Las causas de la diversidad: Genética y epigenética

Angel Carracedo

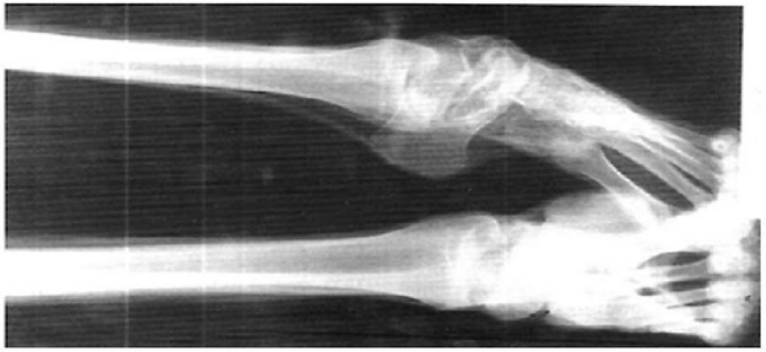
Fundación Galega de Medicina Xenómica-Servicio Galego de Saúde

Instituto de Ciencias Forenses e Centro Nacional de Xenotipado-Universidade de Santiago de Compostela

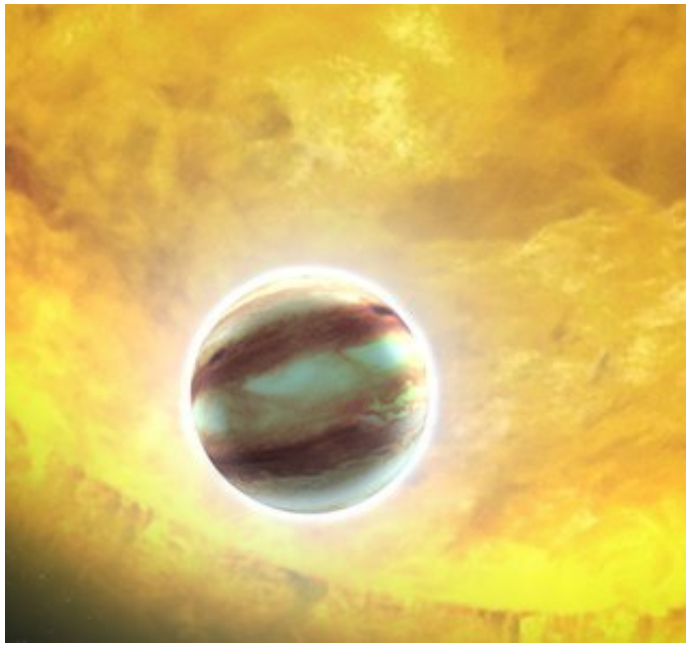
Somos genes y ambiente. El ambiente y las circustancian también condicionan lo que somos

Tanto genes como ambiente no son siempre favorables

Lo primero que permite la ciencia es entender las causas de lo que pasa y no atribuirlas a fenómenos supranaturales



Momia de Siptah

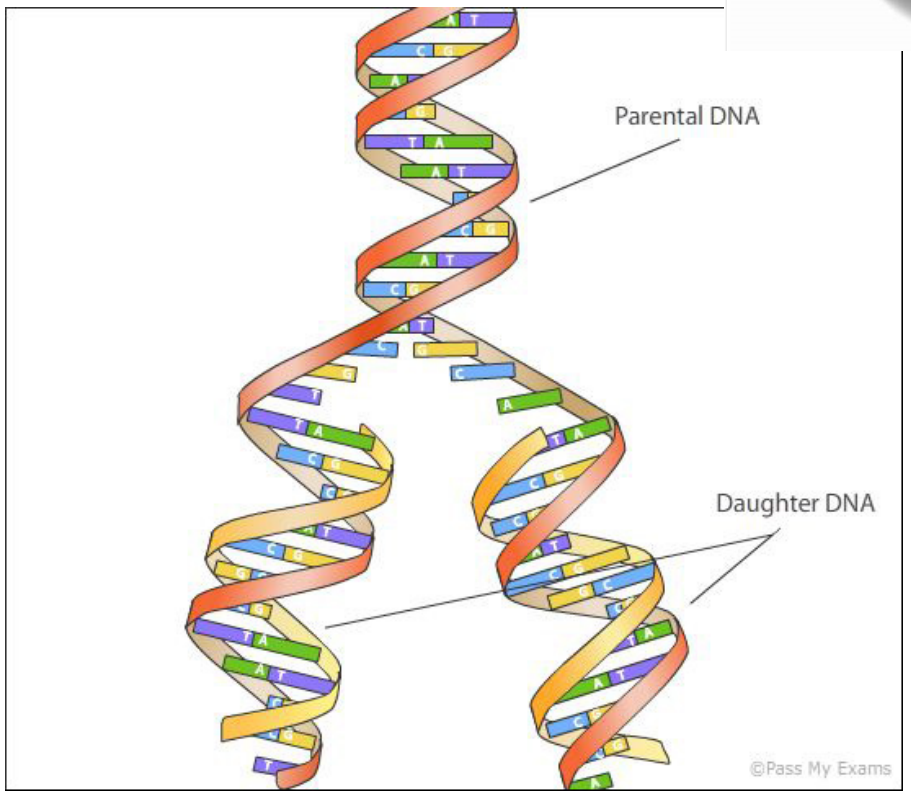


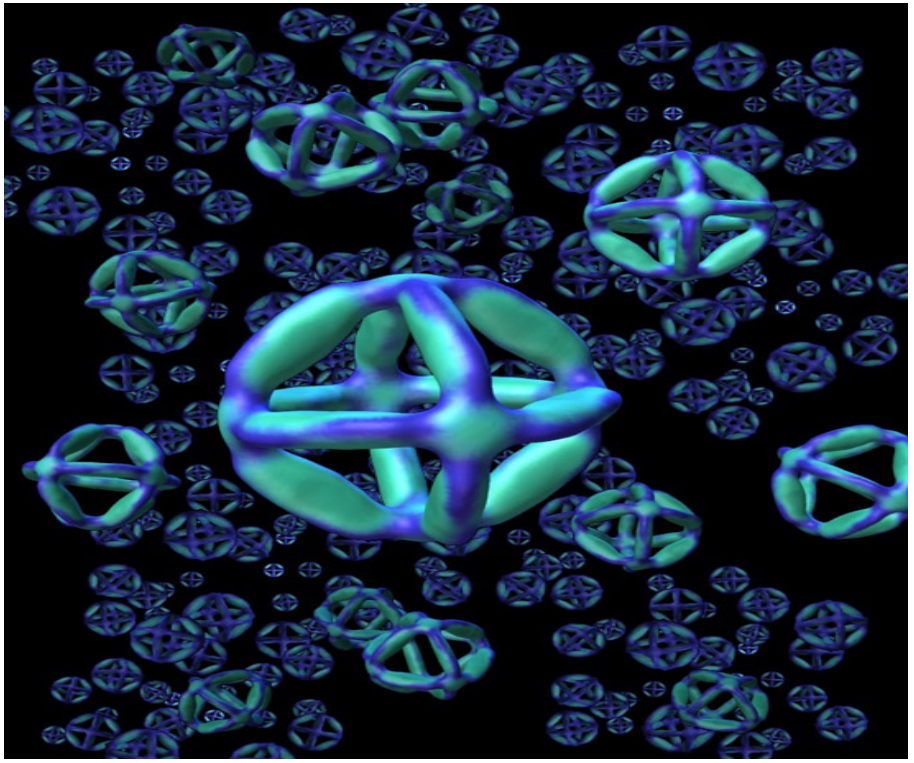
4500 millones de años

4000 millones de anos

ATCG

TAT ATC CCG ATC TGG …
3,300 millones de pares de bases



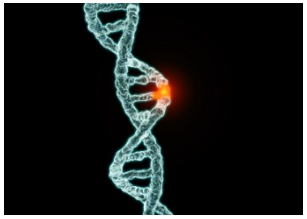


TAT ACT GCG TCG GAT GCT GCG ATT GCT GAC CAA CAT CGT GAC AGT TAG ACA AAC GAT TGA CTG TTA GGA TTG ACCA CCA ATT ACG ATG ACG TTG GAC … 3,3 x 10^9

Fundación Pública Galega de Medicina Xenómica

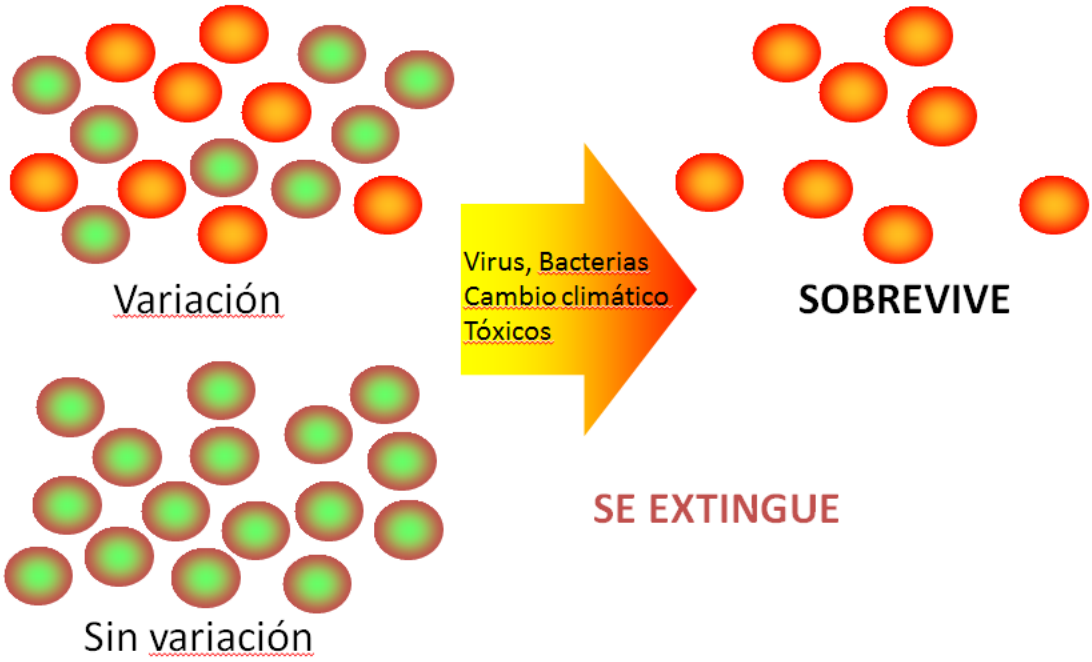
USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

MUTACIONES



AGC CAA TGG CAG TGA TGG
ATG GTA GCT GAG TGC TGG….

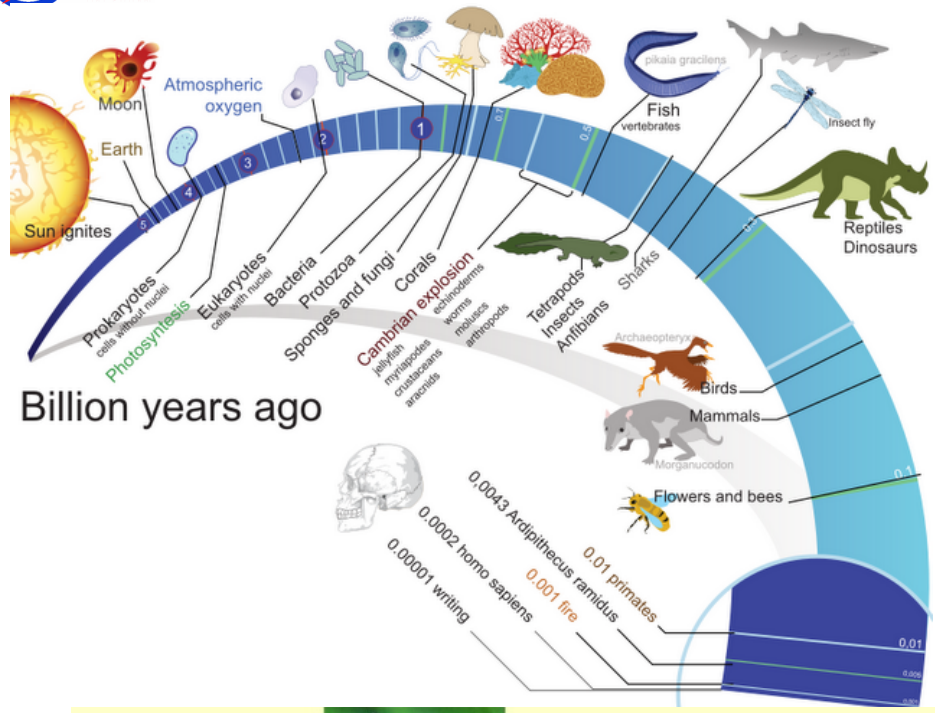
Silent mutation	Missense mutation	Nonsense mutation
TGT → TGC	TGT → TGG	TGT → TGA
Cys → Cys	Cys → Trp	Cys → Stop

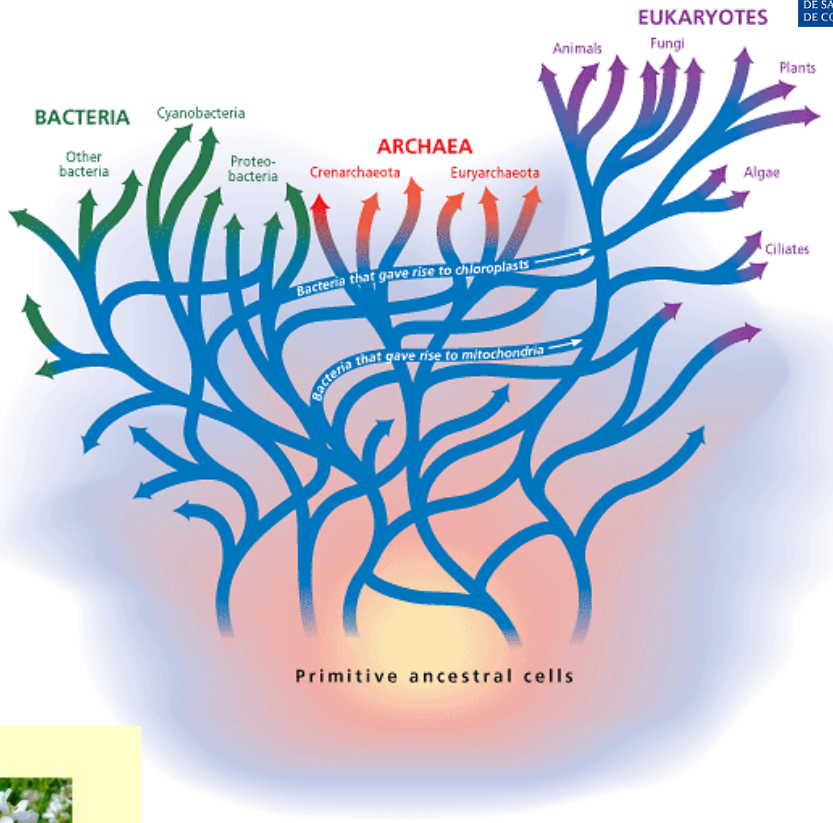


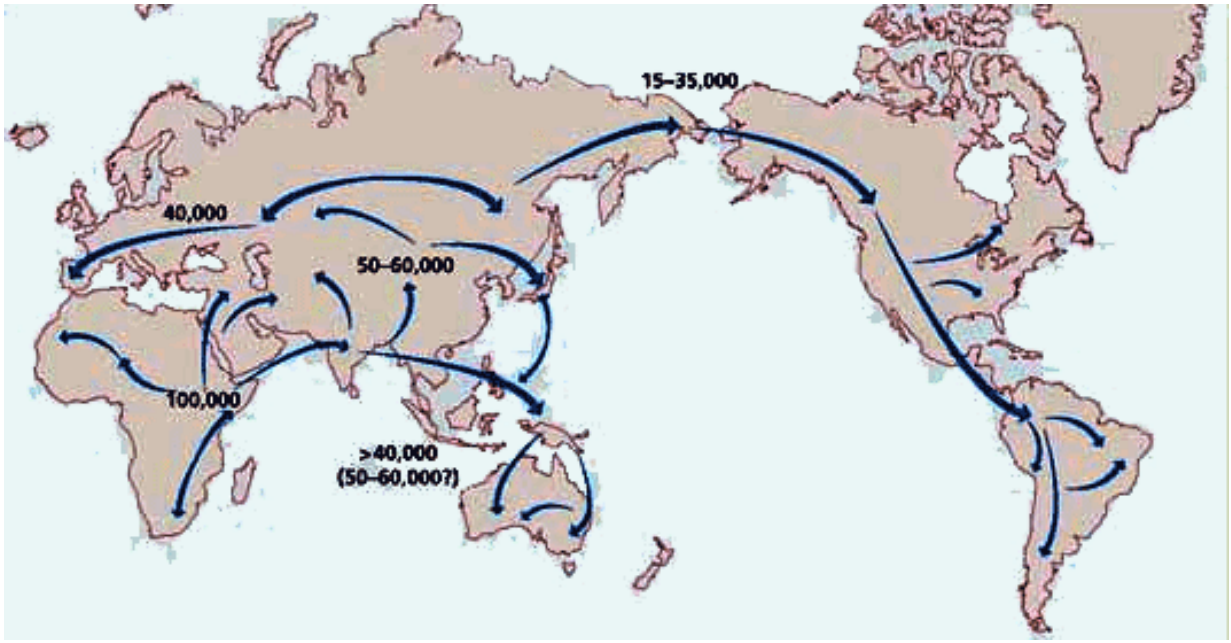
CON ESE SOL HAY MAS LUZ
CON ESA SAL HAY MAS LUZ
ONE SES OLH AYM ASL UZ

Fundación Pública Galega de Medicina Xenómica

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

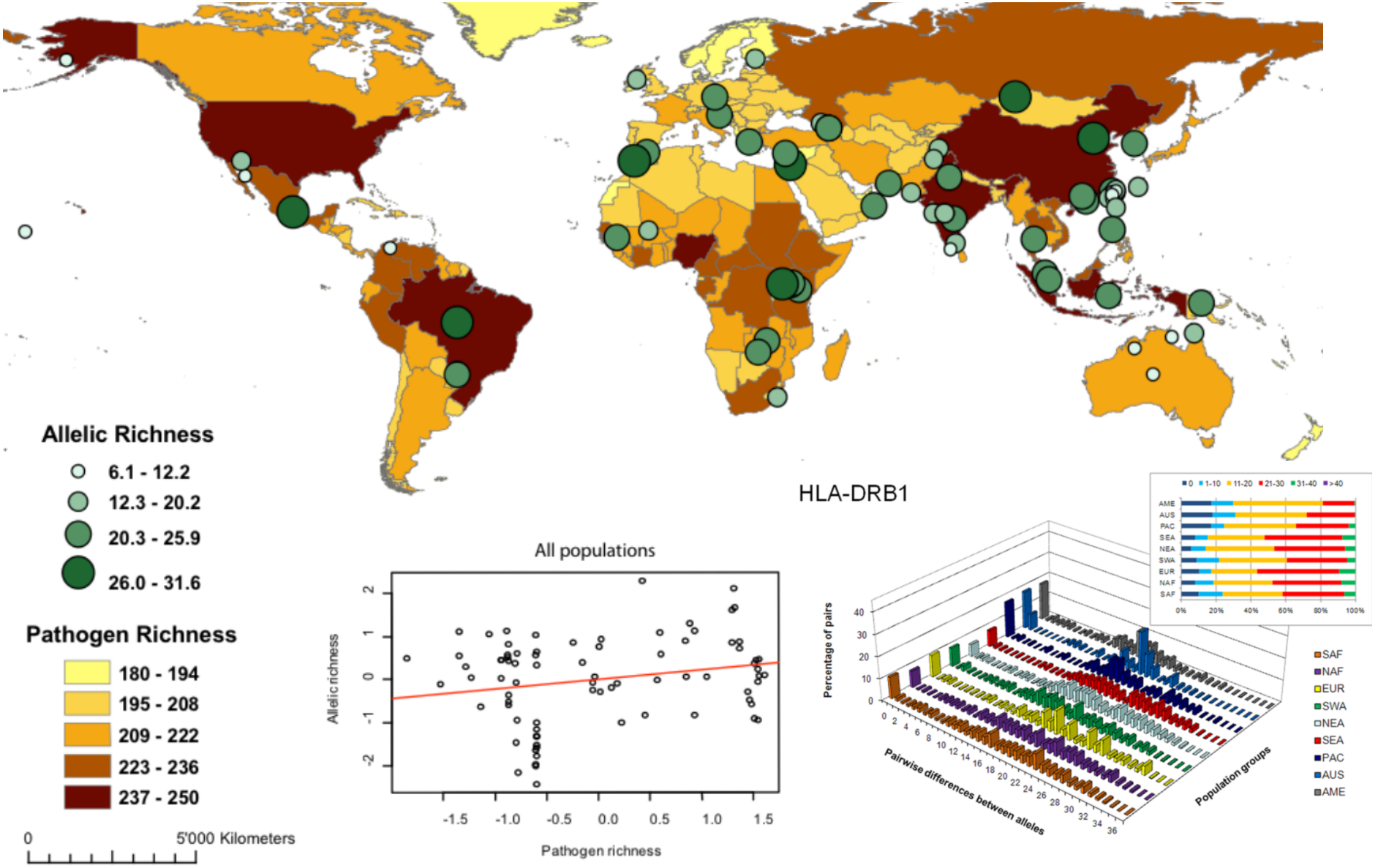


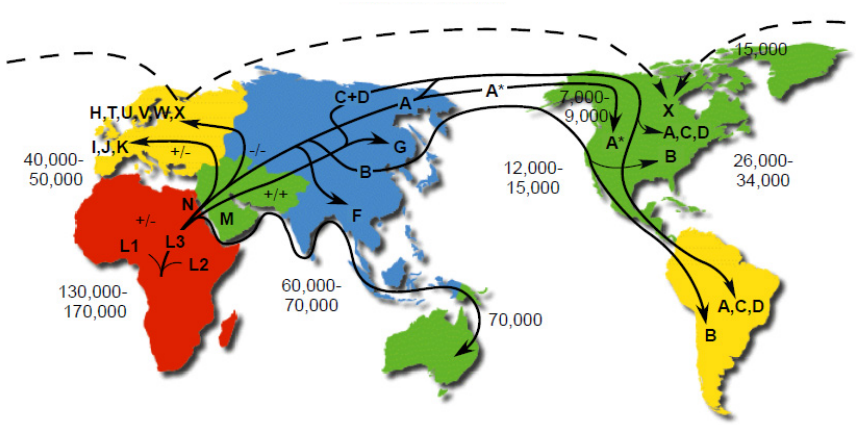


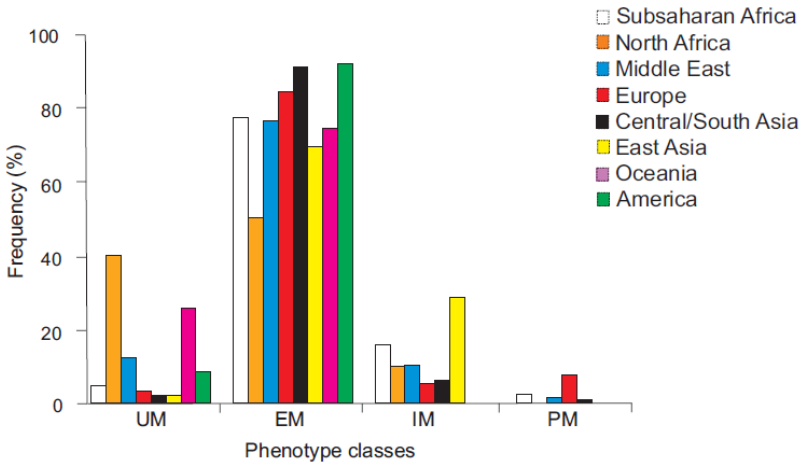

15–35,000
40,000
50–60,000
100,000
>40,000
(50–60,000?)


www.harunyahya.org

Diversidad de HLA y riqueza de patógenos







UM High freq North Africa/Saudi Arabia/ Medium East

Mozabites 40% UM CYP2D6

40% UM

Decreased-function variants *CYP2D6*10*, *CYP2D6*17*, and *CYP2D6*41* are common in Asian, African, and Western Asian populations
Null function variant *CYP2D6*4* is common in European populations.

EPIGENÉTICA: COMO EL AMBIENTE INFLUYE EN LOS GENES

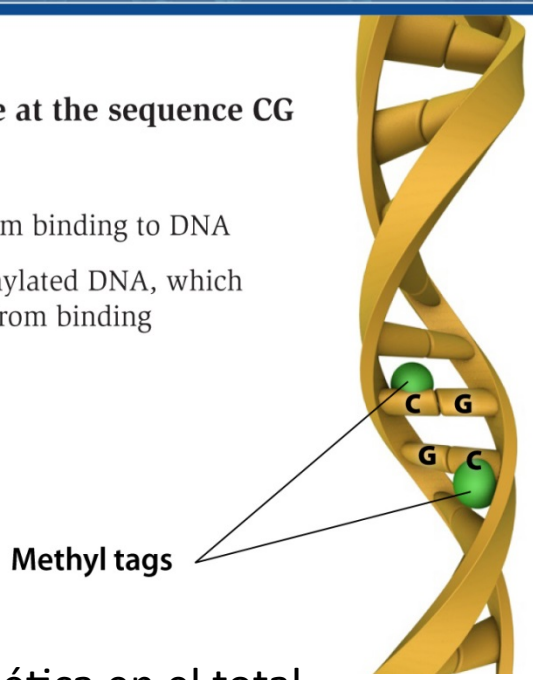
SAL CON ESE./
HAY MAS LUZ!!!

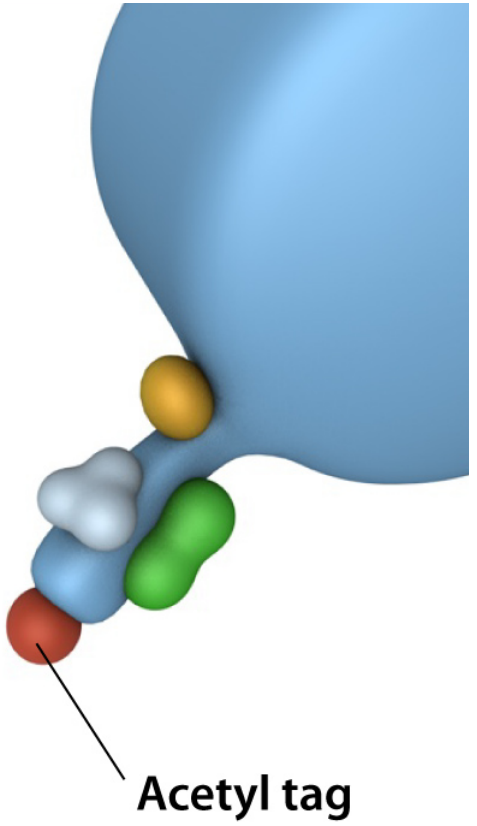
Methyl tags usually turn genes off

Methyl tags are added to a cytosine at the sequence CG

They silence genes by:

- Blocking transcription machinery from binding to DNA
- Recruiting proteins that bind to methylated DNA, which then block transcription machinery from binding

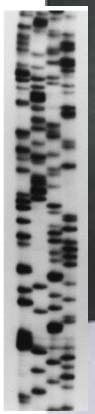


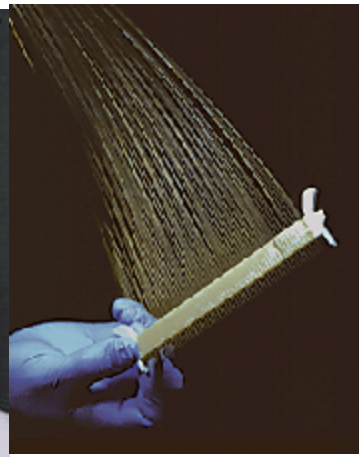


Heredabilidad: Varianza genética en el total de la varianza genética más ambiental
Cáncer de colon: 35%
Cáncer de mama: 28%
Esquizofrenia: 82%
Autismo: 85%

Fundación Pública Galega de Medicina Xenómica

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA



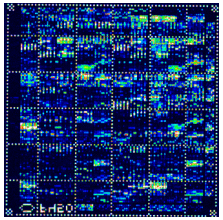


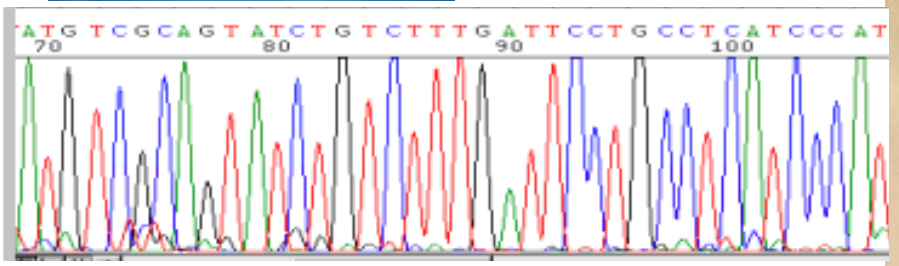
OMIM
Online Mendelian Inheritance in Man
Johns Hopkins University

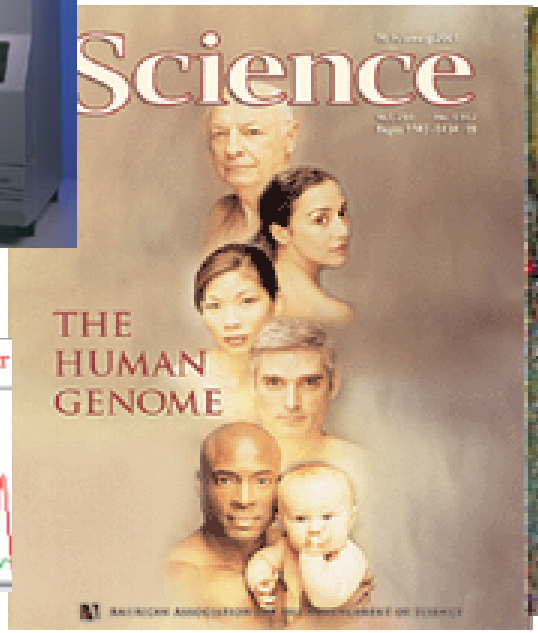
GENETests

HGMD™
The Human Gene Mutation Database
Cardiff

GeneCards™

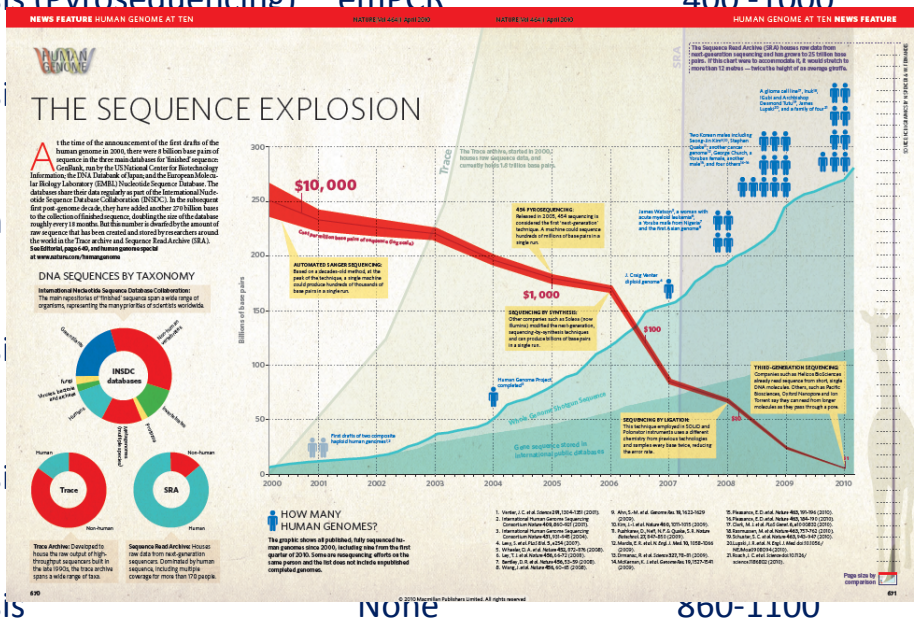






Next-Generation Sequencing Technologies

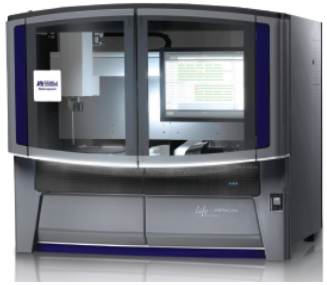
Technology	Sequencing method	Ampliifcation method	Read lenght (bp)	Throughput (Mb/run)
454	Synthesis (Pyrosequencing)	emPCR	400 -1000	50-500-900
Illumina	Synthesi			1020-600000
SOLiD	Ligation			100000-180000
HeliScope	Synthesi			28000
Ion Torrent	Synthesi			10 -100-1000
PacBio	Synthesis	None	860-1100	

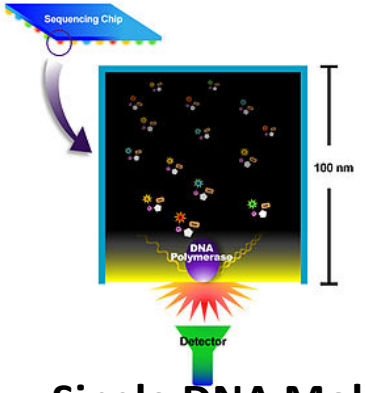

NEWS FEATURE HUMAN GENOME AT TEN

THE SEQUENCE EXPLOSION

DNA SEQUENCES BY TAXONOMY

HOW MANY HUMAN GENOMES?





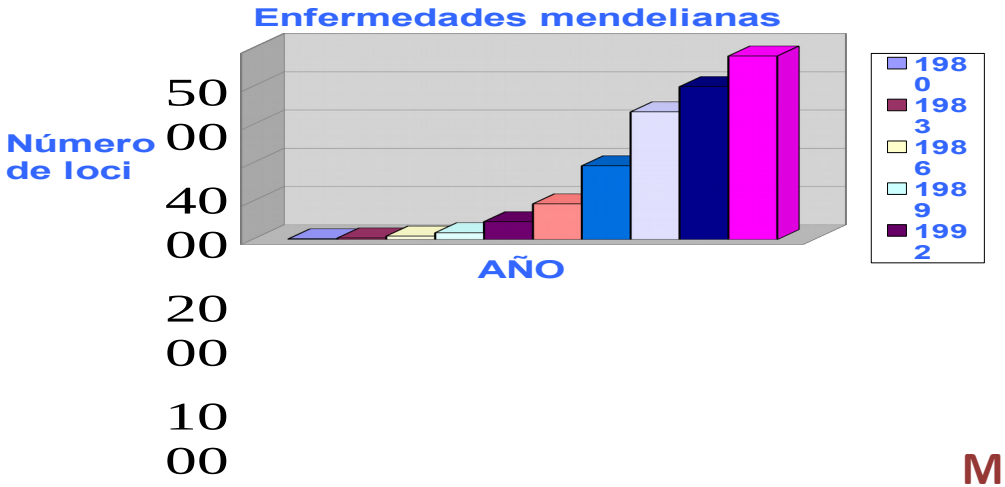
Single DNA Molecule Technologies

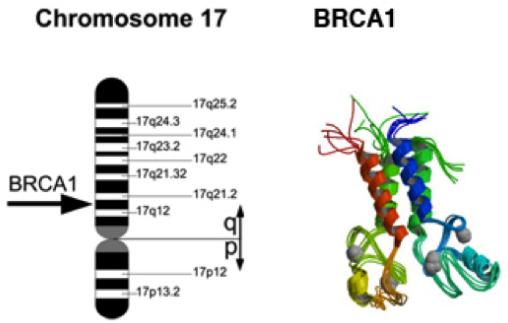
Fundación Pública Galega de Medicina Xenómica

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

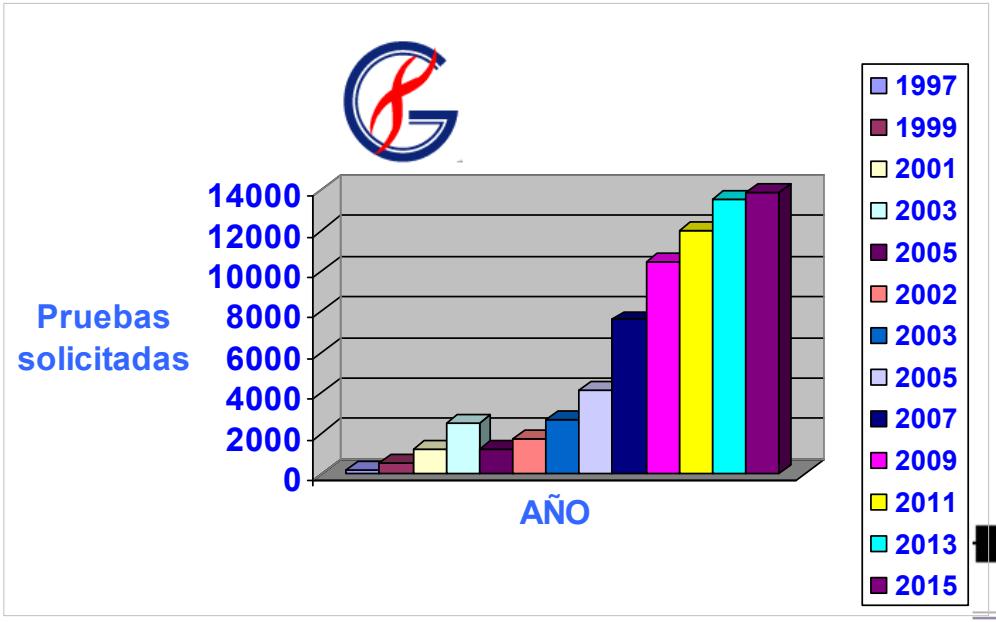
Fundación Galega de Medicina Xenómica

SERGAS





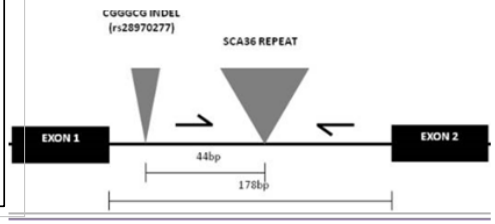
Mutación de splicing "gallega": c.330A>G; Arg71Gly del gen *BRCA1*

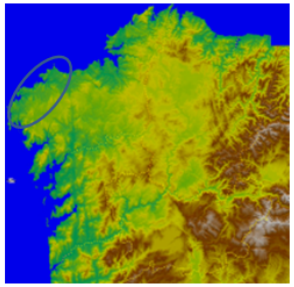


Brain. May 2012; 135(5): 1423–1435. PMCID: PMC3338926
Published online Apr 3, 2012. doi: 10.1093/brain/aws069

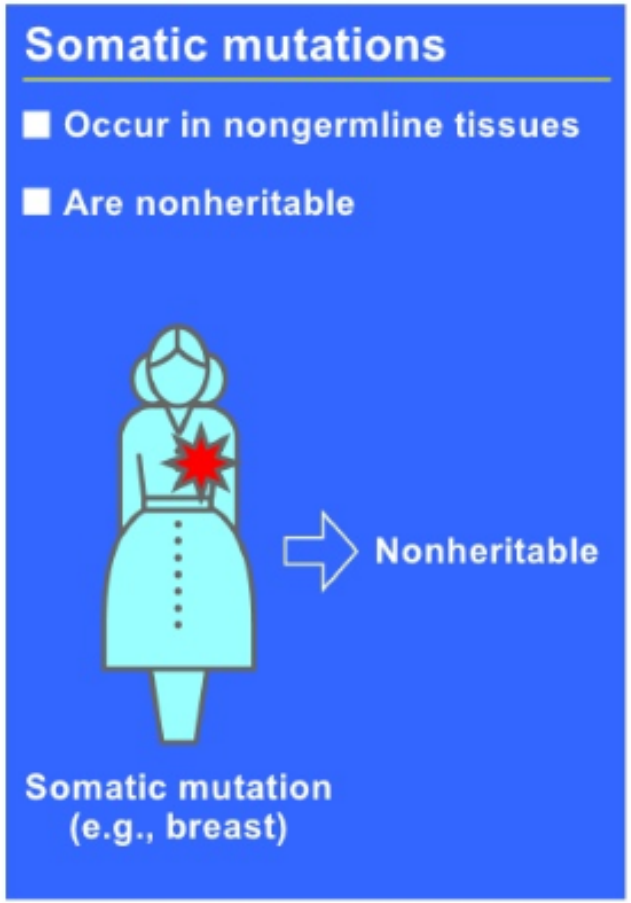
'Costa da Morte' ataxia is spinocerebellar ataxia 36: clinical and genetic characterization

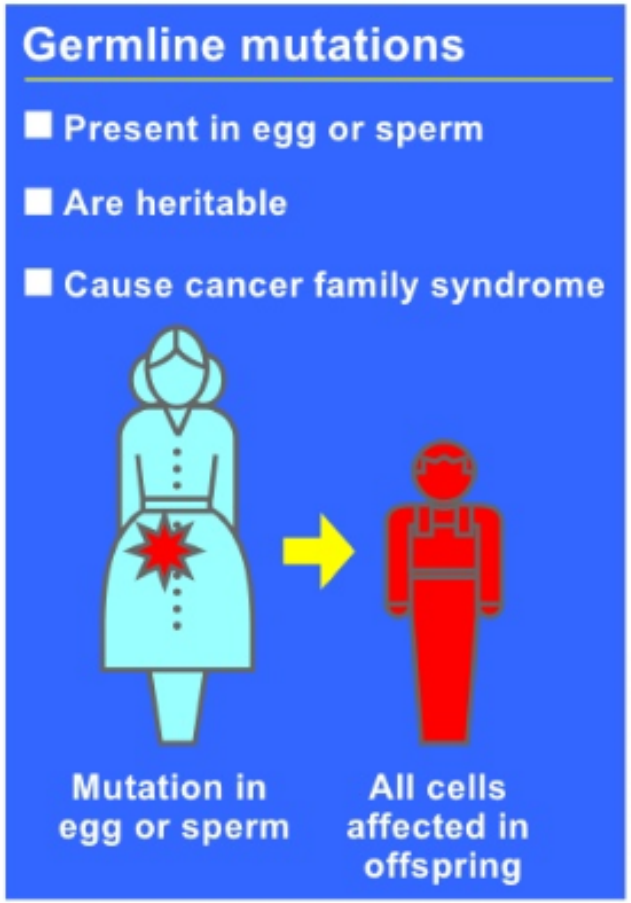
María García-Murias,[1,2,*] Beatriz Quintáns,[3,4,*] Manuel Arias,[5,*] Ana I. Seixas,[6] Pilar Cacheiro,[2] Rosa Tarrío,[2,4] Julio Pardo,[5] María J. Millán,[1] Susana Arias-Rivas,[5] Patricia Blanco-Arias,[1,4] Dolores Dapena,[5] Ramón Moreira,[7] Francisco Rodríguez-Trelles,[8] Jorge Sequeiros,[6,9] Ángel Carracedo,[1,2,4] Isabel Silveira,[6] and María J. Sobrido[001,4]



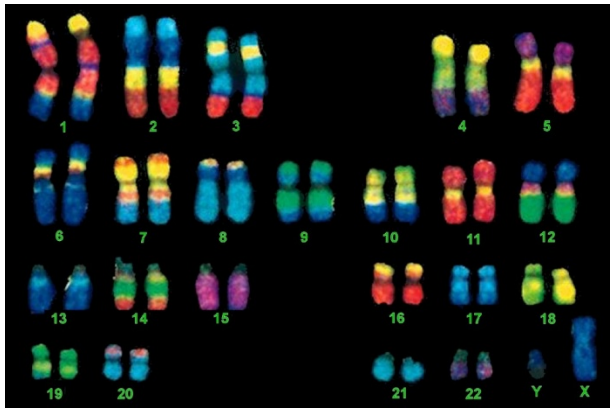


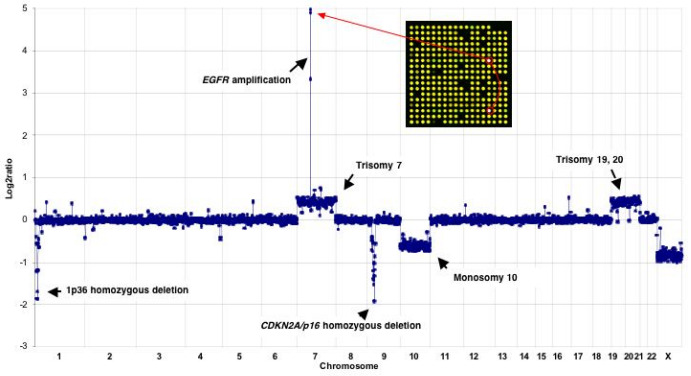
Analysis of variation



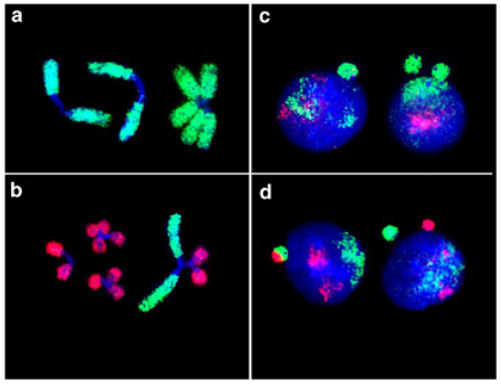


Cromosopatías y defectos estructurales



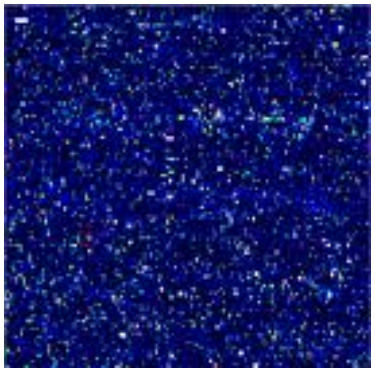


Cariotipo



PCR

Arrays de CGH (Hibridación genómica comparada)

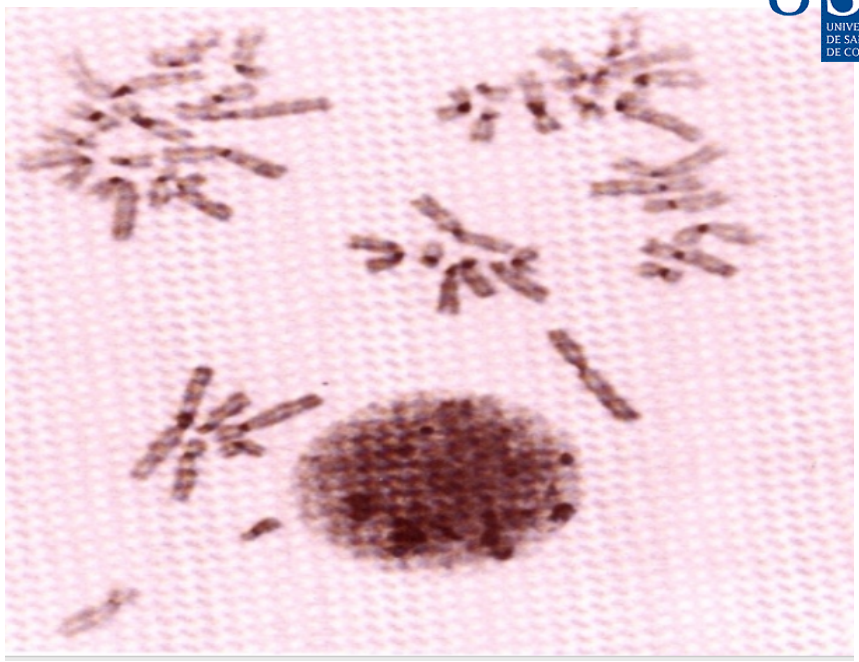


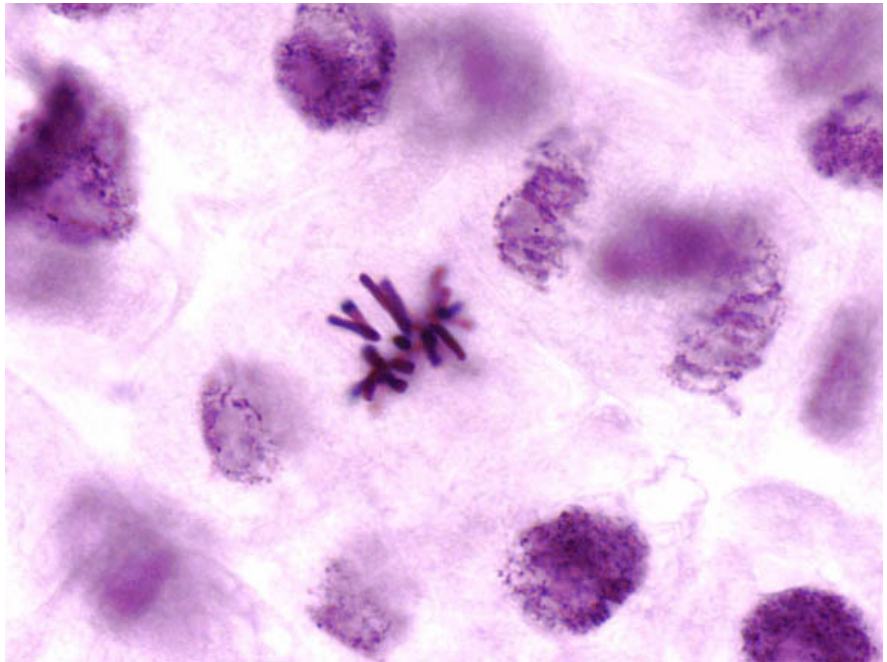
FISH Hibridación fluorescente in situ

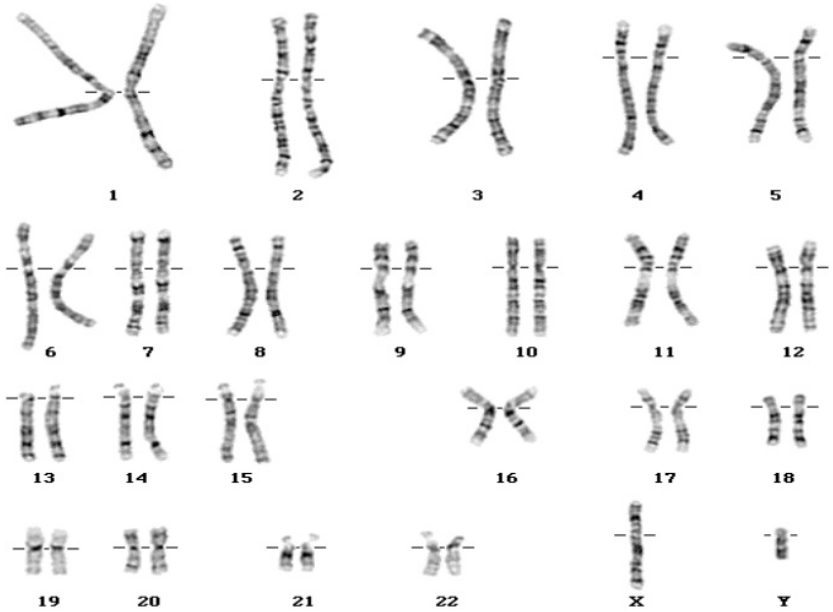
Microarrays de SNPs y sondas para CNVs

Fundación Pública Galega de Medicina Xenómica

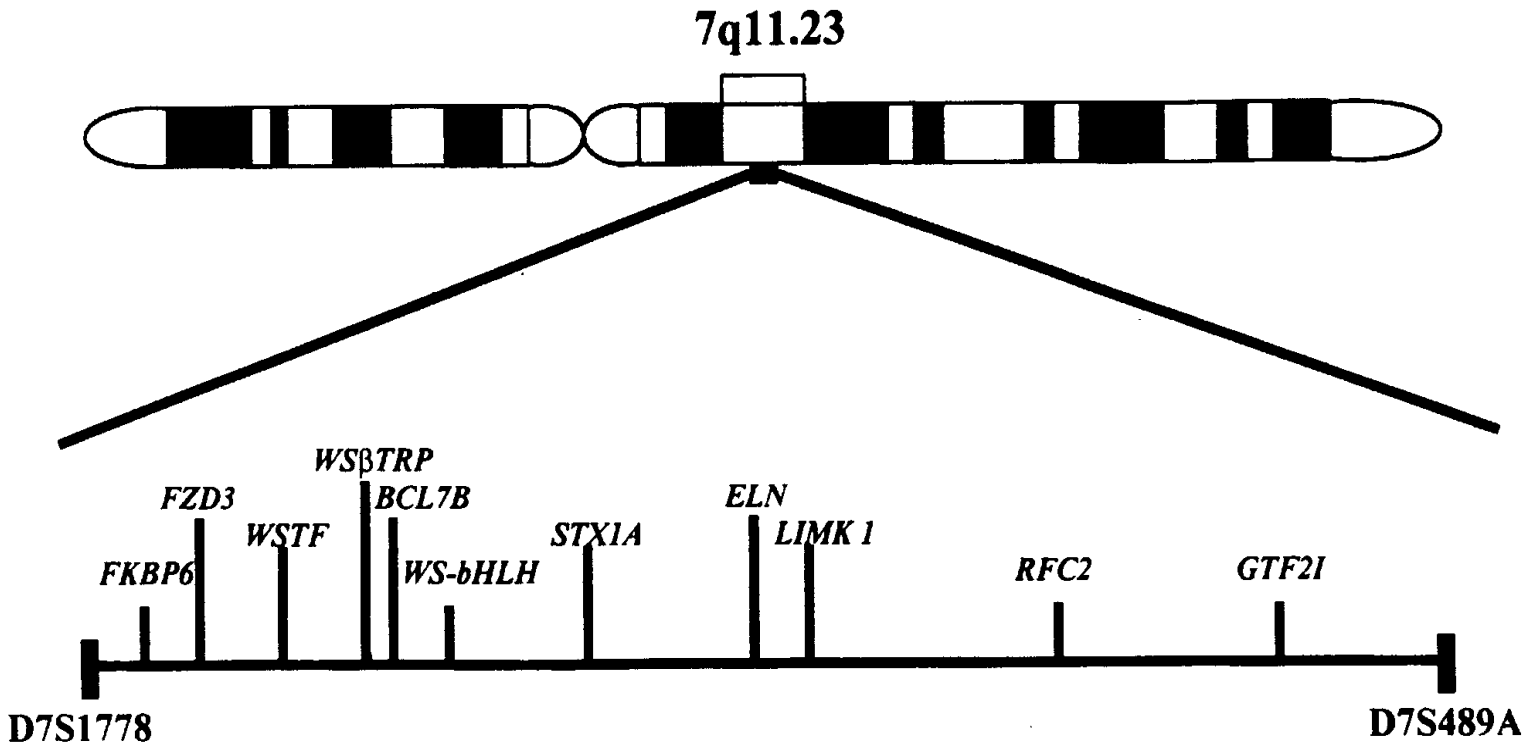
USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA







Williams Deletion Region



Williams Syndrome Common Deletion Region

Fundación Pública Galega de Medicina Xenómica

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

Chromosome Analysis Suite [For Research Use Only ... ostic procedu

File View Reports Analysis Preferences Help

X: 67.085.014 - 67.735.862

No New Updates

Files
- 1H240.cyhd.c
- 8E011.cy2wg.
- BACs
- DGV
- FISH Clones
- Genes

Named Setting

Data Types
- Copy Number State
  - Gain
  - Loss
- Log2 Ratio
- Weighted Log2 Ra
- Copy Number Stat
- LOH
- Allele Peaks
- LOH
- SmoothSignal
- Genotype Calls
- Mosaicism

Karyoview | Segments | CytoRegions | Overlap Map | Graphs

1H240.cyhd.cychp: Copy Number State (segments)

8E011.cy2wg.cychp: Copy Number State (segments)

1H240.cyhd.cychp: Copy Number State

8E011.cy2wg.cychp: Copy Number State

Genes

OPHN1

OMIM ®

300127 Mental_retardation_X-linked_with_cerebellar_hypoplasia_and_distinctive_facial_appearance(300486):NM_002547 (OPHN1)

67100kb 67200kb 67300kb 67400kb 67500kb 67600kb 67700kb

q12

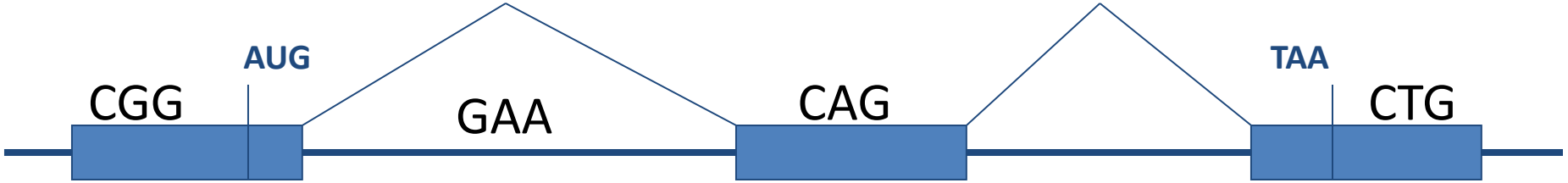
p22.33 p22.31 p22.2 p21.3 p21.1 p11.4 p11.3 p11.23 p11.22 p11.21 q12 q13.1 q21.1 q21.31 q21.33 q22.1 q22.3 q23 q24 q25 q26.2 q26.3 q27.3 q28

Detail View | QC and Sample Info | Chromosome Summary Data

ChAS Browser : NetAffx 32 (hg19) | Restricted Mode: Off | User: Affymetrix

ES 17:26 30/08/2012

Unstable Trinucleotide Repeat Disorders in Humans



Fredreich's Ataxia

Myotonic Dystrophy

Fragile X Syndrome

Fragile XE MR

Spinobulbar Muscular Atrophy

Huntington's Disease

Dentatorubral-Pallidoluyslan Atropphy

Spinocerebellar Ataxia Type 1

Spinocerebellar Ataxia Type 1

Spinocerebellar Ataxia Type 2

Spinocerebellar Ataxia Type 6

Spinocerebellar Ataxia Type 7 GCG(2)GCA(3).

Spinocerebellar Ataxia Type 8 DMOF

Spinocerebellar Ataxia Type 12

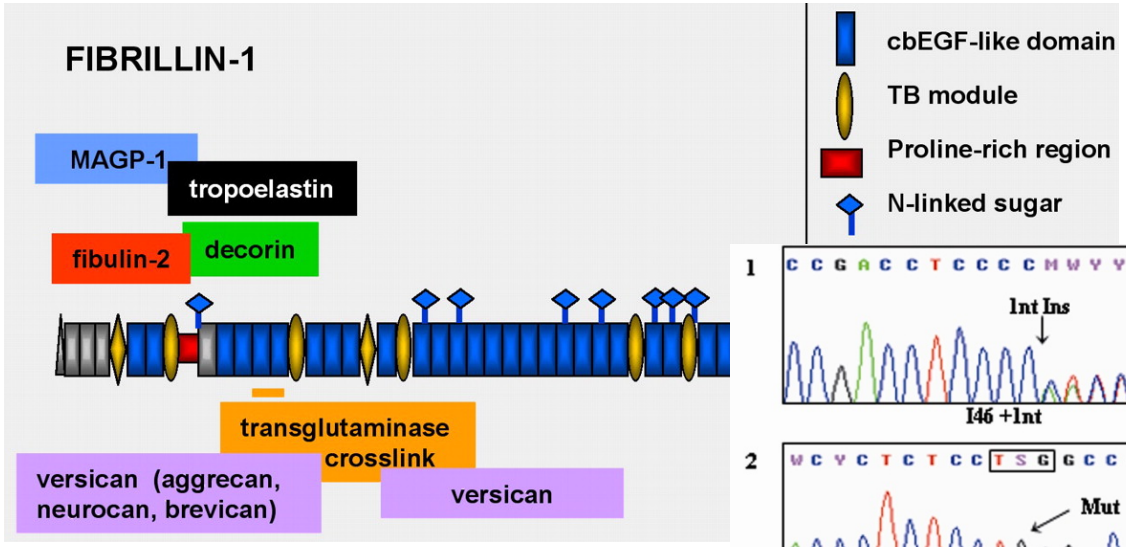
Machado-Joseph Disease (SCA3)

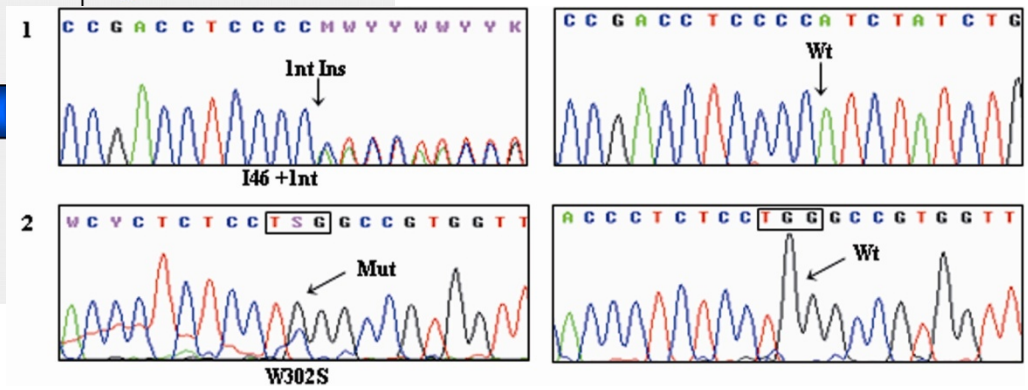
OXFORD JOURNALS Brain

Brain. 2012 May; 135(5): 1423–1435. PMCID: PMC3338928
Published online 2012 April 3. doi: 10.1093/brain/aws069

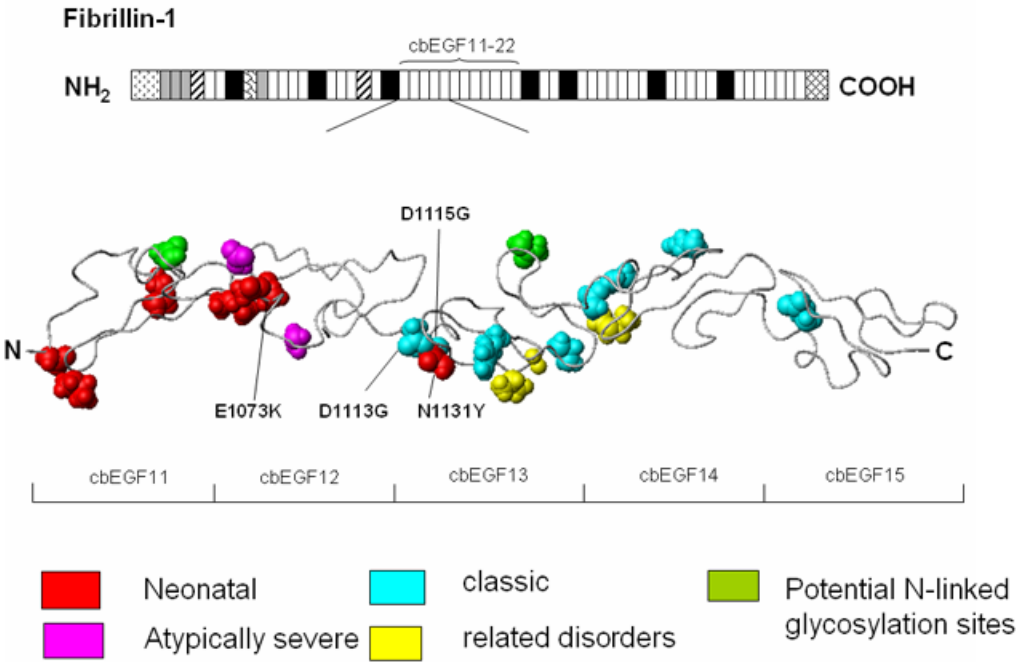
'Costa da Morte' ataxia is spinocerebellar ataxia 36: clinical and genetic characterization

María García-Murias,[1,2,*] Beatriz Quintáns,[3,4,*] Manuel Arias,[5,*] Ana I. Seixas,[6] Pilar Cacheiro,[2] Rosa Tarrío,[2,4] Julio Pardo,[5] María J. Millán,[1] Susana Arias-Rivas,[5] Patricia Blanco-Arias,[1,4] Dolores Dapena,[5] Ramón Moreira,[7] Francisco Rodríguez-Trelles,[8] Jorge Sequeiros,[6,9] Ángel Carracedo,[1,2,4] Isabel Silveira,[6] and María J. Sobrido[1,4]

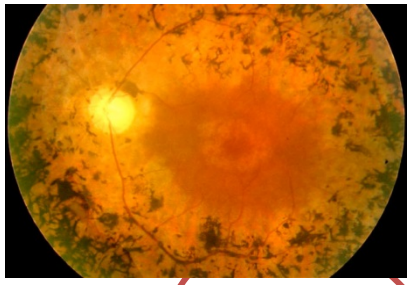


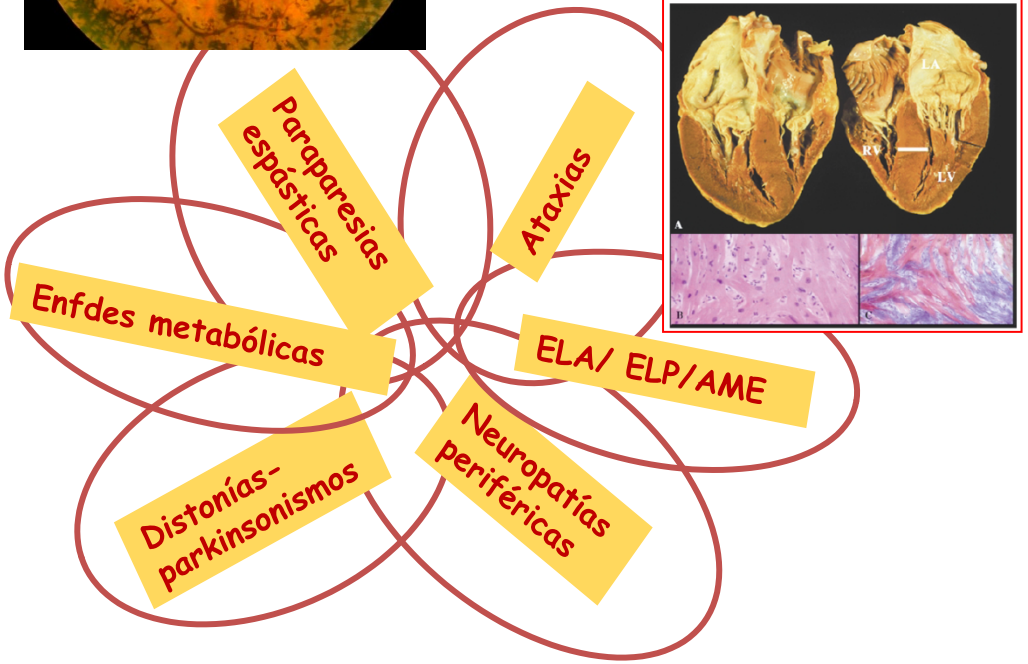


Marfan Syndrome Fibrillin 1



La heterogeneidad de la enfermedad es la norma pero no solo para enfermedades comunes sino para las mendelianas



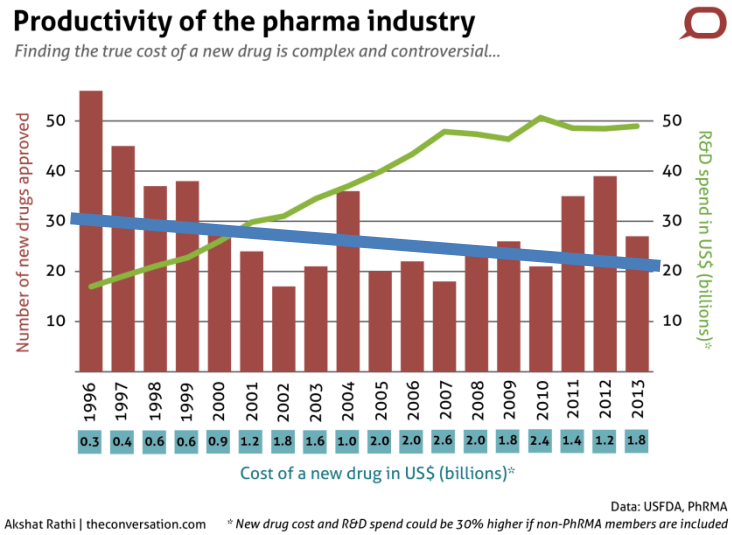


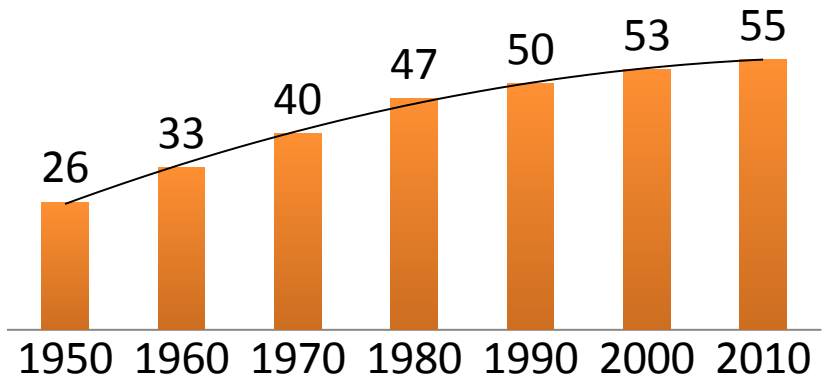
GLOMERULAR DISEASES	OMIM No.	MOI	Characteristic signs and features	*Gene symbol(s)*, gene product(s)
Congenital SRNS (Finnish type)	#256300	AR	congenital nephrotic syndrome, CKD	*NPHS1*, nephrin
SRNS type 2	#600995	AR	SRNS, FSGS, CKD	*NPHS2*, podocin
SRNS type 3	#610725	AR	SRNS (SSNS), DMS, FSGS, CKD	*PLCE1*, phospholipase C
SRNS type 4	#600995	AR, (AD)	SRNS, FSGS	*CD2AP*, CD2AP
Pierson syndrome	#609049	AR	SRNS and microcoria	*LAMB2, laminin-β2*
SRNS, adult-onset			, CKD	*NPHS2*, α-actinin-4 (*ACTN4*)
SRNS, adult-onset			, CKD	*TRPC6*, transient receptor potential cation channel C6
Denys-Drash syndrome, Frasier syndrome				*WT1*, WT suppressor gene
Nail-Patella syndrome			ella,	*LMX1B*, LIM homeodomain protein
Schimke immuno-osseous dystrophy	#242900	AR	Bone abnormalities, immunodeficiency, SRNS	*SMARCAL1*, HepA-related protein (HARP)
Mitochondrial disorders with SRNS	#607426	AR	SRNS +/− neurologic impairment/SND	*COQ2, PDSS2, MTTL1*
Lysosomal disorders with SRNS	#254900	AR	Action myoclonus, SRNS, CKD	*SCARB2*, lysosomal integral membrane protein (LIMP2)
Glomerulopathy with fibronection deposits	#601894	AD	Proteinuria, dRTA	*FN1*, fibronectin-1
Alport syndrom	#301050	XD	Nephritis, SND, CKD	*COL4A5*, α5(IV)-collagen
Alport syndrom with leiomyomatosis	#308940	XD	Alport syndrom with leiomyomatosis, CKD	*COL4A6*, α6(IV)-collagen
Alport syndrom	#203780	AR	Alport syndrome or benign familial hematuria	*COL4A3*, α3(IV)-collagen

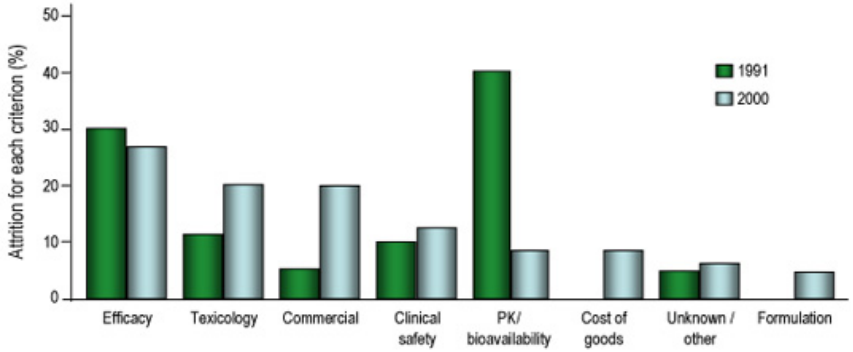
Syndrome	Genes
HCM	MYH7, TNNT2, TPM1, MyBPC3, TNNI3, MYL2, MYL3, ACTC, TTN, PRKAG2, MYH6, GLA, MYO6, MYLK2, TNNC1, TCAP,…
DCM	MYH7, TNNT2, TPM1, ACTC, TNNC1, TTN, TCAP, ZASP, PLN, LMNA, DES, ABCC9, ACTN2, CSRP3
ARVD	PKP2, DSP, JUP, DSC2, DSG2, RYR2, TGFB3, LAMR1, PTPLA, ZASP, DES,..
LQTS	KCNQ1, KCNH2, SCN5A, ANKB, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B,…
SQTS	KCNH2, KCNQ1, KCNJ2, CACNA1C, CACNB2,…
WPW	PRKAG2
CPVT	RyR2, CASQ2
PCCD	SCN5A
Brugada	SCN5A

Cambio de paradigma: El diagnóstico de la enfermedad lo orienta a menudo el propio análisis genético y no el fenotipo

Limited therapeutic efficacy in many TAs







- In 1991 unpredictable PK was the main reason for failure
- Today main reason for failure is lack of efficacy

ADRs

5% hospital admissions

4th cause of death (100.000 d / year USA)

4billions$/year

La heterogeneidad en la enfermedad es la norma

Que es la fiebre una enfermedad o un síntoma?

Y la hipertensión, diabetes, asma, artritis, esquizofrenia ….?

Los conceptos de enfermedad, síntoma y signo se han asimilado erróneamente

Los tratamientos sintómaticos no solucionan el problema si no se soluciona por si solo

Debido a la heterogeneidad, los pocos tratamientos contra las causas tienen eficacia solo para un subgrupo (por ejemplo: una antibiótico para la fiebre tendría una eficacia de alrededor del 20%)

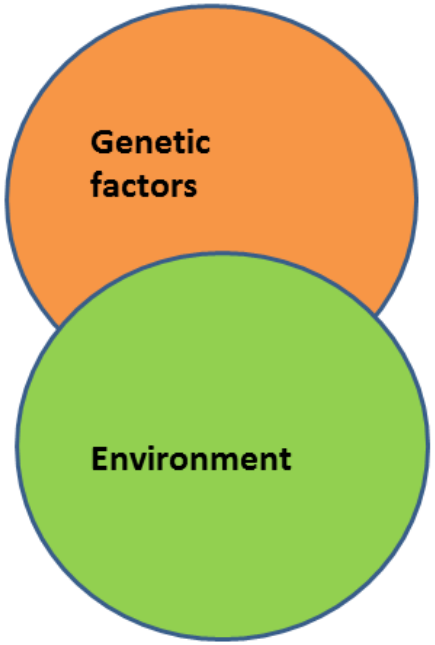
Necesitamos **estratifica**r la enfermedad

EFFICACY

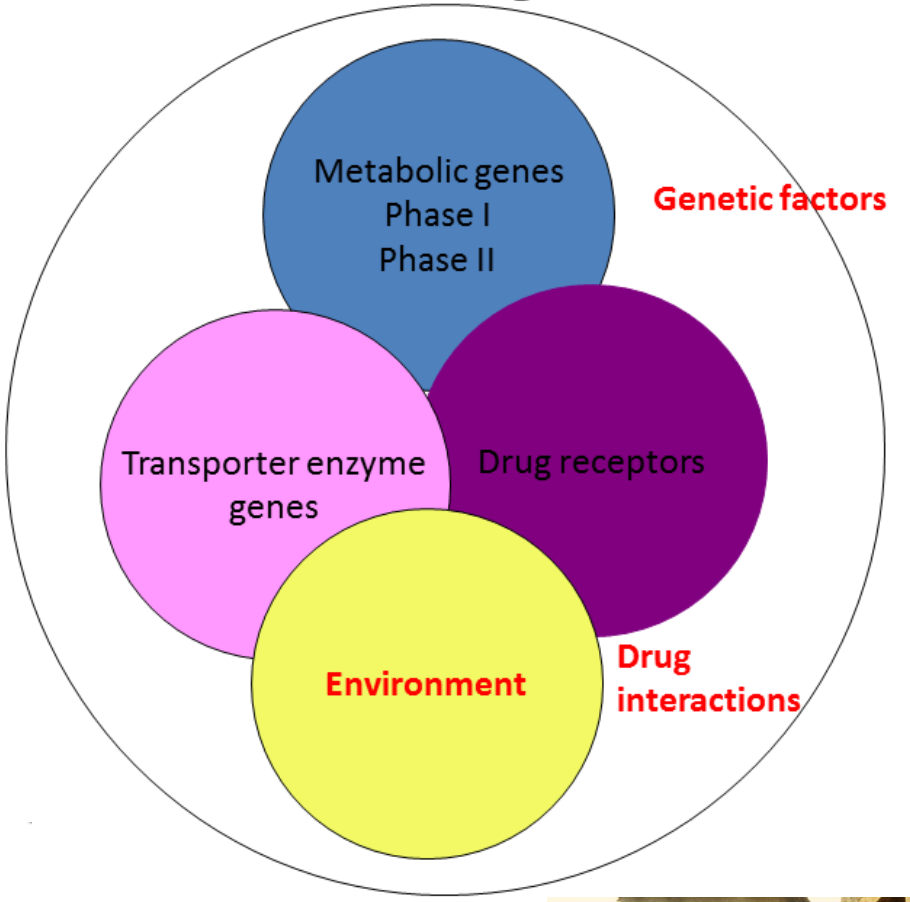
SAFETY

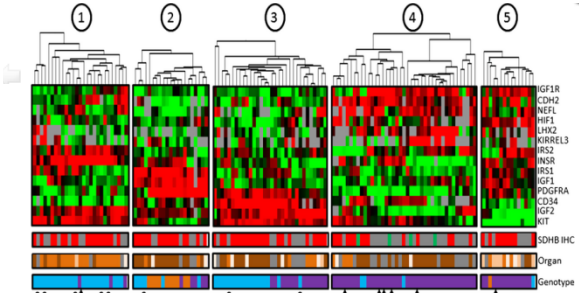
Disease

Heterogeneity of disease



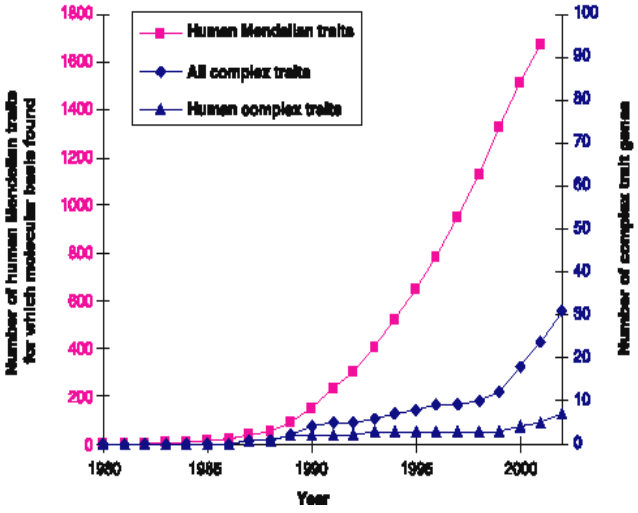
Drug





SNP: SINGLE NUCLEOTIDE POLYMORPHISM

ATCGGCGTACCTGATTCCGAATCCGTATCG
ATCGGCGTACCTGAATCCGAATCCGTATCG

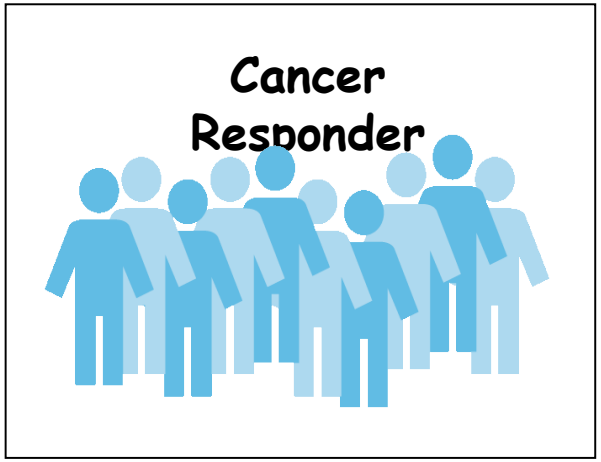


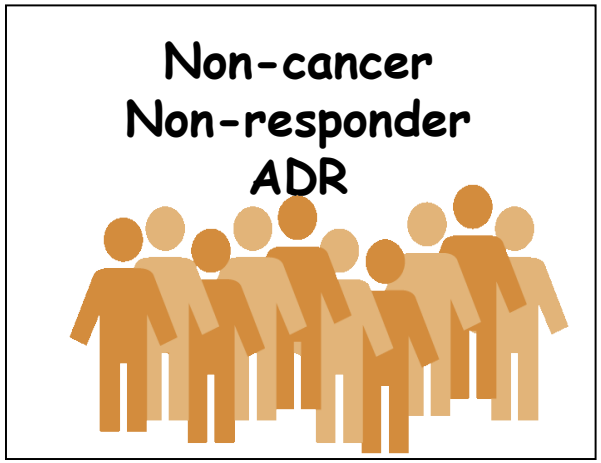
3.3 Gigabases Human Genome / >20 M SNP

1 SNP/<150 bp

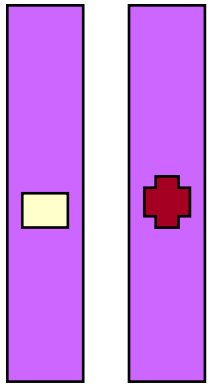
1M SNPs

Human Genetic Association Study Design





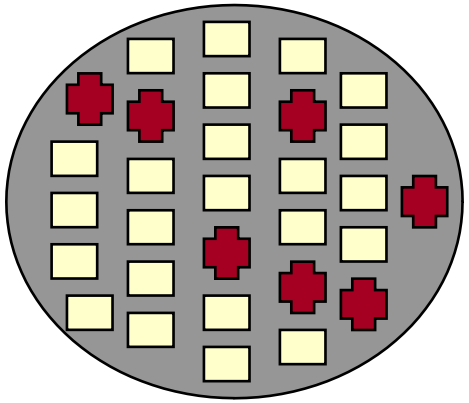
SNPs are the ideal markers



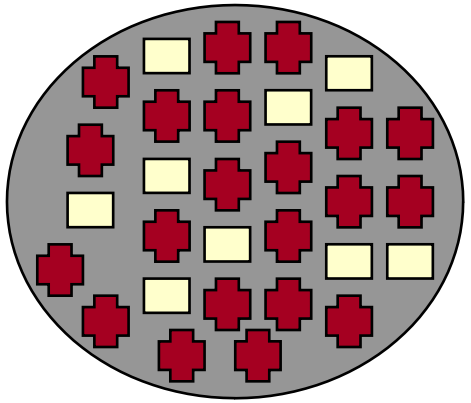
Allele 1

Allele 2

Marker A:
Allele 1
Allele 2



Marker A is associated with Phenotype



CENTRO NACIONAL DE GENOTIPADO CEGEN-ISCIII

Instituto de Salud Carlos III

GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

Scientific advisory board

Board

Coordination USC

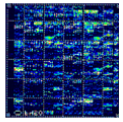
NODE 1 Santiago de Compostela (USC)

USC

Management unit

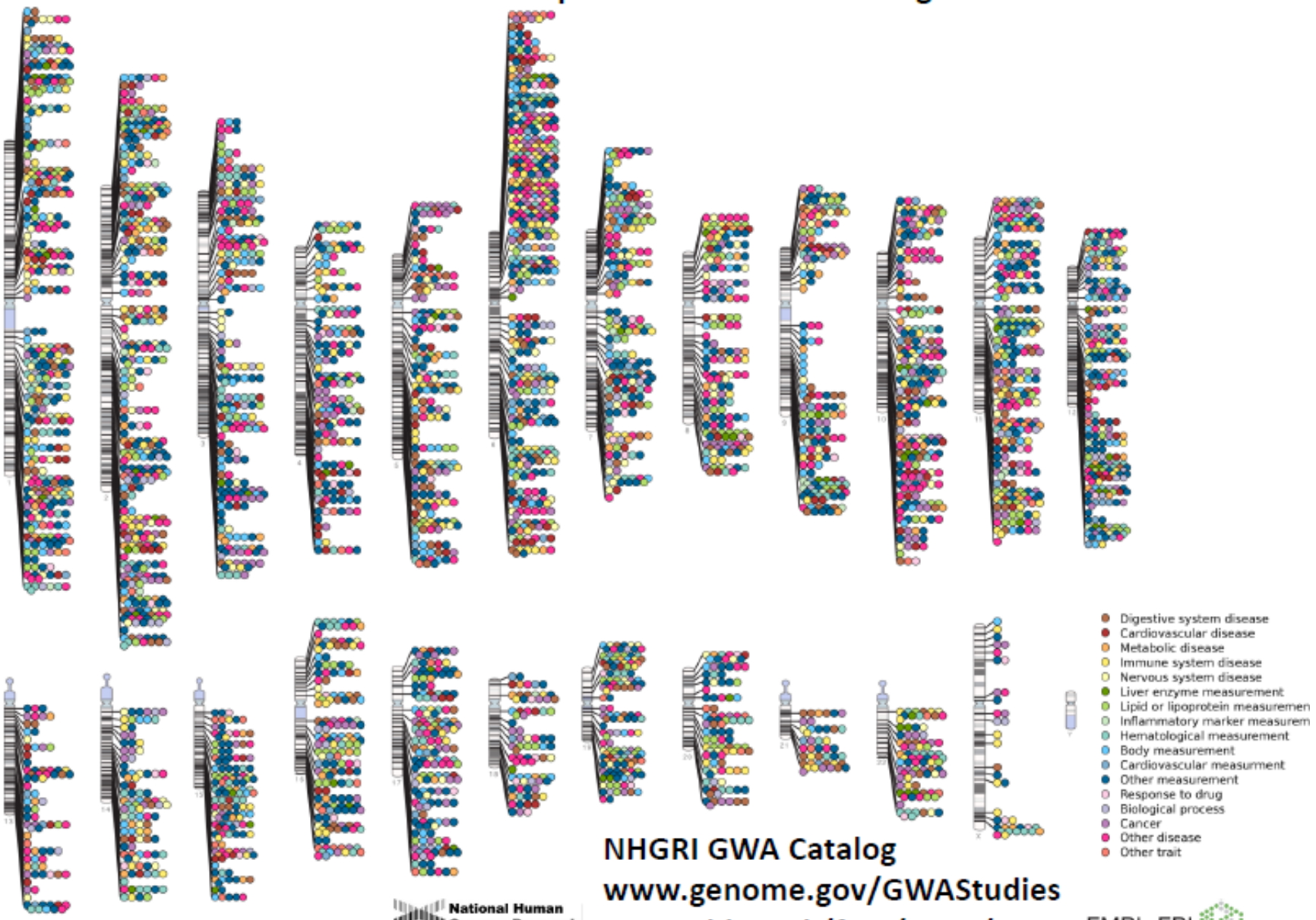
NODE 2 Madrid (CNIO)

CNIO Centro Nacional de Investigaciones Oncológicas



Published Genome-Wide Associations through 12/2013

Published GWA at p≤5X10^{-8} for 17 trait categories



NHGRI GWA Catalog
www.genome.gov/GWAStudies
www.ebi.ac.uk/fgpt/gwas/

National Human Genome Research Institute

EMBL-EBI

Common variants conferring risk of schizophrenia

Nature Stefansonn et al. Aug 2009 (SGENE Consortium)

Genome-wide significant association of seven markers with schizophrenia

ne/ SNP[allele]	Frequency	SGENE-plus* (2,663 cases; 13,498 controls)		Follow-up (4,999 cases; 15,555 controls)		SGENE-plus + follow-up (7,662 cases; 29,053 controls)		SGENE-plus + follow-up + ISC + MGS (12,951 cases; 34,594 controls)		Region/ neighbouring gene
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	
rs6913660[C]†☆	0.85	1.22 (1.10, 1.36)	0.00023	1.11 (1.04, 1.19)	0.0021	1.14 (1.08, 1.21)	4.7×10^{-6}	1.15 (1.10, 1.21)	1.1×10^{-9}	MHC/ *HIST1H2BJ*
rs13219354[T]‡☆	0.90	1.25 (1.11, 1.42)	0.00043	1.19 (1.08, 1.30)	0.00022	1.21 (1.12, 1.30)	4.4×10^{-7}	1.20 (1.14, 1.27)	1.3×10^{-10}	MHC/ *PRSS16*
rs6932590[T]§☆	0.78	1.15 (1.05, 1.26)	0.0024	1.17 (1.10, 1.25)	4.9×10^{-7}	1.17 (1.11, 1.23)	4.4×10^{-9}	1.16 (1.11, 1.21)	1.4×10^{-12}	MHC/ *PRSS16*
rs13211507[T]‖☆	0.92	1.24 (1.08, 1.42)	0.0027	1.27 (1.15, 1.40)	3.1×10^{-6}	1.26 (1.16, 1.36)	3.1×10^{-8}	1.24 (1.16, 1.32)	8.3×10^{-11}	MHC/ *PGBD1*
rs3131296[G]¶☆	0.87	1.21 (1.08, 1.36)	0.0011	1.20 (1.11, 1.30)	5.3×10^{-6}	1.21 (1.13, 1.29)	2.1×10^{-8}	1.19 (1.13, 1.25)	2.3×10^{-10}	MHC/ *NOTCH4*
rs12807809[T]	0.83	1.19 (1.08, 1.32)	0.00045	1.13 (1.06, 1.21)	0.00022	1.15 (1.09, 1.22)	5.0×10^{-7}	1.15 (1.10, 1.20)	2.4×10^{-9}	*NRGN*
rs9960767[C]#☆	0.056	1.30 (1.11, 1.51)	0.0011	1.20 (1.08, 1.33)	0.00044	1.23 (1.13, 1.34)	2.2×10^{-6}	1.23 (1.15, 1.32)	4.1×10^{-9}	*TCF4*

19,000 cases and 35,000 controls from Iceland, Denmark (Aarhus), Denmark (Copenhagen), Germany (Bonn), Germany (Munich), Hungary, the Netherlands, Norway, Russia, Sweden, Finland; Spain (Santiago) and Spain (Valencia)

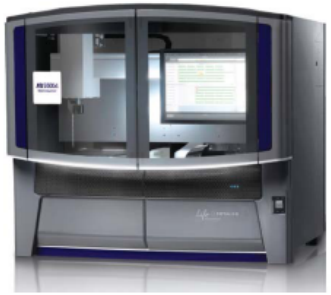
1st 2,663 cases and 13,498 controls

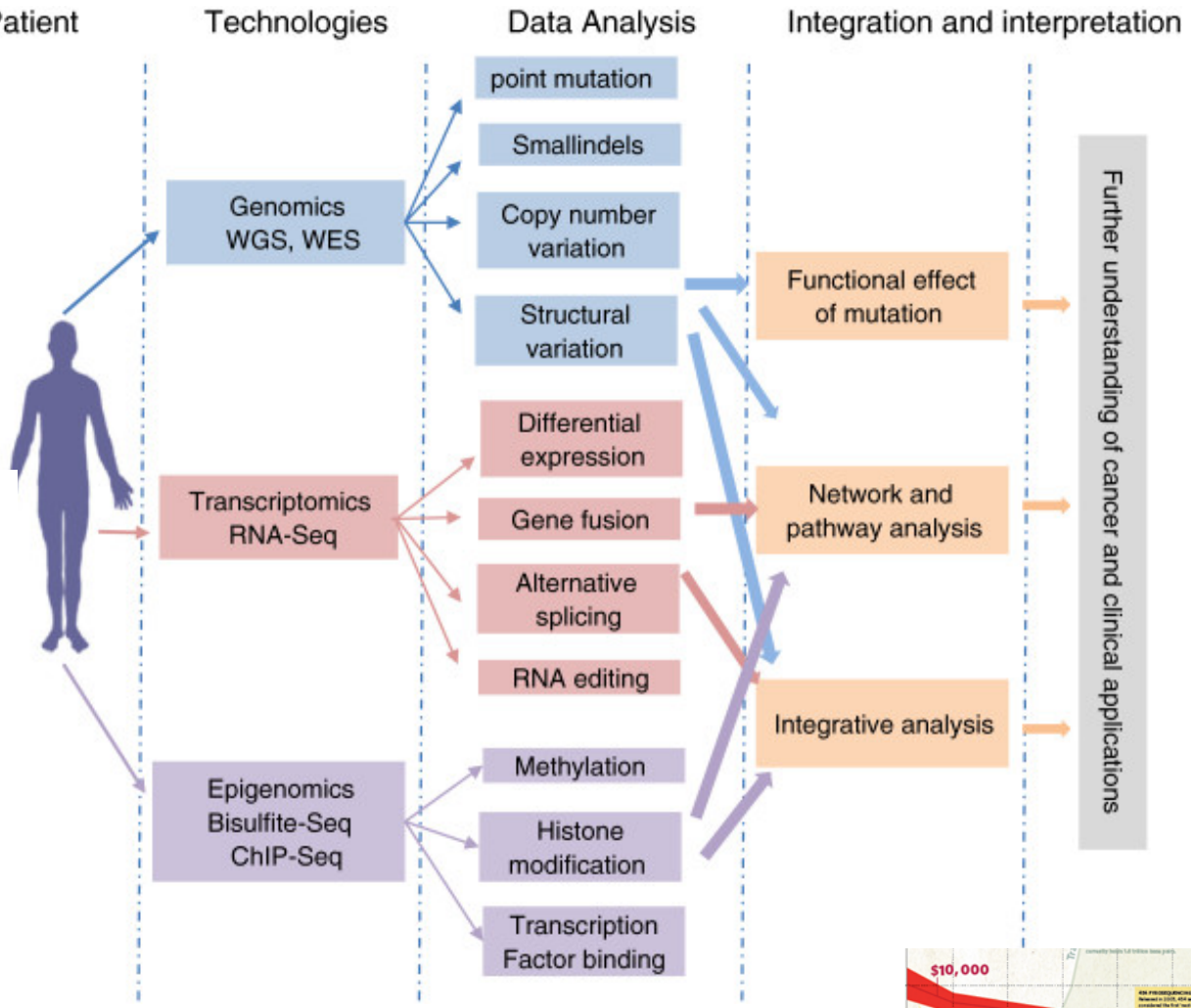
2nd top 1,500 in 4500 cases and 4500 controls

3rd top 25 in 4,999 cases and 15,555 controls

4th top 10 in 14,000 cases and 16,000 controls

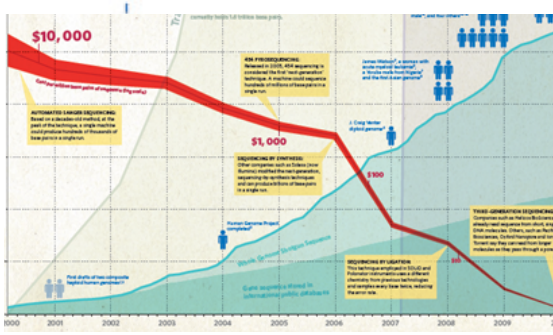
Illumina 300 and 550 K

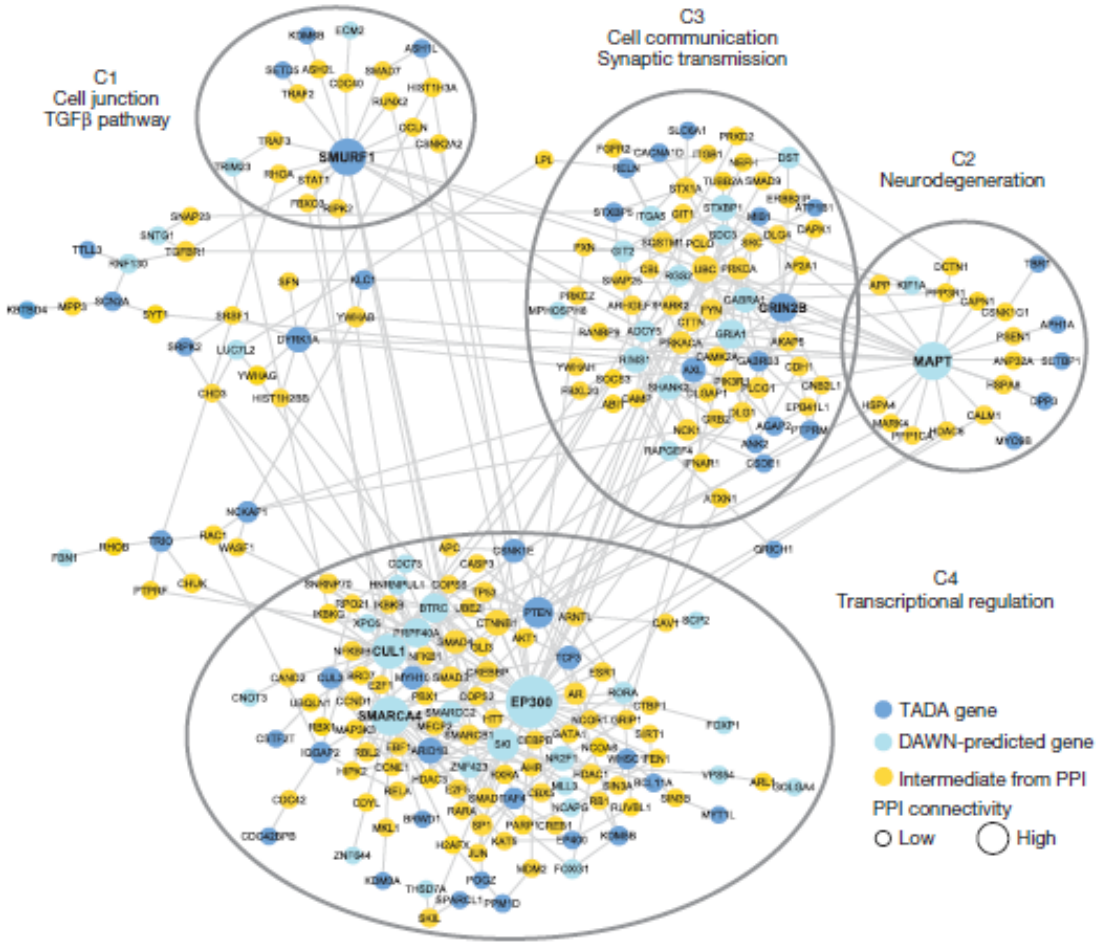




Genomics
Micro RNA
Transcriptomics
Epigenomics
Metagenomics

The sequence explosion

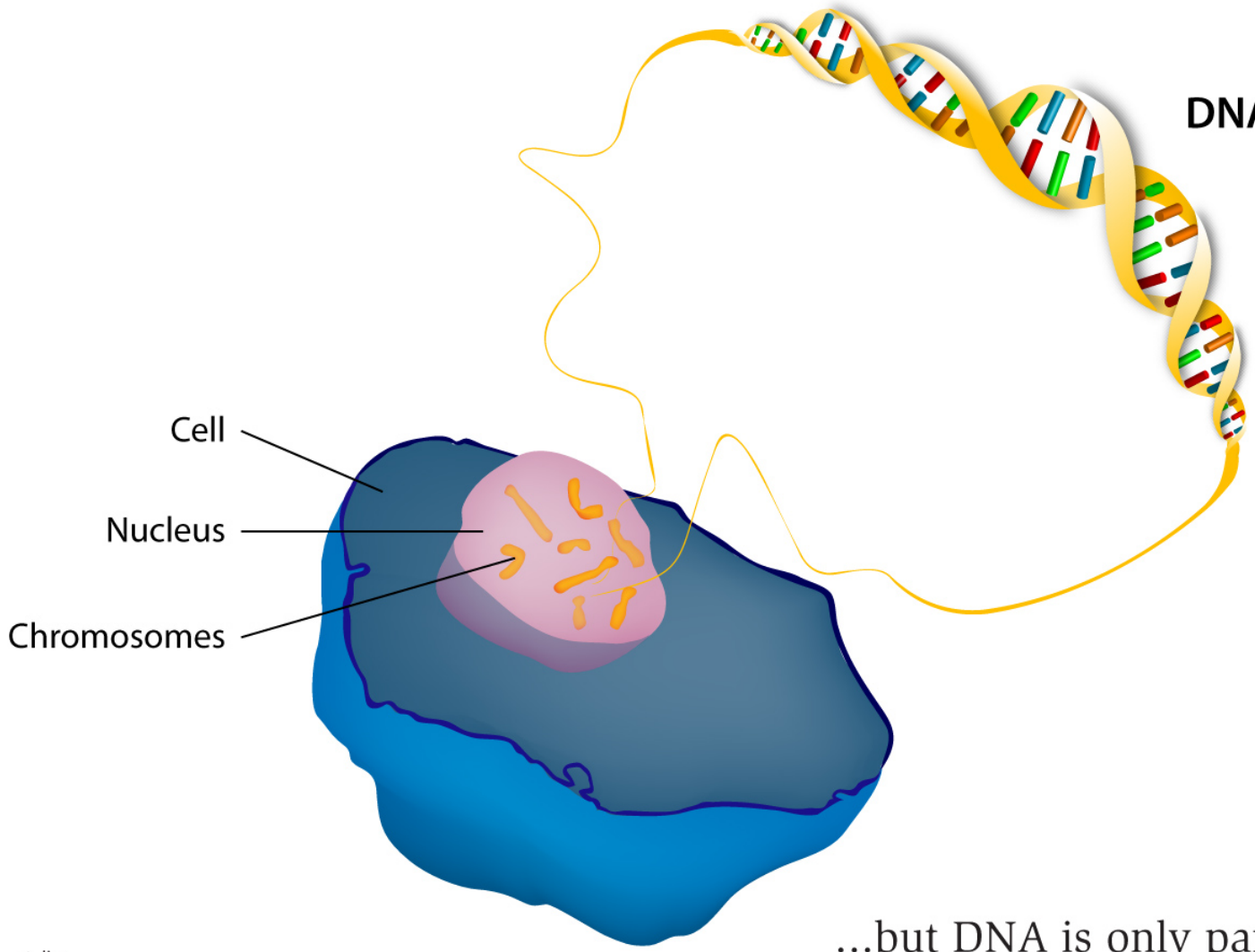




Synaptic, transcriptional and chromatin genes disrupted in autism
De Rubeis et al. Nature (2014) 4000 casos y 10,000 controles

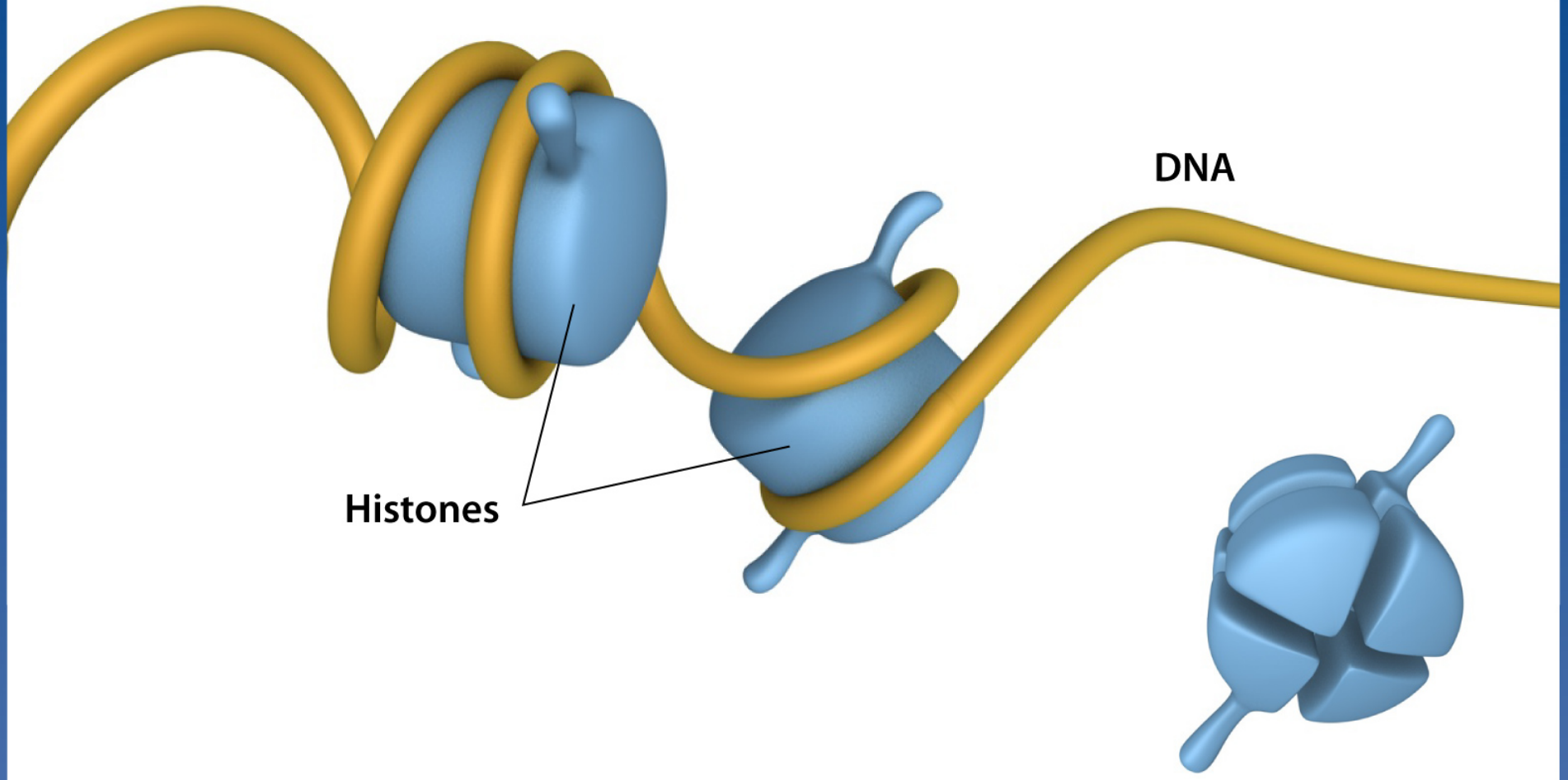
Epigenetics

DNA contains the instructions for building and maintaining all parts of the body



...but DNA is only part of the story

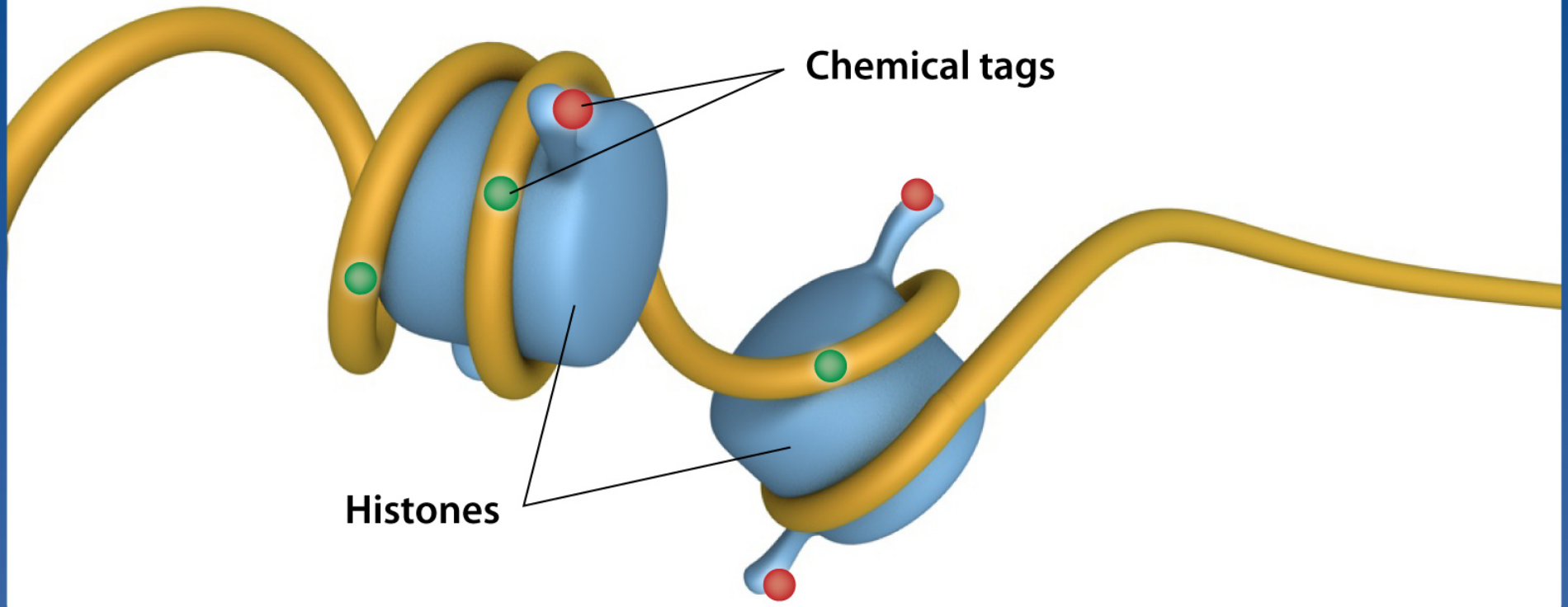
The DNA in our cells is wrapped around proteins called histones



A group of 8 histone proteins come together to form a spool.

National Human Genome Research Institute

DNA and histones are covered with chemical tags



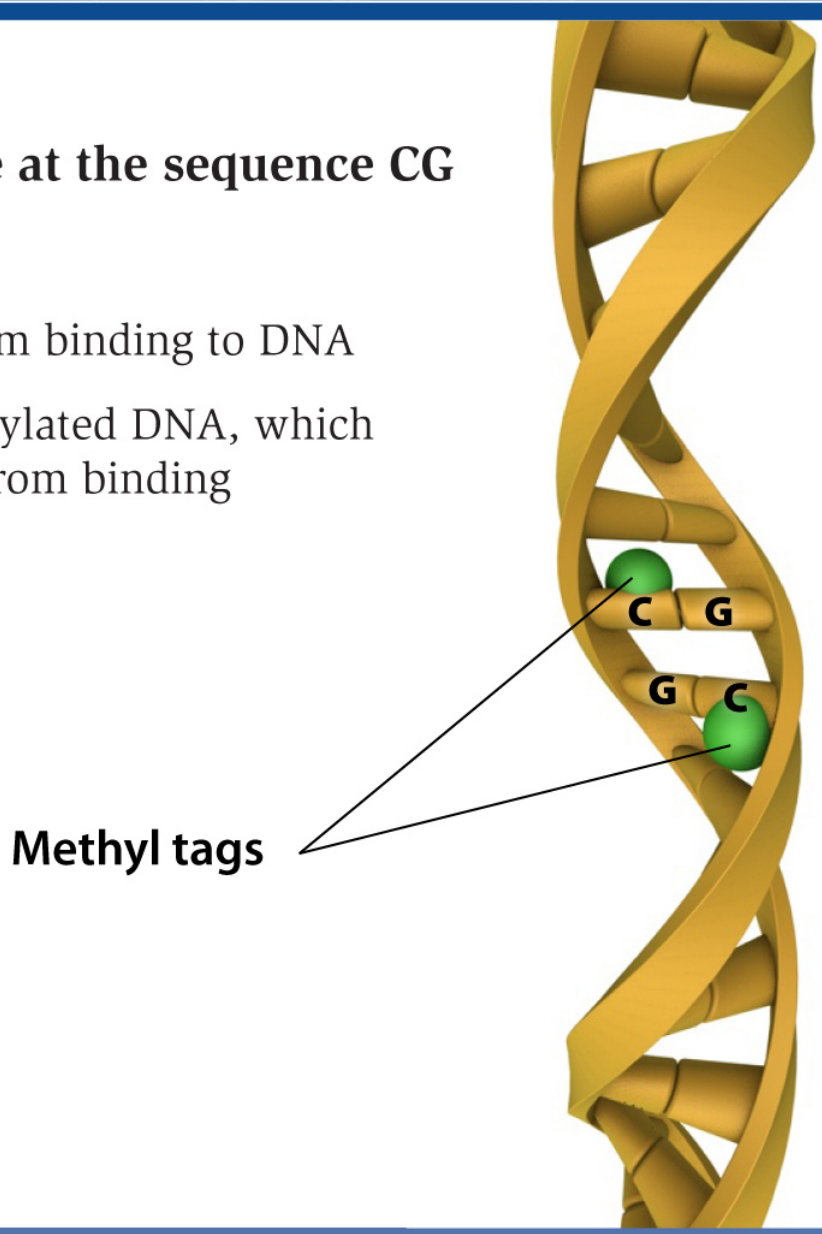
This second layer of structure, in the form of proteins and chemical tags, is called the **epigenome** ("epi" means above, on, or in addition to).

Methyl tags usually turn genes off

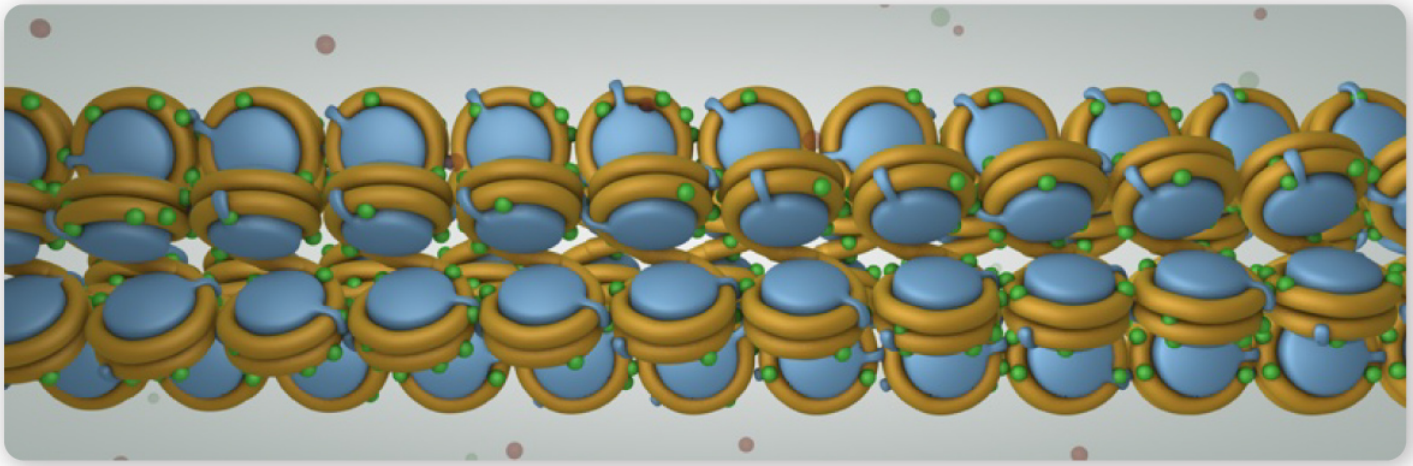
Methyl tags are added to a cytosine at the sequence CG

They silence genes by:

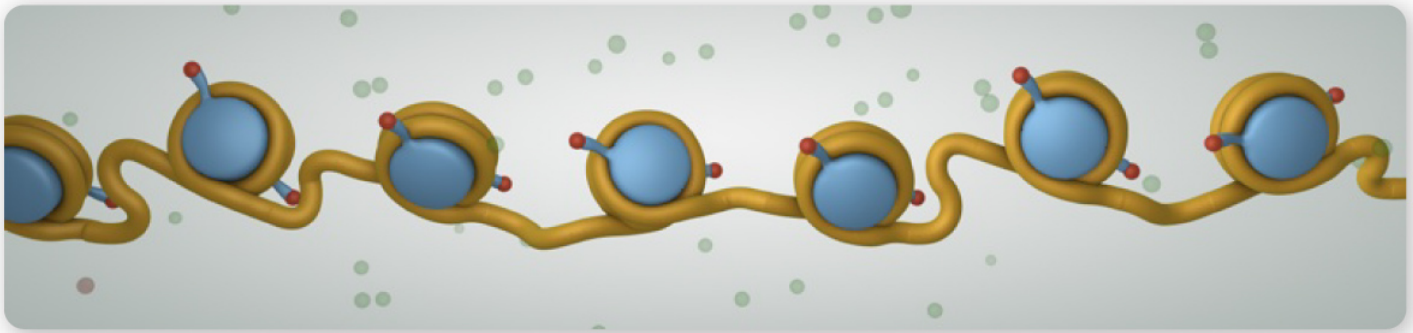
- Blocking transcription machinery from binding to DNA
- Recruiting proteins that bind to methylated DNA, which then block transcription machinery from binding



The epigenome shapes the physical structure of the genome



The epigenome tightly wraps **inactive** genes, making them unreadable.



The epigenome relaxes **active** genes, making them easily accessible.

The DNA code remains fixed for life, but the epigenome is flexible

Factors from the environment interact with the epigenome, affecting gene expression

- Diet
- Toxins
- Physical activity
- Stress

Identical twins have the exact same genetic information

But their epigenomes become increasingly different over time

- Epigenetic changes can cause dramatic differences between twins, including many cases where one twin develops a disease and the other does not.

Diet affects the epigenome

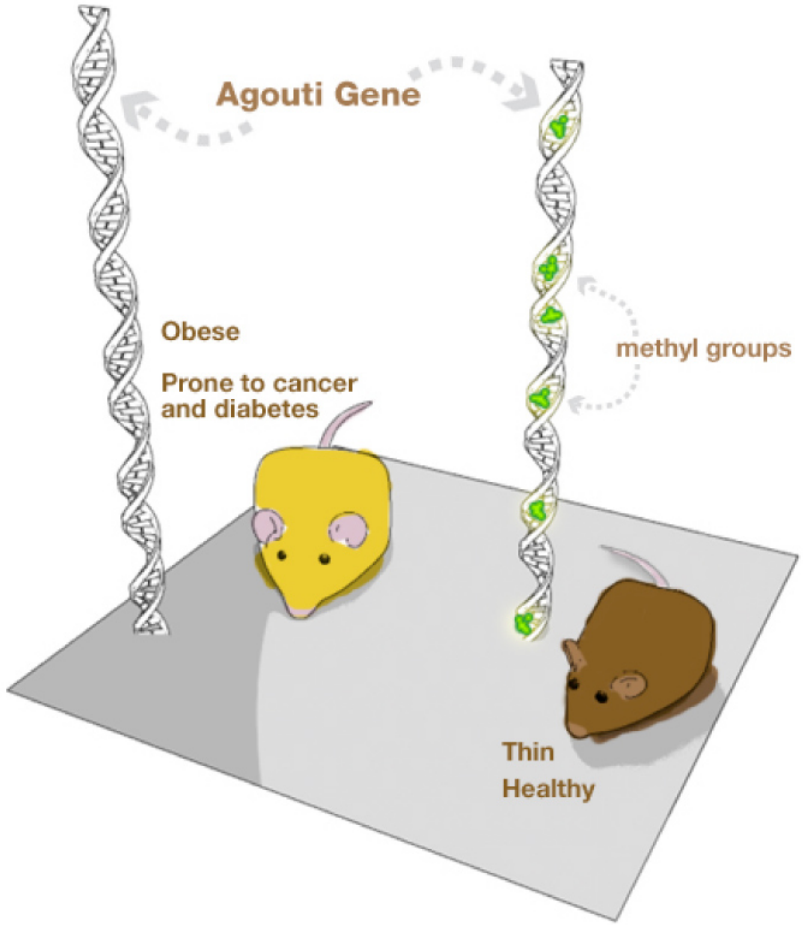
These two mice are genetically identical.

During pregnancy, the mother of the brown mouse ate a diet rich in methyl groups.

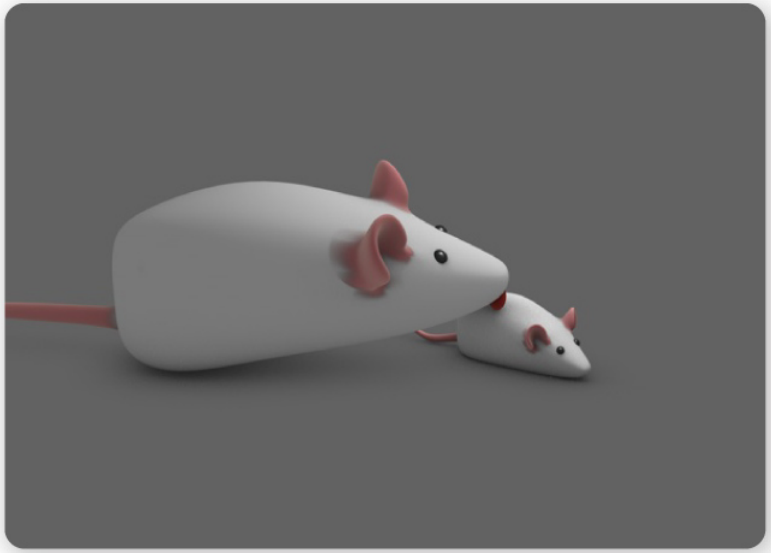
The mother of the yellow mouse ate regular mouse food.

The high methyl diet affected the developing mouse's epigenome, causing it to be born brown, thin and healthy.

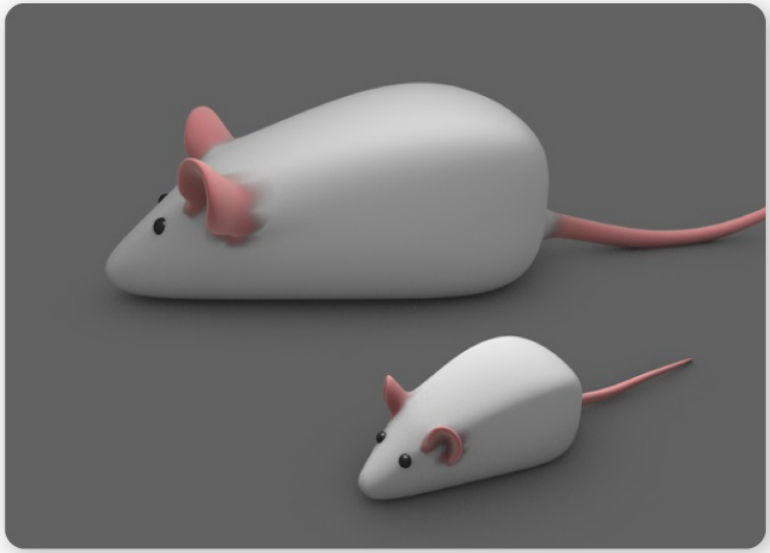
Waterland and Jirtle, 2003. Mol. Cell Biol 23(15): 5293-300.



Maternal care affects the epigenome



Highly nurtured rat pups tend to grow up to be calm adults.



Rat pups who receive little nurturing tend to grow up to be anxious adults.

(Wever et al, 2004. Nature Neuroscience, 7, 847)

The Human Epigenome Project hopes to clarify connections between gene expression and disease

Human Epigenome Project Goals:

- Identify methylation patterns in all of the body's major tissues
- Compare healthy and disease methylation patterns
- Understand interactions between genes, the epigenome, and the environment

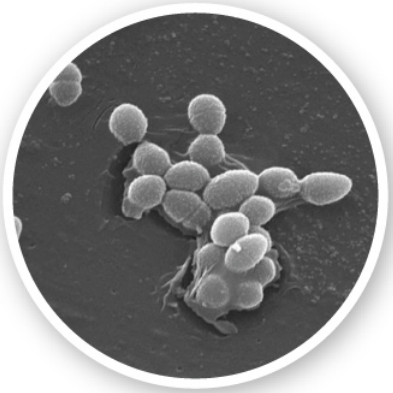
Human Microbiome Project

National Human Genome Research Institute

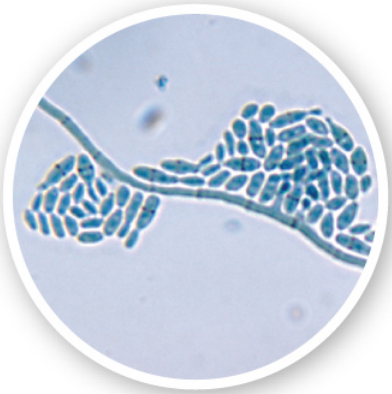
Using large-scale DNA sequencing to understand how microbes affect our health

The cells in our bodies are outnumbered 10:1 by microbes

- About 3 to 4 pounds of microbes live on and in our bodies.
- These microbes represent thousands of different species, and include bacteria, fungi, archaea and viruses.

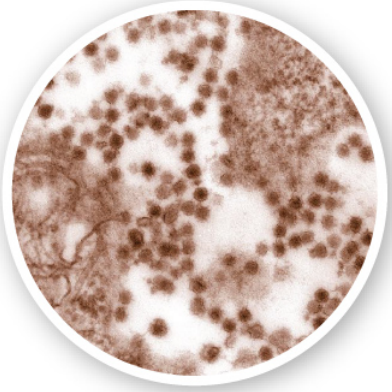


Bacteria



Fungi
(CDC/Dr. Libero Ajello)

Archaea
(P.M. Poon)

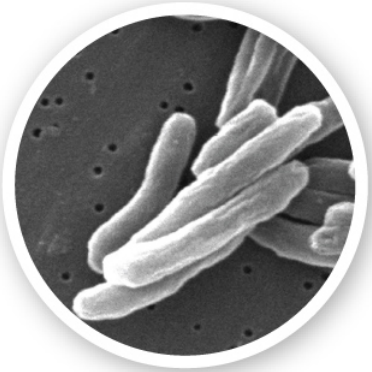


Viruses
(CDC/Cynthia Goldsmith)

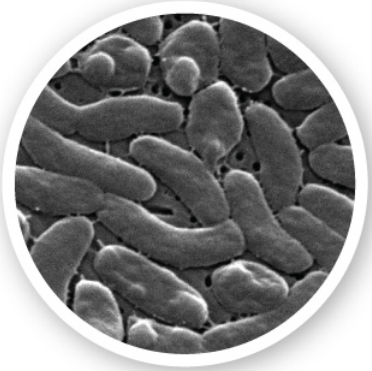
Some microbes cause disease

Many disease-causing microbes have been sequenced, including:

Bacillus anthracis (Anthrax)
Bacillus cereus (foodborne illness)
Borrelia burgdorferi (Lyme disease)
Camphylobacter, multiple species (diarrheal illness)
Chlamydia trachomatis (STD)
Clostridium botulinum (Botulism)
F. tularensis holarctica (tularemia)
Legionella pneumophila (Legionnaires' disease)
Listeria monocytogenes (foodborne illness)
Mycobacterium tuberculosis (Tuberculosis)
Neisseria gonorrhoea (STD)
Rickettsia rickettsii (Rocky mountain spotted fever)
Salmonella enterica (foodborne illness)
Streptococcus pneumoniae (Pneumonia)
Vibrio cholerae (Cholera)



Tuberculosis bacteria



Cholera bacteria

Images: CDC/Janice Carr

Microbes are important for many normal body functions

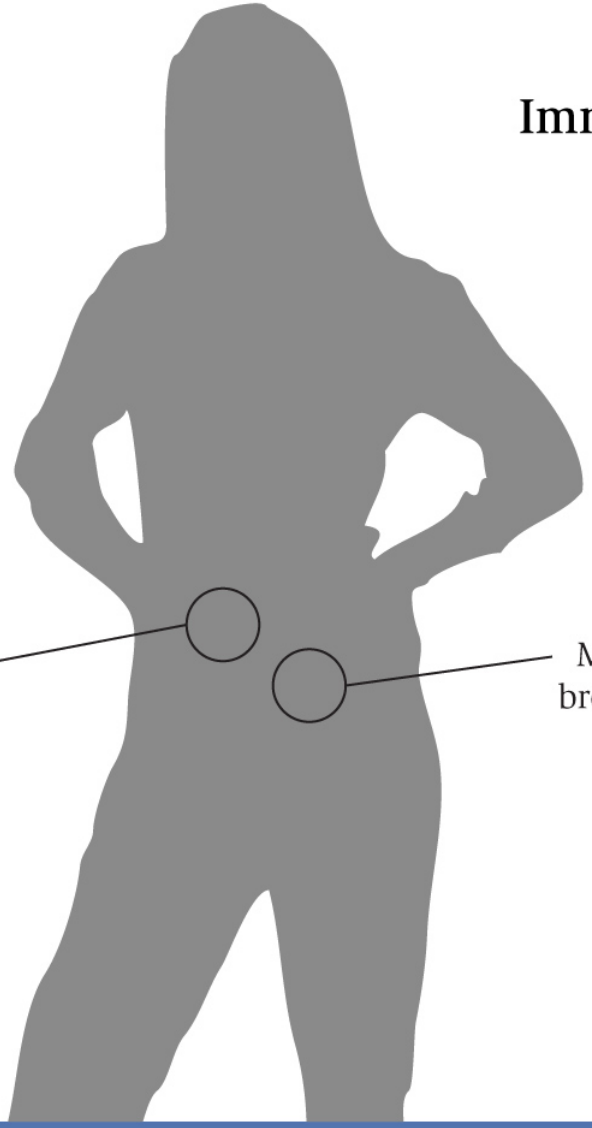
Digestion

Immunity

Nutrition

...and more

Metabolism



Microbes in our intestines produce vitamin K, which helps our blood clot.

Microbes in our intestines break down certain foods so we can absort them.

National Human Genome Research Institute

Variations in "healthy" microbe populations may be associated with complex diseases

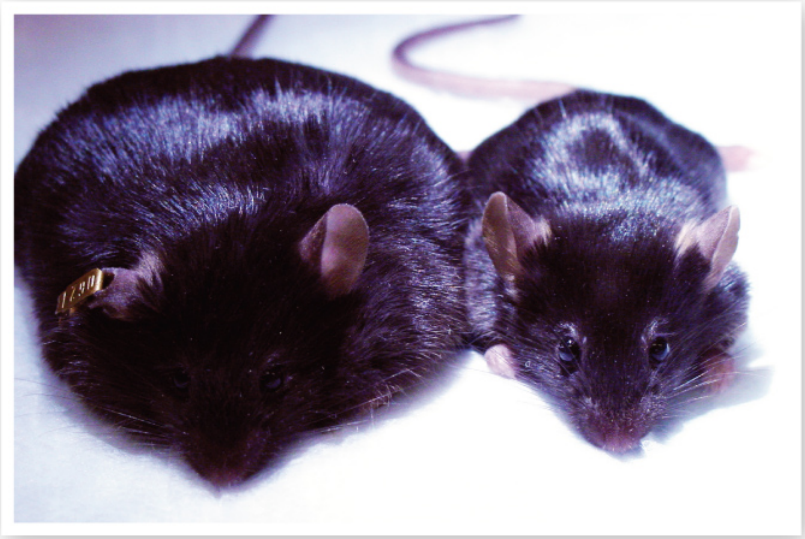


Photo: Umut Ozcan

Genetically obese mice contain gut microbes that are more efficient than normal at harvesting energy from their food.

Transferring these microbes to genetically normal mice causes the thin mice to gain body fat.

(Turnbaugh et al., Nature 444, 1027-131)

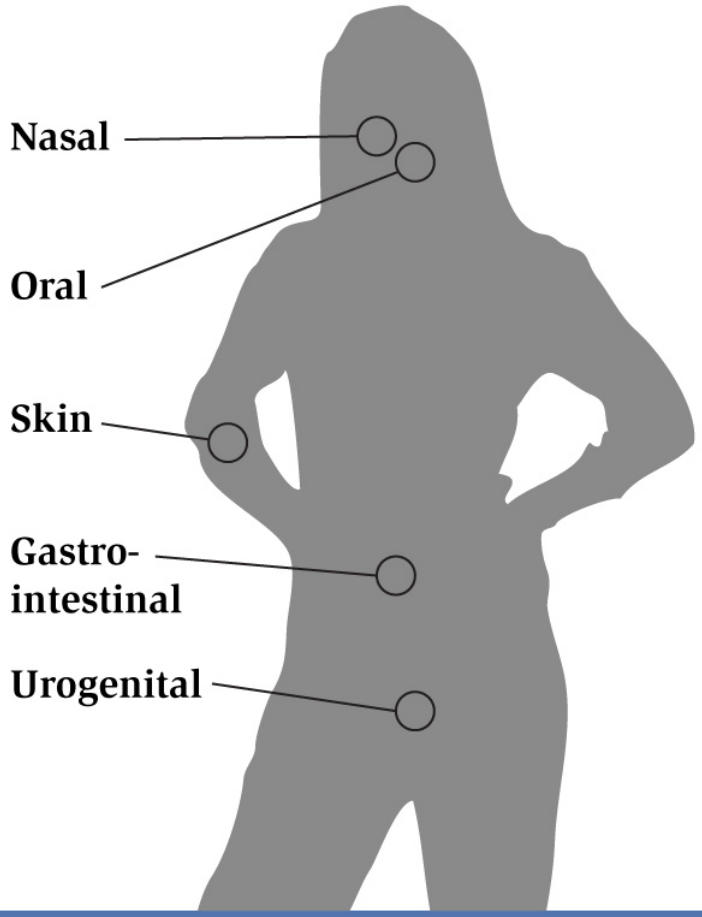
Studies suggest that obese and thin humans also have different gut microbes.

The Human Microbiome Project

Part 1: Identify and characterize the microorganisms that are found on and in the human body (the microbiome)

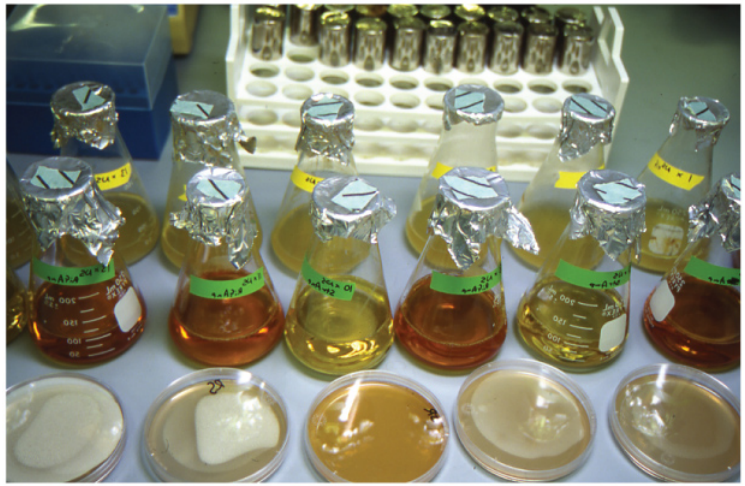
- Build a basic data set based on about 1,000 different microbes

The human microbiome project will focus on the microbe populations in 5 body regions:



Microbes live in specialized environments around the body

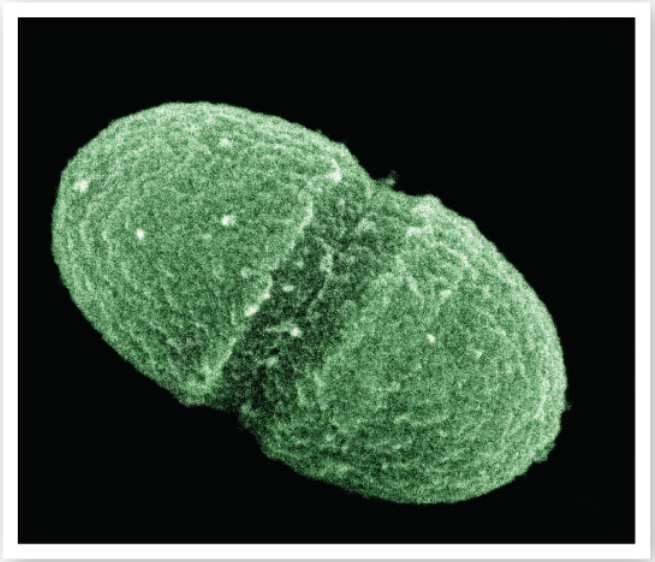
- Most of our resident microbes cannot be cultured outside of the body.
- New "metagenomics" tools can analyze large populations of microbes directly and simultaneously.
  - DNA sequences
  - RNA sequences
  - Protein sequences
  - Metabolic products



The Human Microbiome Project

Part 2: Examine the species represented in samples from healthy people

- Do humans share a common microbiome?
- Is the microbiome more similar between relatives? Members of a community?
- How does the microbiome change over the course of a day? year? lifetime?

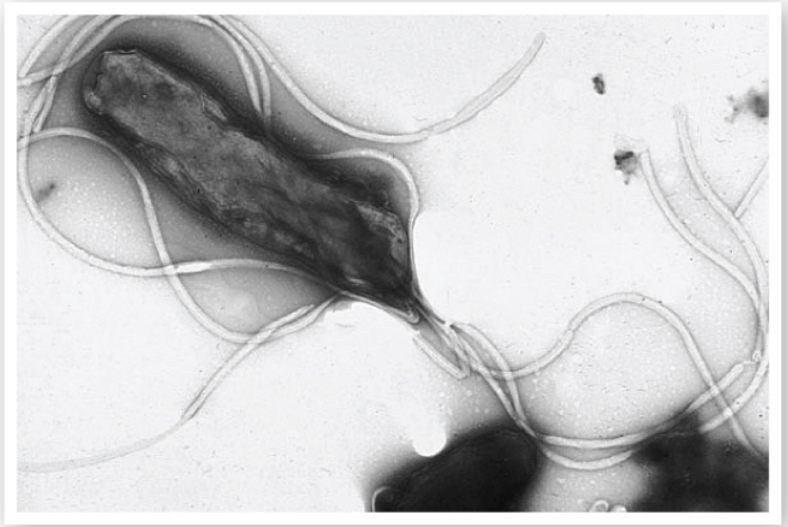


Enterococcus faecalis, a bacterium that lives in the gut.

The Human Microbiome Project

Part 3: Examine the species represented in samples from people with diseases

- How do changes in the microbiome correlate with changes in human health?



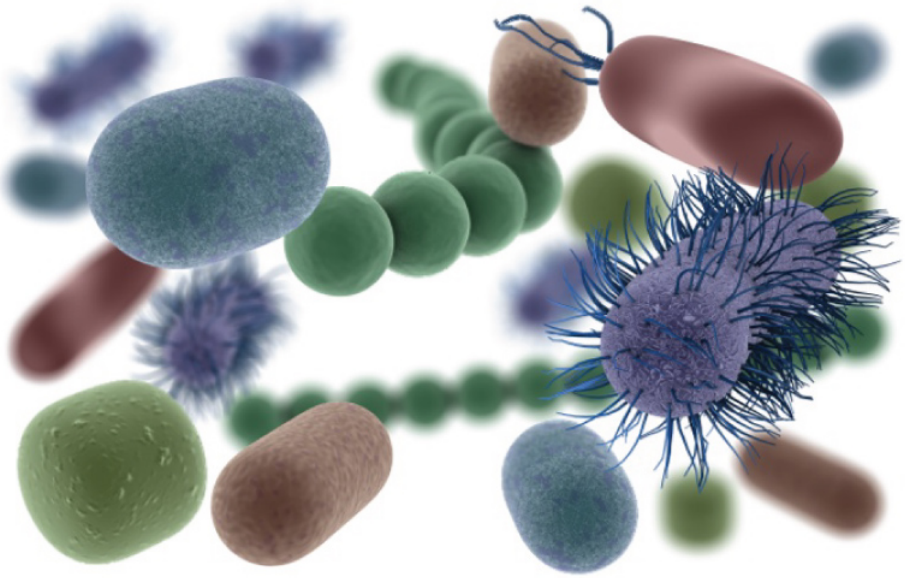
Helicobacter pylori, a bacterium that causes stomach ulcers.
(Yutaka Tsutsumi, M.D.)

The Human Microbiome Project

Diseases that may be affected by microbes include:

- Obesity
- Acne
- Asthma
- Diabetes
- Gall stones
- Stomach ulcers
- Inflammatory bowel disease
- Antibiotic-associated diarrhea
- Chronic periodontal (gum) disease
- Dental cavities
- Stomach and colon cancer

One day doctors may be able to make changes to an individual's microbiome to treat these and other diseases.



Fundación Pública Galega de Medicina Xenómica

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

BRIEFING ROOM | ISSUES | THE ADMINISTRATION | PARTICIPATE | 1600 P

Home • Briefing Room • Statements & Releases

The White House

Office of the Press Secretary

For Immediate Release

FACT SHEET: President Obama's Preci… Initiative

nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Curr

Archive | Volume 517 | Issue 7536 | News | Article

NATURE | NEWS

US precision-medicine proposal

Announcement by President Obama comes amidst grow

The NEW ENGLAND JOURNAL of MEDICINE

HOME | ARTICLES & MULTIMEDIA | ISSUES | SPECIALTIES & TOPICS | FOR AUTHOR

Perspective

A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

N Engl J Med 2015; 372:793-795 | February 26, 2015 | DOI: 10.1056/NEJMp1500523

European Commission

RESEARCH & INNOVATION

Health

European Commission > Research & Innovation > Health > Policies > Personalised Medicine

Home | Policies | Key Research Areas | Funded Projects

Policies

Genomics england

About Us | 100,000 Genomes Project | Taking Part | For Healthcare Professionals | Research | Industry Partnerships | News & Events

Home > The 100,000 Genomes Project

The 100,000 Genomes Project

The project will sequence 100,000 genomes from around 70,000 people. Participants are NHS patients with a rare disease, plus

Useful links

Cancer
Introduction to cancer in the 100,000 Genomes Project.

HELIX

The **H**uman **E**arly-**Li**fe E**x**posome – novel tools for integrating early-life environmental exposures and child health across Europe

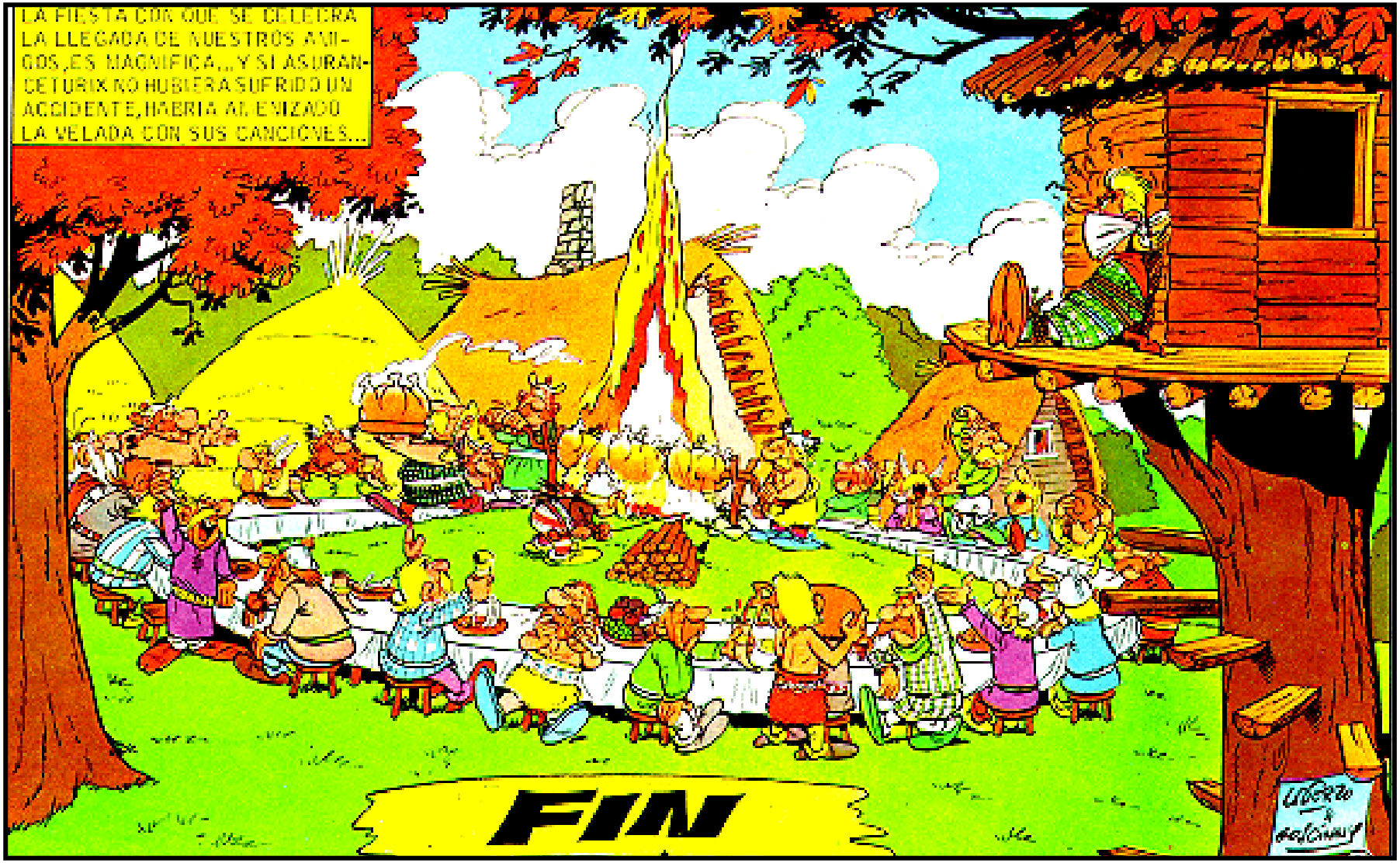
Study Protocol - Pregnancy Panel Study

V2, 7 March 2013

A. Introduction

B. Methods

1) Overview
2) Study population
3) Health parameters
4) Biological samples
5) Exposure assessment
6) Field work


LA FIESTA CON QUE SE CELEBRA LA LLEGADA DE NUESTROS AMIGOS,ES MAGNIFICA...Y SI ASURANCETURIX NO HUBIERA SUFRIDO UN ACCIDENTE,HABRIA AMENIZADO LA VELADA CON SUS CANCIONES...
FIN