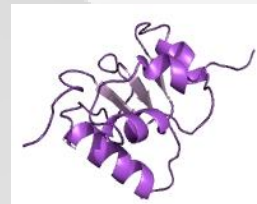
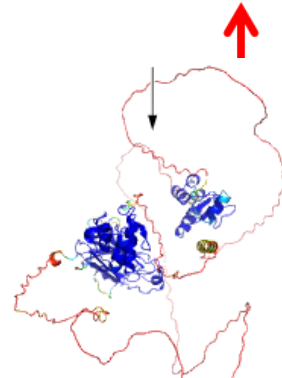
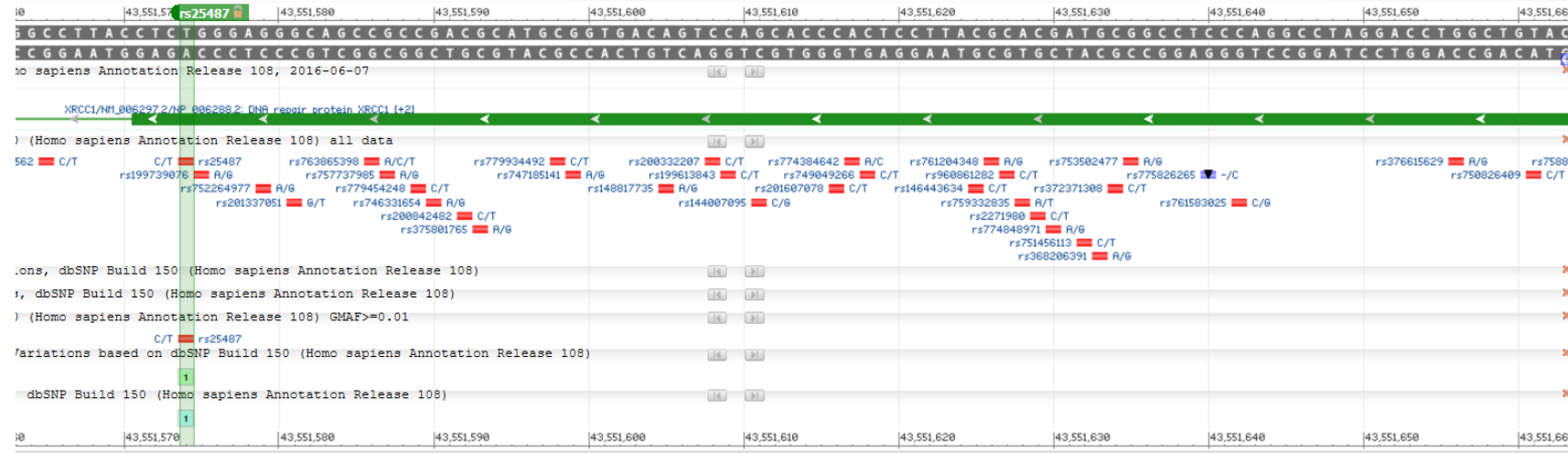
Primary Assembly Mapping

Assembly	SNP to Chr	Chr	Chr position	Contig
GRCh38.p7	Rev	19	43551574	NT_011109.17

a 82pb



43.551.656 C>T

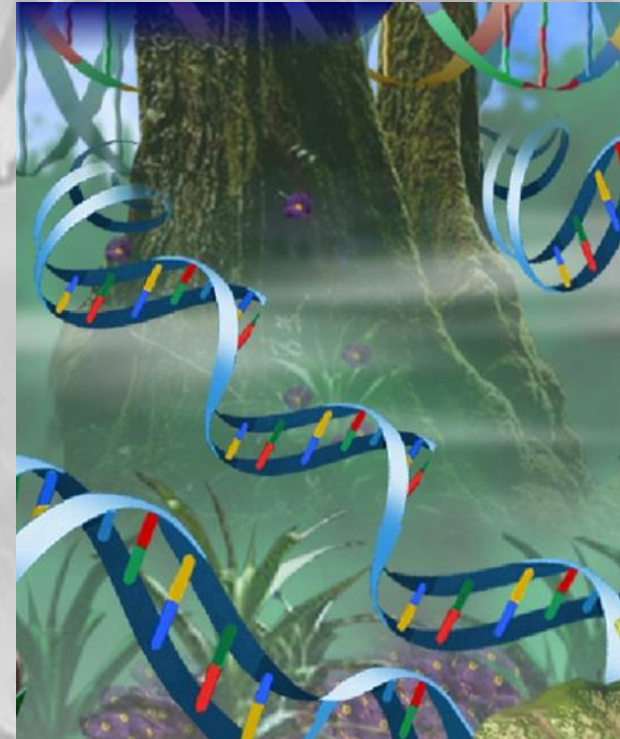


Allele
Variation Class: SNV: single nucleotide variation
RefSNP Alleles: A/G (REV)
Allele Origin:
Ancestral Allele: G
Variation View:
Clinical Significance: With drug-response allele [ClinVar]
MAF/MinorAlleleCount: T=0.2168/20373 (ESP), T=0.2604/1304 (1000 Genomes), T=0.2908/3782 (GO-ESP), T=0.2639/7685 (TOPMED)



NÚCLEO DE QUITO

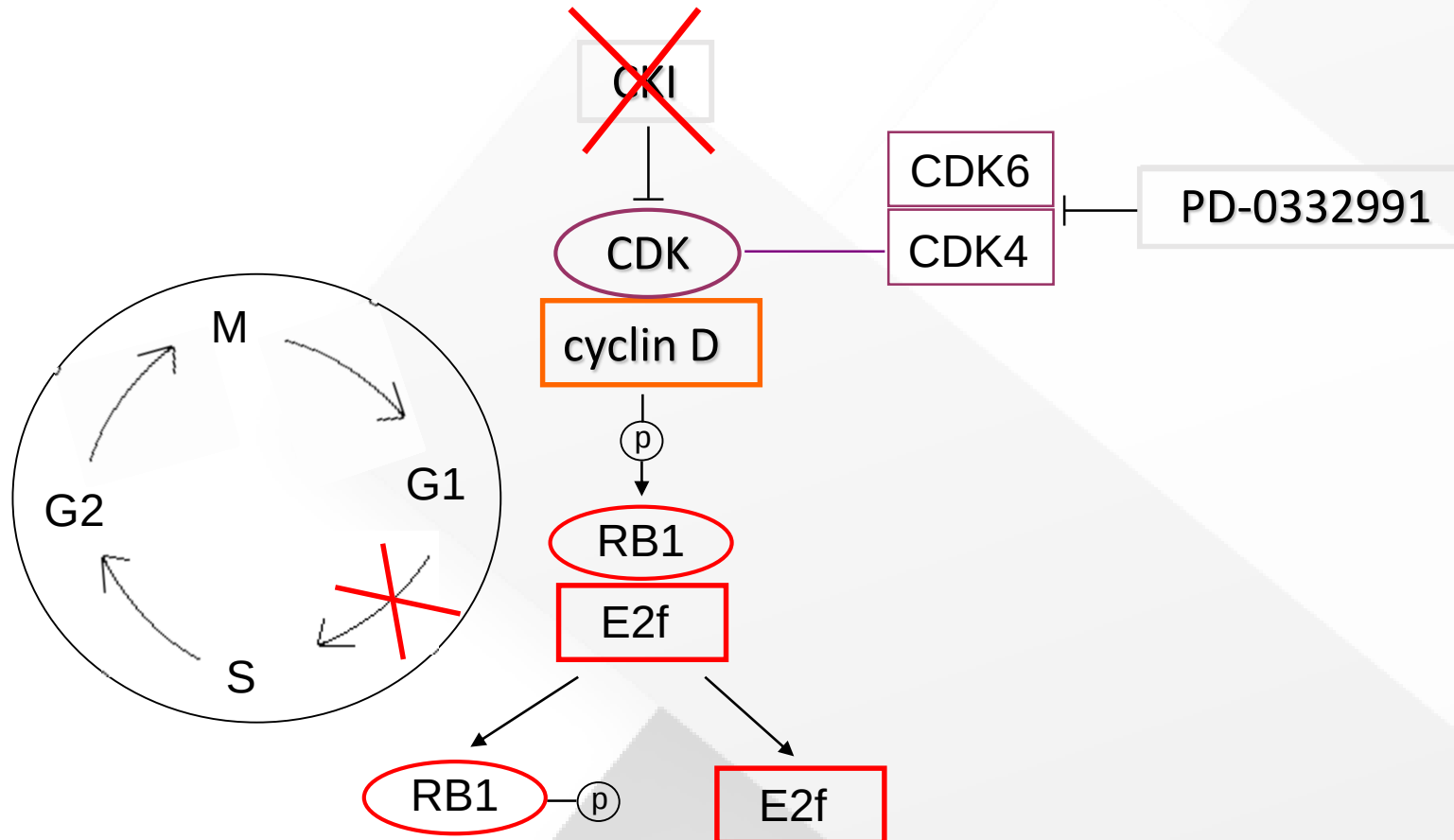
ADN: base del cáncer





NÚCLEO DE QUITO

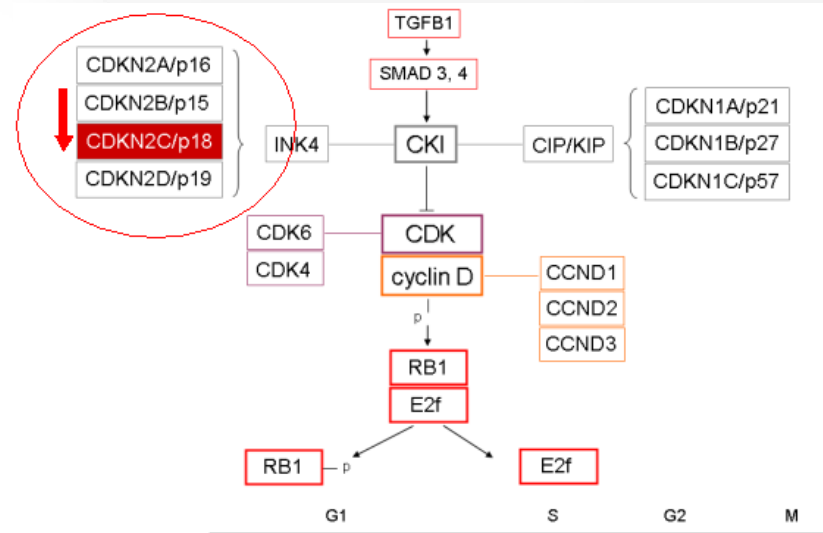
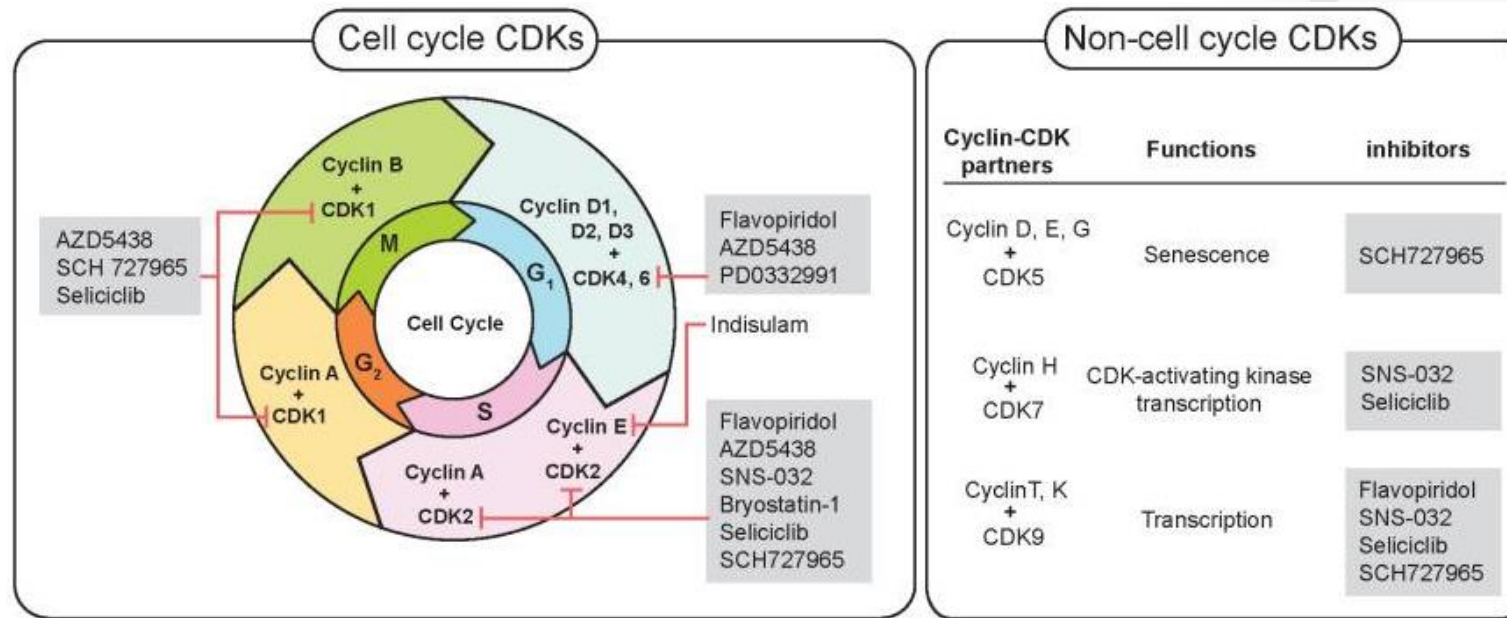
PD-0332991: Inhibidor de CDK4 y CDK6





NÚCLEO DE QUITO

Inhibidores de CDKs





NÚCLEO DE QUITO

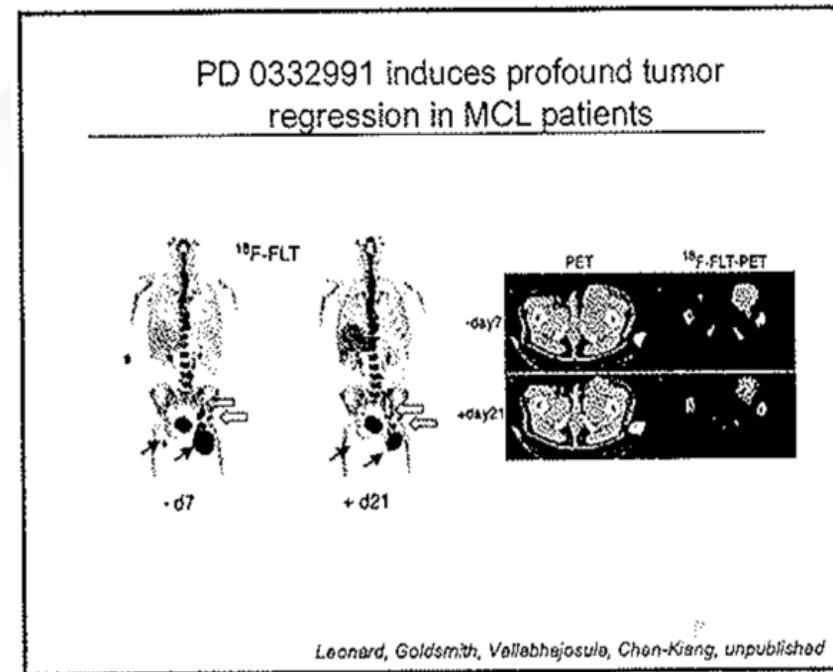
www.aacrjournals.org

Clin Cancer Res 2008;14(19), 2008

Human Cancer Biology

Deletions of *CDKN2C* in Multiple Myeloma: Biological and Clinical Implications

Paola E. Leone,¹ Brian A. Walker,¹ Matthew W. Jenner,¹ Laura Chiecchio,² GianPaolo Dagrada,² Rebecca K.M. Protheroe,² David C. Johnson,¹ Nicholas J. Dickens,¹ Jose Luis Brito,¹ Monica Else,¹ David Gonzalez,¹ Fiona M. Ross,² Selina Chen-Kiang,³ Faith E. Davies,¹ and Gareth J. Morgan¹



Fuente: *Emerging Approaches in Apoptotic and Cell Cycle Control of Hematopoietic Malignancies*, ASH 2008



NÚCLEO DE QUITO

Ensayo clínico usando PD-0332991 en Mieloma

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

[Home](#) [Search](#) [Study Topics](#) [Glossary](#)

Search

[Full Text View](#) [Tabular View](#) [No Study Results Posted](#) [Related Studies](#)

An Investigational Drug, PD 0332991, Is Being Studied In Combination With Velcade And Dexamethasone In Patients With Multiple Myeloma. Patients Must Have Received Prior Treatment For Multiple Myeloma.

This study is currently recruiting participants.

Verified by Pfizer, May 2010

First Received: November 8, 2007 Last Updated: May 20, 2010 [History of Changes](#)

Sponsor:	Pfizer
Information provided by:	Pfizer
ClinicalTrials.gov Identifier:	NCT00555906

palbociclib

► Purpose

This is a Phase 1/2 study evaluating the safety and anti-tumor activity of PD 0332991 in combination with Velcade and dexamethasone in patients who have received at least one previous treatment for multiple myeloma.

Condition	Intervention	Phase
Multiple Myeloma	Drug: Bortezomib Drug: Dexamethasone Drug: PD 0332991	Phase I Phase II

Further study details as provided by Pfizer:

Estimated Enrollment: 62
Study Start Date: January 2008
Estimated Study Completion Date: February 2013
Estimated Primary Completion Date: February 2012 (Final data collection date for primary outcome measure)

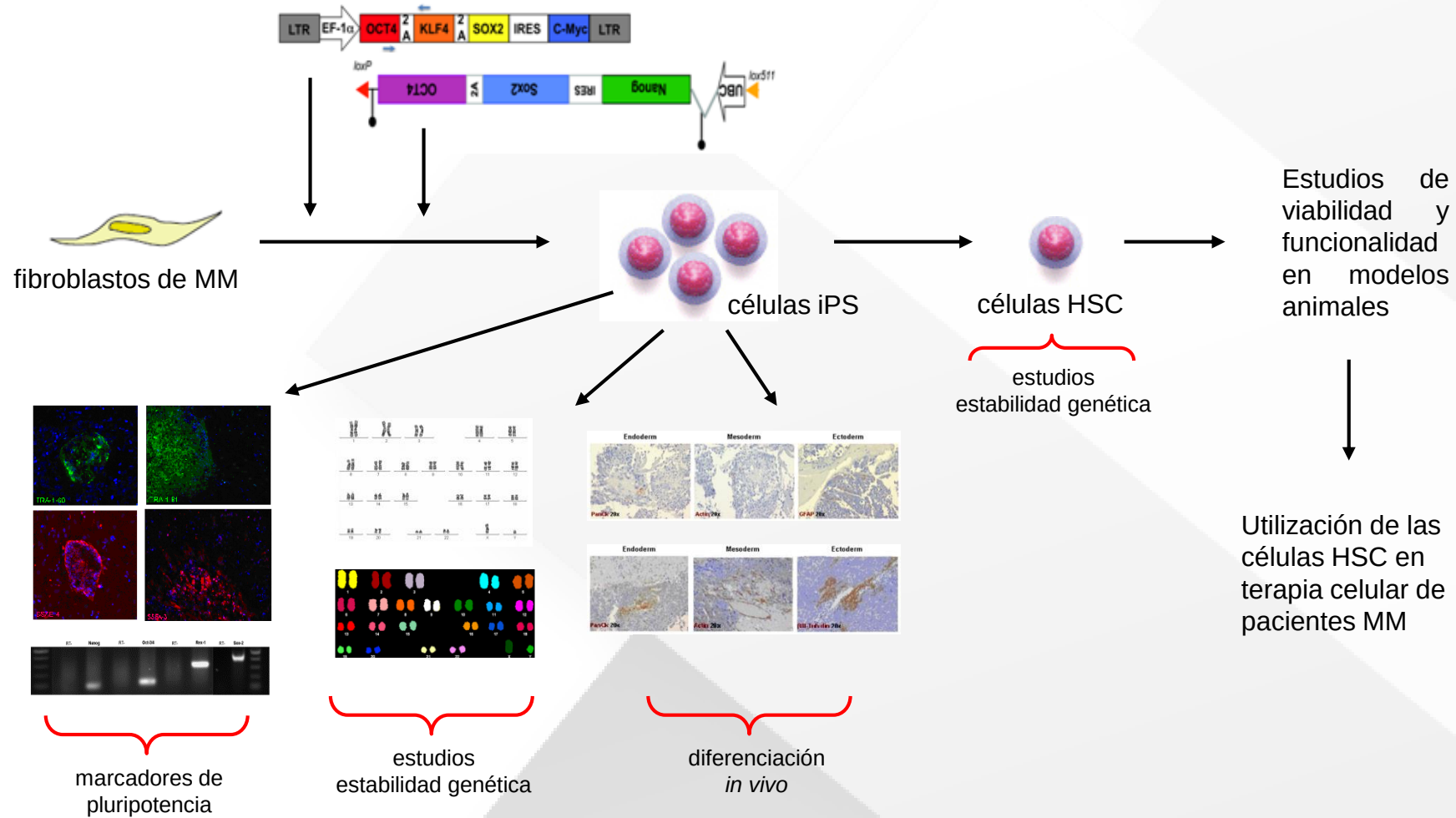
Arms	Assigned Interventions
1: Experimental	Drug: Bortezomib Escalating doses of bortezomib will be administered intravenously on Days 8, 11, 15 and 18 of a 28-day cycle (Schedule A) or of a 21-day cycle (Schedule B). The planned doses to be evaluated are 0.7, 1 and 1.3 mg/m ² in combination with PD 0332991 and dexamethasone. Drug: Dexamethasone 20 mg, orally on Days 8, 11, 15 and 18 of a 28 day cycle (Schedule A) or of a 21-day cycle (Schedule B) in combination with PD 0332991 and bortezomib. Drug: PD 0332991 Escalating doses of PD 0332991 will be administered orally on Days 1-21 of a 28-day cycle for Schedule A and on Days 1-12 of a 21-day cycle for Schedule B. The planned doses to be evaluated are 50, 75, 100 mg and 125 mg once daily in combination with bortezomib and dexamethasone.

Fuente: modificado de <http://clinicaltrials.gov/ct2/show/NCT00555906>



NÚCLEO DE QUITO

Reprogramación células madre pluripotentes

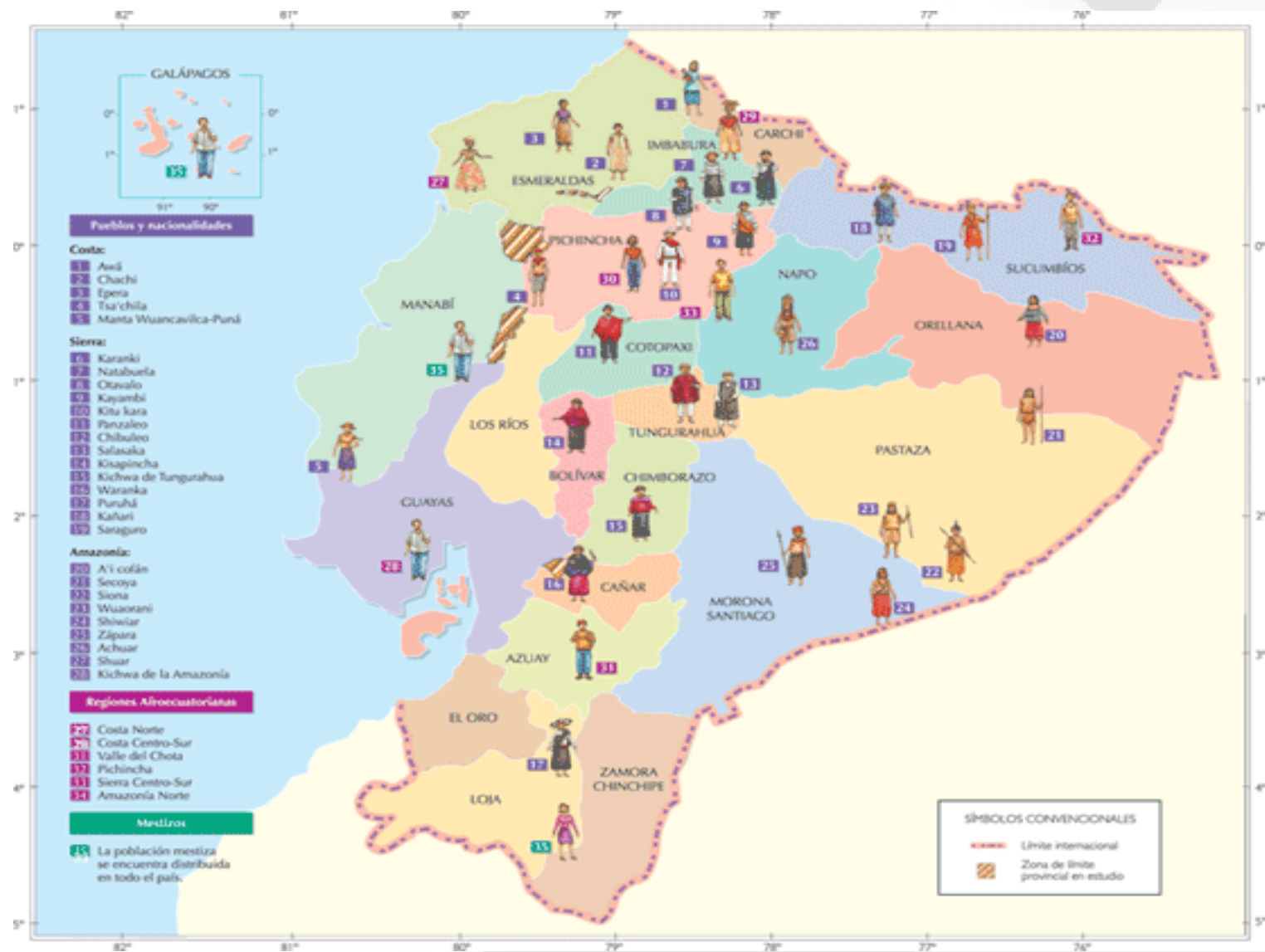


Proyecto de Investigación en Salud – ISCIII. PI11/00125: Generación de células madre pluripotentes humanas a partir de fibroblastos de pacientes con mieloma múltiple



NÚCLEO DE QUITO

Grupos étnicos del Ecuador



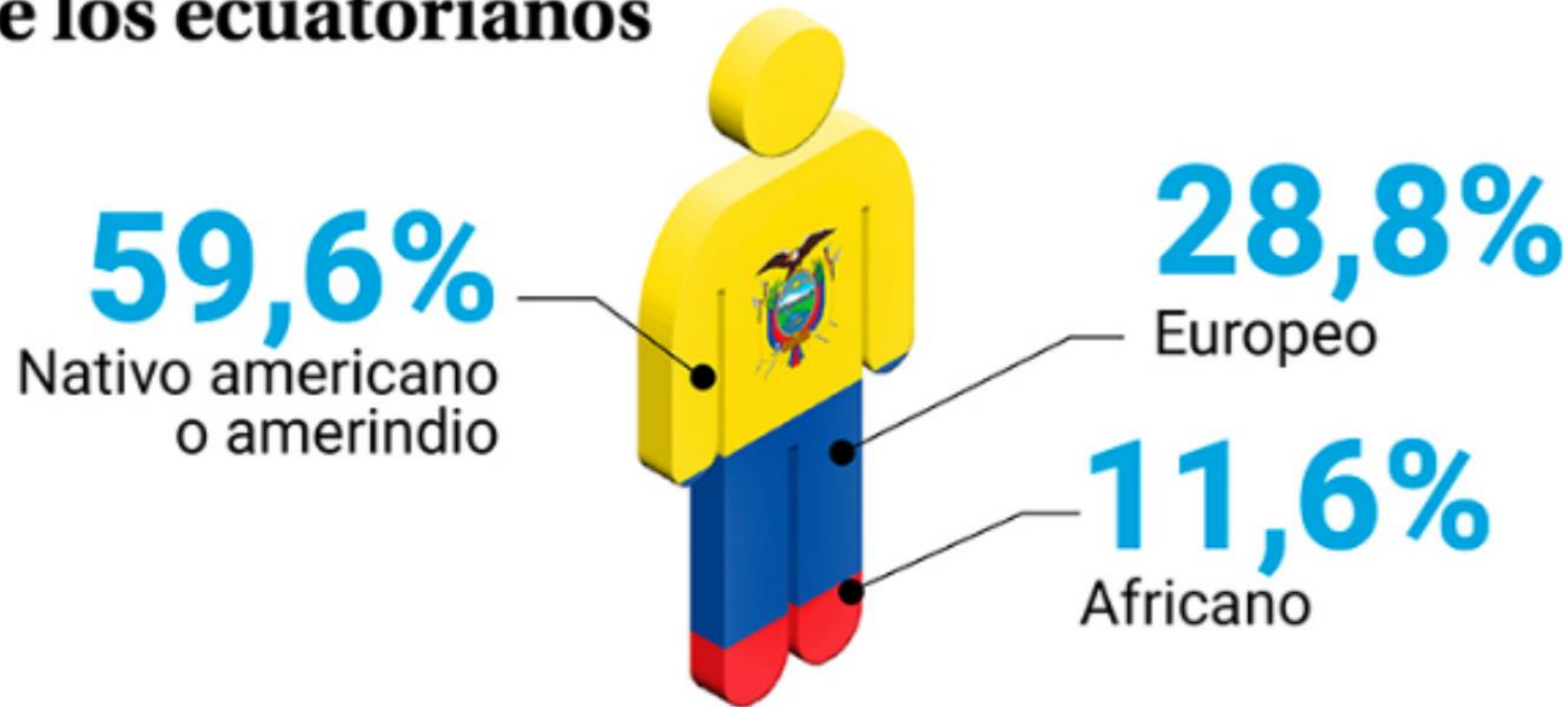


NÚCLEO DE QUITO

Población ecuatoriana: Trihíbrida

Composición genética de los ecuatorianos

PRIMICIAS

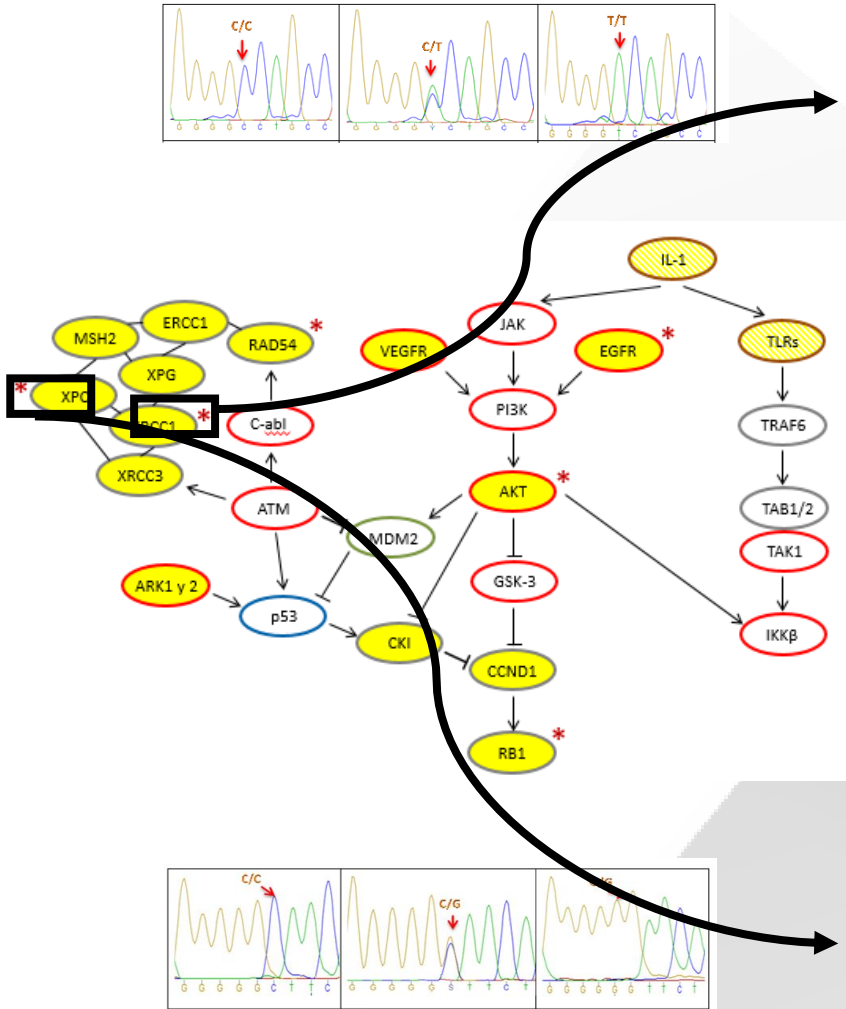


Composición genética de los ecuatorianos Fuente: Centro de Investigación Genética y Genómica – CIGG de la Universidad UTE

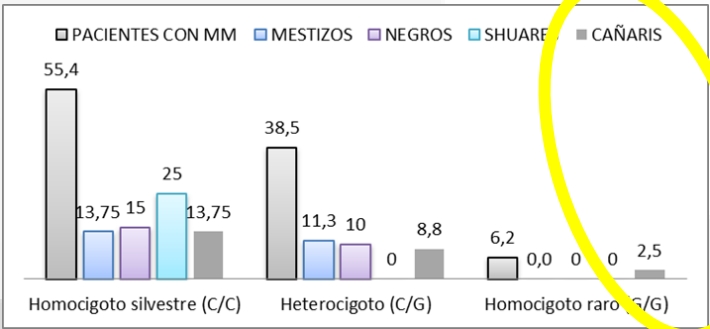
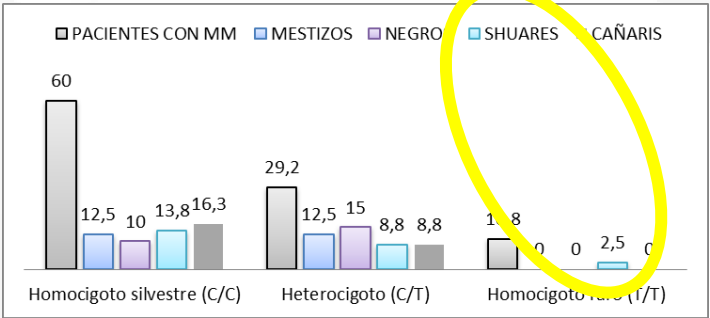


NÚCLEO DE QUITO

Mieloma múltiple: afectados



mutación	proteína	tipo	gen
43.551.656 C>T	Q426Stop	Nonsense	exon 10



mutación	proteína	tipo	gen
14.146.053 C>G	W904S	Missense	exon 15



Protein

CAGCAGCAG...

≤ 21

Cáncer

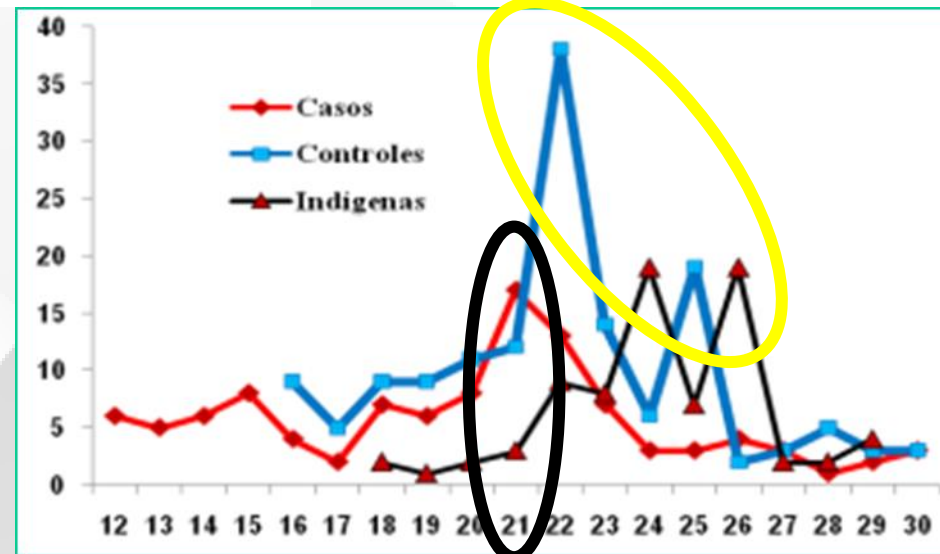
Triplet Repeat

CAGCAGCAGCAGCAGCAGCAGCAGCAGCAG...

≥ 22

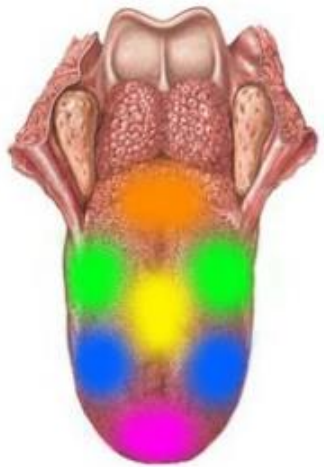
Normal

Protein



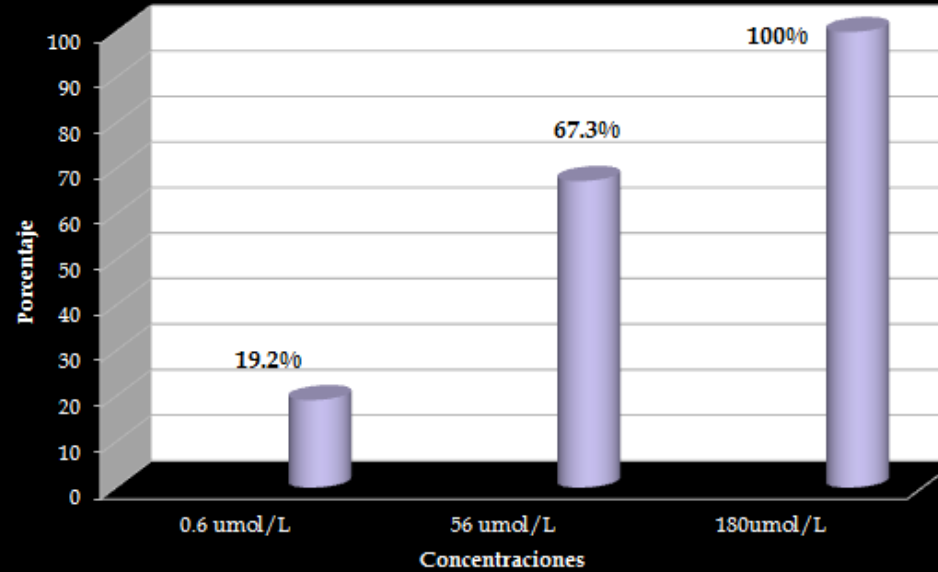


NÚCLEO DE QUITO



- Amargo
- Ácido / Agrio
- Umami
- Salado
- Dulce

Percepción del sabor amargo



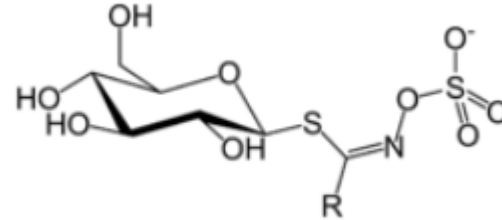
	Dosis (totales)		
	0,001%	0,08%	0,25%
# Individuos	10/52	35/52	52/52
Porcentaje	19,2%	67,3%	100%

Concentración umbral: inferior a 0,6 umol/L – 0,001% (Wittig de Penna, 2001)



NÚCLEO DE QUITO

Falta de percepción de sabor amargo asociado a cáncer de Tiroides y Colon



Zonas abundante Yodo

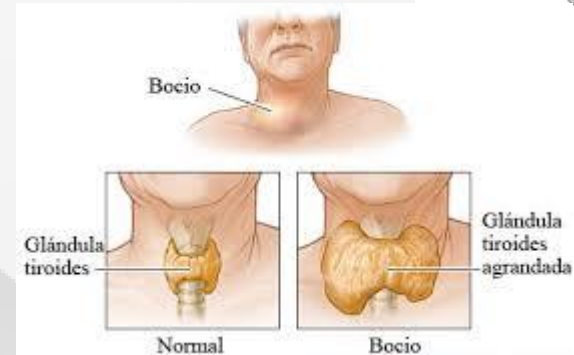
glucosinolato no inhibe la función de tiroides

Ventaja: no detectar el sabor

Zonas bajo Yodo

glucosinolato podría ser dañino salud

Ventaja: poseer variante sensible

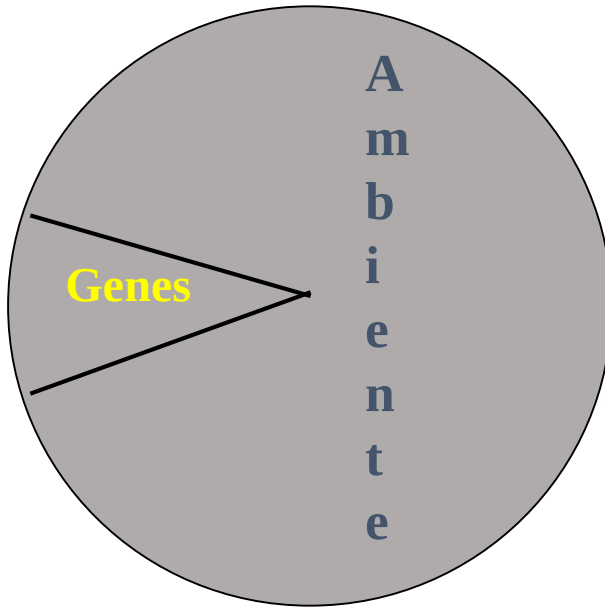




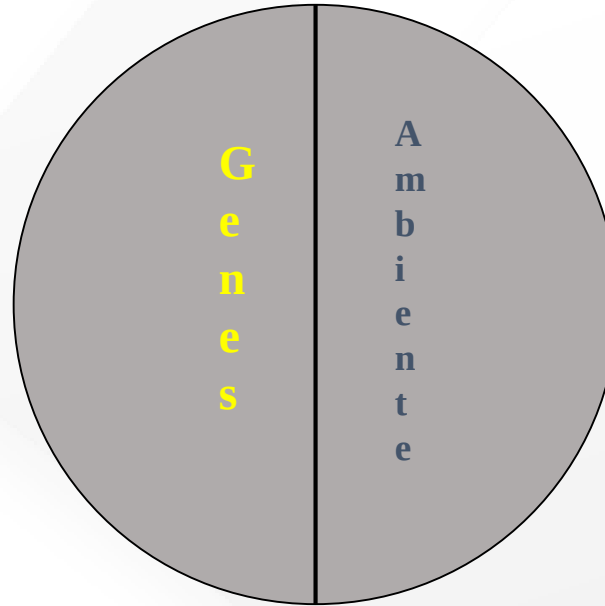
NÚCLEO DE QUITO

Relación Genes y ambiente

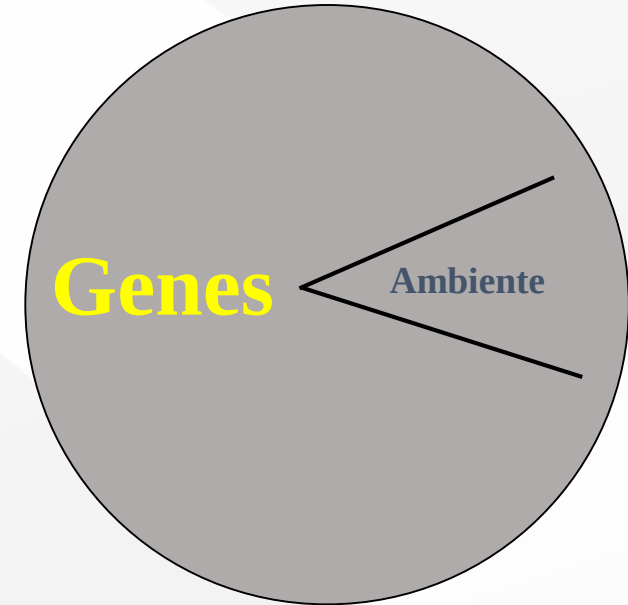
$$\text{FENOTIPO} = \text{GENOTIPO} + \text{AMBIENTE}$$



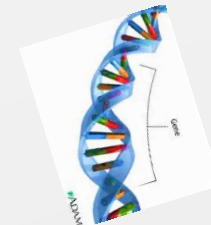
Multifactorial



Multifactorial/Poligénico

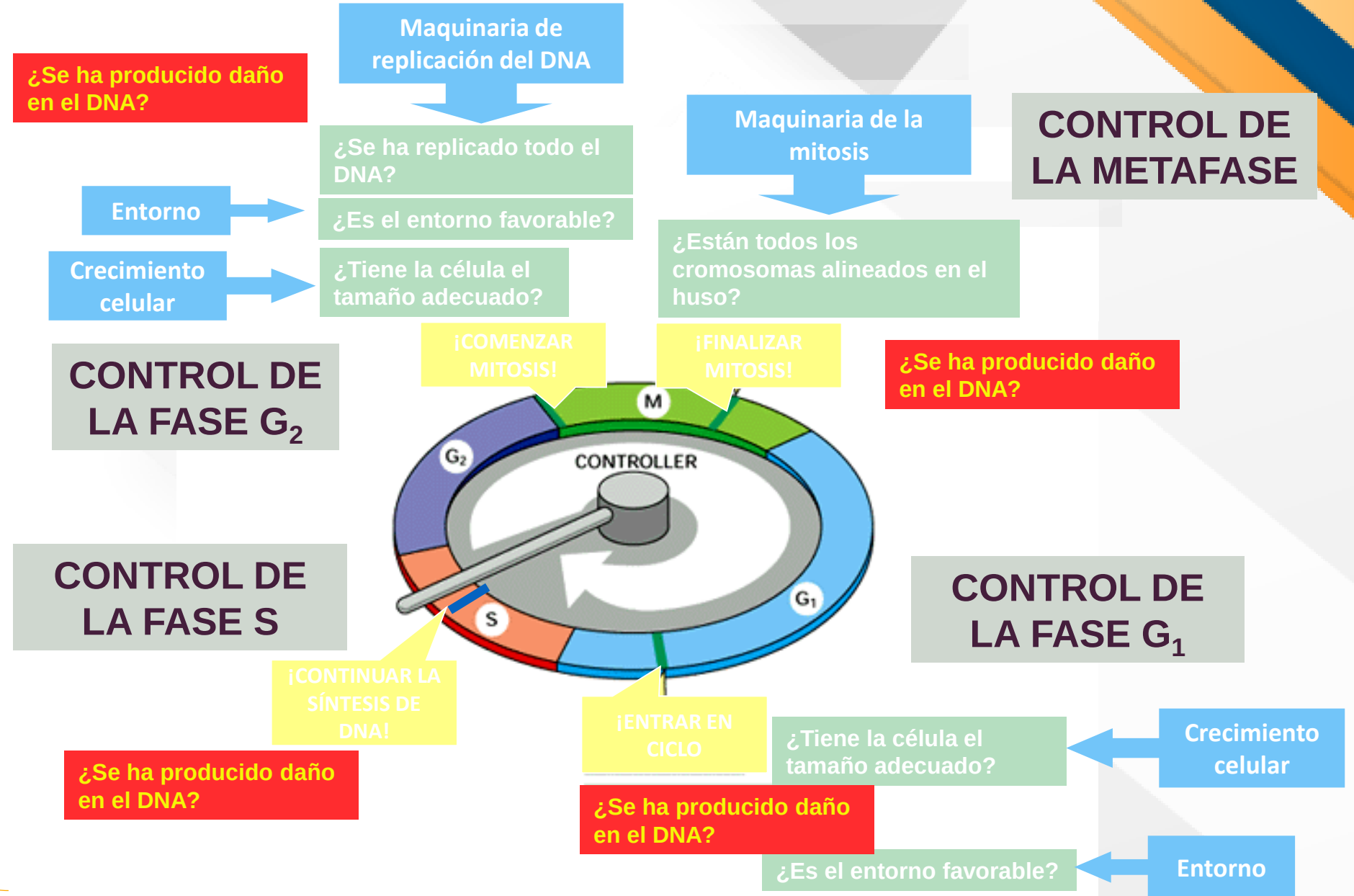
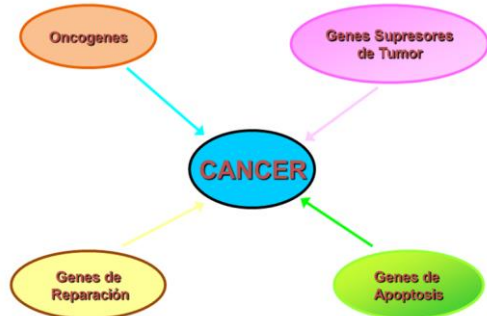


Monogénico





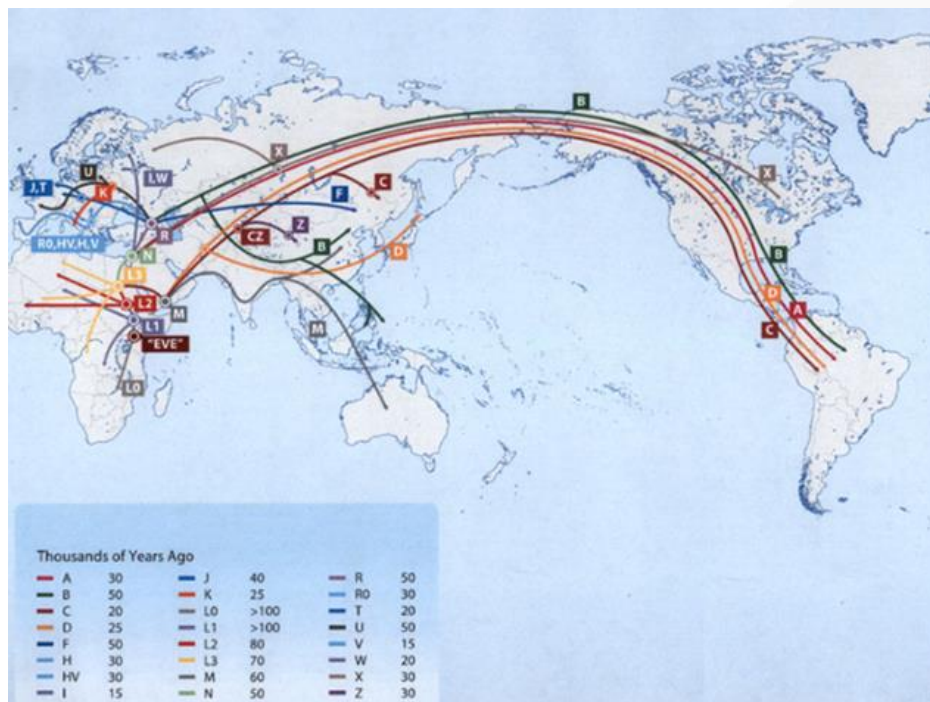
NÚCLEO DE QUITO



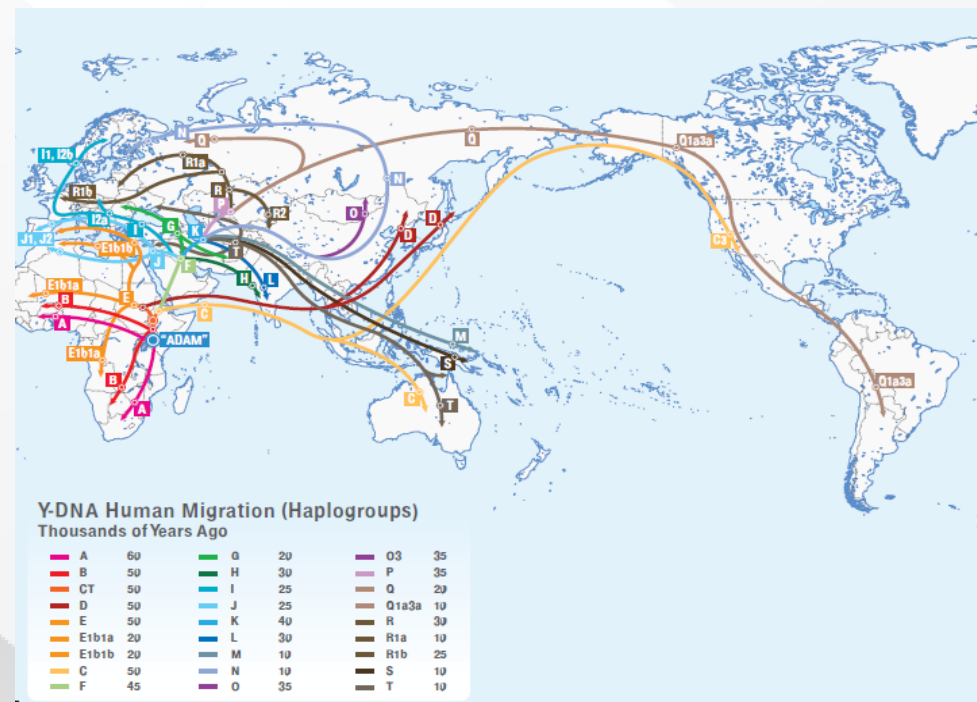


NÚCLEO DE QUITO

Origen de la población americana



ADN mitocondrial

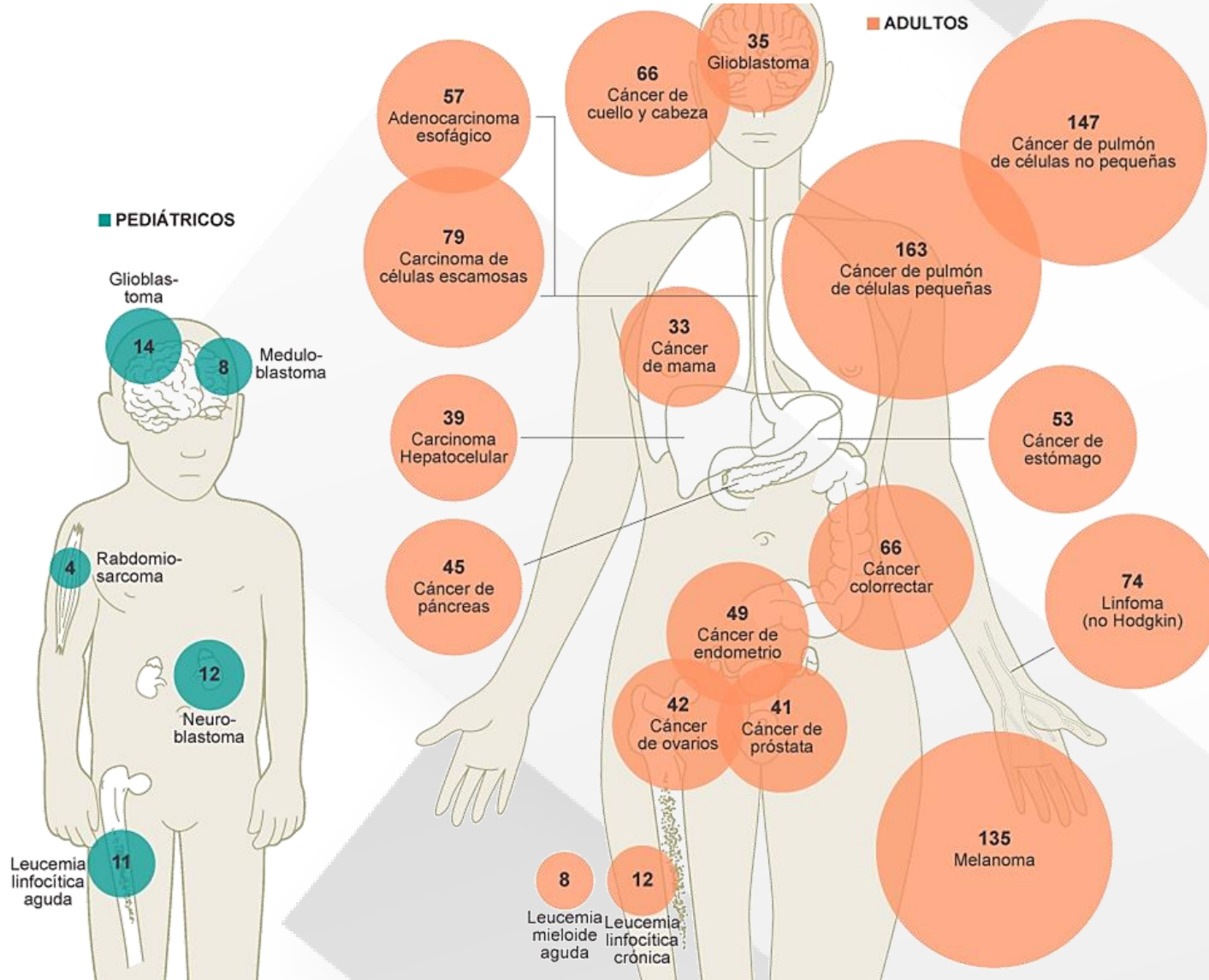


ADN cromosoma Y



NÚCLEO DE QUITO

Genes del cáncer



Tomado de Science, 2013



NÚCLEO DE QUITO

Población ecuatoriana trihíbrida

- Incidencia de enfermedades
- Pronóstico de enfermedades
- Diferente frecuencia de mutaciones
- Mutaciones nuevas
- Diferente respuesta a tratamientos



NÚCLEO DE QUITO

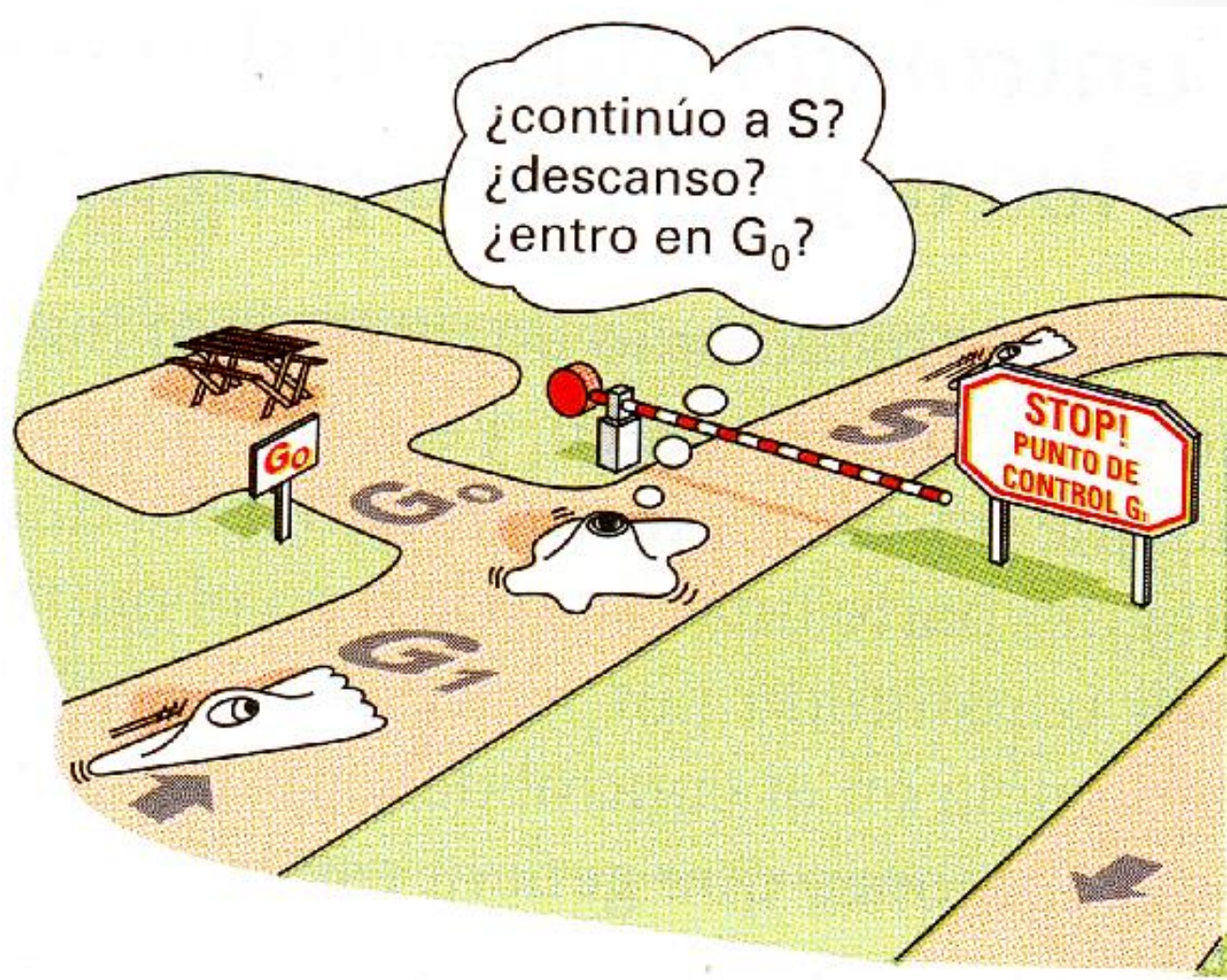
Conclusiones

- El **control** del **ciclo celular** es importante en biología celular y genética.
- Tiene importantes implicaciones prácticas en la **lucha contra el cáncer**, al estar producido por **alteraciones** en la **capacidad** de la célula **de regular** su propia **división**.
- El descubrimiento de genes que codifican **inhibidores** del **ciclo celular**, puso en marcha la **síntesis** de **nuevos** tipos de **fármacos anticancerígenos** que **bloquean** el **crecimiento celular descontrolado** imitando los efectos de estos inhibidores.

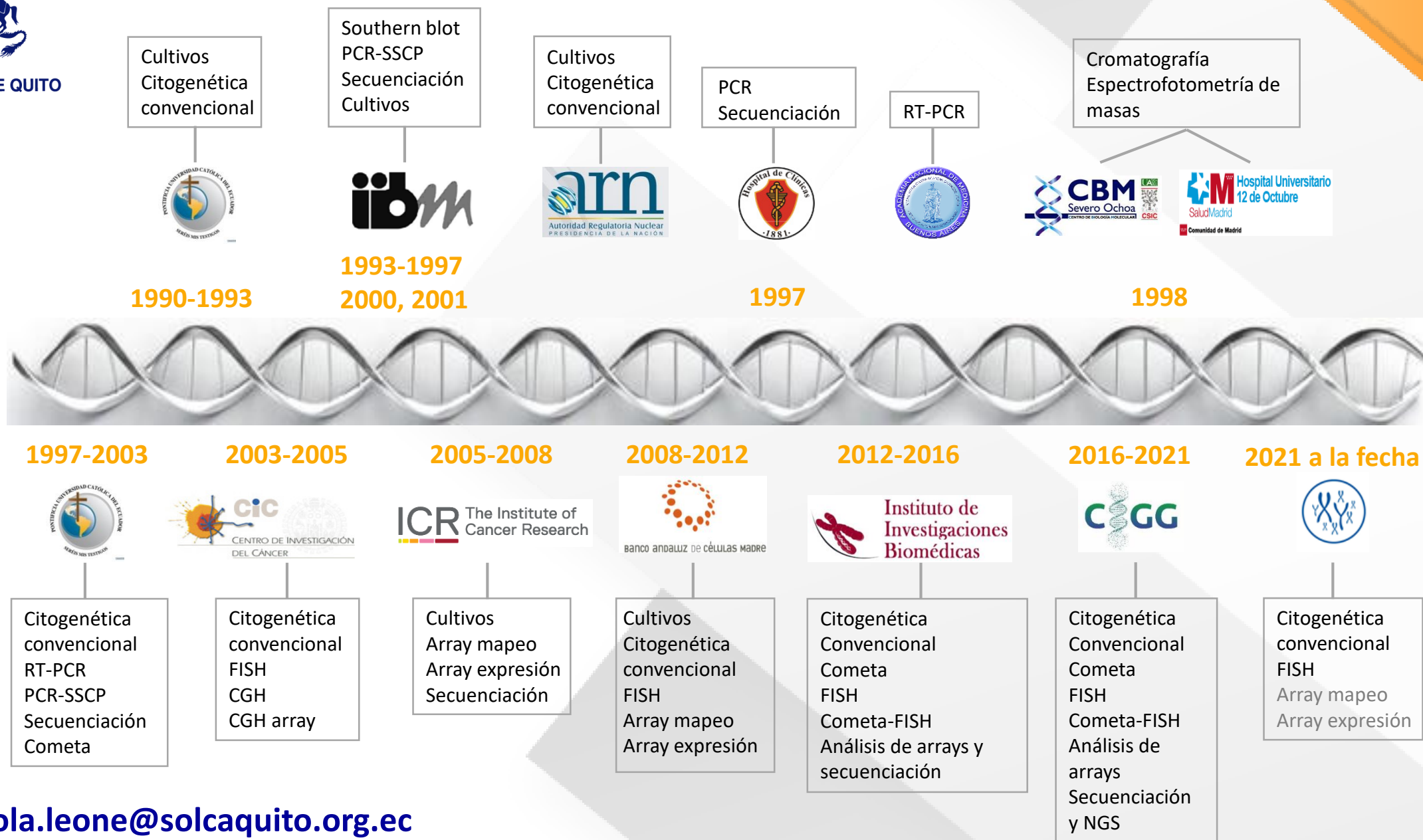


NÚCLEO DE QUITO

... y ahora?



Agradecimientos





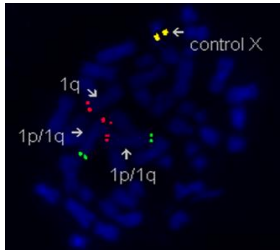
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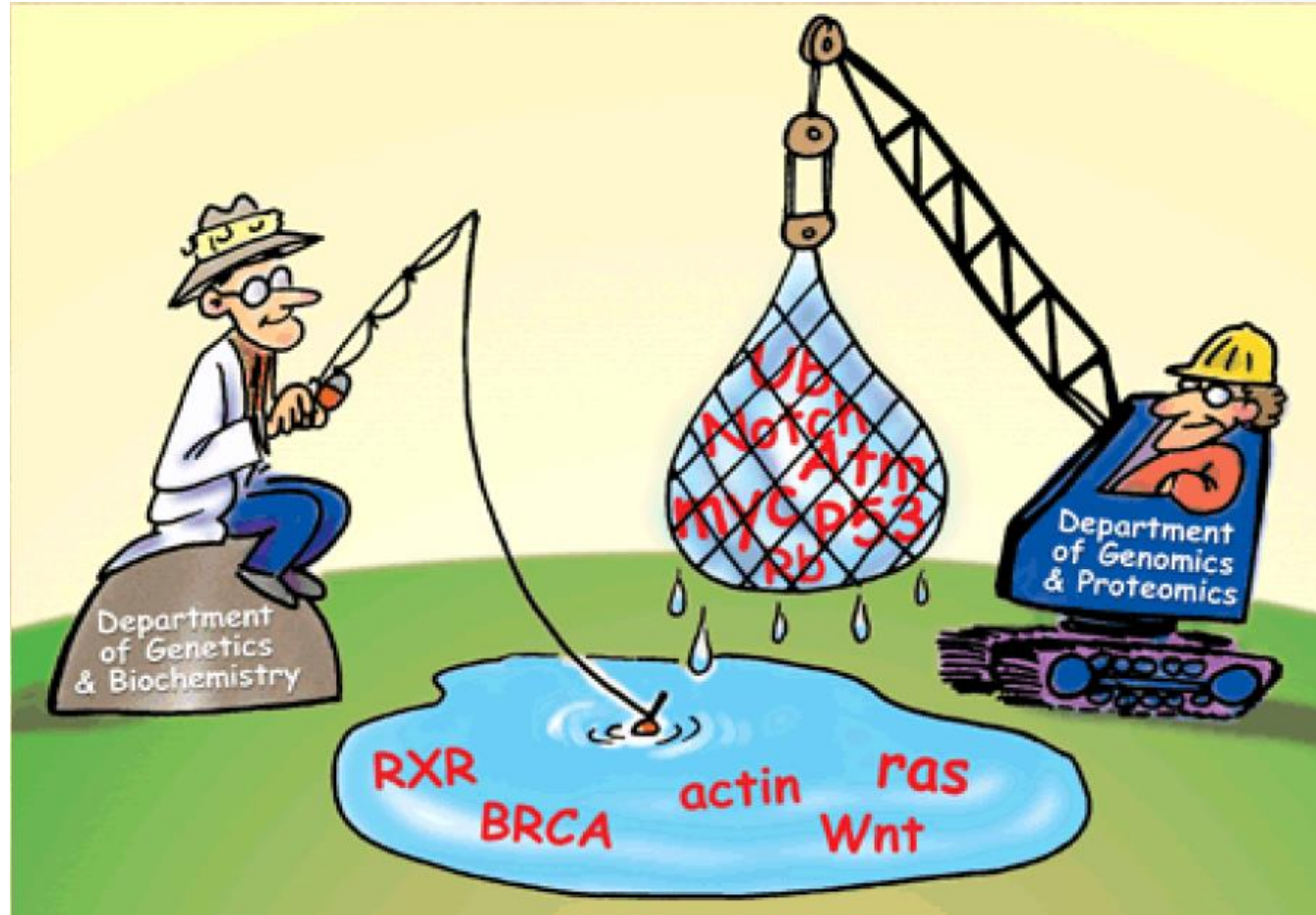


NÚCLEO DE QUITO

Estudio del Genoma completo



FISH



CHIP

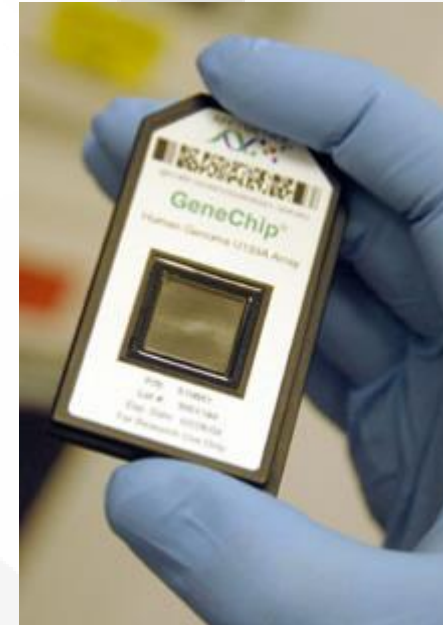
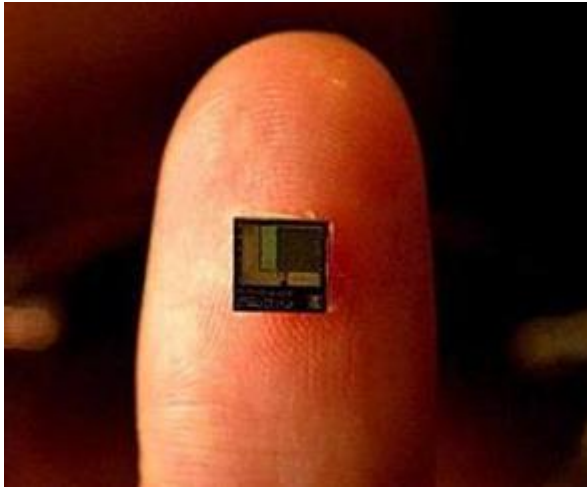
Genoma Humano

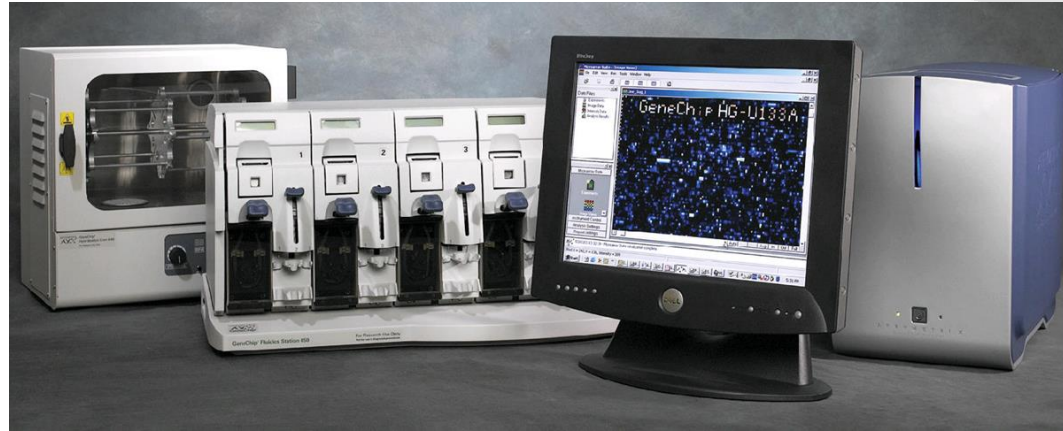




NÚCLEO DE QUITO

Arrays o chips





Equipamiento para realizar los estudios de Arrays



Array de mapeo genético



Array de expresión



NÚCLEO DE QUITO



Secuenciación masiva de genes



MiSeq
15-25 millones de lecturas



NextSeq
130-400 millones de lecturas

Arrays de mapeo genético



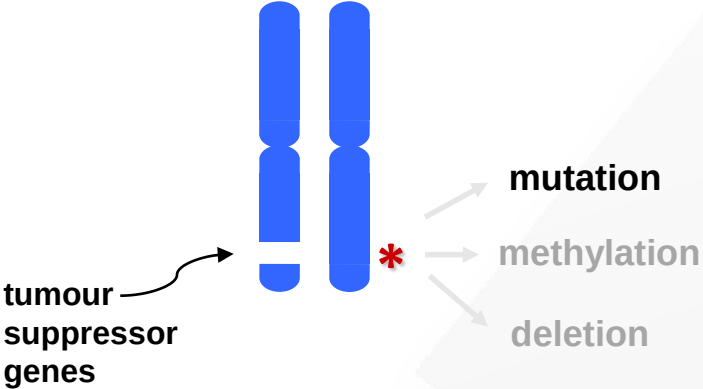
Secuenciación masiva de genes



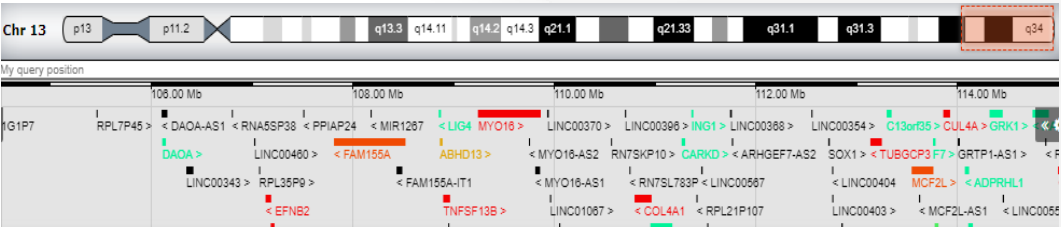


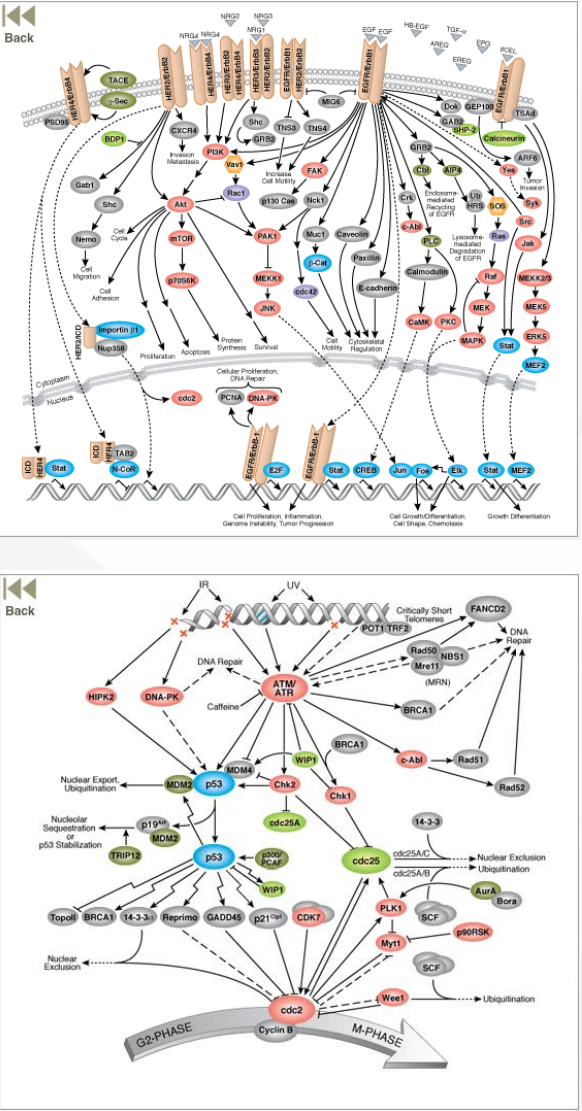
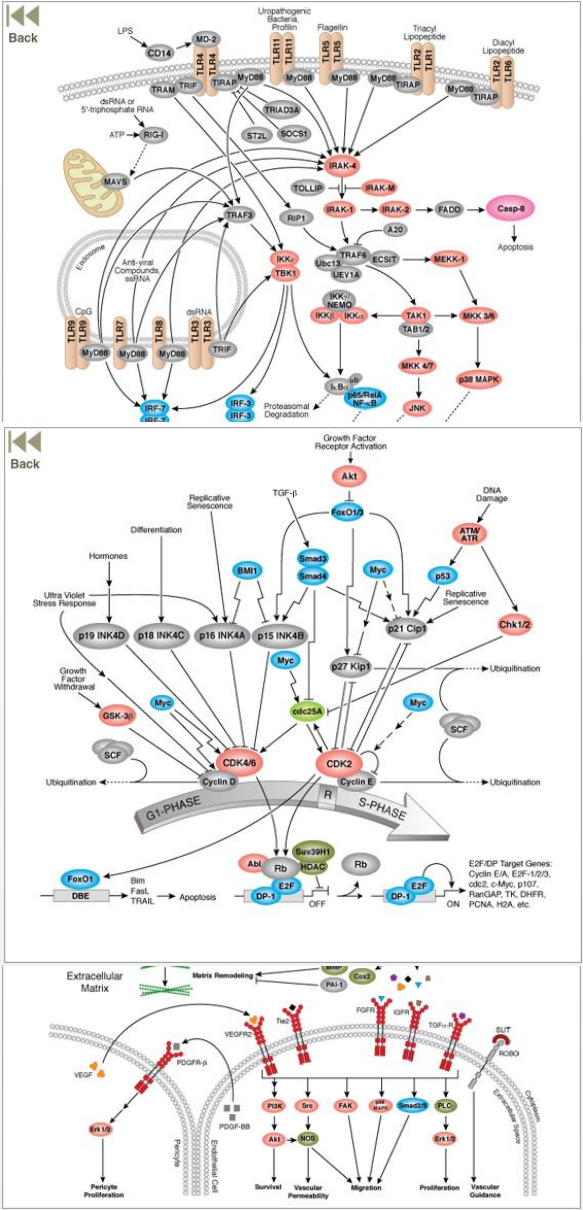
NÚCLEO DE QUITO

En búsqueda de alteraciones del segundo cromosoma



Variante	Gen	Consecuencia	Estado	Significado	Herencia
chr13:103528002	ERCC5	Missense NM_000123.3 c.3310G>C p.(Asp1104His)	Homocigoto	Incierto	HAR
chr17:73513677	TSEN54	Missense NM_207346.2 c.409A>C p.(Ile137Leu)	Homocigoto	Incierto	HAR

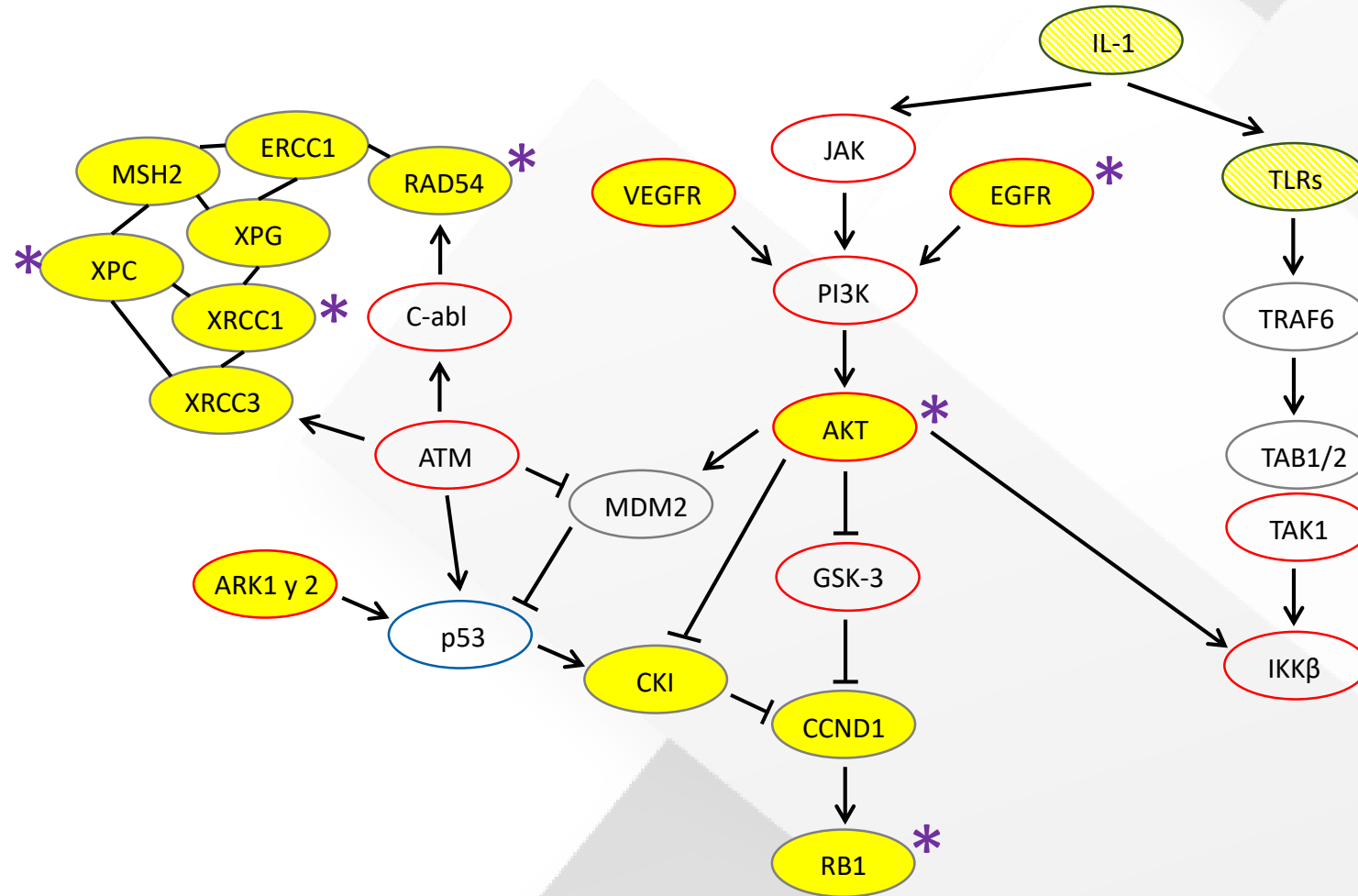






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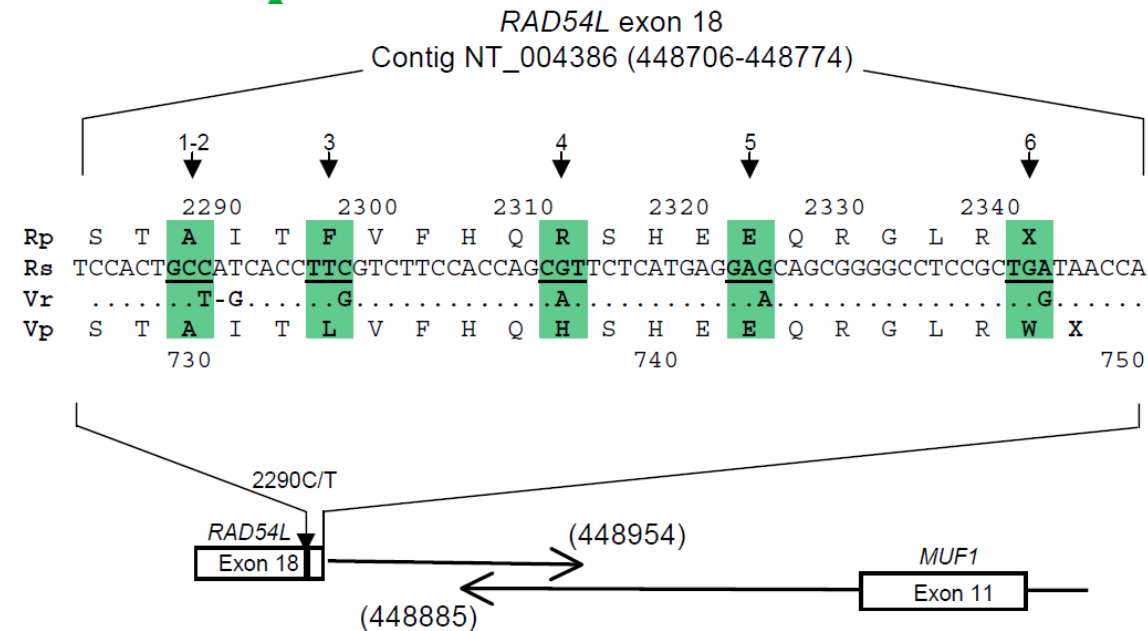
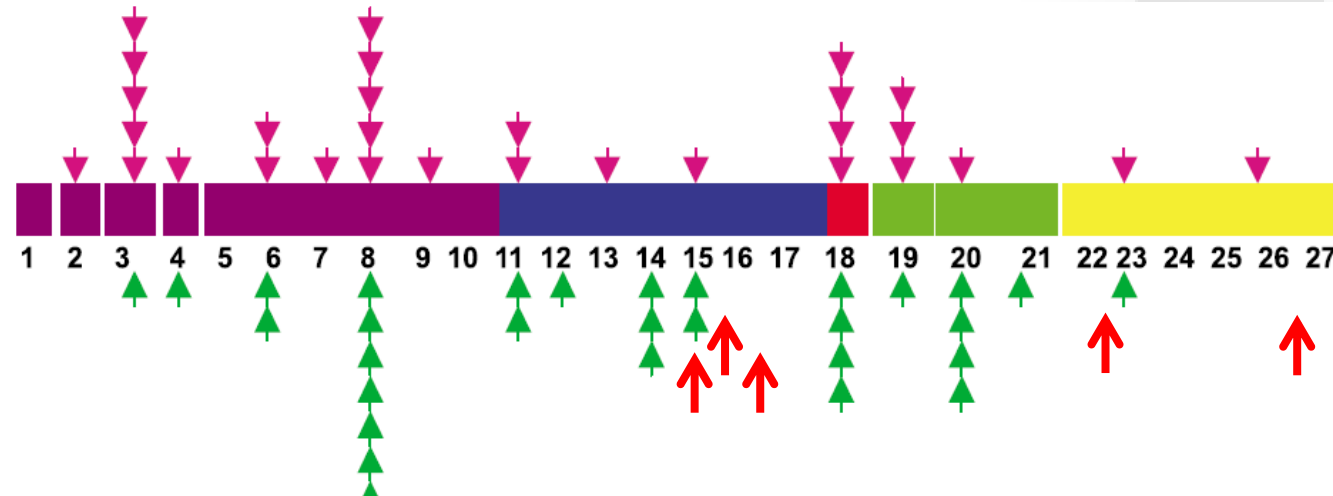
Búsqueda de genes asociados





NÚCLEO DE QUITO

Ecuador: mutaciones nuevas



ABERRACIONES CROMOSÓMICAS



Roturas de cromátide



Roturas cromosómicas



Gap de cromátide



Gap cromosómico



Dicéntrico



Acéntrico



Doble minute



Anillo