CÁNCER HEREDO-FAMILIAR

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CASO CLÍNICO

- Paciente varón
- 15 años
- Tumoración en rodilla derecha 6 meses de evolución
- Informe AP: Osteosarcoma clásico

PREDISPOSICION GENÉTICA AL CÁNCER INFANTIL

- Sindromes que predisponen al cáncer infatil.
  - Qué son realmente?
    - Cambios (o mutaciones) de determinados genes se transmiten de un pariente consanguíneo a otro. Las personas que heredan uno de estos cambios en los genes tendrán una mayor probabilidad de sufrir cáncer a lo largo de su vida.
    - Determinados genes controlan el crecimiento, reproducción y/o muerte de las células manteniéndolas en equilibrio. Las mutaciones ocurridas en estos genes alteran este equilibrio y aumentan el riesgo de desarrollar un tumor. El cáncer es el resultado de la acumulación de mutaciones en varios genes que son importantes en la regulación del ciclo de vida de las células.

ALGUNAS DEFINICIONES

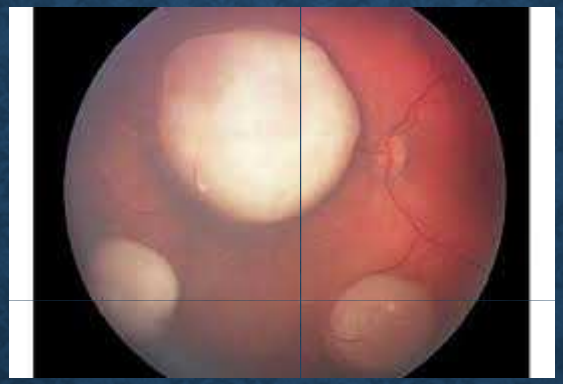
- La predisposición y el alto riesgo de cáncer observado en los casos hereditarios, se expresa en las familias con características particulares que muchas veces ayudan a su sospecha y detección:

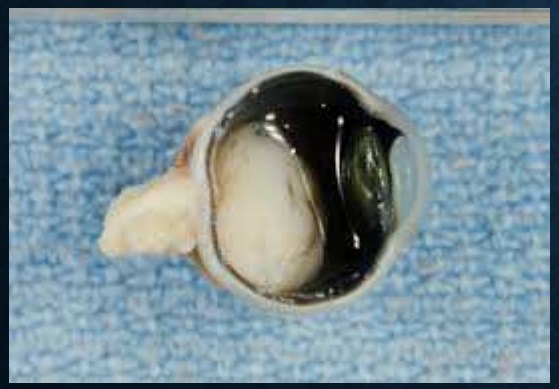
- Aparición de tumores a edades más tempranas que las esperadas en la población general.
- Varios miembros de la familia afectados con el mismo cáncer.
- Más de una generación de familiares que tuvieron el mismo cáncer.
- Afección de órganos múltiples o bilaterales en el caso de órganos pares (ejemplo: mamas, riñón, polipos colónicos múltiples, etc.)
- Casos donde se observa más de un tumor en el mismo individuo (dos o más tumores diferentes a lo largo de la vida)
- Determinados tumores en etnias específicas (Ej.: Judíos ashkenazies para cáncer de mama-ovario hereditario)
- Aparición de tumores raros en un solo individuo o varios en la familia (Ej.: cáncer medular de tiroides, feocromocitoma, retinoblastoma, etc.)

ALGUNAS DEFINICIONES

- La gran mayoría de las mutaciones causales de los cánceres hereditarios se transmiten de padres a hijos y de generación en generación con un patrón llamado autosómico dominante. Esto significa que para que el riesgo de desarrollar cáncer aumente, debemos heredar una mutación de uno solo de nuestros progenitores, ya sea el materno o el paterno.
- La probabilidad que tiene un individuo portador de una mutación de desarrollar la enfermedad es denominada Penetrancia. La magnitud de este riesgo es variable y depende de cada gen en cada Síndrome y también de las características familiares de los individuos y de la población a la que pertenecen.

RETINOBLASTOMA- PROTOTIPO DEL CÁNCER INFANTIL HEREDITARIO





RETINOBLASTOMA- PROTOTIPO DEL CÁNCER INFANTIL HEREDITARIO

Proc. Nat. Acad. Sci. USA
Vol. 68, No. 4, pp. 820–823, April 1971

Mutation and Cancer: Statistical Study of Retinoblastoma

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Communicated by James V. Neel, February 8, 1971

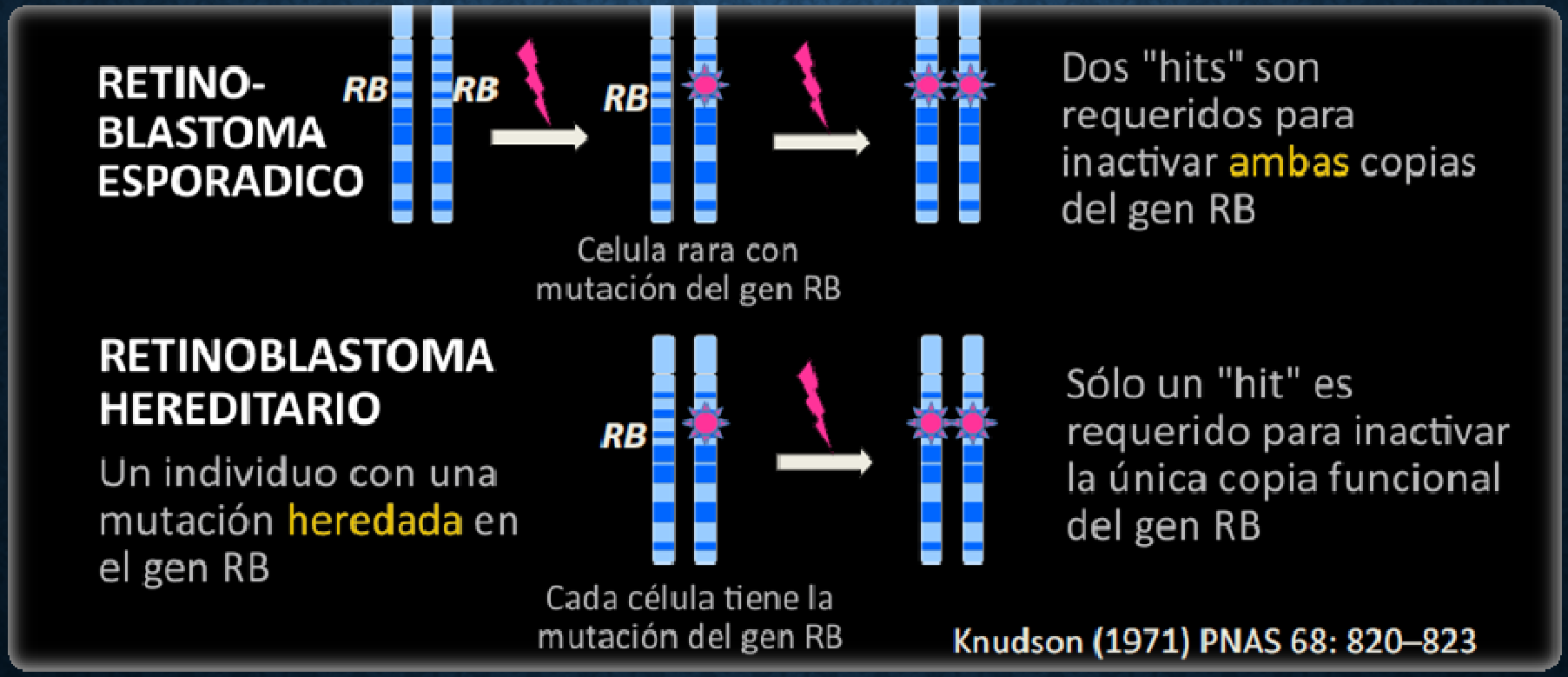
PATIENT DATA

The records of all retinoblastoma patients admitted to the M. D. Anderson Hospital, some 48 cases during the period 1944–1969, were reviewed. These cases are tabulated (Table 1) with respect to unilaterality or bilaterality, sex, age at diagnosis, and family history. Whenever possible, the number of tumors in each eye was estimated.

RETINOBLASTOMA- PROTOTIPO DEL CÁNCER INFANTIL HEREDITARIO

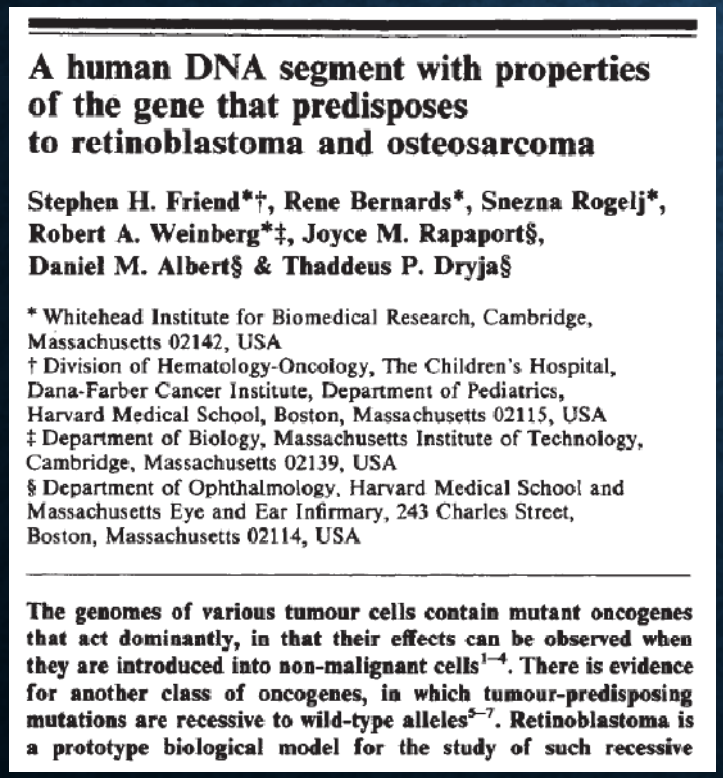
Feature	Non-heritable	Heritable
Tumor	Unilateral	Bilateral
Family history	None	20% of cases
Age at dx	2 years	<1 year
Increased risk of second primaries?	No	osteosarcoma, sarcomas, pineal involvement

HIPOTESIS DE LOS DOS HITS DE KNUDSON



RETINOBLASTOMA- PROTOTIPO DEL CÁNCER INFANTIL HEREDITARIO

- RB1 es identificado como un gen que predispone al cáncer.
- SH Friend et al, Science, 1986



A human DNA segment with properties of the gene that predisposes to retinoblastoma and osteosarcoma

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The genomes of various tumour cells contain mutant oncogenes that act dominantly, in that their effects can be observed when they are introduced into non-malignant cells[1–4]. There is evidence for another class of oncogenes, in which tumour-predisposing mutations are recessive to wild-type alleles[5–7]. Retinoblastoma is a prototype biological model for the study of such recessive oncogenes[8]. This malignant tumour, which arises in the eyes of children, can be explained as the result of two distinct genetic changes, each causing loss of function of one of the two homologous copies at a single genetic locus, *Rb* (refs 9–12), assigned to the q14 band of human chromosome 13 (refs 13–22). Mutations affecting this locus may be inherited from a parent, may arise during gametogenesis or may occur somatically. Those who inherit a mutant allele at this locus have a high incidence of non-ocular, second tumours[23], almost half of which are osteosarcomas believed to be caused by the same mutation[24,25]. Here we describe the isolation of a complementary DNA segment that detects a chromosomal segment having the properties of the gene at this locus. The gene is expressed in many tumour types, but no RNA transcript has been found in retinoblastomas and osteosarcomas. The cDNA fragment detects a locus spanning at least 70 kilobases (kb) in human chromosome band 13q14, all or part of which is frequently deleted in retinoblastomas and osteosarcomas.

OMIM, ONLINE MENDELIAN INHERITANCE IN MAN

SYNDROME (OMIM ENTRY)	PRIMARY COMPONENT TUMORS[a]	INHERITANCE	GENES
HEREDITARY BREAST CANCER SYNDROMES			
Hereditary breast and ovarian cancer (113705, 600185, 605724-*FANCD1*)	Breast cancer, ovarian cancer	Dominant	*BRCA1, BRCA2*
	Prostate cancer, pancreatic cancer, melanoma	Dominant	*BRCA2*
	Fanconi anemia (*FANCD1*) in biallelic carriers, medulloblastoma	Recessive	*BRCA2*
Partner and localizer of *BRCA2* (610355)	See *BRCA2* above	Dominant	*PALB2 (FANCN)*
BRCA1-interacting protein 1 (605882, 609054 *BRIP1*)	See *BRCA1* above; Fanconi anemia (*FANCJ*) in biallelic carriers	Recessive	*BRIP1*
Li-Fraumeni syndrome (151623)	Breast cancer, sarcomas (soft tissue/ osteosarcoma), brain tumors, adrenocortical carcinoma	Dominant	*p53*
Cowden syndrome (158350-*PTEN*, 612105-*Killin*)	Breast, thyroid, endometrial cancers	Dominant	*PTEN, KILLIN*
Bannayan-Riley-Ruvalcaba syndrome (153480)	Breast cancer, meningioma, thyroid follicular cell tumors	Dominant	*PTEN*
Ataxia telangiectasia (208900)	Leukemia	Recessive	*ATM*
Other hereditary breast cancer (604373)	Breast cancer (2-fold risk)	Dominant	*CHEK2*

OMIM, ONLINE MENDELIAN INHERITANCE IN MAN

HEREDITARY GASTROINTESTINAL MALIGNANCIES			
Lynch syndrome (also known as HNPCC) (120435, 613244-*EPCAM/TACSTD1*)	Colon, endometrial cancers; gastric, hepatobiliary, ovarian, pancreatic, renal, pelvis, small bowel, and ureteral cancers	Dominant	*MLH1, MSH2 (including EPCAM), MSH6, PMS2*
Includes Turcot syndrome (276300)	Glioblastoma		
Familial adenomatous polyposis, including attenuated phenotype (175100)	Colon cancer; gastric, duodenal, ampullary cancers	Dominant	*APC*
Includes Turcot syndrome (276300)	Medulloblastoma		
MYH-associated polyposis (608456)	Colon cancer	Recessive	*MYH*
Mismatch repair cancer syndrome (276300)	Colon, CNS, hematologic, and other cancers	Recessive	*MLH1, MSH2 MSH6, PMS2*
Hereditary diffuse gastric cancer (137215)	Gastric cancer; lobular breast cancer	Dominant	*CDH1*
Juvenile polyposis (174900)	Gastrointestinal cancers; Pancreatic cancer	Dominant	*SMAD4 (DPC4), BMPR1A*
Peutz-Jeghers syndrome (175200)	Colon, small bowel, breast, ovarian, and pancreatic cancers	Dominant	*STK11*
Hereditary pancreatic cancer (600185, 260350)	Pancreatic cancer; breast and ovarian cancers	Dominant	*BRCA2, PALB2*
Hereditary melanoma pancreatic syndrome (606179)	Pancreatic cancer, melanoma	Dominant	*CDKN2A (p16)*
Hereditary pancreatitis (167800)	Pancreatic cancer	Dominant	*PRSS1*
Familial gastrointestinal stromal syndrome (606764)	Gastrointestinal stromal tumors	Dominant	*KIT*
Oligodontia-colorectal cancer syndrome (608615)	Colon cancer	Dominant	*AXIN2*

OMIM, ONLINE MENDELIAN INHERITANCE IN MAN

GENODERMATOSES WITH CANCER PREDISPOSITION			
Melanoma syndromes (155600, 155601, 609048, 608035)	Malignant melanoma	Dominant	*CDNK2 (p16), CDK4, CMM*
Basal cell carcinoma/nevus syndrome/Gorlin syndrome (109400)	Basal cell cancers; medulloblastoma, ovarian cancer	Dominant	*PTCH*
Cowden syndrome	See above	Dominant	*PTEN*
Neurofibromatosis 1 (162200)	Neurofibrosarcoma, pheochromocytoma, optic gliomas, meningiomas	Dominant	*NF1*

SYNDROME (OMIM ENTRY)	PRIMARY COMPONENT TUMORS[a]	INHERITANCE	GENES
Neurofibromatosis 2 (101000)	Vestibular schwannoma	Dominant	*NF2*
Tuberous sclerosis (191100)	Renal cancer, multiple bilateral renal angiomyolipoma, myocardial rhabdomyoma, ependymoma, giant cell astrocytoma	Dominant	*TSC1, TSC2*
Carney complex (160980, 605244)	Myxoid subcutaneous tumors, primary adrenocortical nodular hyperplasia, testicular Sertoli cell tumor, atrial myxoma, pituitary adenoma, mammary fibroadenoma, thyroid carcinoma, schwannoma	Dominant	*PRKAR1A*
Muir-Torre syndrome (variant of Lynch syndrome; 158320)	Sebaceous neoplasia (adenoma, keratoacanthoma, carcinoma); see Lynch syndrome above for other component tumors	Dominant	*MLH1, MSH2, MSH6*
Xeroderma pigmentosum (278730, 278700, 278720, 278760, 274740, 278780, 278750, 133510)	Skin cancer, melanoma, leukemia	Recessive	*XPA–G, POLH*
Rothmund-Thomson syndrome (268400)	Basal and squamous cell carcinoma, osteogenic sarcoma	Recessive	*RECQL4*
LEUKEMIA/LYMPHOMA PREDISPOSITION SYNDROMES			
Bloom syndrome (210900)	Leukemia, carcinoma of the tongue, squamous cancers, Wilms tumor	Recessive	*BLM*
Fanconi anemia, several complementation groups (227650)	Leukemia; squamous cancers; hepatoma; and brain, skin, vulvar, and cervical cancers; see hereditary breast cancer above (*FANCD1, J*)	Recessive	*FANCA, B, C, D2, E, F, G, I, L, M, N (FANCH is FANCA)*
Shwachman-Diamond syndrome (260400)	Myelodysplasia, acute myelogenous leukemia	Recessive	*SBDS*
Nijmegen breakage syndrome (251260)	Lymphoma, glioma, medulloblastoma, rhabdomyosarcoma	Recessive	*NBS1*
Canale-Smith syndrome (601859)	Lymphoma	Dominant	*FAS, FASL*
Hodgkin lymphoma (236000)	Hodgkin lymphoma	Recessive	*KLHDC8B*
IMMUNODEFICIENCY SYNDROMES			
Wiskott-Aldrich syndrome (301000)	Hematopoietic malignancies	X-linked recessive	*WAS*
Severe combined immune deficiency (102700, 300400, 312863, 601457, 600802, 602450)	B-cell lymphoma	X-linked recessive Recessive	*IL2RG, ADA, JAK3, RAG1, RAG2, IL7R, CD45, Artemis*
X-linked lymphoproliferative syndrome (308240)	Lymphoma	X-linked recessive	*SH2D1A*
GENITOURINARY CANCER PREDISPOSITION SYNDROMES			
Hereditary prostate cancer (176807, 601518)	Prostate cancer	Dominant	*HPC1, HPCX, HPC2/ELAC2, PCAP, PCBC, PRCA*
Simpson-Golabi-Behmel syndrome (312870)	Embryonal tumors, Wilms tumor	X-linked recessive	*GPC3*
Von Hippel-Lindau syndrome (193300)	Hemangioblastomas (retina and CNS), renal cell cancer (clear cell), pheochromocytomas, endolymphatic sac tumors	Dominant	*VHL*
Beckwith-Wiedemann syndrome (130650)	Wilms tumor, hepatoblastoma, adrenal carcinoma, gonadoblastoma	Dominant	*CDKN1C, NSD1*
Wilms tumor syndrome (194070)	Wilms tumor	Dominant	*WT1*
Wilms tumor, aniridia, genitourinary abnormalities, mental retardation (WAGR) (194072)	Wilms tumor, gonadoblastoma	Dominant	*WT1*
Birt-Hogg-Dubé syndrome (135150)	Renal tumors	Dominant	*FLCN*
Papillary renal cancer syndrome (605074)	Papillary renal tumor	Dominant	*MET, PRCC*

RÁPIDA EVOLUCIÓN

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ermline *HABP2* Mutation Causing Familial Nonmedullary yroid Cancer

lheer Kumar Gara, Ph.D., Li Jia, Ph.D., Maria J. Merino, M.D., Sunita K. Agarwal, Ph.D., a Zhang, Ph.D., Maggie Cam, Ph.D., Dhaval Patel, M.D., and Electron Kebebew, M.D.
ocrine Oncology Branch (S.K.G., L.Z., D.P., E.K.), Bioinformatics Core (L.J.) and Laboratory athology (M.J.M.), Center for Cancer Research, and the Office of Science and Technology ources (M.C.), National Cancer Institute, and the Metabolic Diseases Branch, National itute of Diabetes and Digestive and Kidney Diseases (S.K.A.) — both in Bethesda, MD

MMARY

Familial nonmedullary thyroid cancer accounts for 3 to 9% of all cases of thyroid cancer, but the susceptibility genes are not known. Here, we report a germline variant of *HABP2* in seven affected members of a kindred with familial nonmedullary thyroid cancer and in 4.7% of 423 patients with thyroid cancer. This variant was associated with increased HABP2 protein expression in tumor samples from affected family members, as compared with normal adjacent thyroid tissue and samples from sporadic cancers. Functional studies showed that *HABP2* has a tumor-suppressive effect, whereas the G534E variant results in loss of function

nature genetics

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Mutations in the transcriptional repressor *REST* predispose to Wilms tumor

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- Predisposición al Cáncer puede estar desencadenada por gran variedad de mutaciones de la línea germinal:
  - Gen supresor inactivo,
  - Gen de reparación Inactivo
  - Un oncogén Activado
- Se abarca un amplio espectro de enfermedades raras
- Cada una de estas tiene sus características clinicas particulares y únicas
- **Se calcula que aproximadamente 8,5% del cancer es heredado.**

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gl J Med. 2015 December 10; 373(24): 2336–2346. doi:10.1056/NEJMoa1508054.

mline Mutations in Predisposition Genes in Pediatric Cancer

ui Zhang, Ph.D.[#], Michael F. Walsh, M.D.[#], Gang Wu, Ph.D.[#], Michael N. Edmonson, Tanja A. Gruber, M.D., Ph.D., John Easton, Ph.D., Dale Hedges, Ph.D., Xiaotu Ma, Xin Zhou, Ph.D., Donald A. Yergeau, Ph.D., Mark R. Wilkinson, B.S., Bhavin daria, B.A., Xiang Chen, Ph.D., Rose B. McGee, M.S., Stacy Hines-Dowell, D.N.P., a Nuccio, M.S., Emily Quinn, M.S., Sheila A. Shurtleff, Ph.D., Michael Rusch, B.A., Patel, M.S., Jared B. Becksfort, M.S., Shuoguo Wang, Ph.D., Meaghann S. Weaver, Li Ding, Ph.D., Elaine R. Mardis, Ph.D., Richard K. Wilson, Ph.D., Amar Gajjar, M.D., W. Ellison, M.D., Ph.D., Alberto S. Pappo, M.D., Ching-Hon Pui, M.D., Kim E. Nichols, and James R. Downing, M.D.

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e authors contributed equally to this work.

ract

ACKGROUND—The prevalence and spectrum of predisposing mutations among children and olescents with cancer are largely unknown. Knowledge of such mutations may improve the derstanding of tumorigenesis, direct patient care, and enable genetic counseling of patients and milies.

ETHODS—In 1120 patients younger than 20 years of age, we sequenced the whole genomes 595 patients), whole exomes (in 456), or both (in 69). We analyzed the DNA sequences of 565 nes, including 60 that have been associated with autosomal dominant cancer-predisposition ndromes, for the presence of germline mutations. The pathogenicity of the mutations was termined by a panel of medical experts with the use of cancer-specific and locus-specific genetic tabases, the medical literature, computational predictions, and second hits identified in the mor genome. The same approach was used to analyze data from 966 persons who did not have own cancer in the 1000 Genomes Project, and a similar approach was used to analyze data from autism study (from 515 persons with autism and 208 persons without autism).

RESULTS—Mutations that were deemed to be pathogenic or probably pathogenic were identified in 95 patients with cancer (8.5%), as compared with 1.1% of the persons in the 1000 Genomes Project and 0.6% of the participants in the autism study. The most commonly mutated genes in the affected patients were *TP53* (in 50 patients), *APC* (in 6), *BRCA2* (in 6), *NF1* (in 4), *PMS2* (in 4), *RB1* (in 3), and *RUNX1* (in 3). A total of 18 additional patients had protein-truncating mutations in tumor-suppressor genes. Of the 58 patients with a predisposing mutation and available information on family history, 23 (40%) had a family history of cancer.

CONCLUSIONS—Germline mutations in cancer-predisposing genes were identified in 8.5% of the children and adolescents with cancer. Family history did not predict the presence of an underlying predisposition syndrome in most patients. (Funded by the American Lebanese Syrian Associated Charities and the National Cancer Institute.)

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re forms provided by the authors are available with the full text of this article at NEJM.org.


TENER EN CUENTA LAS REGIONES NO CODIFICANTES
TENER EN CUENTA LAS VARIANTES EPIGENETICAS

Tumor Type	Differential genetic diagnosis	Gene(s)
Adrenocortical	Li-Fraumeni (LFS)	*TP53*
Atypical Teratoid Rhabdoid	Rhabdoid tumor syndrome	*SMARCB1/INI1*
Breast cancer, early onset	**LFS**	***TP53***
Choroid plexus carcinoma	LFS	*TP53*
Desmoid tumor	Familial adenomatous polyposis (FAP)	*APC*
Glioblastoma	Turcot/Lynch syndrome, LFS	*MLH1, MSH2, MSH6, PMS2, TP53*
Hemangioblastoma	Von-Hippel Lindau (VHL)	*VHL*
Hepatoblastoma	FAP, BWS/IHH	*APC, 11p15*
Medulloblastoma	Turcot/FAP, Nevoid Basal Cell Carcinoma Syndrome	*APC, PTCH1*
Medullary Thyroid Cancer	MEN, type 2 (MEN2)	*RET*

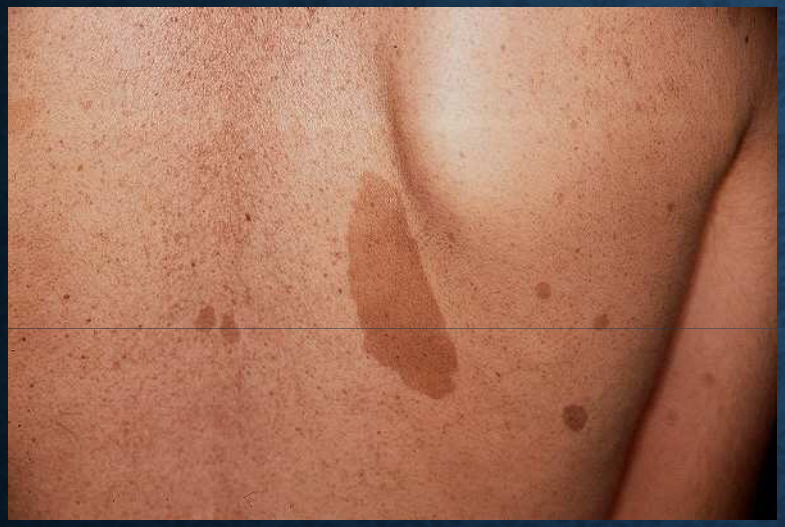
Tumor Type	Differential genetic diagnosis	Gene(s)
Neuroblastoma	Familial neuroblastoma	*ALK, PHOX2B*
Optic pathway tumor	Neurofibromatosis, type 1 (NF1)	*NF1*
Ovarian sex cord-stromal; Sertoli-Leydig cell tumors	PPB family tumor syndrome	*DICER1*
Paraganglioma/Pheochromocytoma	Familial PGL/PCC, VHL, MEN2, NF1	*SDHB, C D, A, AF2, TMEM127, MAX; VHL; RET; NF1*
Retinoblastoma (RB)	Familial RB	*RB1*
Pleuropulmonary blastoma (PPB)	PPB family tumor syndrome	*DICER1*
Sarcomas (OS, Rhabdo, lipo)	**LFS**, PPB tumor syndrome, BWS	***TP53***, *DICER1, 11p15*
Schwannoma	Neurofibromatosis, type 2 (NF2)	*NF2*
Wilms tumor	Wilms tumor syndromes, BWS/IHH	*WT1, 11p15*

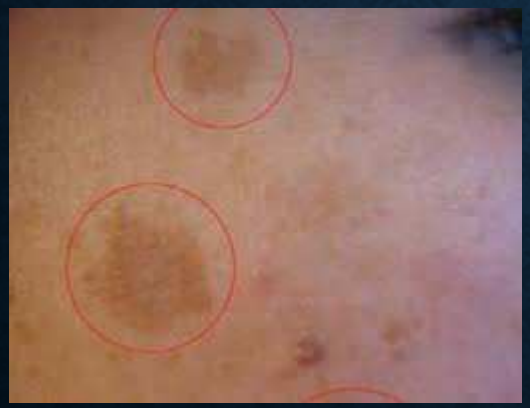
CARACTERÍSTICAS CLÍNICAS DE LOS SMES GENÉTICOS ASOCIADOS A CÁNCER

- TENER EN CUENTA QUE PODEMOS HACER HALLAZGOS CLINICOS PREVIOS A LA APARICION DEL CANCER

  - CARACTERISTICAS ESPECIFICAS DE UN SME PARTICULAR
  - RETRASO DEL CRECIMIENTO O SESARROLLO, AUTISMO
  - MACROCEFALIA, SOBRECRECIMIENTO, HEMIHIPERTROFIA
  - MANCHAS CAFE CON LECHE, PECAS, QUISTES
  - PIEZAS DENTARIAS EXTRAS O FALTANTES
  - NODULOS DE LISCH, TELANGIECTASIA

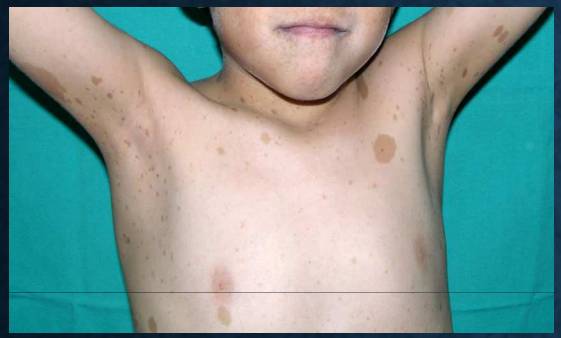
MANCHAS CAFÉ CON LECHE



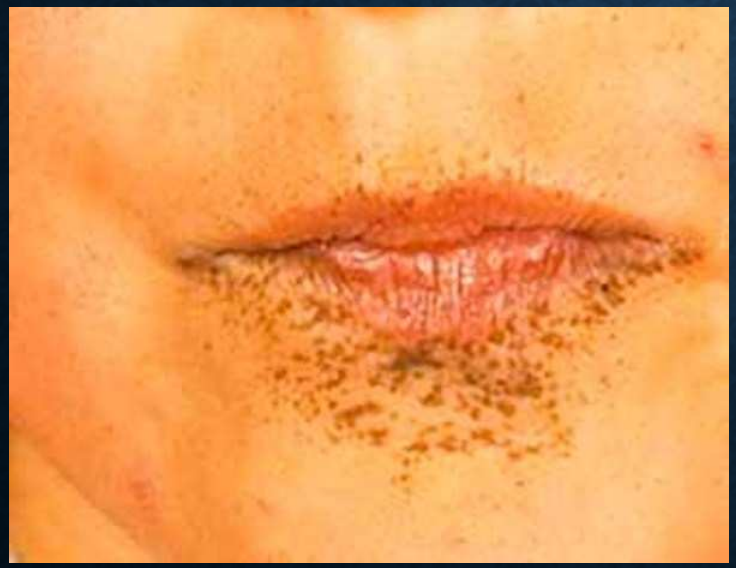


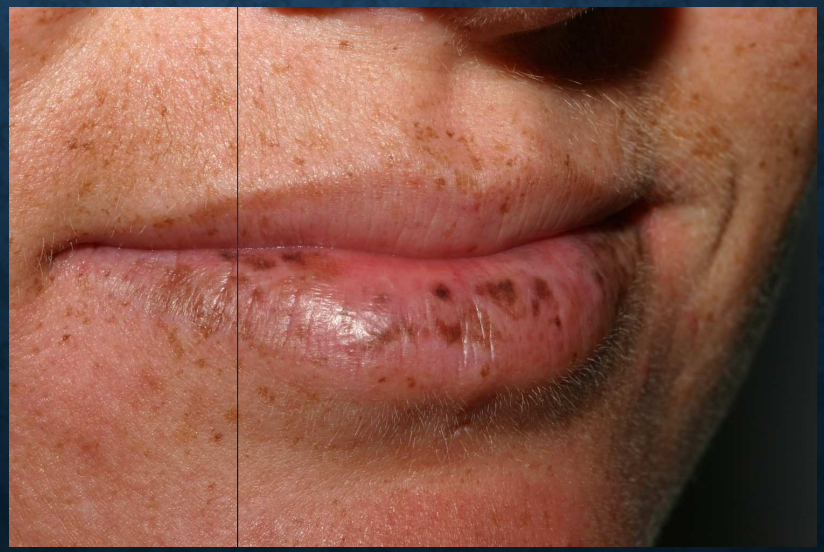
Manifestaciones típicas de NF1

PECAS



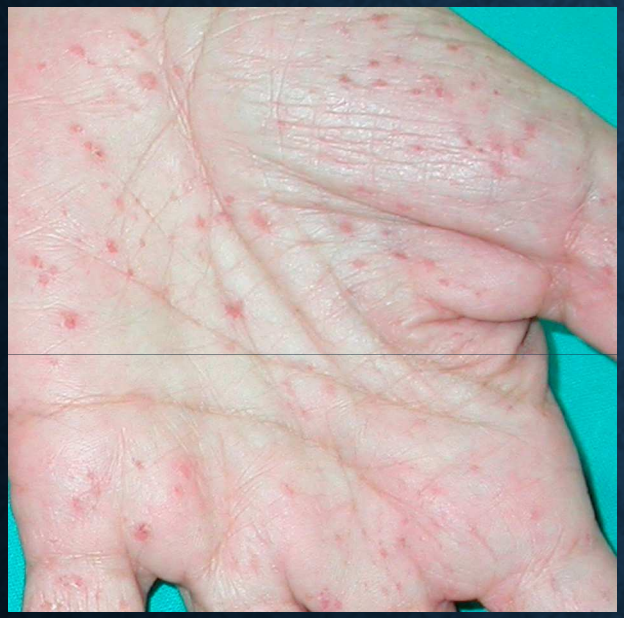
NF1



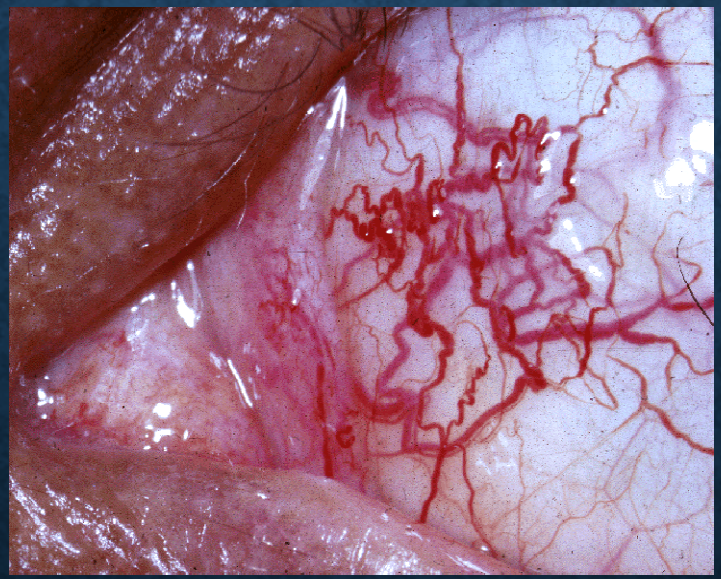


Puetz Jehgers Syndrome

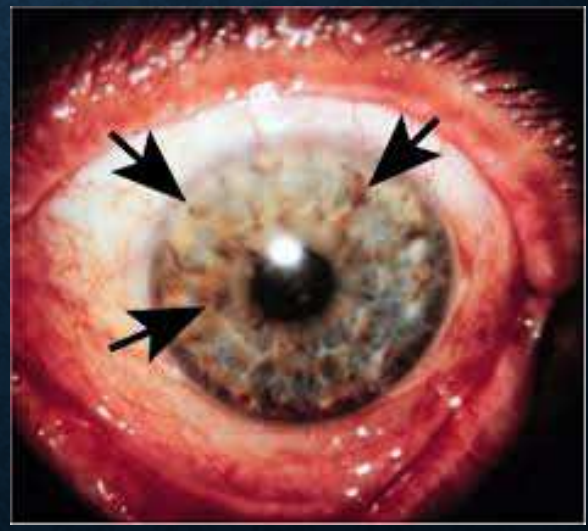
PITS / TELANGIECTASIAS/N. DE LISCH



Gorlin
Syndrome

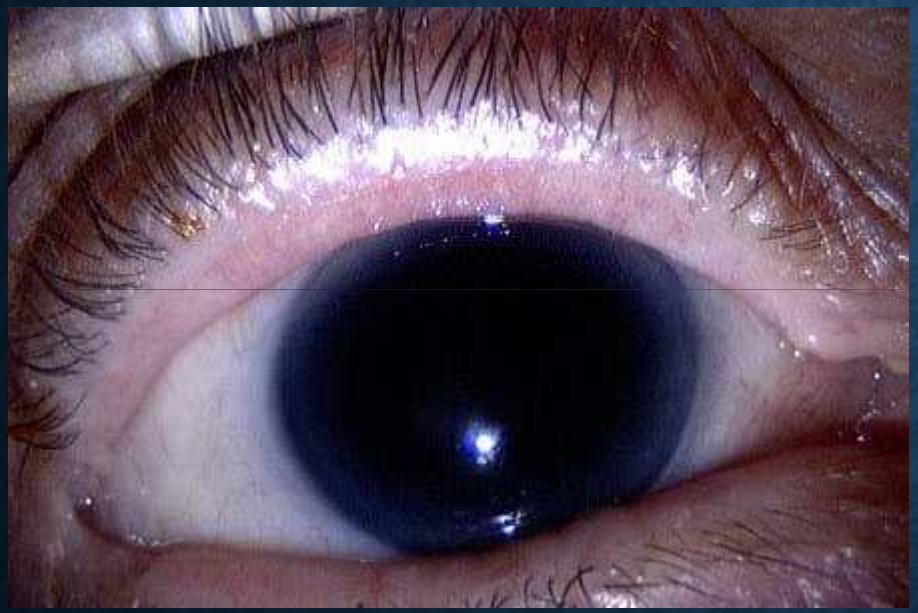


Ataxia
Telangiectasia

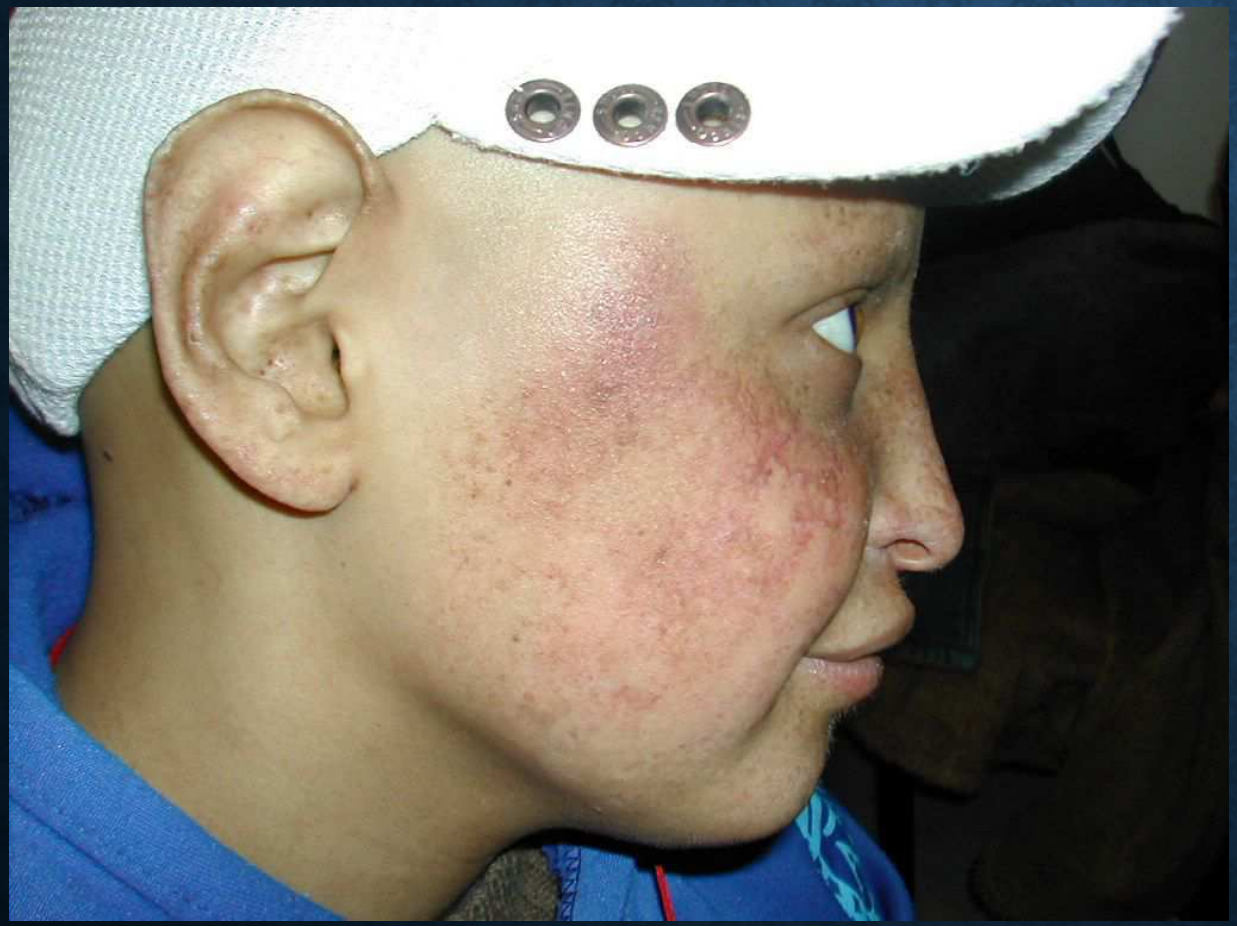


NF1

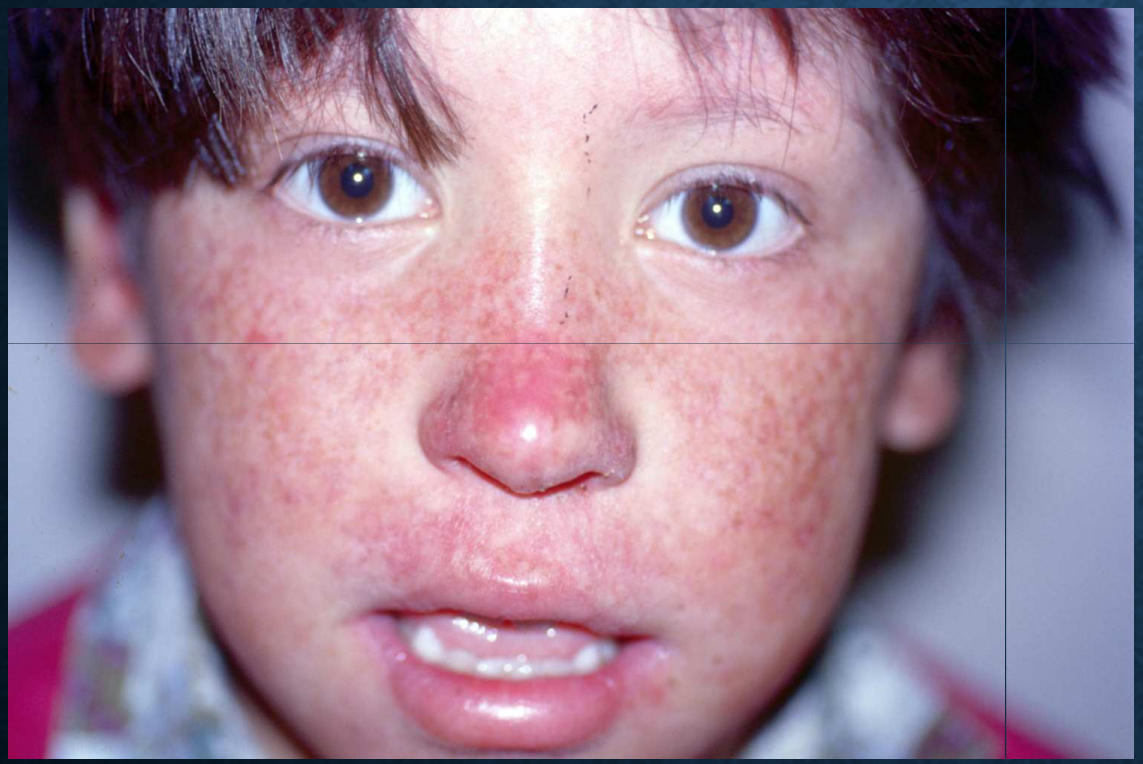
ANIRIDIA



Tumor de Wilms
Aniridia
Malformaciones G.ur.
Retraso Mental
(Sindrome de WAGR)



15 años



5 años

SME DE ROTHMUND - THOMPSON

- A P de bajo peso y falla en el crecimiento.
- Lesiones cutáneas a partir de los primeros meses de vida.
- Eritema difuso de las mejillas con telangiectasias e hipopigmentación que evoluciona rápidamente en parches reticulados rojo amarronados y asociados con atrofia (Poiquilodermia congénita)
- Fotosensibilidad con vesiculación y ampollas.
- Hiperqueratosis verrucosa en manos, pies, rodillas y tobillos
- Anormalidades dentarias.
- Cataratas.
- **Alta frecuencia de Cancer fundamentalmente Osteosarcoma**

A QUIEN Y CUANDO HACER UN TEST?

- Sobre poner ante todo el principio de PRIMUM NON NOCERE
  - Historia Familiar
  - Tipo de Tumor
  - Características Clínicas

HISTORIA FAMILIAR

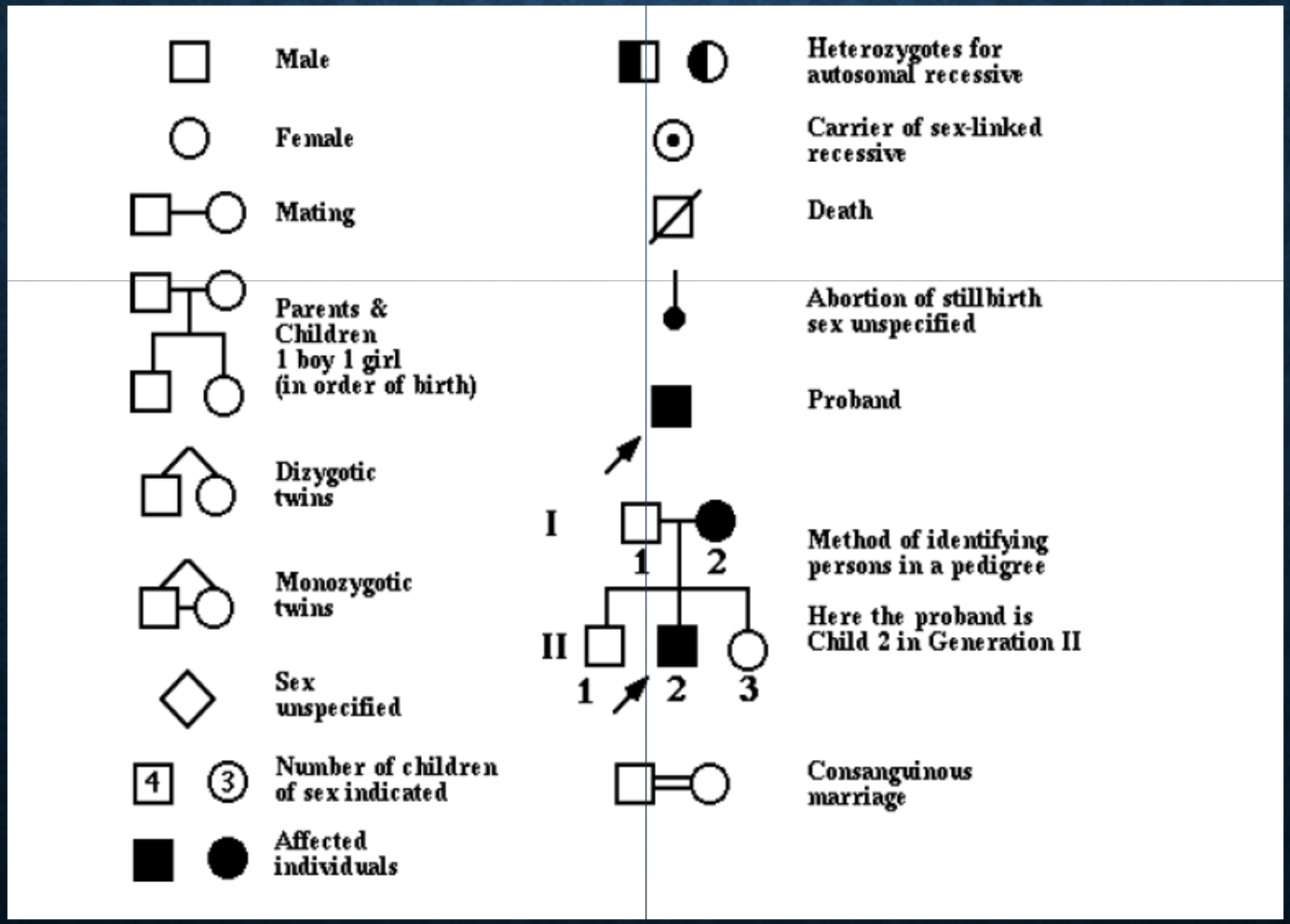
- La historia familiar es un elemento clave para la evaluación de riesgo.
- Se confecciona un árbol genealógico donde constan al menos tres generaciones consecutivas o hasta los familiares de segundo grado afectados

PRIMER GRADO	SEGUNDO GRADO	TERCER GRADO
PADRE / MADRE	ABUELO / ABUELA	BISABUELO / BISABUELA
HIJO/ HIJA	NIETO / NIETA	BISNIETO / BISNIETA
HERMANO /HERMANA	TIO / TIA	SOBRINO / SOBRINA

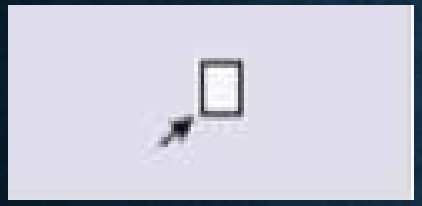
HISTORIA FAMILIAR

- Familiares sanos, afectados y fallecidos
- Tipo de cáncer o canceres presentes en la familia
- Edad actual y edad de diagnóstico de cáncer
- Numero de tumores, distinguiendo entre segundos tumores primarios o recidivas
- Localización de o los tumores
- Fecha, edad y causa de muerte
- Patologías asociadas de interés
- Otros datos que puedan resultar relevantes (abortos, recién nacidos muertos, malformaciones, retraso mental, etc)
- Estudios genéticos realizados si los hubiera

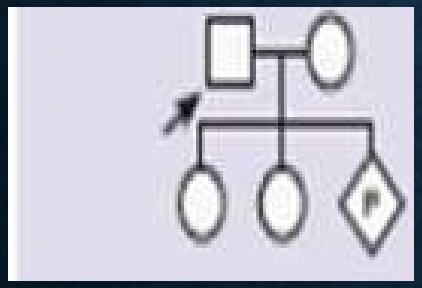
SIMBOLOGÍA DEL ÁRBOL GENEALÓGICO O PEDIGREE



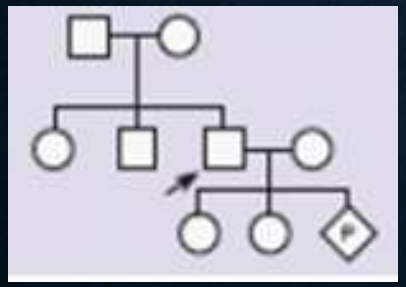
PEDIGREE



La gráfica inicia con la persona que se entrevista y se marcará c



Pareja e hijos



Padres y hermanos

A QUIÉN Y CUANDO HACER UN TEST II?

- Sobreponer ante todo el principio de PRIMUM NON NOCERE
  - Tenemos chance de encontrar una mutación
  - Existe un test disponible?
    - Es sensible y especifico?
  - Nos debe ayudar
    - Definir el espectro de un tumor especifico
    - Edad y sitio de aparición
    - Opciones de vigilancia, prevención y tratamiento

- El testeo puede ser hecho
    - Paciente pre sintomático
        - Población de riesgo
        - Comenzar con screening, detección temprana y tratamiento precoz
        - Educación y cambios de hábitos
    - En el niño con cáncer
        - Modificar tratamiento
        - Vigilancia para segundos tumores

- Sin Embargo
    - Es caro por el momento
    - Toma tiempo
    - Se desconoce el real impacto
    - Se interponen cuestiones éticas/emocionales/sociales

CONCLUSION

- El espectro de los síndromes de predisposición al cáncer aumenta día a día
- Muchos Sindromas Asociados al cáncer se manifiestan en la niñez
- La prueba genética puede mejorar la calidad de vida de los pacientes ayudando al diagnóstico precoz y el tratamiento oportuno.

CONCLUSIÓN II

- De nada vale el testeo genético si nos olvidamos de **preguntar** cuando hacemos la historia clínica

- De nada vale el testeo genético si nos olvidamos de **revisar al paciente de pies a cabeza cuando viene a nuestra consulta aunque sea por una simple angina**

CONCLUSIÓN III

- Porqué llegar a

CONCLUSIÓN III

- Si tenemos

GRACIAS !!!