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7 DÉCADAS
desde 1954
de atención especializada en cáncer

Genética del cáncer de mama en el Ecuador

Quito, 19 de julio de 2024

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7 DÉCADAS desde 1954
de atención especializada en cáncer

Estudios genéticos realizados en Ecuador desde 1990

Paola E. Leone, PhD, Acad

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Declaración de conflictos de interés	
Título	Genética del cáncer de mama en el Ecuador
Autor	Paola E. Leone
Institución	Laboratorio de Genética y Genómica, SOLCA Quito

No hay conflictos de interés por declarar

Estudios genéticos: Fragilidad cromosómica

5 ml sangre periférica

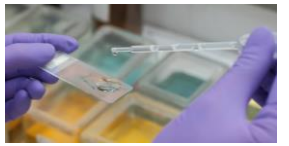
Sembrar en 125 ml RPMI + fitohemaglutinina + afidicolina

Incubar a 37 ºC 72 h

Añadir colchicina

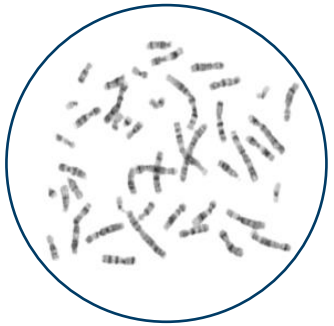
Solución hipotónica salina

Fijación de células

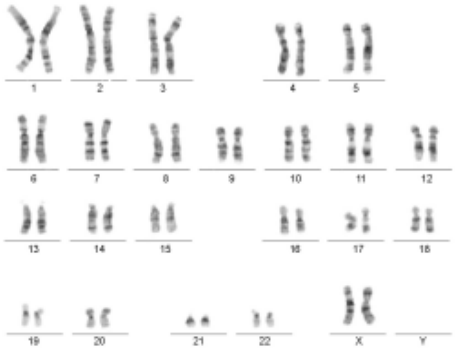


Extensión sobre un portaobjetos por goteo

Tinción



Metafase



Cariotipo

Análisis y Fotografía

Estudios genéticos: Fragilidad cromosómica

No. Interno	Edad
14	64
15	34
25	40
27	32
29	48
33	63
34	56
36	61
45	42
48	50
49	70
68	51
69	52
95	40
103	41
105	68
116	39
127	62
130	62
131	58

Grupo	Medio	No. Metafases analizadas	No. Metafases con Fra	Porcentaje	*P*	
Ca. mama	N	2.000	606	30,3	< 0,001	< 0,001
Ca. mama	Af	2.000	970	48,5		
Control	N	2.000	36	1,8	> 0,04	
Control	Af	2.000	50	2,5		

Grupo	Medio	No. Metafases analizadas	Espaciamiento (g)		Rotura (b)		Fragmento acéntrico
			cromátide	cromosómico	cromátide	cromosómico	
Ca. mama	N	2.000	448	674	34	14	34
Ca. mama	Af	2.000	692	840	50	24	12
Control	N	2.000	13	29	3	3	
Control	Af	2.000	19	32	4	2	1

No.	Sexo	Edad (años)		
		rango	media	mediana
20	F	32 - 70	51,7	51,5

1990-1997: **20** Ca. Mama / 20 controles

Cancer Genet Cytogenet. 1997; 94(2),120-4;
Am J Hum Genet. 1991; 49(4),247

Estudios genéticos: Fragilidad cromosómica

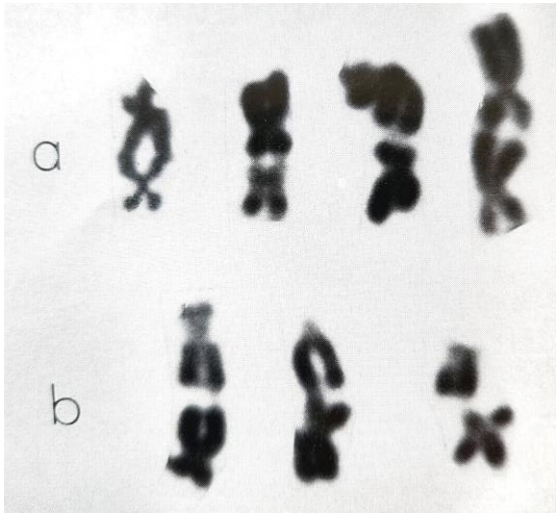
Grupo	Medio	No. Metafases analizadas	Hipodiploidía		Hiperdiploidía	Poliploidía	*P*
			44	45	(47 - 57)	(± 92)	
Ca. mama	N	2.000	150	242	48	40	< 0,001
Ca. mama	Af	2.000	134	328	44	22	
Control	N	2.000	2	2		8	
Control	Af	2.000	1	2		4	

1990-1997: **20** Ca. Mama / 20 controles

Cancer Genet Cytogenet. 1997; 94(2),120-4;

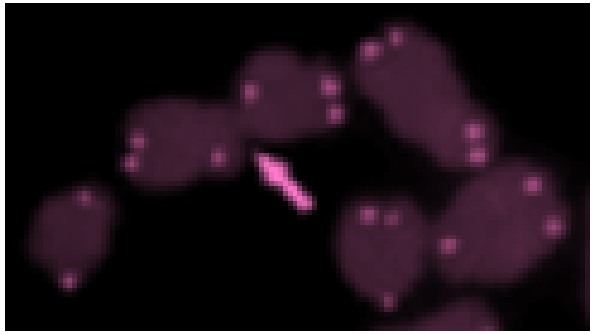
Am J Hum Genet. 1991; 49(4),247

Estudios genéticos: Asociaciones teloméricas



Grupo	Medio	No. Metafases analizadas	No. Metafases con AT	Porcentaje	*P*	
Ca. mama	N	2.000	191	9,55	< 0,05	< 0,001
Ca. mama	Af	2.000	227	11,35		
Control	N	2.000	2	0,10	> 0,05	
Control	Af	2.000	2	0,10		

1990-1997: **20** Ca. Mama / 20 controles



Cancer Genet Cytogenet. 1997; 98(2),115-8

Estudios genéticos: Citogenética en pieza tumoral

Fecha	No. Interno	HC	Sexo	Edad	Cariotipo
29/1/1999	154	49.293	F	43	46,XX[20]
23/10/2000	392	55.077	F	58	NM
20/6/2001	527	51.768	F	52	46,XX[20]
6/9/2001	577	58.808	F	22	NM
21/1/2002	663	59.445	F	62	46,XX[20]
8/5/2002	763	61.442	M	74	NM
6/5/2003	1001	58.927	M	33	46,XY[20]
30/3/2006	1639	101.444	F	43	46,XX[20]
14/8/2006	1719	59.238	F	53	46,XX[20]
6/2/2007	1814	107.656	F	64	46,XX[20]
9/2/2007	1817	85.414	F	70	46,XX[20]/89,XX[1]
21/3/2007	1835	97.666	F	61	46,XX[20]/46,XX,del(16)(q2?)[1]
13/9/2007	1924	106.950	F	34	46,XY[20]
18/1/2008	1971	125.321	F	59	46,XX[8]
23/1/2008	1973	99.429	F	40	46,XX[5]
5/3/2008	1993	101.472	F	57	NM
14/7/2008	2059	141.474	F	44	NM
10/12/2008	2140	85.695	F	43	46,XX[20]/160,XX[1]

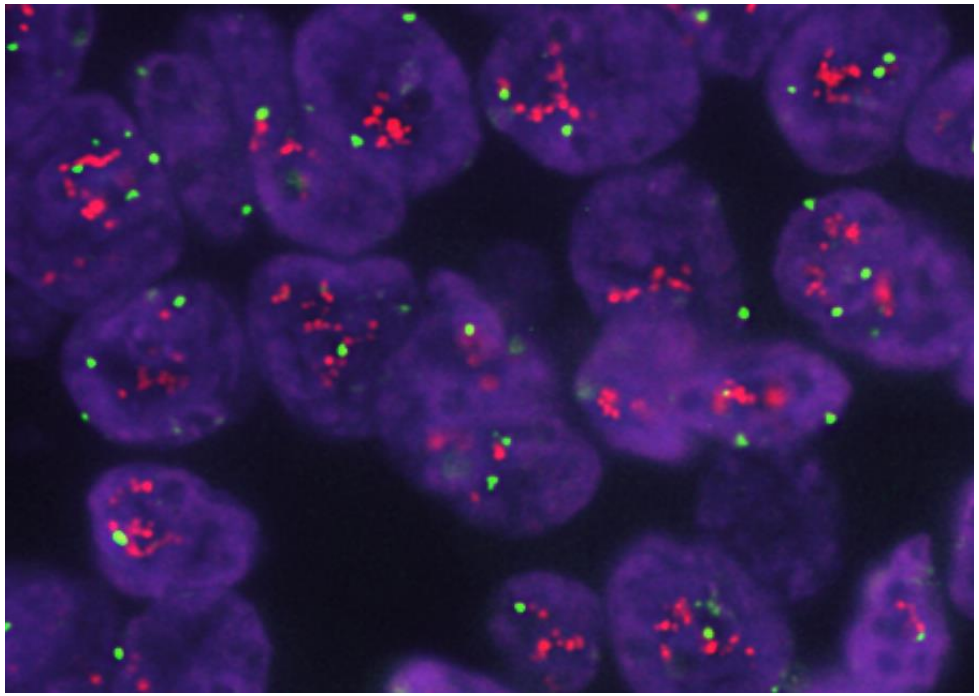
Fecha	No. Interno	HC	Sexo	Edad	Cariotipo
19/2/2010	2411	126.360	F	61	NM
14/4/2010	2436	84.584	F	50	46,XX[20]
5/5/2010	2444	102.408	F	72	46,XX[20]
19/7/2010	2477	144.838	F	52	46,XX[16]/47,XX,+ace[4]
6/1/2011	2533	147.164	F	47	46,XX[20]
28/4/2011	2580	84.046	F	68	46,XX[20]/94,XX[1]
19/5/2011	2589	112.557	F	61	46,XX[20]
14/2/2012	2713	149.045	M	41	46,XX[20]
16/3/2012	2732	74.535	F	58	46,XX[20]
7/6/2012	2771	111.419	F	46	46,XX[3]
3/10/2012	2838	116.754	F	77	46,XX[20]
8/10/2012	2843	65.482	F	66	46,XX[20]
10/10/2012	2845	58.024	F	62	NM
27/11/2012	2868	102.289	F	60	46,XX[20]
11/12/2012	2878	186.546	F	57	46,XX[15]/47,X,-X,+mar?[1]
26/3/2013	2931	200.540	F	67	46,XX[20]/47,XX,-9,+2mar[1]/89,XY[1]
9/4/2013	2936	174.659	F	53	46,XX[15]
18/4/2013	2942	177.967	F	68	46,XX[20]/88,XX[1]

No.	Sexo	Edad (años)		
		rango	media	mediana
33	F	22 - 77	55,5	58
3	M	33 - 74	49,3	41

1996-2013: **36** Ca. Mama (11,5 %) / 313 tumores sólidos

Datos del Laboratorio de Genética y Genómica, SOLCA

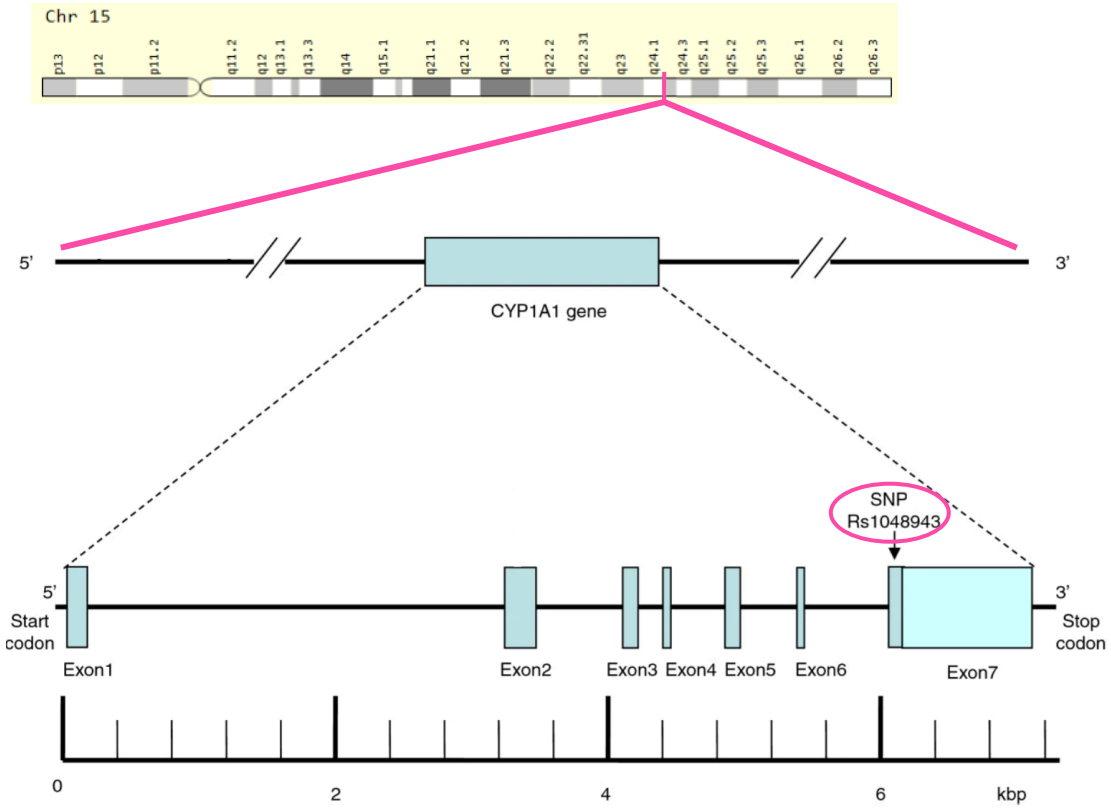
Estudios genéticos: Hibridación *in situ* fluorescente



2011-2020: **82** Ca. Mama (26,8 % amplificación *HER2*)

Datos del Laboratorio de Genética y Genómica, SOLCA

Estudios genéticos: Gen *CYP1A1*



Genotipo	Control	Casos	*P*
Ile/Ile	9	14	> 0,05
Ile/Val	67	59	
Val/Val	15	9	
TOTAL	91	82	

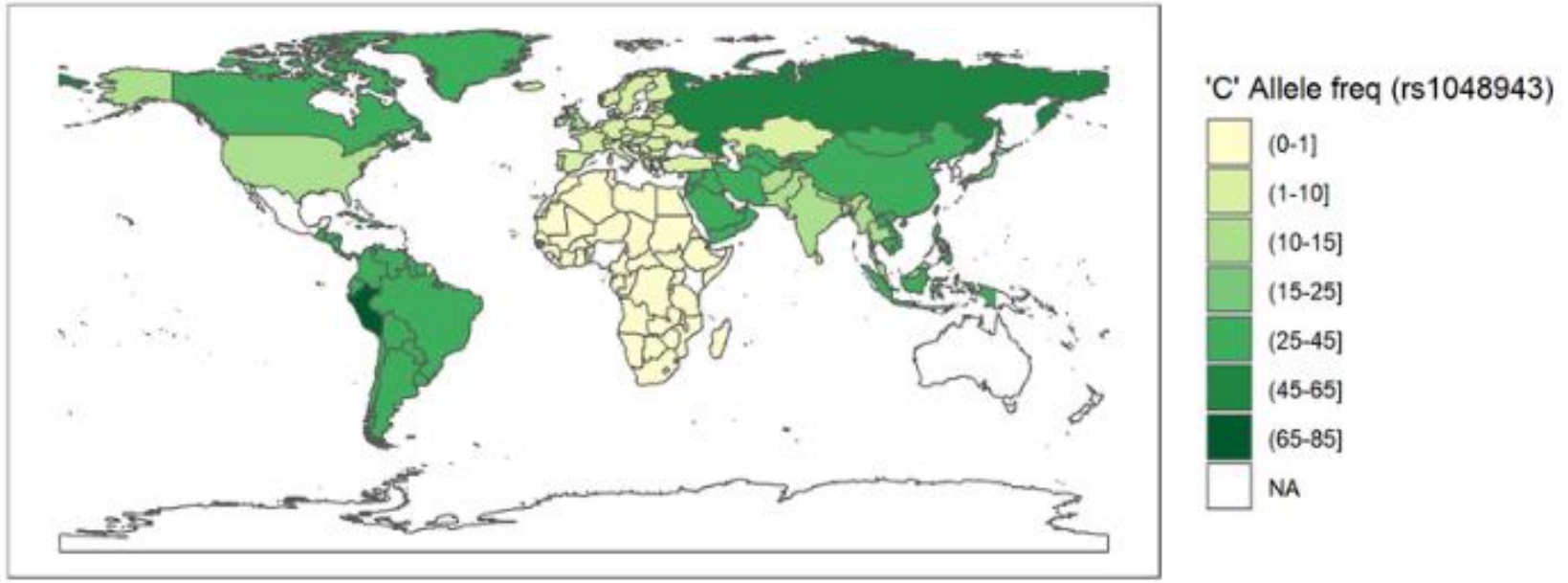
Frecuencia alélica	Control	Casos	*P*
A	0,47	0,53	> 0,05
G	0,53	0,47	

82 Ca. Mama / 91 controles

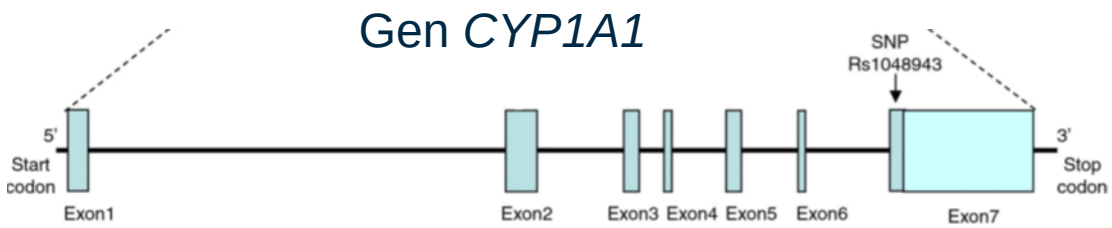
Rev Oncol. 2010; 20(3-4),85-91

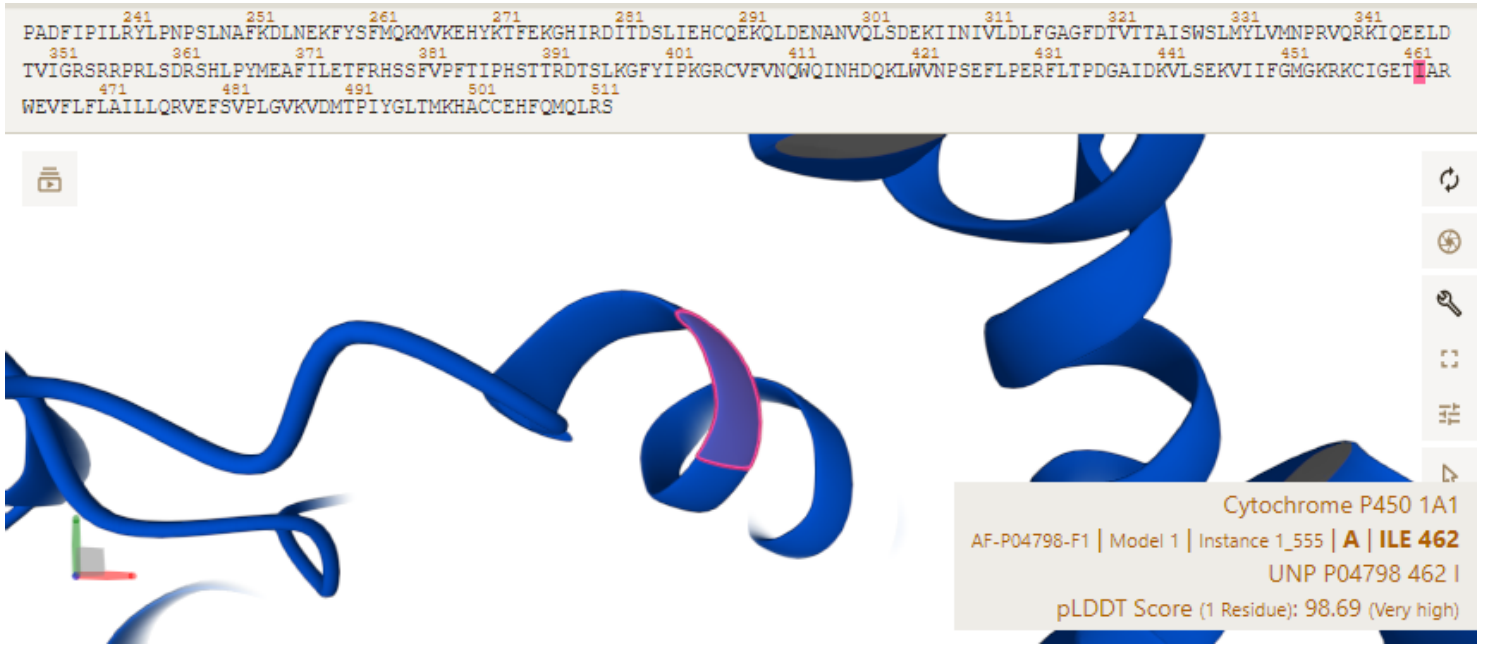
Estudios genéticos: Gen *CYP1A1*

Frecuencia de rs1048943 p.Ile462Arg **similar** a **Asia**



Estudios genéticos: Gen *CYP1A1*

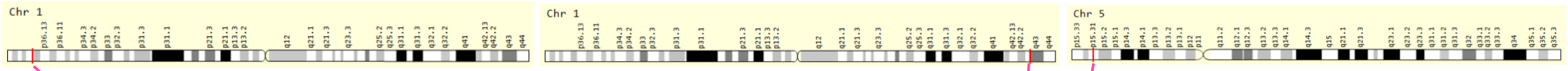




Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
CYP1A1	rs1048943	missense	c.2455 A>G	p. Ile462Arg	Significado incierto

GeneCards. 2023

Estudios genéticos: Genes *MTHFR, MTR* y *MTRR*



Genes	Genotype	Genotypic frequency			Allele frequency			*P* value HWE
		Cases	Controls	All	Cases	Controls	All	
MTHFR C677T rs1801133	C/C	0.22	0.35	0.30	0.55	0.64	0.605	0.78
	C/T	0.66	0.58	0.61				
	T/T	0.12	0.07	0.09	0.45	0.36	0.395	
MTHFR A1298C rs1801131	A/A	0.965	0.980	0.974	0.98	0.99	0.98	0.68
	A/C	0.026	0.015	0.019				
	C/C	0.009	0.005	0.007	0.02	0.01	0.02	
MTR A2756G rs1805087	A/A	0.82	0.63	0.70	0.90	0.79	0.83	0.94
	A/G	0.16	0.32	0.26				
	G/G	0.02	0.05	0.04	0.10	0.21	0.17	
MTRR A66G rs1801394	A/A	0.03	0.03	0.03	0.485	0.475	0.48	0.42
	A/G	0.91	0.89	0.90				
	G/G	0.06	0.08	0.07	0.515	0.525	0.52	

HWE Hardy-Weinberg equilibrium of all study population

114 Ca. Mama / 195 controles

Tumor Biol. 2015; 36(89),6451-61

Estudios genéticos: Genes *MTHFR, MTR* y *MTRR*

Table 5 Association of genotypes with histopathological and immunohistochemical characteristics

	MTHFR C677T rs1801133		MTHFR A1298C rs1801131		MTRR A66G rs1805087		MTR A2756G rs1801394	
Variable	C/C	C/T+T/T	A/A	A/C+C/C	A/A	A/G+G/G	A/A	A/G+G/G
Breast affected								
Right	15 (13 %)	51 (45 %)	64 (56 %)	2 (2 %)	2 (2 %)	64 (56 %)	38 (33 %)	10 (9 %)
Left	10 (9 %)	38 (33 %)	46 (40 %)	2 (2 %)	1 (1 %)	47 (41 %)	56 (49 %)	10 (9 %)
OR (95 % CI)	1.1 (0.5–2.8)		1.4 (0.2–10.2)		1.5 (0.1–16.7)		0.7 (0.3–1.8)	
P value	0.990		1		1		0.590	
Tumor stage[a]								
T1–T2	17 (15 %)	66 (58 %)	80 (70 %)	3 (3 %)	2 (2 %)	81 (71 %)	67 (59 %)	16 (14 %)
T3–T4	4 (4 %)	14 (12 %)	17 (15 %)	1 (1 %)	1 (1 %)	17 (15 %)	15 (13 %)	3 (3 %)
OR (95 % CI)	0.9 (0.3–3.1)		1.6 (0.2–16)		0.4 (0.04–4.9)		0.8 (0.2–3.2)	
P value	1		1		1		1	
LN status								
+	14 (12 %)	42 (37 %)	54 (47 %)	2 (2 %)	2 (2 %)	54 (47 %)	47 (41 %)	9 (8 %)
−	11 (10 %)	47 (41 %)	56 (49 %)	2 (2 %)	1 (1 %)	57 (50 %)	47 (41 %)	11 (10 %)
OR (95 % CI)	0.7 (0.3–1.7)		1 (0.1–7.6)		0.5 (0.4–5.4)		0.8 (0.3–2.2)	
P value	0.581		1		0.975		0.873	
ER status								
+	19 (17 %)	53 (46 %)	69 (60 %)	3 (3 %)	2 (2 %)	70 (61 %)	59 (52 %)	13 (11 %)
−	6 (5 %)	36 (32 %)	41 (36 %)	1 (1 %)	1 (1 %)	41 (36 %)	35 (31 %)	7 (6 %)
OR (95 % CI)	2.2 (0.8–5.9)		0.6 (0.6–5.6)		1.2 (0.1–13.3)		0.9 (0.3–2.5)	
P value	0.203		1		1		1	
PR status								
+	16 (14 %)	51 (45 %)	64 (56 %)	3 (3 %)	2 (2 %)	65 (57 %)	50 (44 %)	17 (15 %)
−	9 (8 %)	38 (33 %)	46 (40 %)	1 (1 %)	1 (1 %)	46 (40 %)	44 (38 %)	3 (3 %)
OR (95 % CI)	1.3 (0.5–3.3)		0.5 (0.05–4.6)		1.4 (0.1–16.1)		0.2 (0.06–0.7)	
P value	0.711		0.877		1		0.018	
HER2 status								
+	7 (6 %)	26 (23 %)	31 (27 %)	2 (2 %)	1 (1 %)	32 (28 %)	28 (25 %)	5 (4 %)
−	18 (16 %)	63 (55 %)	79 (69 %)	2 (2 %)	2 (2 %)	79 (69 %)	66 (58 %)	15 (13 %)
OR (95 % CI)	0.9 (0.4–2.5)		0.4 (0.05–2.9)		1.2 (0.1–14.1)		1.3 (0.4–3.8)	
P value	1		0.701		1		0.875	
Surgical margins								
+	17 (15 %)	63 (55 %)	77 (67 %)	3 (3 %)	1 (1 %)	79 (69 %)	65 (57 %)	15 (13.2 %)
−	8 (7 %)	26 (23 %)	33 (29 %)	1 (1 %)	2 (2 %)	32 (28 %)	29 (25.4 %)	5 (4.4 %)
OR (95 % CI)	1.1 (0.4–2.9)		1.3 (0.1–12.8)		4.9 (0.4–56.4)		1.3 (0.4–4.0)	
P value	0.983		1		0.439		0.802	

LN lymph node, *PR* progesterone receptor, *ER* estrogen receptor, *HER* human epidermal growth factor receptor

[a] Analyses of 101 individuals

Genes	Genotype	Cases (n=114), n (%)	Controls (n=195), n (%)	OR	95 % CI	*P* value
MTHFR	C/C[a]	25 (21.93)	69 (35.38)	1.0		
C677T	C/T	75 (65.79)	113 (57.95)	1.8	1.1–3.2	0.039
rs1801133	T/T	14 (12.28)	13 (6.67)	2.9	1.2–7.2	0.025
	C/T+T/T	89 (78.07)	126 (64.62)	1.9	1.1–3.3	0.019
MTHFR	A/A[a]	110 (96.49)	191 (97.95)	1.0		
A1298C	A/C	3 (2.63)	3 (1.54)	1.7	0.3–8.8	0.803
rs1801131	C/C	1 (0.88)	1 (0.51)	1.7	0.1–28.0	1.000
	A/C+C/C	4 (3.51)	4 (2.05)	2.3	0.5–10.5	0.472

Tumor Biol. 2015; 36(89),6451-61

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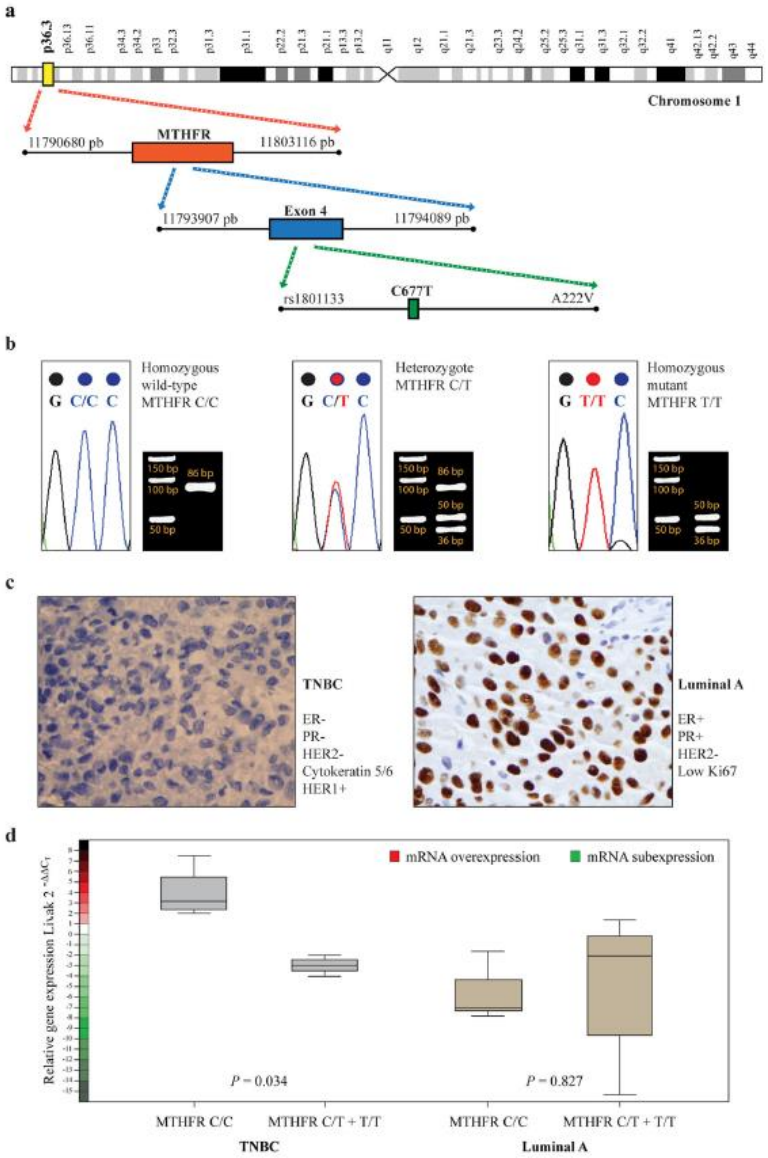
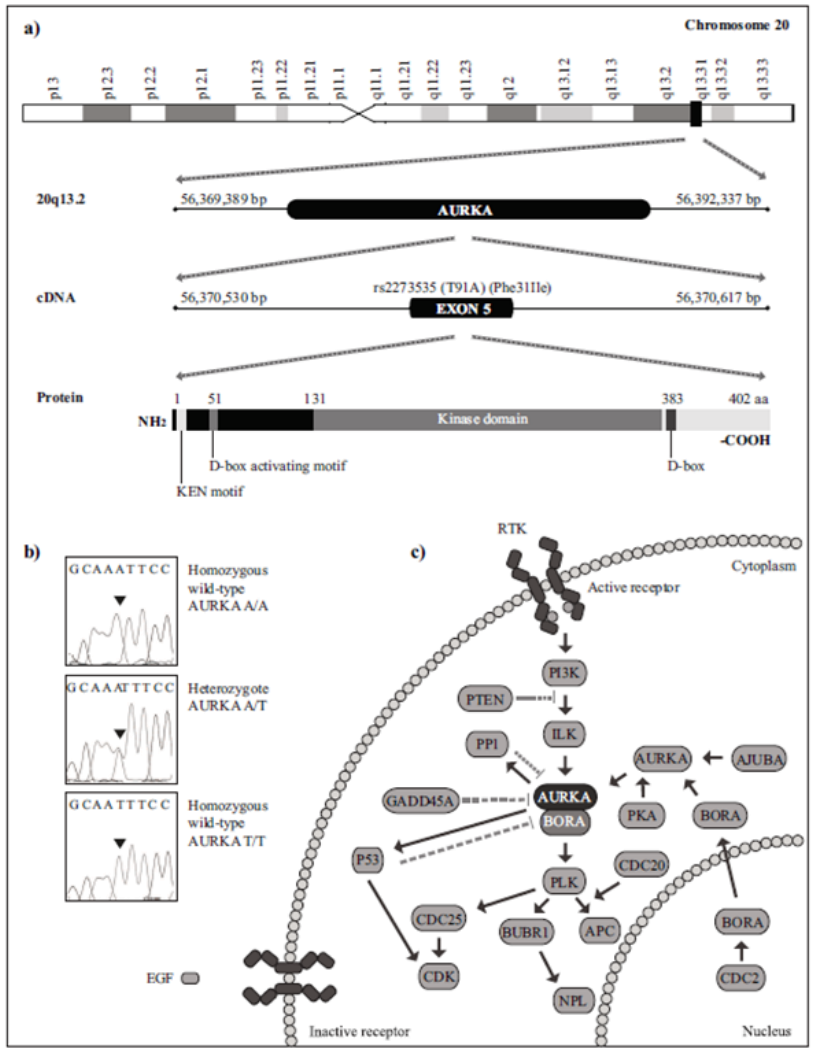
Estudios genéticos: Gen *MTHFR*

Genes	Genotype	Cases (n=114), n (%)	Controls (n=195), n (%)	OR	95 % CI	P value
MTHFR	C/C[a]	25 (21.93)	69 (35.38)	1.0		
C677T	C/T	75 (65.79)	113 (57.95)	1.8	1.1–3.2	0.039
rs1801133	T/T	14 (12.28)	13 (6.67)	2.9	1.2–7.2	0.025
	C/T+T/T	89 (78.07)	126 (64.62)	1.9	1.1–3.3	0.019
MTHFR	A/A[a]	110 (96.49)	191 (97.95)	1.0		
A1298C	A/C	3 (2.63)	3 (1.54)	1.7	0.3–8.8	0.803
rs1801131	C/C	1 (0.88)	1 (0.51)	1.7	0.1–28.0	1.000
	A/C+C/C	4 (3.51)	4 (2.05)	2.3	0.5–10.5	0.472



Tumor Biol. 2015; 36(89),6451-61

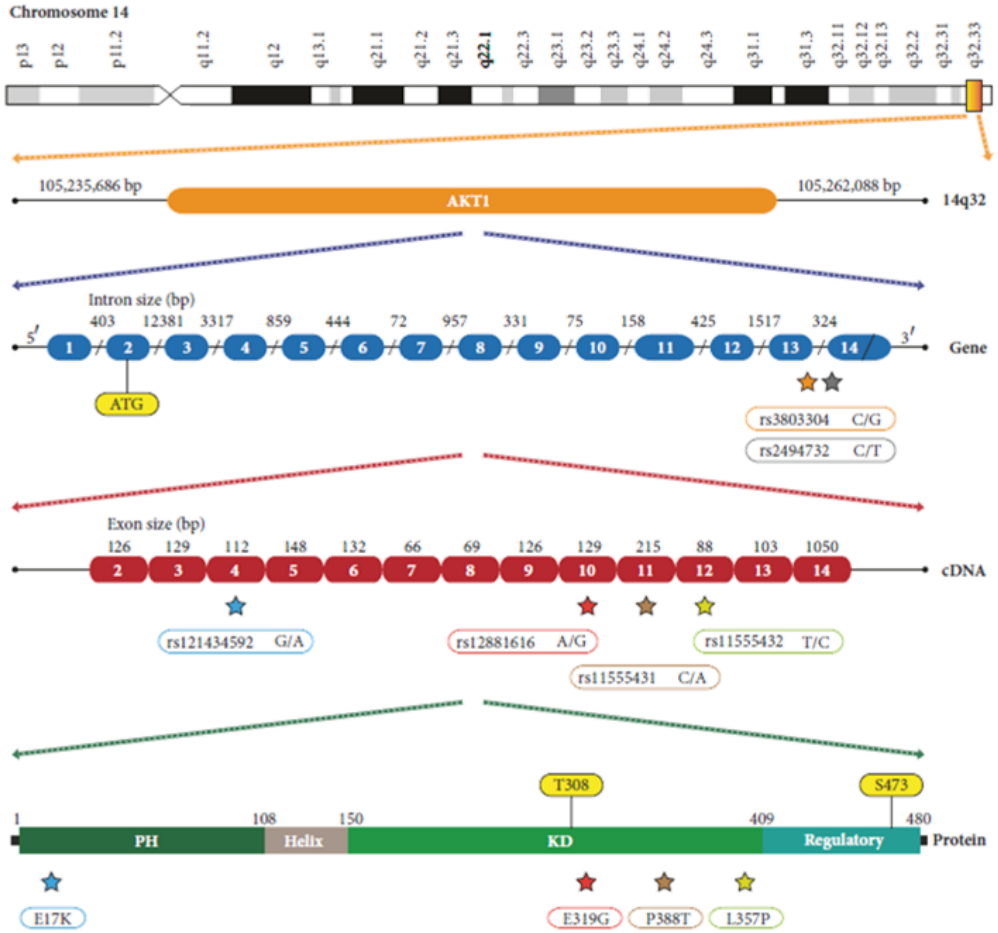
Estudios genéticos: Gen *AURKA*



	Phe/Phe (AA)		Phe/Ile (AT)		Ile/Ile (TT)		Total		*P* value
	n	%	n	%	n	%	n	%	
Samples									
Healthy	46	46.0	42	42.0	12	12.0	100	50	0.002
Affected	23	23.0	54	54.0	23	23.0	100	50	
Breast affected									
Right	14	24.6	29	50.9	14	24.6	57	57	0.931
Left	10	23.3	21	48.8	12	27.9	43	43	
Pathology									
Invasive ductal carcinoma	14	20.0	36	51.4	20	28.6	70	79.5	0.398
Lobular carcinoma in situ	3	37.5	4	50.0	1	12.5	8	9	
Papillary carcinoma	2	50.0	2	50.0	0	0.0	4	4.5	
Mucinous carcinoma	0	0.0	4	66.7	2	33.3	6	7	
Tumor grade (SBR) [a]									
SBR III	5	26.3	4	21.1	10	52.6	19	29	Reference
SBR II	5	17.2	18	62.1	6	20.7	29	45	0.017
SBR I	6	35.3	10	58.8	1	5.9	17	26	0.007
ER Status [b]									
+	15	23.4	37	57.8	12	18.8	64	68	0.561
-	8	26.7	14	46.7	8	26.7	30	32	
PR Status									
+	13	23.6	30	54.5	12	21.8	55	58.5	0.972
-	10	25.6	21	53.8	8	20.5	39	41.5	
HER2 Status									
+	6	28.6	11	52.4	4	19.0	21	22	0.875
-	17	23.3	40	54.8	16	21.9	73	78	
Metastasis									
+	5	16.1	19	61.3	7	22.6	31	31	0.499
-	17	24.6	34	49.3	18	26.1	69	69	
Ki-67 [c]									
< 20	15	31.2	31	64.6	2	4.2	48	66	0.000
≥ 20	5	20.0	9	36.0	11	44.0	25	34	
Immunohistotype									
ER+ PR+ HER2+	1	16.7	4	66.7	1	16.7	6	6.3	Reference
ER+ PR+ HER2-	10	22.2	25	55.6	10	22.2	45	47.4	0.875
ER+ PR- HER2+	2	40.0	2	40.0	1	20.0	5	5.3	0.632
ER+ PR- HER2-	2	25.0	5	62.5	1	12.5	8	8.4	0.922
ER- PR+ HER2+	1	50.0	1	50.0	0	0.0	2	2.1	0.587
ER- PR+ HER2-	1	33.3	0	0.0	2	66.7	3	3.2	0.153
ER- PR- HER2+	2	28.6	3	42.9	2	28.6	7	7.4	0.692
ER- PR- HER2-	4	22.2	9	50.0	5	27.8	19	20	0.771

Pathol Oncol Res. 2018; 24(3),457-65

Estudios genéticos: Gen *AKT1*



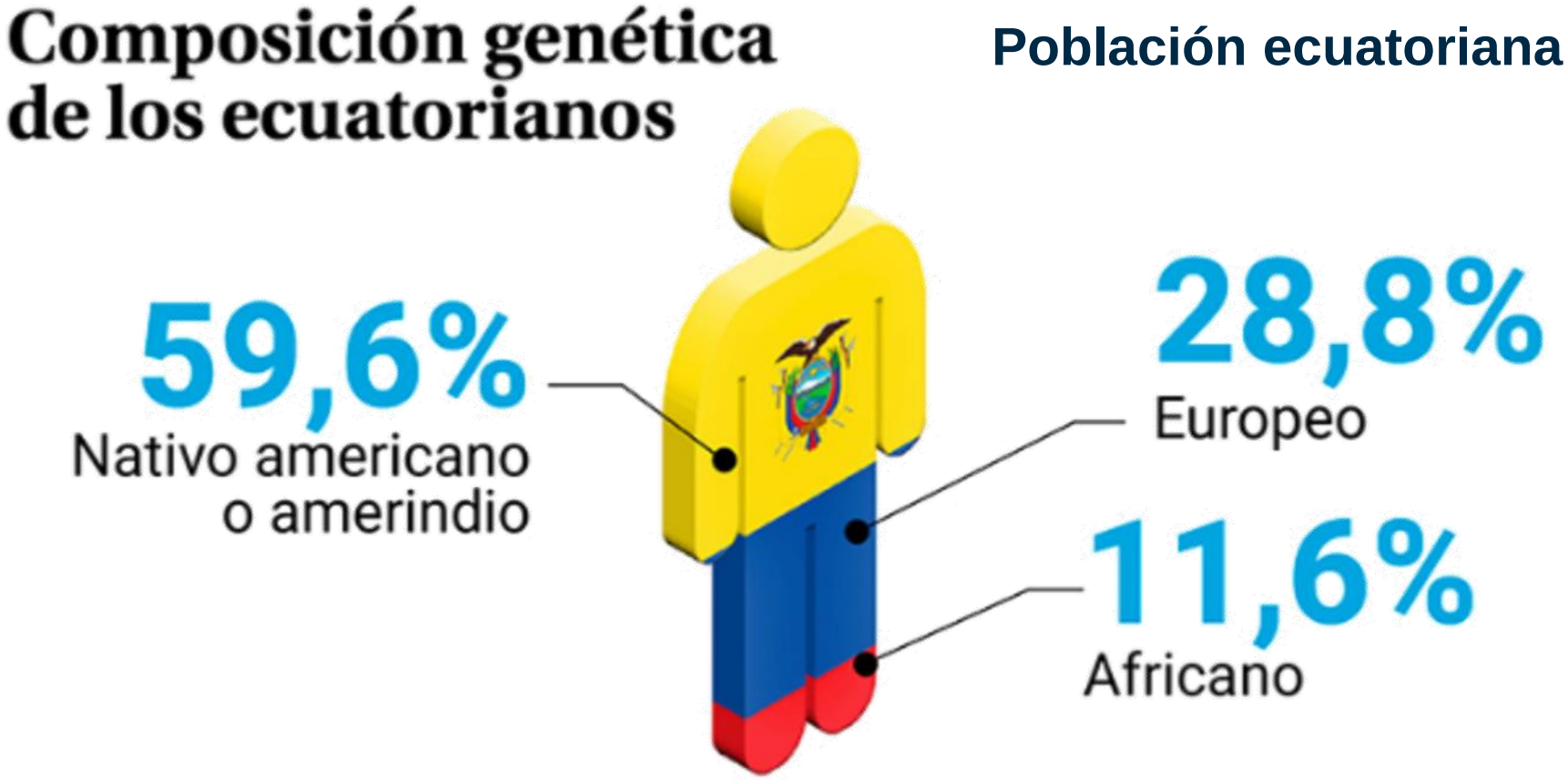
Mutations	Genotypes	Genotypic frequency			Allele frequency		
		Cases	Controls	All	Cases	Controls	All
rs121434592 E17K	GG	0.98	1.00	0.99	0.98	1.00	0.99
	GA	0.00	0.00	0.00			
	AA	0.02	0.00	0.01	0.02	0.00	0.01
rs12881616 E319G	AA	1.00	1.00	1.00	1.00	1.00	1.00
	AG	0.00	0.00	0.00			
	GG	0.00	0.00	0.00	0.00	0.00	0.00
rs11555432 L357P	TT	1.00	1.00	1.00	1.00	1.00	1.00
	TC	0.00	0.00	0.00			
	CC	0.00	0.00	0.00	0.00	0.00	0.00
rs11555431 P388T	CC	1.00	1.00	1.00	1.00	1.00	1.00
	CA	0.00	0.00	0.00			
	AA	0.00	0.00	0.00	0.00	0.00	0.00
rs2494732	CC	0.45	0.30	0.34	0.65	0.54	0.57
	CT	0.41	0.48	0.46			
	TT	0.14	0.22	0.20	0.35	0.46	0.43
rs3803304	CC	0.59	0.65	0.63	0.76	0.82	0.80
	CG	0.33	0.33	0.33			
	GG	0.08	0.02	0.04	0.24	0.18	0.20

91 Ca. Mama / 185 controles

¡Juntos somos esperanza de vida!

BioMed Res. 2018; 7463832

Estudios genéticos: Composición genética



Población ecuatoriana: Trihíbrida

Scientific Reports. 2019; 9(1), 9247

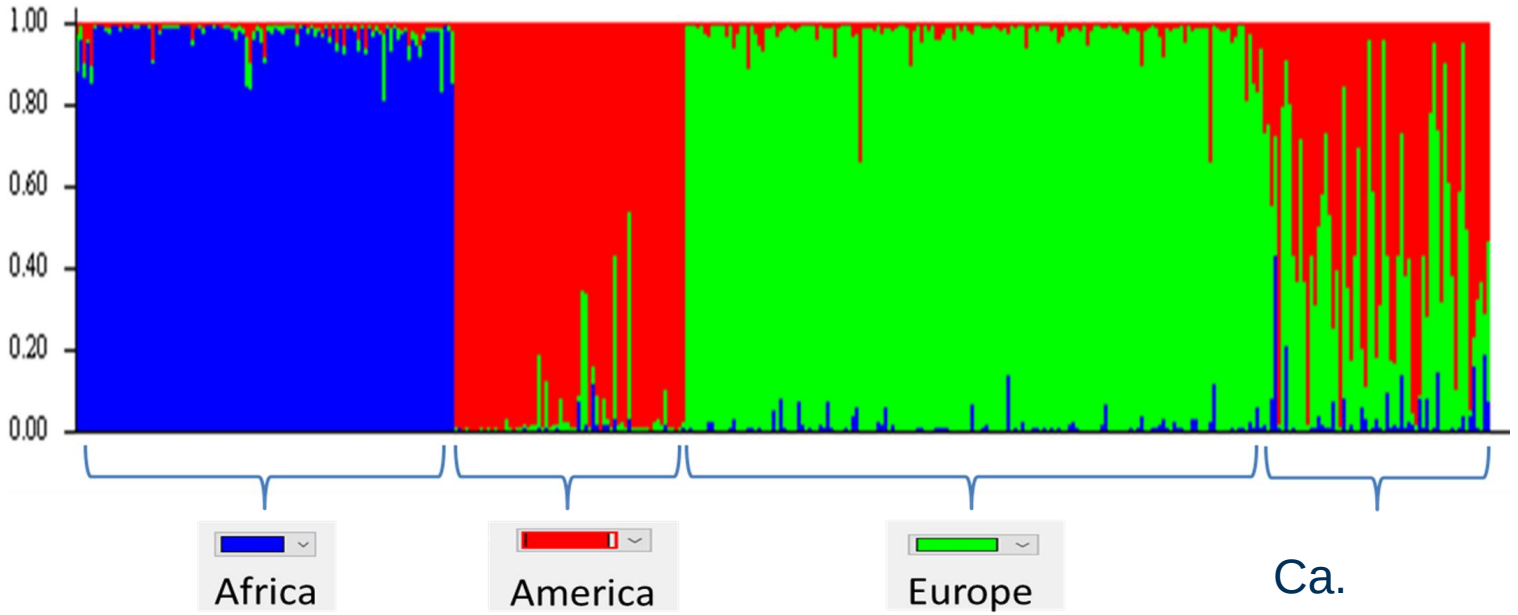
Estudios genéticos: Composición genética

59,6%
Nativo americano
o amerindio

Forensic Sci Int. 2019; 7, 140-1; Mol Genet Genomic Med. 2015; 4(1), 9-17; Open J Blood Dis. 2013; 3(4), 108-15; Hum Biol 2005; 77(4), 521-6; Ann Hematol. 2005; 84(2), 103-5; Cancer Genet Cytogenet. 2002; 137, 72-4

Estudios genéticos: Composición genética

Población ecuatoriana: Trihíbrida



NA: 60,58 %
E: 34,57 %
A: 3,7 %

Ca. mama

Forensic Sci Int. 2017; 6:e231-2

Estudios genéticos: NGS

94 genes y 284 SNPs

illumina®

Panel	Genes
TruSight Cancer	94
TruSight Inherited Disease	552
TruSight One	4813

TruSight Cancer Target Genes and SNPs			
Genes	SNPs		
AIP	rs17401966	rs2180341	rs9510787
ALK	rs9430161	rs9485372	rs753955
APC	rs7538876	rs2046210	rs9600079
ATM	rs11249433	rs651164	rs9573163
BAP1	rs7412746	rs9364554	rs9543325
BLM	rs3790844	rs7758229	rs7335046
BMPR1A	rs6691170	rs4487645	rs944289
BRCA1	rs6687758	rs11978267	rs116909374
BRCA2	rs801114	rs4132601	rs4444235
BRIP1	rs1465618	rs6465657	rs4779584
BUB1B	rs7579899	rs1495741	rs4924410
CDC73	rs1432295	rs1512268	rs4775302
CDH1	rs721048	rs2439302	rs8030672
CDK4	rs10187424	rs16892766	rs7176508
CDKN1C	rs17483466	rs1016343	rs8034191
CDKN2A	rs12621278	rs1456315	rs1051730
CEBPA	rs2072590	rs16901979	rs8042374
CEP57	rs13016963	rs2456449	rs3803662
CHEK2	rs13393577	rs16902094	rs4784227
CYLD	rs3768716	rs445114	rs3112612
DDB2	rs6435862	rs13281615	rs9929218
DICER1	rs13387042	rs1562430	rs391525
DIS3L2	rs966423	rs10505477	rs258322
EGFR	rs13397985	rs6983267	rs1805007
EPCAM	rs7584330	rs7014346	rs4785763
ERCC2	rs2292884	rs1447295	rs4795519
ERCC3	rs757978	rs4242382	rs4430796
ERCC4	rs4973768	rs4242384	rs7501939
ERCC5	rs1052501	rs7837688	rs7210100
EXT1	rs2660753	rs9642880	rs1859962
EXT2	rs9284813	rs2019960	rs17674580
EZH2	rs17181170	rs10088218	rs7238033
FANCA	rs9841504	rs891835	rs4939827
FANCB	rs10934853	rs4295627	rs8170
FANCC	rs6763931	rs2294008	rs8102137
FANCD2	rs6774494	rs7040024	rs10411210
FANCE	rs10936599	rs755383	rs8102476
FANCF	rs10936632	rs3814113	rs11083846
FANCG	rs4488809	rs7023329	rs2735839
FANCI	rs10937405	rs2157719	rs961253
FANCL	rs17505102	rs1412829	rs910873
FANCM	rs710521	rs1011970	rs4925386
FH	rs2131877	rs4977756	rs6010620
FLCN	rs798766	rs965513	rs4809324
GATA2	rs1494961	rs865686	rs372883
GPC3	rs12500426	rs505922	rs2014300
HNF1A	rs17021918	rs10795668	rs45430
HRAS	rs1229984	rs11012732	rs1547374

KIT	rs971074	rs3123078	rs738722
MAX	rs7679673	rs10993994	rs36600
MEN1	rs10069690	rs10821936	rs2284063
MET	rs2242652	rs7089424	rs1014971
MLH1	rs2736100	rs10822013	rs5759167
MSH2	rs2853676	rs10995190	rs5768709
MSH6	rs4635969	rs224278	rs1327301
MUTYH	rs4975616	rs704010	rs5945572
NBN	rs401681	rs3765524	rs5945619
NF1	rs31489	rs2274223	rs5919432
NF2	rs12653946	rs3781264	rs1321311
NSD1	rs2255280	rs17119461	rs3824999
PALB2	rs13361707	rs12413624	rs5934683
PHOX2B	rs2121875	rs11199874	rs2283873
PMS1	rs4415084	rs2981579	rs807624
PMS2	rs889312	rs2981575	rs1027643
PRF1	rs10052657	rs1219648	rs3755132
PRKAR1A	rs20541	rs2981582	rs790356
PTCH1	rs4624820	rs3817198	rs5955543
PTEN	rs10058728	rs7127900	rs10974944
RAD51C	rs872071	rs110419	rs1210110
RAD51D	rs12210050	rs1945213	rs7555566
RB1	rs4712653	rs11228565	rs1364054
RECQL4	rs6939340	rs7931342	rs6734275
RET	rs4324798	rs10896449	rs7584993
RHBDF2	rs29232	rs7130881	rs17272796
RUNX1	rs3129055	rs7105934	rs1155741
SBDS	rs2860580	rs614367	rs161792
SDHAF2	rs2517713	rs1393350	rs11940551
SDHB	rs6457327	rs1801516	rs9293511
SDHC	rs130067	rs3802842	rs9352613
SDHD	rs2894207	rs498872	rs685449
SLX4	rs2596542	rs735665	rs7808249
SMAD4	rs2248462	rs2900333	rs1106334
SMARCB1	rs3117582	rs718314	rs11017876
STK11	rs204999	rs10875943	rs9572094
SUFU	rs9268542	rs11169552	rs4905366
TMEM127	rs6903608	rs902774	rs4775699
TP53	rs2395185	rs995030	rs1528601
TSC1	rs2858870	rs3782181	rs11655512
TSC2	rs674313	rs4474514	rs4793172
VHL	rs28421666	rs11066015	rs242076
WRN	rs2647012	rs671	rs6603251
WT1	rs10484561	rs4767364	AMG_mid100
XPA	rs9275572	rs2074356	MITF_rs149617956
XPC	rs210138	rs11066280	ATM_SNP
	rs10484761	rs4765623	HOXB13_rs138213197
	rs339331	rs1572072	

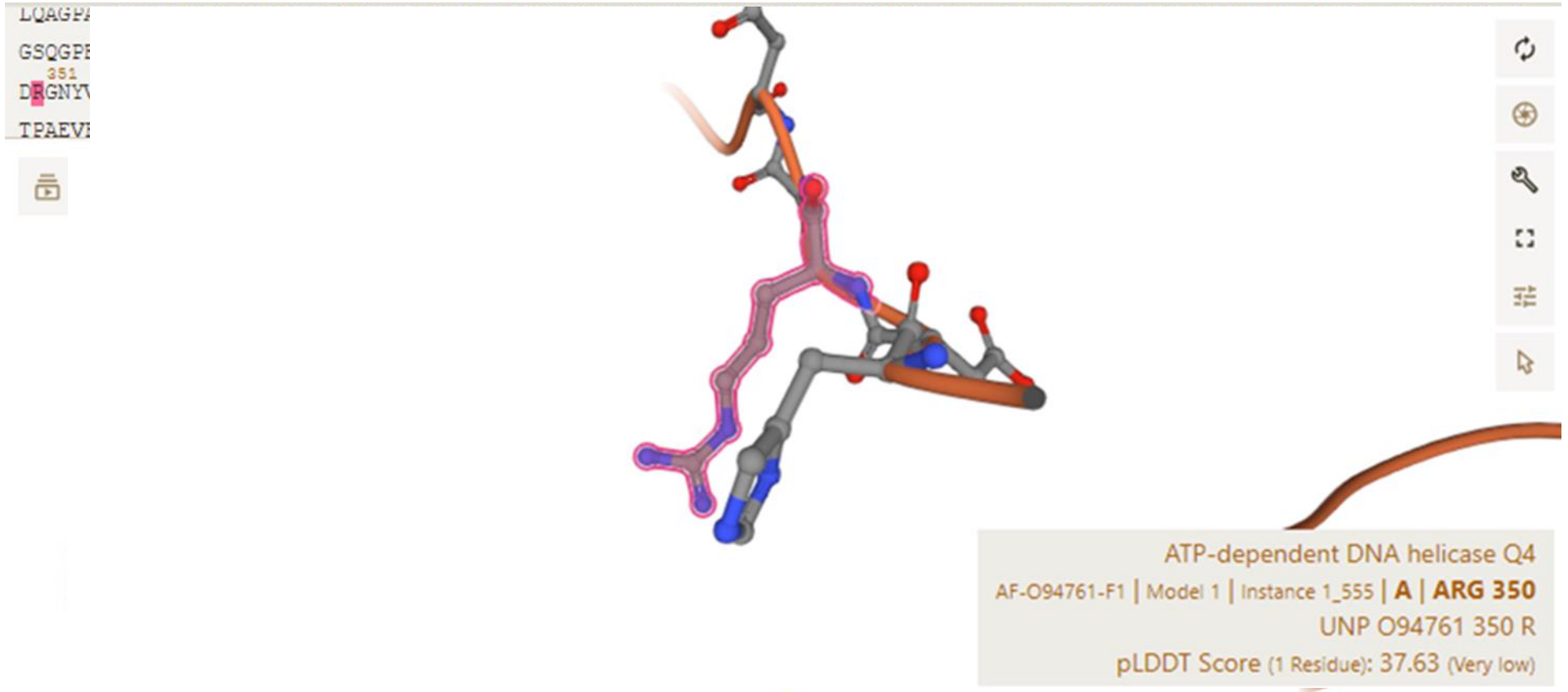
Estudios genéticos: NGS

Resultados	%
Hallazgos	83
negativo	17

Significado clínico	%	Genes
Patogénica	19	*ATM, BRCA1, BRCA2, MUTYH, PALB2, PTEN, RECQL4*
Probablemente patogénica	2	*DIS3L2, SDHB*
Significado incierto	77	*AIP, APC, ATM, BARD1, BRCA1, BRCA2, CDKN1B, DIS3L2, MEN1, MET, MLH1, MSH2, MSH3, MSH6, NF1, NF2, NTHL1, PALB2, PMS2, POLD1, POLE, RAD51C, RB1, RECQL4, RET, SMARCE1, TSC1, TSC2, TP53, WRN*
Probablemente beningo	2	*BRCA2, WT1*

J Basic Appl Genet. 2019; 30(1), 273

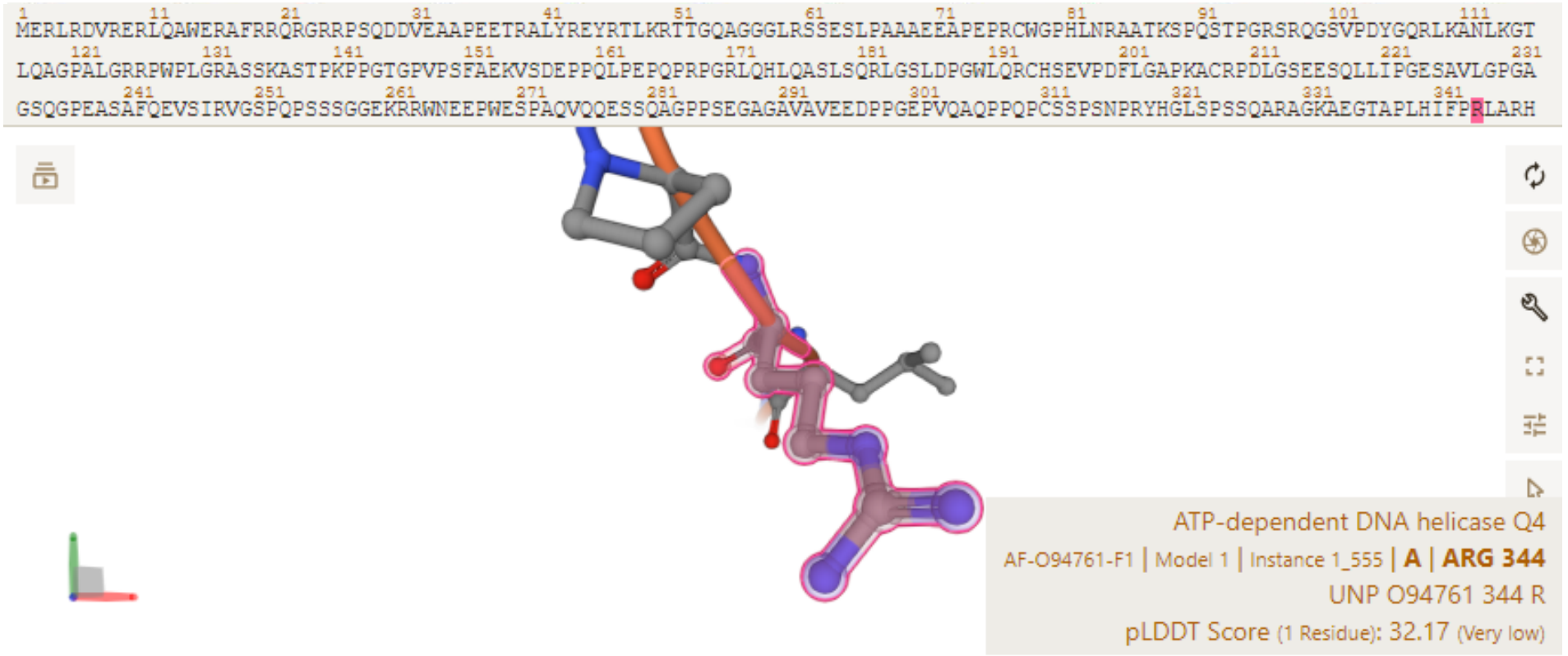
Estudios genéticos: NGS



Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
RECQL4	rs746636748	frameshift	c.1048_1049 del	p. Arg350Gly	Patológico

GeneCards. 2023

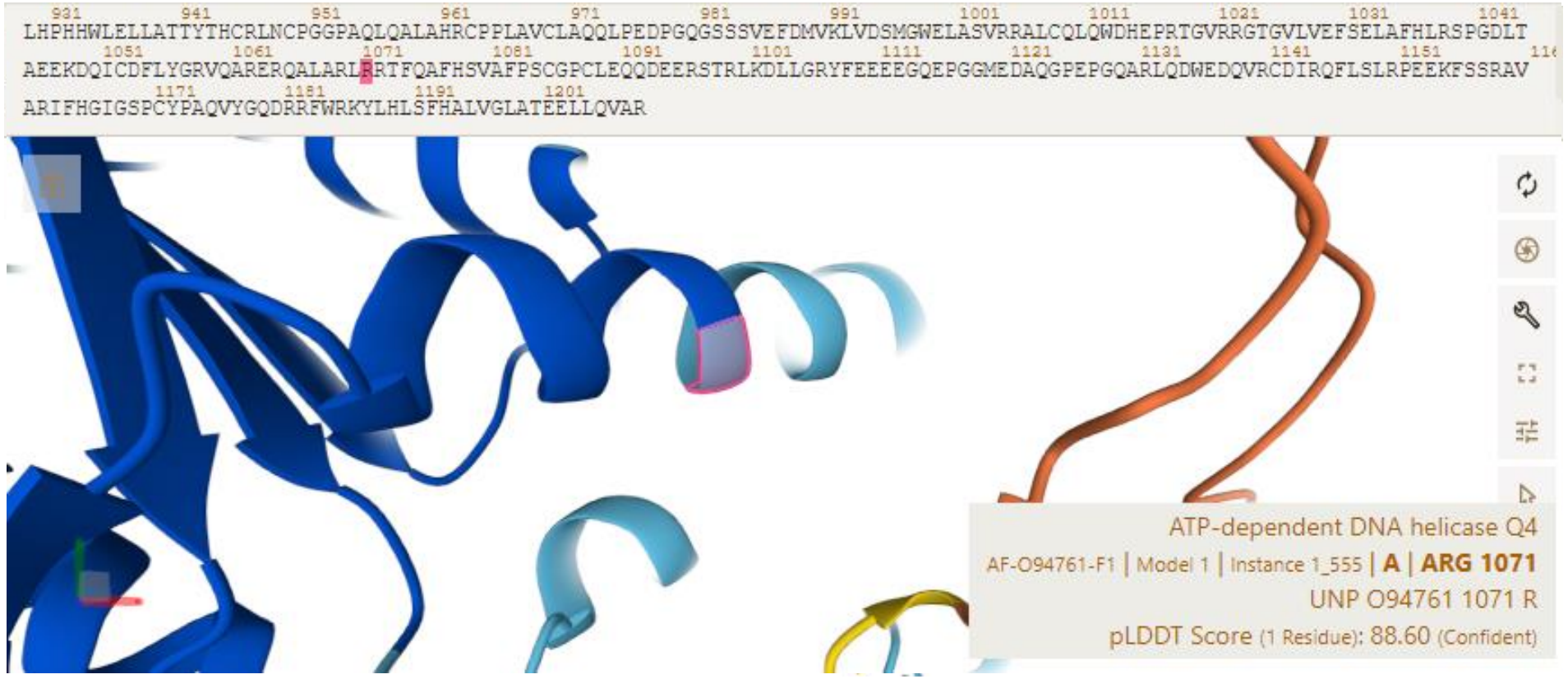
Estudios genéticos: NGS



Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
RECQL4	rs745874353	missense	c.1031 G>A	p. Arg344Gln	Significado incierto

GeneCards. 2023

Estudios genéticos: NGS



Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
RECQL4	rs773856131	missense	c.3212 G>A	p. Arg1071His	Significado incierto

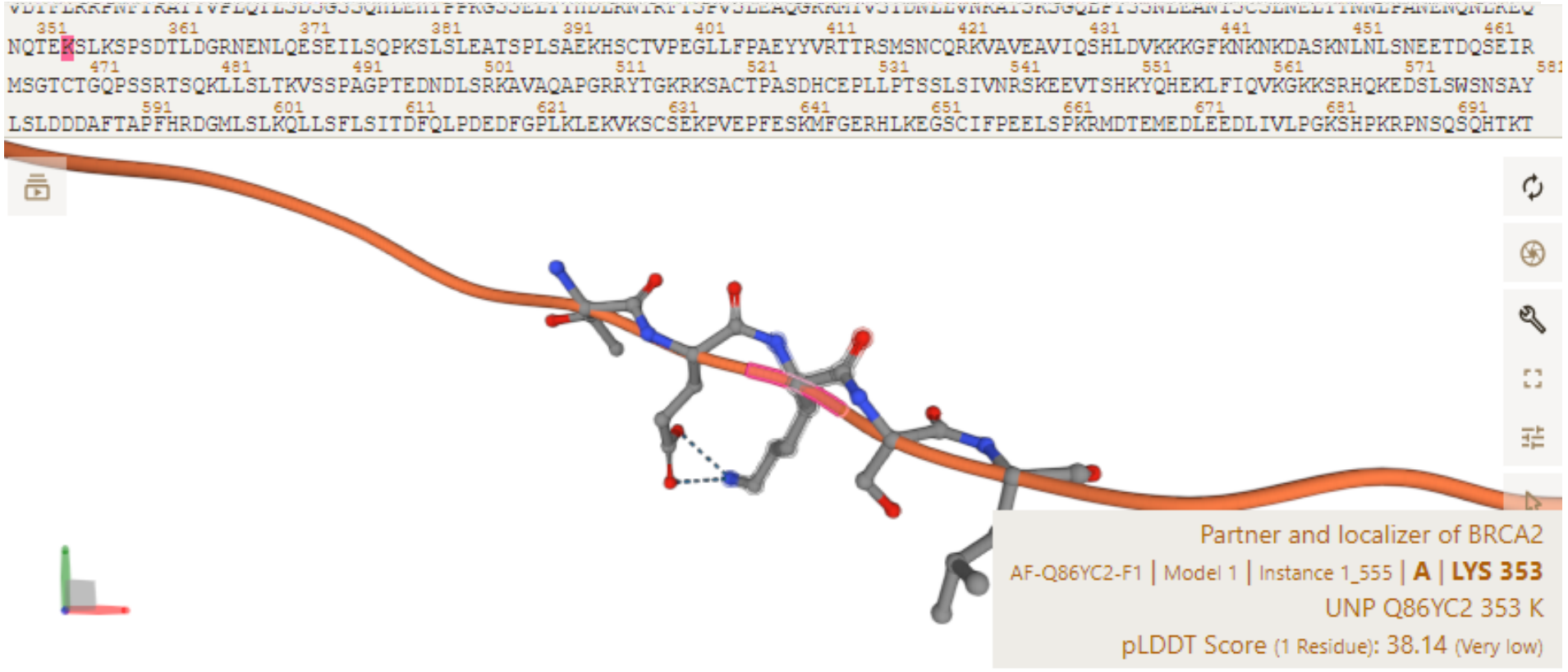
GeneCards. 2023

Estudios genéticos: NGS

Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
PTEN	c.39_40dup	nonsense	c.39_40dup	p. Arg14fs*11	Patológico

GeneCards. 2023

Estudios genéticos: NGS



Gen	SNP	Tipo	Cambio	Efecto	Significado clínico
PALB2	rs180177099	nonsense	c.1056_1057del	p. Lys353llefs*7	Patológico

GeneCards. 2023

Estudios genéticos: NGS

Gen	SNP	Ecuador		Asia		Europa	
		Alelo de referencia	Alelo alternativo	Alelo de referencia	Alelo alternativo	Alelo de referencia	Alelo alternativo
AIP	rs267606568	0,998	0,002	1,000	0,000	1,00000	0,00000
APC	rs1060503350	0,998	0,002	1,000	0,000	1,00000	0,00000
	rs1377799096	1,000	0,000	1,000	0,000	1,00000	0,00000
ATM	rs1060501661	1,000	0,000	1,000	0,000	1,00000	0,00000
	rs55830714	1,000	0,000	1,000	0,000	0,99996	0,00004
	c.8558C>T	1,000	0,000				
BRCA1	c.5075-3C>T	1,000	0,000				
	rs28897696	1,000	0,000	1,000	0,000	0,99950	0,00050
BRCA2	c.4521G>C	1,000	0,000				
DIS3L2	c.1425+1G>A	1,000	0,000				
MEN1	rs1225964479	0,998	0,002	1,000	0,000	1,00000	0,00000
MET	c.4169A>C	1,000	0,000				
MLH1	c.207+4A>G	1,000	0,000				
MSH2	c.1360A>C	1,000	0,000				
	c.1405C>T	1,000	0,000				
MSH3	c.15G>T	1,000	0,000				
MUTYH	c.1187G>A	1,000	0,000				
NF1	rs876660103	1,000	0,000	1,000	0,000	1,00000	0,00000
NTHL1	c.38G>A	1,000	0,000				
	c.535G>A	1,000	0,000				
	c.607G>A	1,000	0,000				
PALB2	c.886dup	1,000	0,000				
	rs180177099	1,000	0,000	1,000	0,000	1,00000	0,00000
POLD1	c.365T>G	1,000	0,000				
POLE	c.3724T>C	1,000	0,000				
PTEN	c.39_40dup	1,000	0,000				
RAD51C	rs876659936	1,000	0,000	1,000	0,000	1,00000	0,00000
RB1	c.208G>A	1,000	0,000				
RECQL4	c.263A>G	1,000	0,000				
	rs746636748	1,000	0,000	1,000	0,000	0,99979	0,00021
	rs773856131	1,000	0,000	1,000	0,000	0,99992	0,00008
	rs745874353	1,000	0,000	1,000	0,000	1,00000	0,00000
RET	rs774347808	1,000	0,000	1,000	0,000	0,99994	0,00006
SDHB	c.269G>T	1,000	0,000				
SMARCE1	c.938G>T	1,000	0,000				
WRN	c.1976A>T	1,000	0,000				
WT1	c.299C>G	1,000	0,000				

Frecuencia similar a Asia

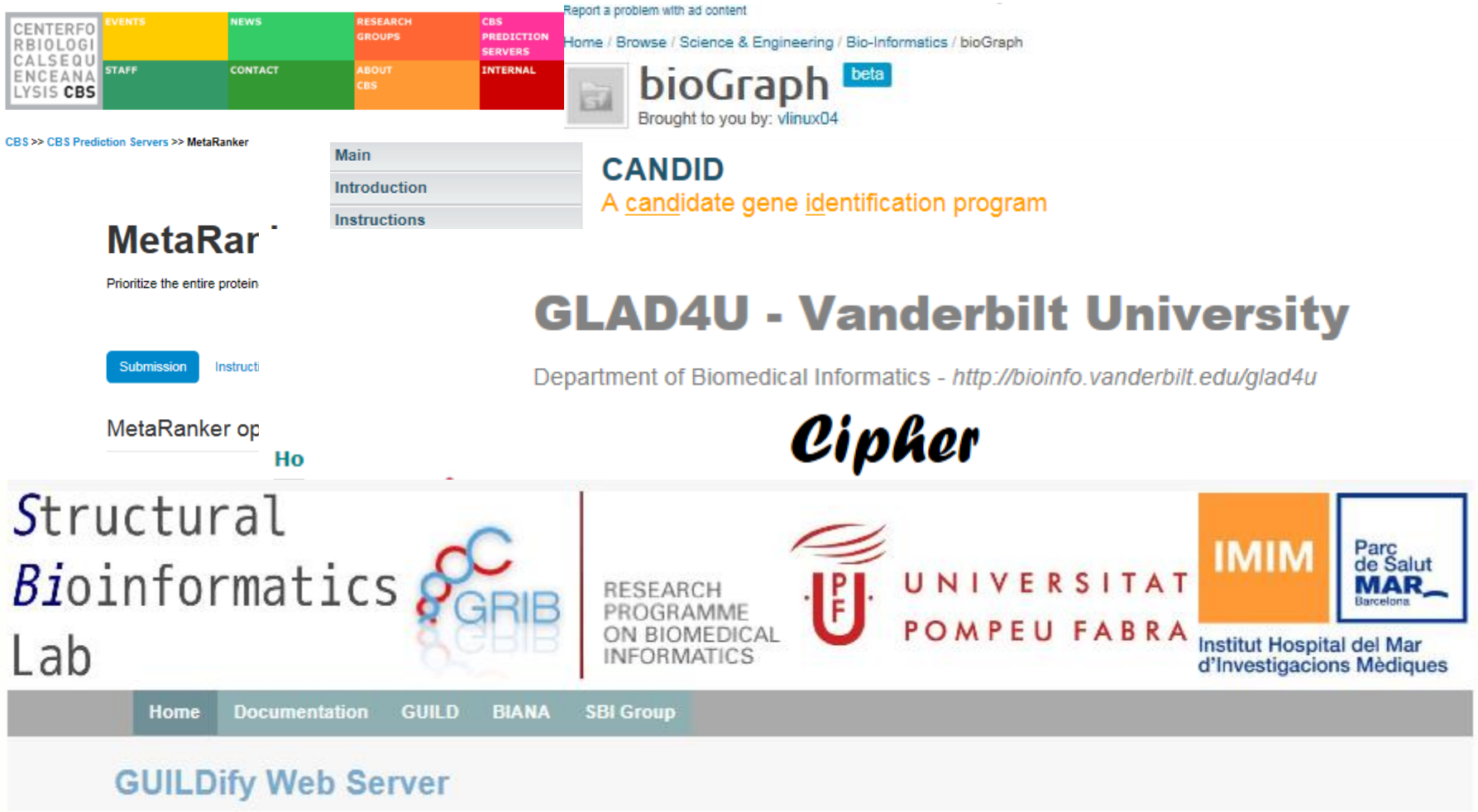
Frecuencia propia

Variantes no descritas en la literatura

J Hum Genet. 2003; 48, 639-41. J Basic Appl Genet. 2019; 30(1), 273

Genes con SNPs: Priorización de genes

OMIM: # 114480 BREAST CANCER



http://omim.org/entry/114480

Genes con SNPs: Priorización de genes

OMIM: # 114480 BREAST CANCER

Summary of GDAs | Evidences for GDAs | Summary of VDAs | Evidences for VDAs | Summary of DDAs | Disease Mappings

BREAST CANCER, SUSCEPTIBILITY TO, C3469522

Source: ALL

1 - 11 of 11 results

Results per page 25

Filter within current res

Gene	UniProt	Gene Full Name	Protein Class	N. diseases $_g$	DSI $_g$	DPI $_g$	pLI	Score $_{gda}$	EL $_{gda}$	EI $_{gda}$	N. PMIDs	N. SNPs $_{gda}$	First Ref.
CHEK2	O96017	checkpoint kinase 2	Kinase	297		0.460	0.808	1.2E-24	0.100		None	0	4
BRCA2	P51587	BRCA2 DNA repair a...	Nucleic acid binding	656		0.379	0.846	2.4E-25	0.100		None	0	4
BRCA1	P38398	BRCA1 DNA repair a...	Enzyme	747		0.367	0.923	9.2E-29	0.100		None	0	1
BARD1	Q99728	BRCA1 associated RI...		75		0.597	0.538	1.4E-24	0.100		None	0	1
WBP1L	Q9NX94	WW domain binding ...		22		0.769	0.462	0.64	0.100		None	0	1
PHB	P35232	prohibitin		177		0.511	0.846	0.76	0.100		None	0	1
ATM	Q13315	ATM serine/threonine...	Kinase	684		0.374	0.885	5.6E-47	0.100		None	0	3
APC	P25054	APC regulator of WN...		703		0.373	0.962	1.00	0.100		None	0	1
C11orf65	Q8NCR3	chromosome 11 open...		45		0.670	0.462	2.0E-14	0.100		None	0	3
CYP17A1	P05093	cytochrome P450 fam...		326		0.462	0.769	2.6E-04	0.100		None	0	1
PALB2	Q86YC2	partner and localizer ...		260		0.485	0.769	3.0E-19	0.100		None	0	8

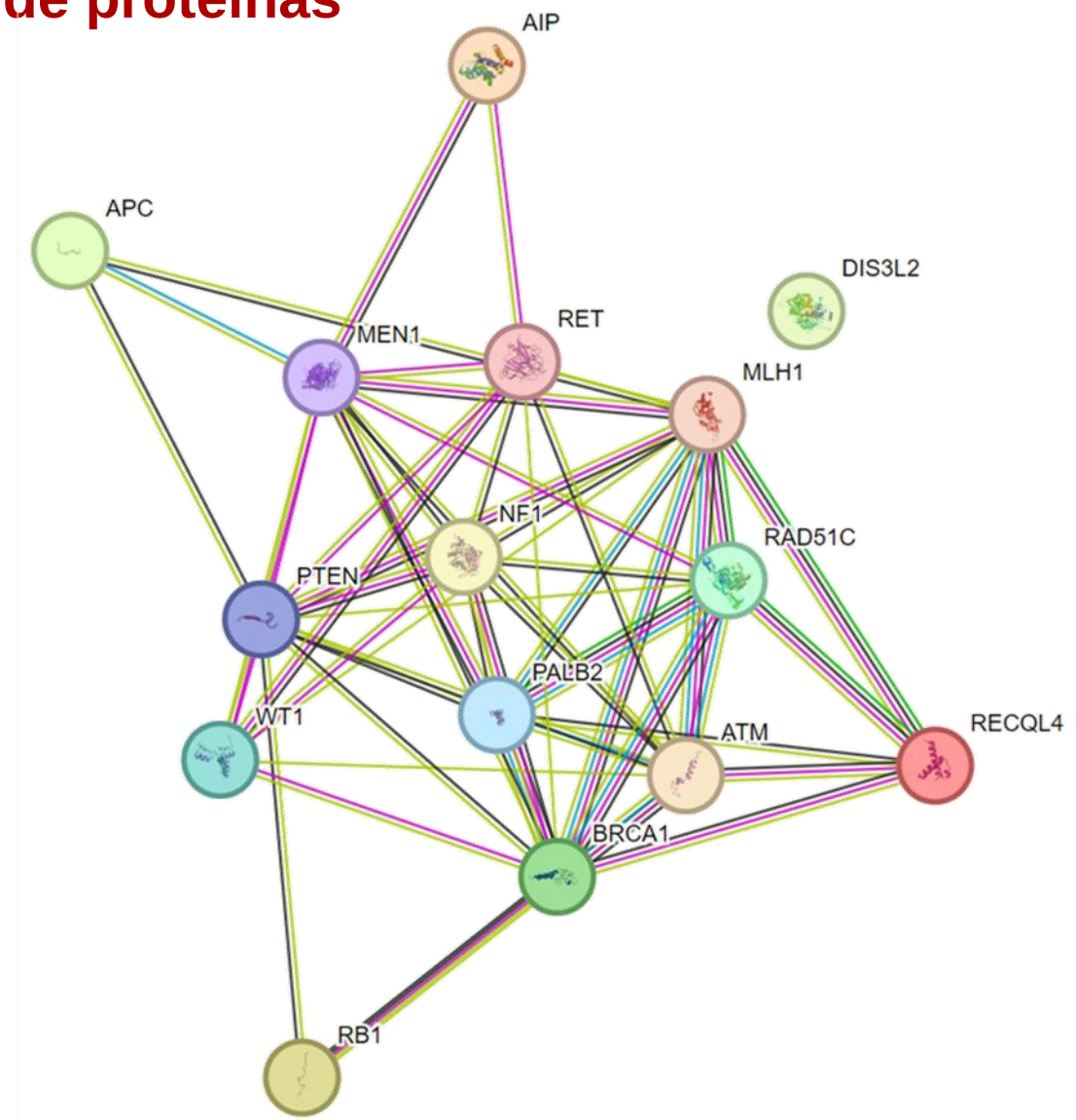
https://www.disgenet.org/

Genes con SNPs: Interacción de proteínas

Gene Ontology

GO-term	Biological process
GO:2001241	positive regulation of extrinsic apoptotic signaling pathway in absence of ligand
GO:0045141	meiotic telomere clustering

GO-term	Cellular component
GO:1990391	DNA repair complex



Known Interactions
- *from curated databases*
- *experimentally determined*

Predicted Interactions
- *gene neighborhood*
- *gene fusions*
- *gene co-occurrence*

Others
- *textmining*
- *co-expression*
- *protein homology*

String. 2023

Genes con SNPs: Historia familiar de cáncer

Gen	SNP	Significado clínico	Estudio realizado a familiares	Presencia de variante en otros estudios
AIP	rs267606568	VUS	–	Ca. Endometrio Ca. Próstata Ca. Tiroides
APC	rs745394881	VUS	–	
	rs1060503350	VUS	–	
	rs1377799096	VUS	+	Pob. Control
ATM	rs587779858	VUS	–	
	rs55633650	VUS	–	
	rs1060501661	VUS	+	Pob. Control
	rs1060501642	PAT	–	
	rs876658322	VUS	–	Ca. Próstata
	rs776938735	VUS	+	Pob. Control
	rs108364109	PAT	+	
	rs55830714	VUS	+	Pob. Control
	rs1555092528	VUS	+	Pob. Control
	rs1374689246	VUS	–	
	c.8558C>T	VUS	+	Pob. Control
BARD1	rs1283527672	VUS	+	Pob. Control
BRCA1	rs80357617	PAT	+	Pob. Control
	rs80357746	PAT	–	
	c.5075-3C>T	VUS	–	
	rs28897696	PAT	+	Ca. Tiroides
BRACA2	rs80359277	PAT	+	Pob. Control
	rs876659509	VUS	–	
	c.4521G>C	VUS	+	Pob. Control
	rs397507404	PAT	–	
CDKN1B	rs200422211	VUS	+	Pob. Control
DIS3L2	c.1425+1G>A	LPAT	–	
	rs756721316	VUS	–	
MEN1	rs376872829	VUS	+	Ca. Ovario Pob. Control
	rs1225964479	VUS	+	Pob. Control
MET	rs1306740707	VUS	–	
	c.4169A>C	VUS	–	
MLH1	c.207+4A>G	VUS	+	
	rs146777069	VUS	–	
MSH2	c.1360A>C	VUS	–	
	c.1405C>T	VUS	–	
MSH3	c.15G>T	VUS	–	
	rs575779178	VUS	–	
MSH6	rs587780673	VUS	+	Pob. Control

Gen	SNP	Significado clínico	Estudio realizado a familiares	Presencia de variante en otros estudios
MUTYH	c.1187G>A	PAT	–	
NF1	rs876660103	VUS	–	Ca. Tiroides
NF2	rs201527155	VUS	–	
NTHL1	c.38G>A	VUS	+	Pob. Control
	c.535G>A	VUS	–	
	c.607G>A	VUS	+	Pob. Control
PALB2	c.886dup	PAT	+	Pob. Control
	rs180177099	PAT	–	
	rs786203879	VUS	–	
	rs587776527	PAT	–	
PMS2	rs876659642	VUS	+	Pob. Control
POLD1	c.365T>G	VUS	–	
	rs753689379	VUS	–	
	rs2038876608	VUS	+	Pob. Control
	rs750085275	VUS	–	
POLE	c.3724T>C	VUS	–	
PTEN	c.39_40dup	PAT	+	
RAD51C	rs876659936	VUS	–	Ca. Tiroides
RB1	c.208G>A	VUS	–	Ca. Tiroides
RECQL4	c.263A>G	VUS	–	
	rs1178719750	VUS	–	
	rs1449551392	VUS	–	
	rs745874353	VUS	–	
	rs746636748	PAT	–	
	rs575020739	VUS	+	Pob. Control
	rs374225917	VUS	–	
	rs773856131	VUS	+	Pob. Control
RET	rs774347808	VUS	–	
SDHB	c.269G>T	LPAT	–	
SMARCE1	c.938G>T	VUS	–	
TSC1	rs1203864892	VUS	–	
TSC2	rs1555496979	VUS	–	
TP53	rs587782461	VUS	+	Pob. Control
WRN	rs781107893	VUS	+	Pob. Control
	c.1976A>T	VUS	–	
	rs769756672	VUS	–	
WT1	c.299C>G	LB	–	

VARIOMA ECUADOR:

Estudio de variantes genómicas y genéticas patogénicas y probablemente patogénicas en población ecuatoriana

PROCER:

Predisposición al cáncer en el Ecuador

PROCER: *2018-126E, MSP-DIS-2019-0283-O*

VARIOMA: *2018-127E, MSP-DIS-2019-0284-O*

SOLCA
NÚCLEO DE QUITO

Conclusiones

La población ecuatoriana tiene un componente trihíbrido de ancestría: Nativo americano, europeo y afroecuatoriano.

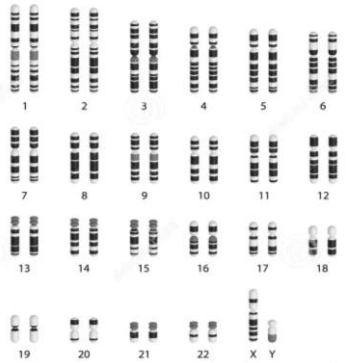
- Los estudios realizados en la población ecuatoriana con cáncer de mama para establecer el perfil genético incluyen la fragilidad cromosómica que se presentó con diferencia estadísticamente significativa en comparación al grupo control.

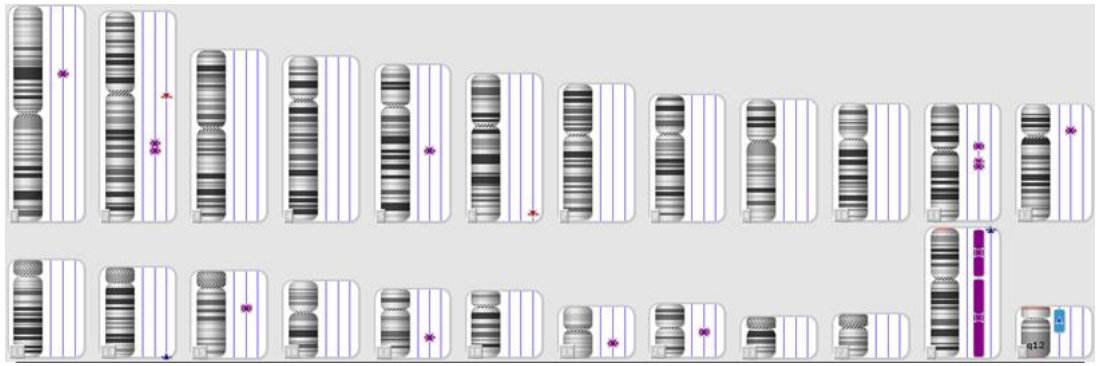
- El análisis de asociaciones teloméricas evidenció mayor presencia en los casos de cáncer de mama que la población control.

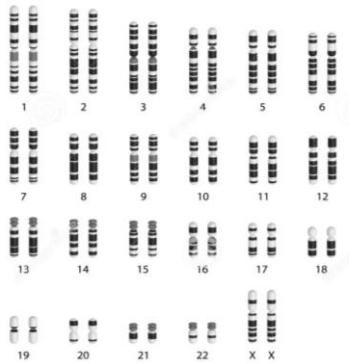
- Los estudios de citogenética convencional, en piezas extraídas quirúrgicamente, mostró cariotipo normal.

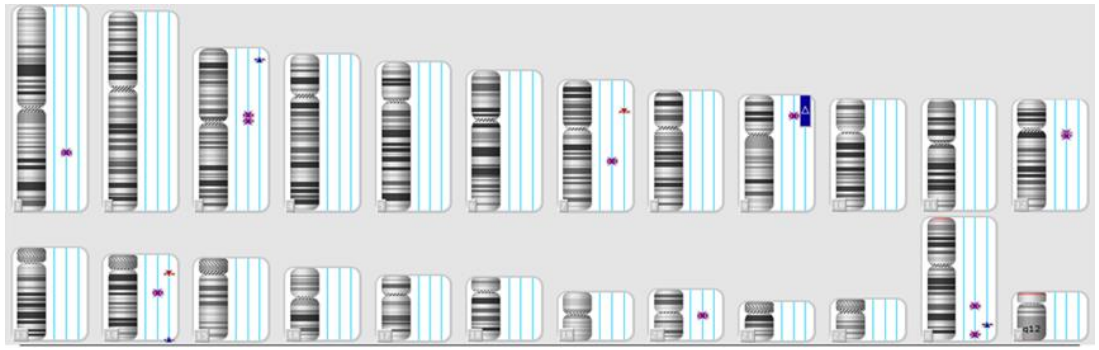
Retos

Detección de alteraciones en el número de copias cromosómicas









10 Mb

Submegabase

- Pérdida
- LOH
- Ganancia

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Conclusiones

- La FISH es una buena técnica, rápida y sensible, para evidenciar la amplificación del gen *HER2*.
- Los estudios de algunos genes, *MTHFR, AURKA* y *AKT1* mostraron estar asociados con el cáncer de mama en la población ecuatoriana.
- Las variantes de significado clínico patológicas identificadas se asociaron a alteraciones como deleciones y duplicaciones con la generación de codón de stop.
- La identificación de variantes genéticas propias de la población ecuatoriana, plantea la necesidad de profundizar la caracterización del perfil genético del cáncer de mama a través de la secuenciación de exoma o secuenciación de genoma completo.

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Retos

Secuenciación de exomas y secuenciación de genomas completos

Identificar nuevas variantes

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Agradecimientos

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desde 1954
7 DÉCADAS
de atención especializada en cáncer

¡Gracias!

julio 2024

UICC Member

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¡Juntos somos esperanza de vida!