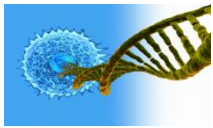


Modelos de Negocios en Biociencias: importancia del proceso de valoración de la investigación y análisis costo beneficio

Dr. Andrés Araya





Claves para re-evaluar el Diagnóstico

Oportunidad



Mercado y Demografía
Costos en salud



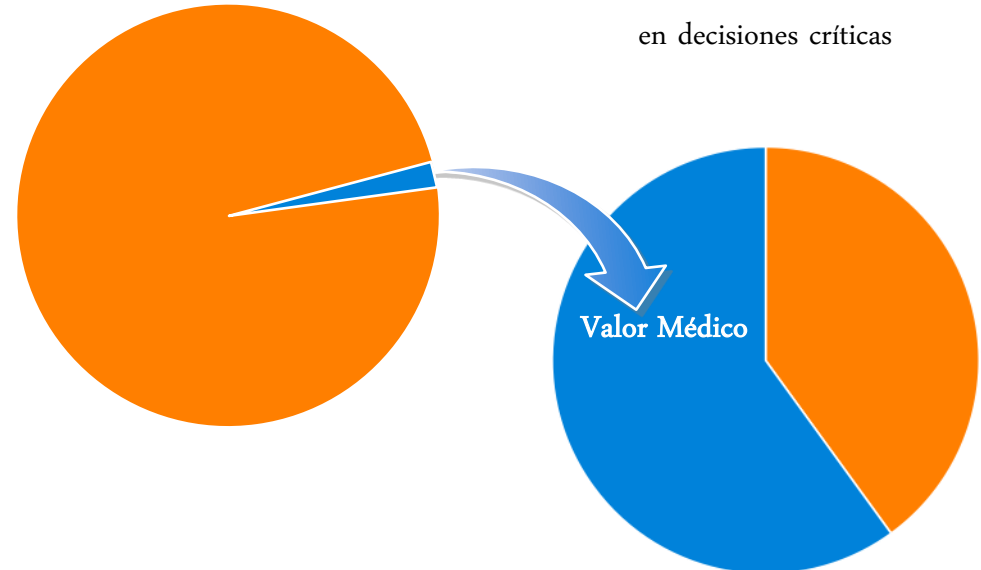
Adelantos en la ciencia
Nuevos descubrimientos

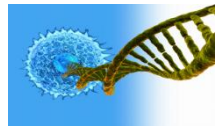


Necesidades Médicas
Medicina Personalizada

...para re-evaluar el diagnóstico

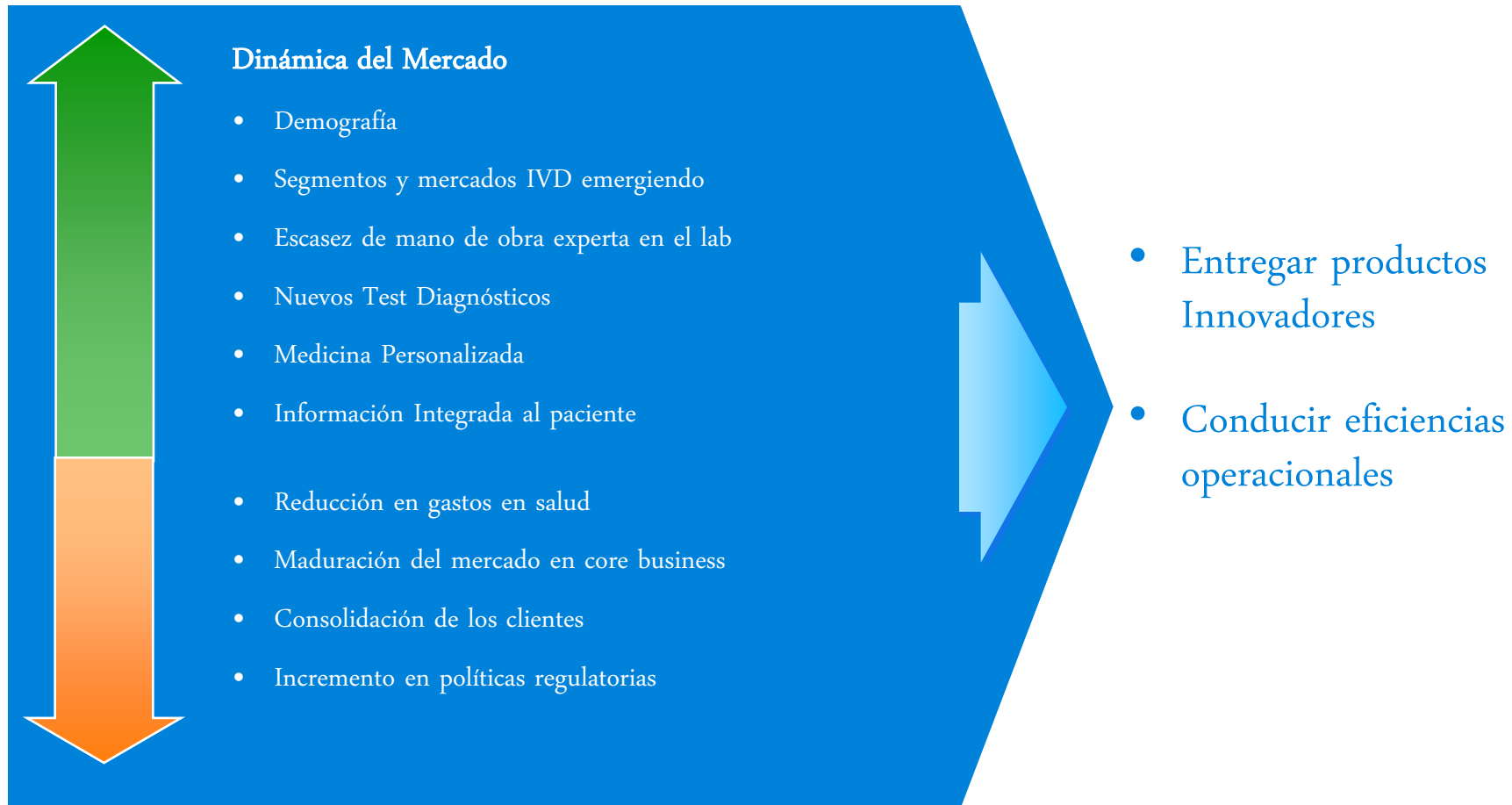
IVD <2 % gasto total en salud



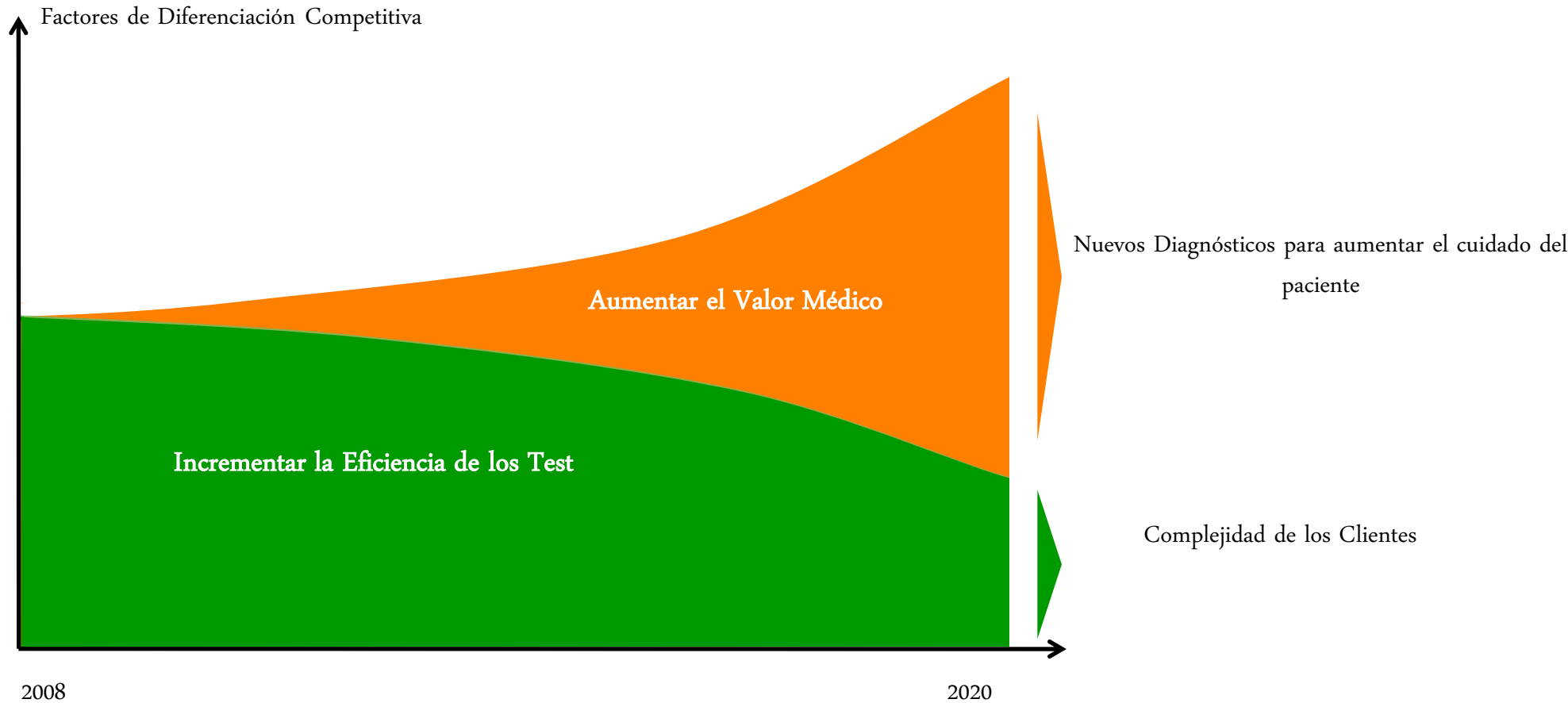
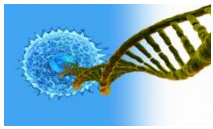


Cambios en el Mercado IVD

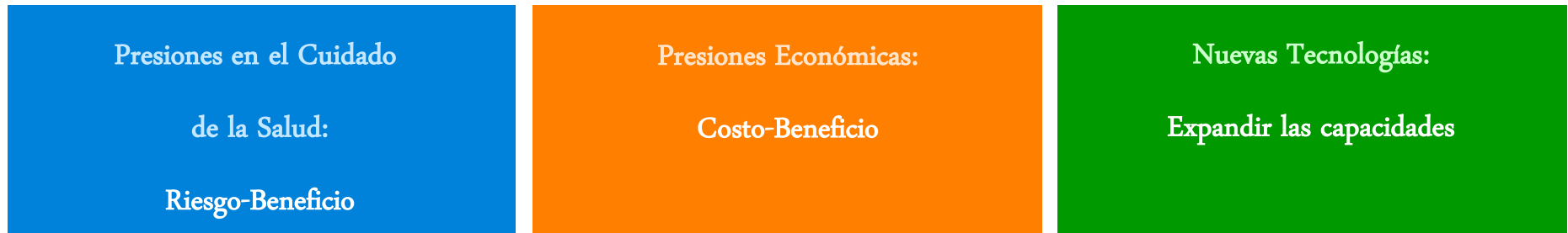
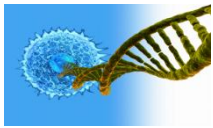
Capitalización sobre las tendencias de mercado



¿Cómo se puede entregar valor?



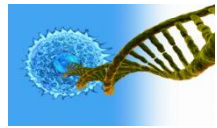
Demostrando Valor a través de la Medicina Personalizada



Medicinas Altamente diferenciadas impactarán positivamente en la salud pública

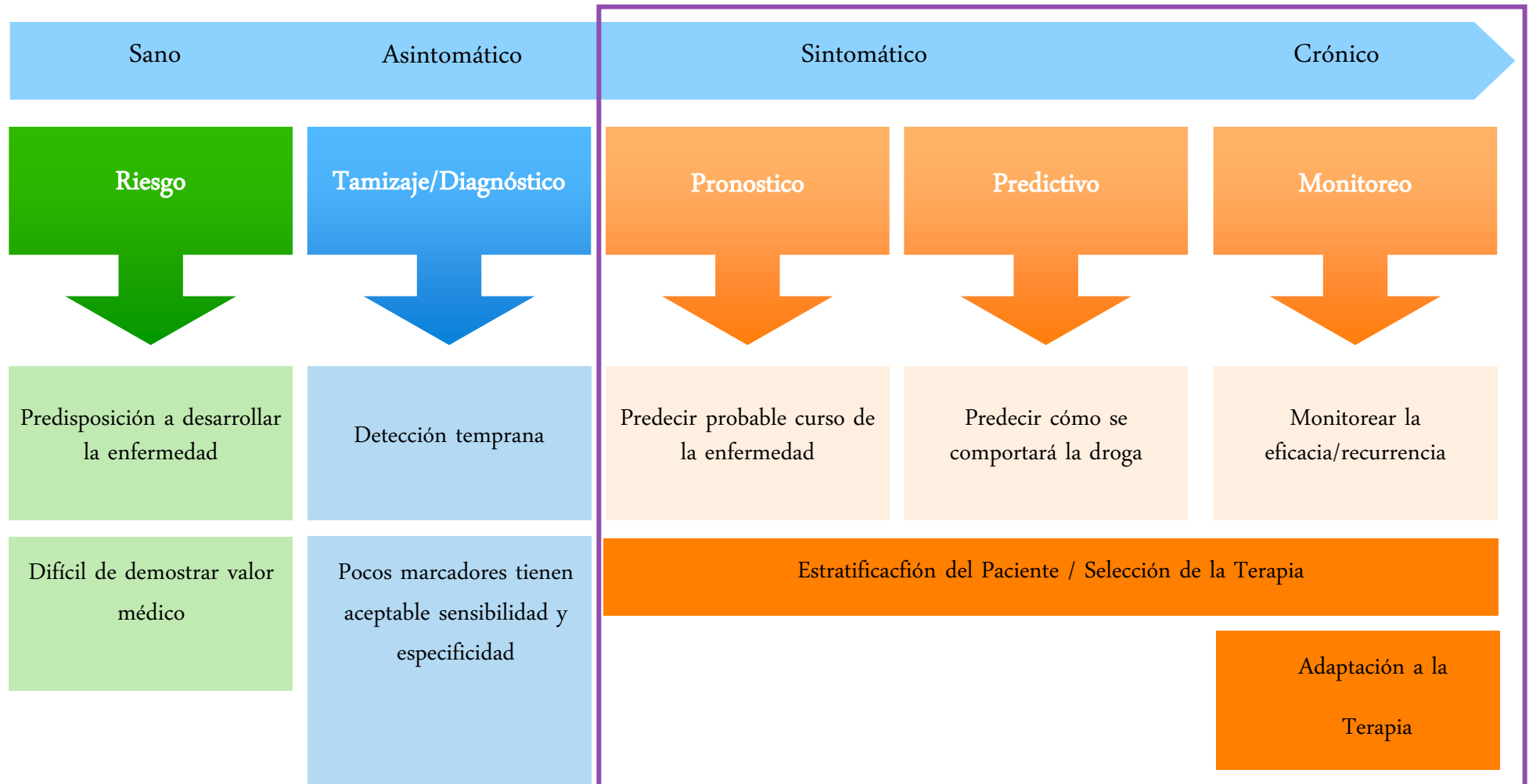


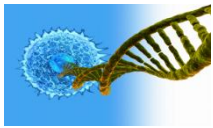
Pacientes compensarán la innovación



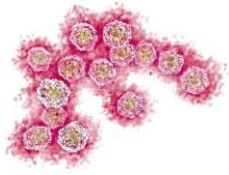
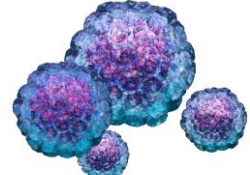
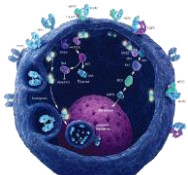
IVDs juegan un rol a lo largo de la vía de tratamiento

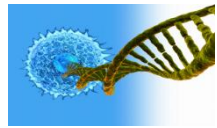
Biomarcadores son claves en la Medicina Personalizada





Necesidades Medicas para Diagnóstico Molecular

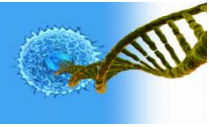
MEDICAL NEED	Blood Screening	Virology	HPV/ CT/NG	Microbiology	Genomics & Oncology
					
	Mas de 80 millones de unidades de sangre donada son distribuídas cada año	Infecciones Virales están entre las mayores causas de muerte en todo el mundo	El Virus Papiloma Humano (HPV) causa la mayoría de los cánceres cervicouterinos. Este cáncer es uno de los más comunes en las mujeres, con mas de 250,000 muertes cada año	Cuidado de la Salud asociada a infecciones intrahospitalarias	Sub tipos de cáncer pueden incidir en la progresión de la enfermedad y en la efectividad del tratamiento



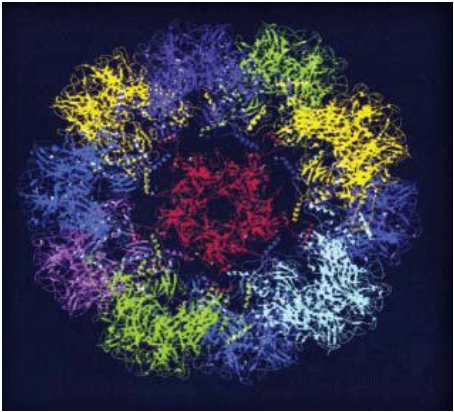
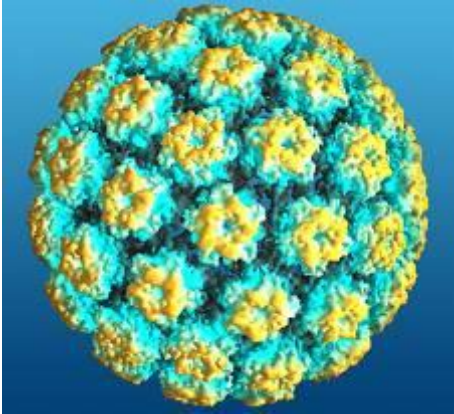
Ejemplo 1:

Control del Cáncer Cervicouterino

Human Papillomavirus (HPV)



99% de los cánceres cervicouterinos son causados por una infección de HPV alto riesgo



- 5th cáncer más comun en todo el mundo
- Infección mas comun transmitida sexualmente
- 75% de las mujeres esta expuesta
- La mayoría de las infecciones por HPV son sanadas
- Sobre 100 tipos distintos de HPV
 - HPV bajo riesgo: verrugas genitales
 - HPV alto riesgo: cáncer cervico uterino
- 16 tipos de HPV son considerados de alto riesgo

¿Qué aporta una intervención nueva frente al manejo actual, ¿porqué **pagar por ella?**

VALOR MÉDICO o Valor Clínico

Si la nueva intervención **es mejor** que el manejo actual, ¿debería tener un **precio mayor?**

Si la nueva intervención **es mejor** que el manejo actual, **¿cuánto vale la pena pagar** por el beneficio obtenido?

COSTO BENEFICIO

COSTO EFECTIVIDAD

Establecer las Ventajas Competitivas

Gran Trial Clínico



1. Demostrar el valor de identificar HPV Genot 16/18
2. Demostrar la performance relativa comparada con el estándar actual
3. Demostrar el valor del resultado del ensayo en algoritmos clínicos

Establecer las Ventajas Competitivas

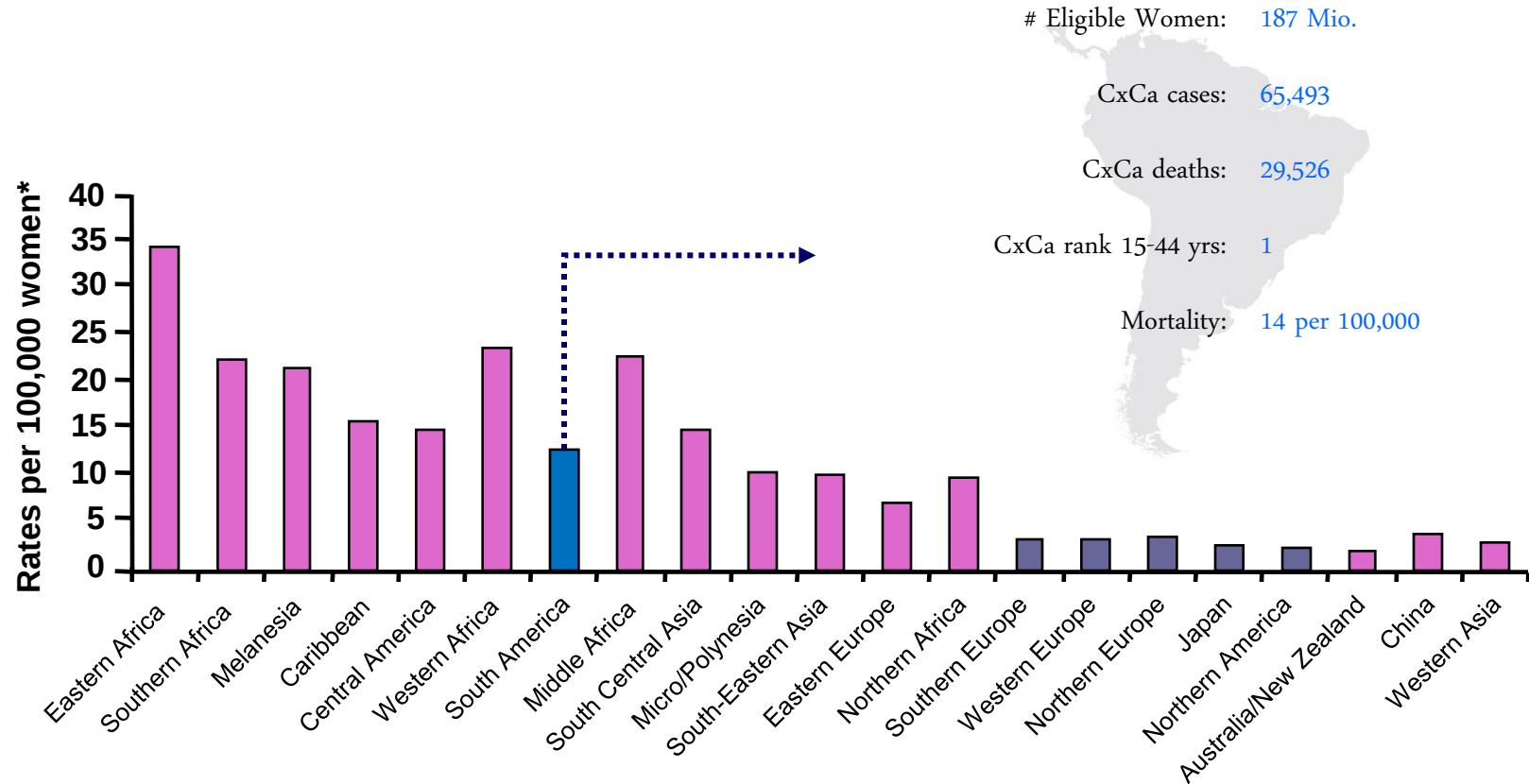
Gran Trial Clínico



1. Demostrar el valor de identificar HPV Genot 16/18
2. Demostrar la performance relativa comparada con el estándar actual
3. Demostrar el valor del resultado del ensayo en algoritmos clínicos

Cervical cancer associated mortality varies worldwide

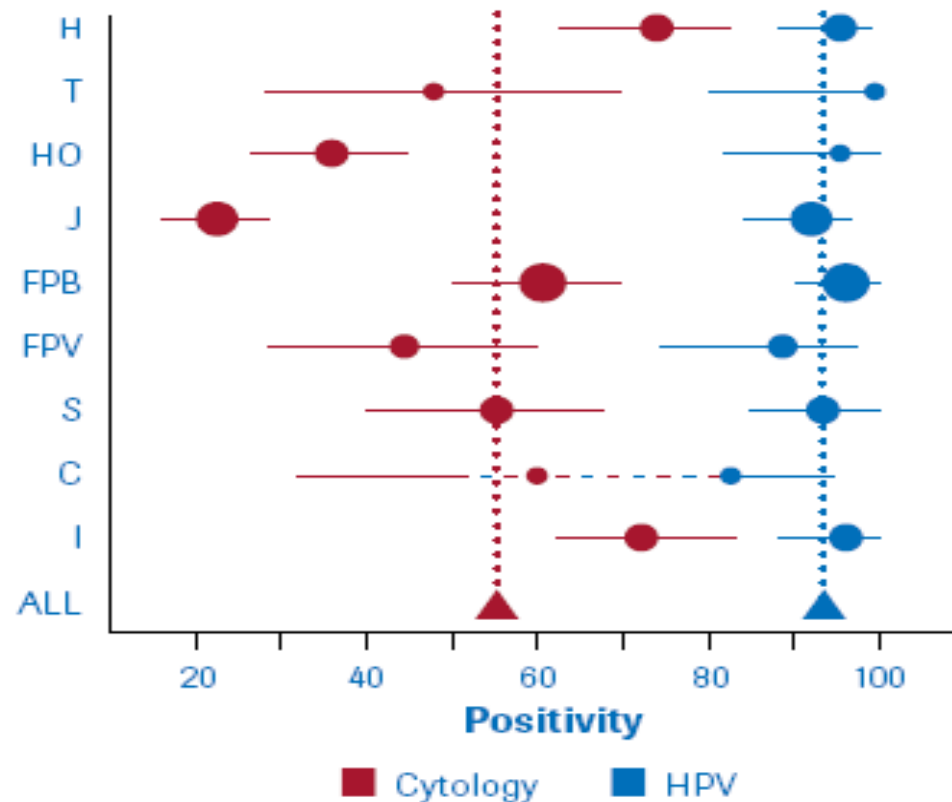
2002 GLOBOCAN series of the IARC



* Estimated age-standardized rates

Screening has reduced cervical cancer mortality in industrialized nations by approximately a half to two-thirds

Test HPV es mas sensible que la citología (PAP) para la detección de la enfermedad



43% ASCUS son HPV HR+

?

Prevalencia $\geq$ CIN2 = 10,3 %²

Estratificación identificando

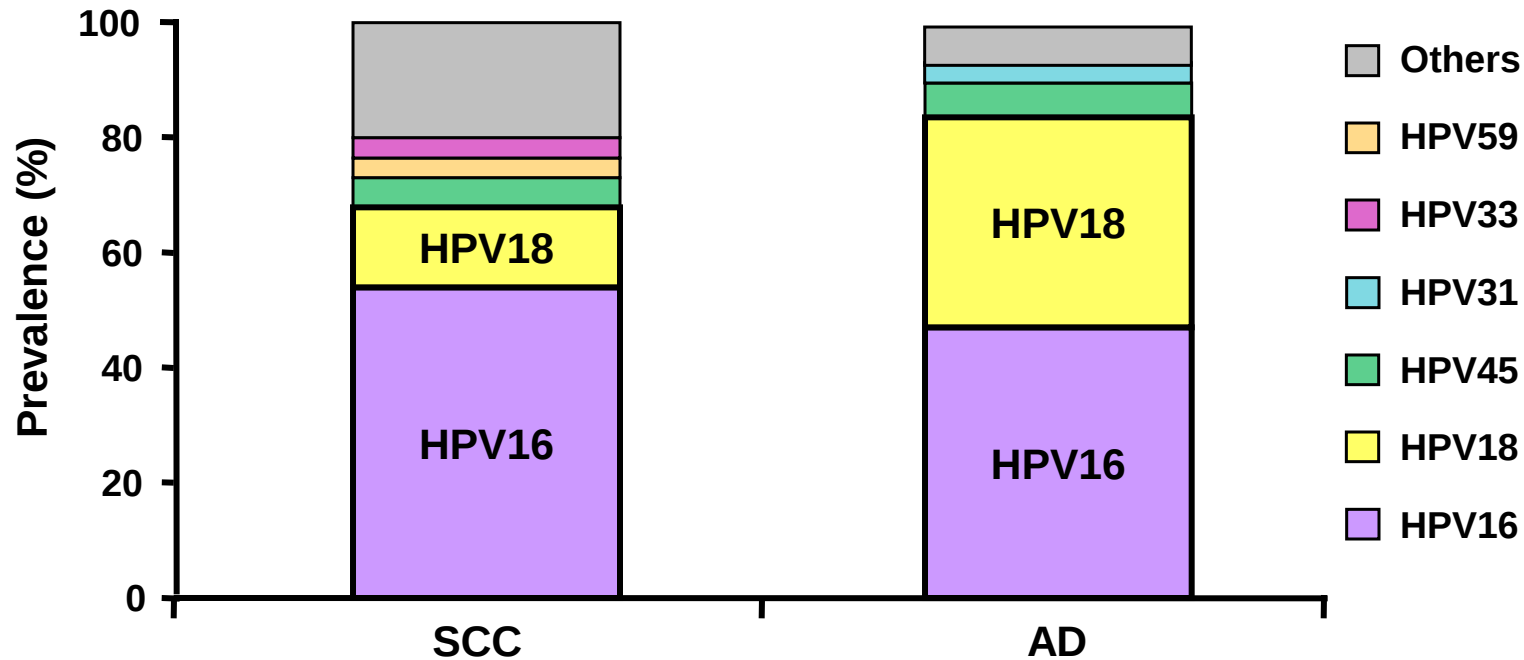
HPV 16/18

Para identificar mujeres con alto riesgo de CIN2 o peor.

Test HPV es sustancialmente mas sensible en detectar CIN2+ (96%) que la citología (53%)¹

Prevalencia de tipos de HPV en cáncer cervical

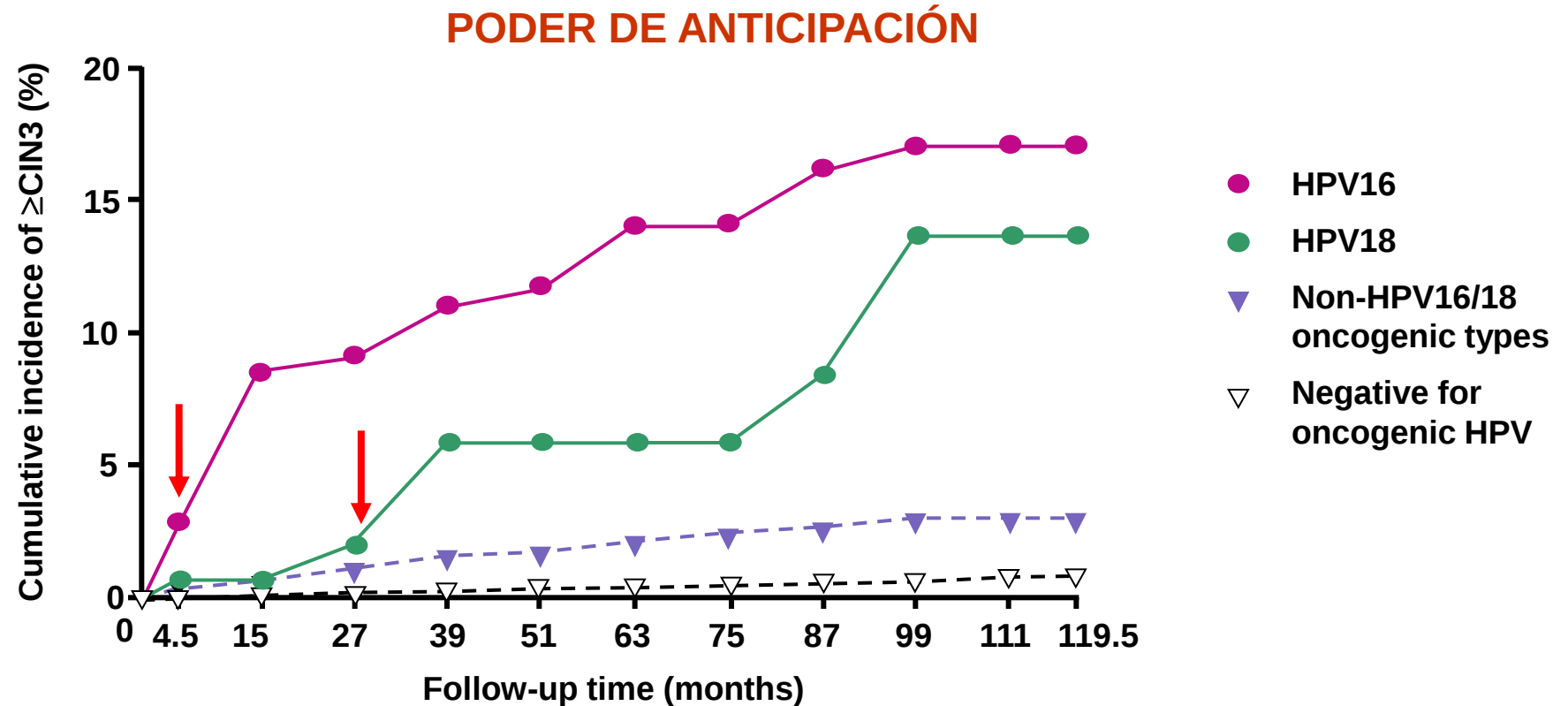
Squamous cell carcinoma y adenocarcinoma



SCC=Squamous Cell Carcinoma
AD=Adenocarcinoma

HPV16 y HPV18 son los dos tipos de HPV oncogénicos mas prevalentes en SCC y AD

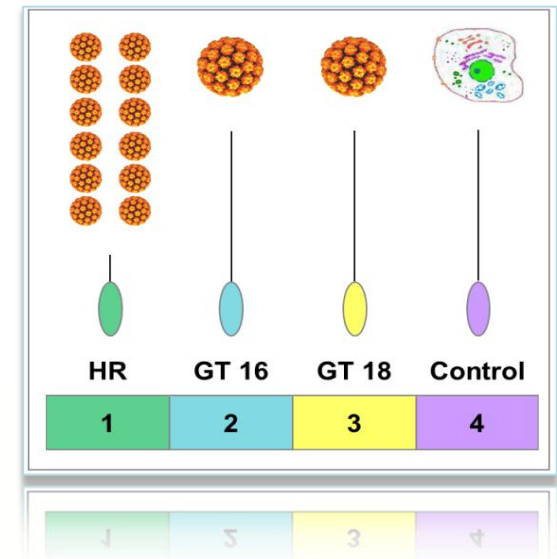
HPV16 y HPV18: riesgo en 10 años de desarrollar precáncer y cáncer



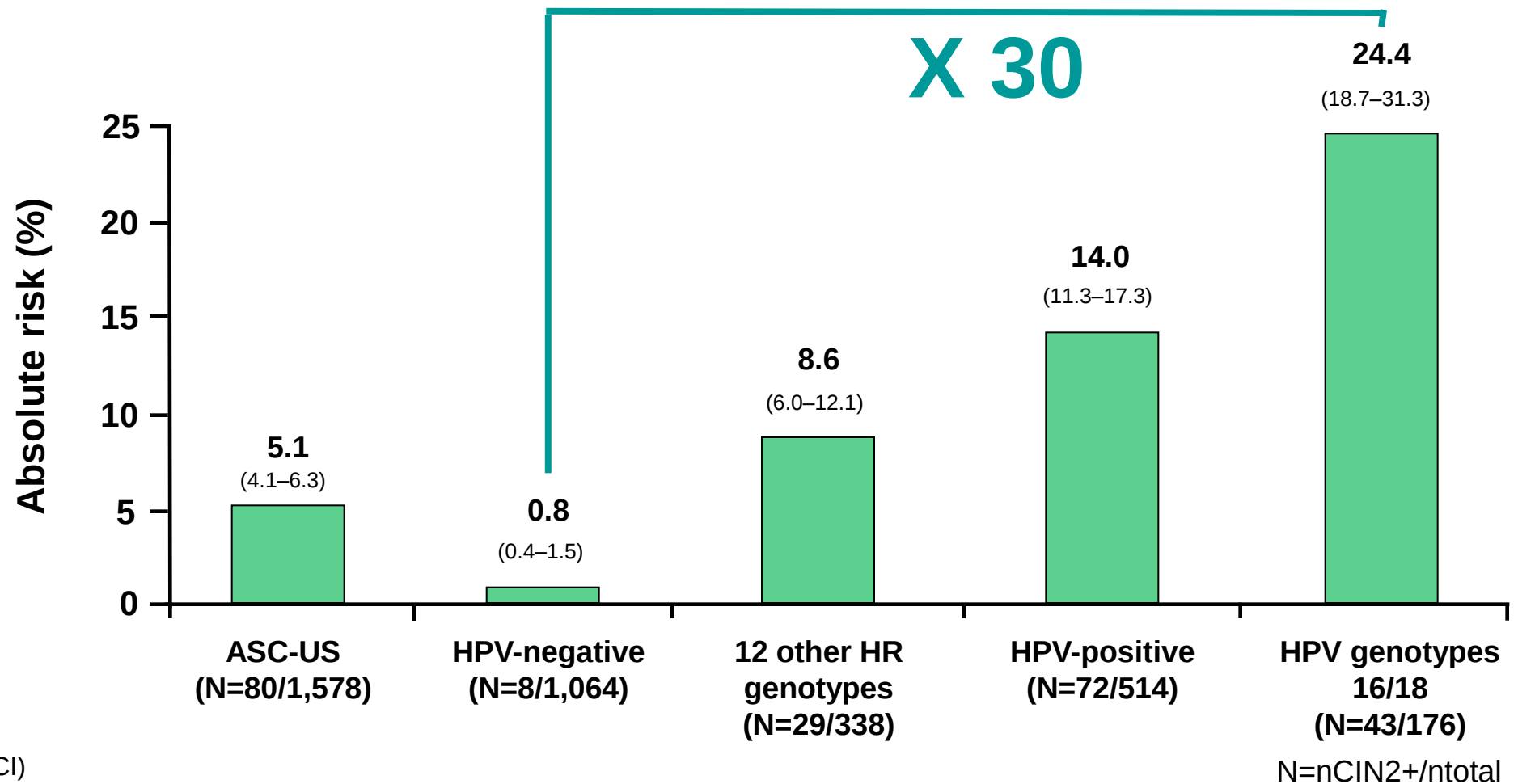
HPV genotyping for HPV16 and HPV18 may identify women at greatest risk of $\geq$ CIN3

The cobas® HPV Test

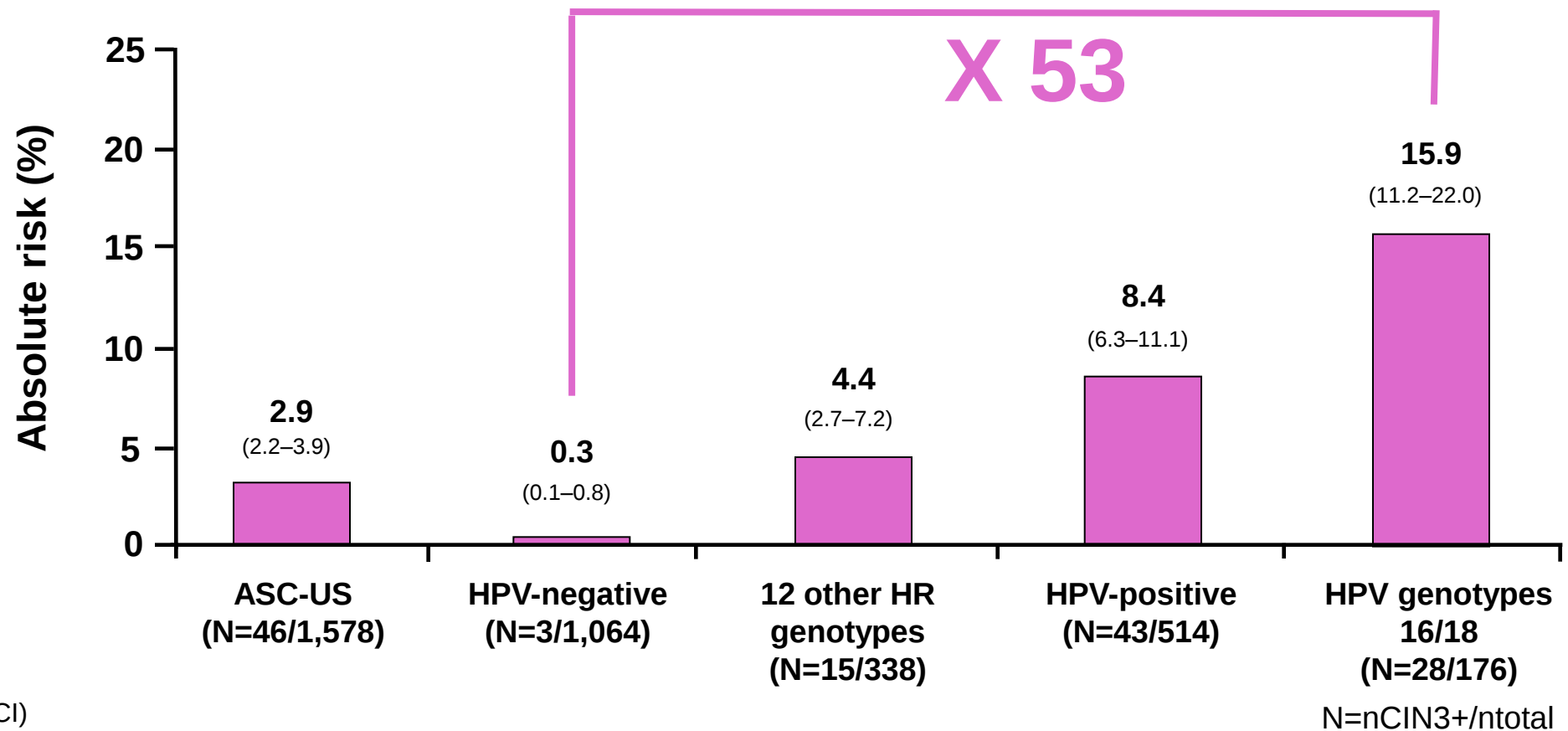
Channel 1	Pool of 12 HR types
Channel 2	HPV Genotype 16
Channel 3	HPV Genotype 18
Channel 4	Control



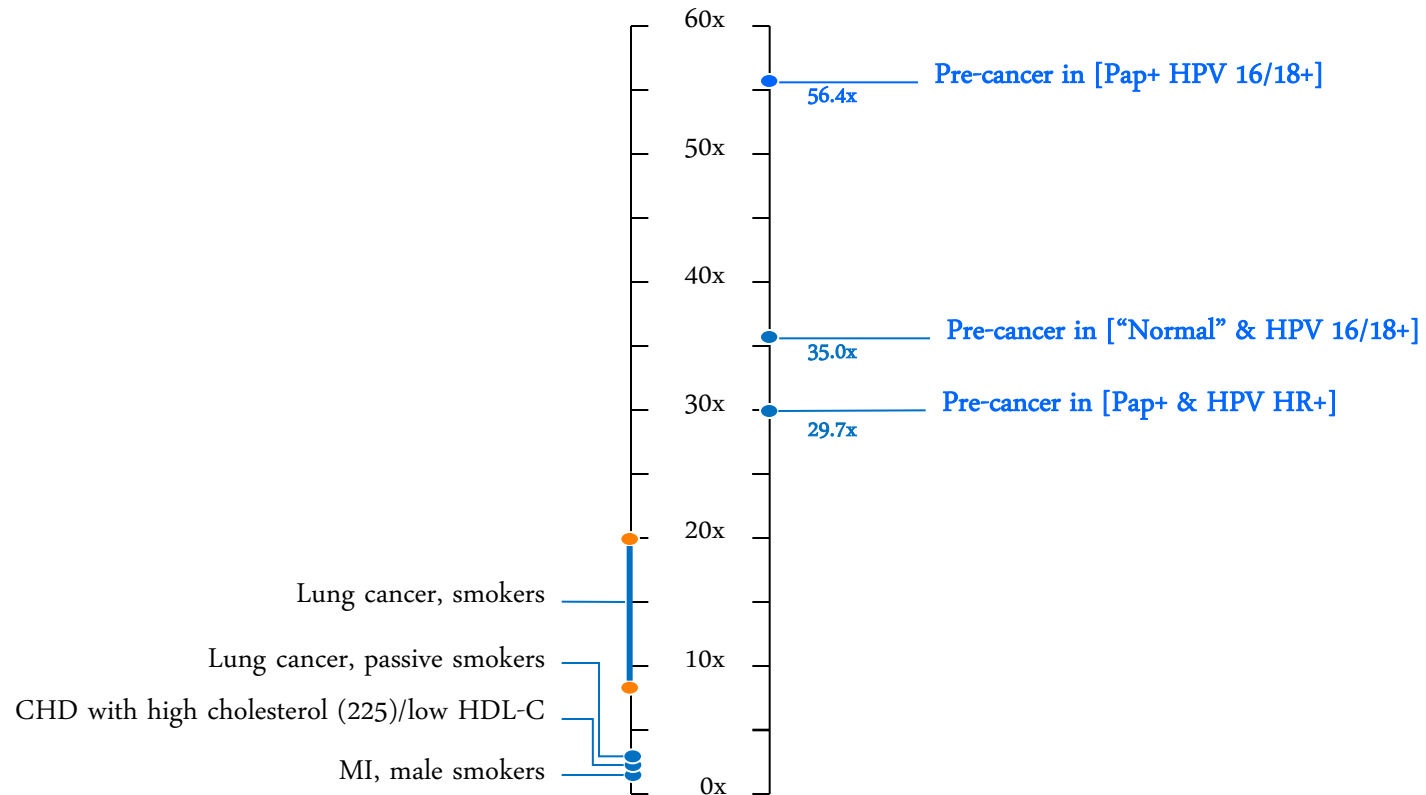
Riesgo absoluto en $\geq \text{CIN2}$ respecto del genotipo de HPV en mujeres ASC-US positivo



Riesgo absoluto en $\geq \text{CIN3}$ respecto del genotipo de HPV en mujeres ASC-US positivo



ATHENA Results: Relative Risk of Pre-cancer



Establecer las Ventajas Competitivas

Gran Trial Clínico



1. Demostrar el valor de identificar HPV Genot 16/18
2. Demostrar la performance relativa comparada con el estándar actual
3. Demostrar el valor del resultado del ensayo en algoritmos clínicos

Sensitivity and specificity of HPV Test for detecting $\geq$ CIN2 and $\geq$ CIN3 in the ASC-US population



	HPV Test		Gold Standard	
	Point estimate	95% CI	Point estimate	95% CI
$\geq$ CIN2 N=80				
Sensitivity	90.0%	(81.5–94.8)	87.2%	(78.0–92.9)
Specificity	70.5%	(68.1–72.7)	71.1%	(68.8–73.4)
$\geq$ CIN3 N=46				
Sensitivity	93.5%	(82.5–97.8)	91.3%	(79.7–96.6)
Specificity	69.3%	(66.9–71.5)	70.0%	(67.7–72.3)

The HPV Test performance is comparable with the Gold Standard

ATHENA trial; Roche Molecular Diagnostics; Data on file 2010.

Establecer las Ventajas Competitivas

Gran Trial Clínico

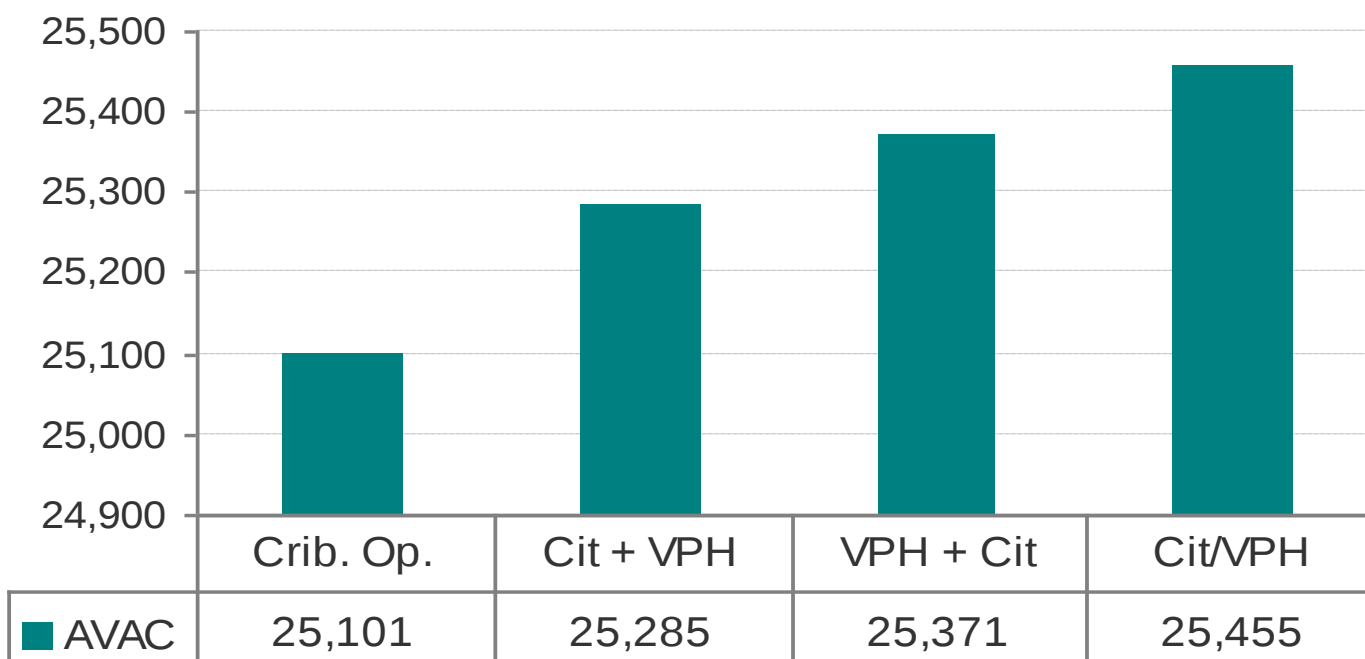


1. Demostrar el valor de identificar HPV Genot 16/18
2. Demostrar la performance relativa comparada con el estándar actual
3. Demostrar el valor del resultado del ensayo en algoritmos clínicos

Modelización Económica del Cribado de Cáncer Cervical

Resultados del modelo - Efectividad

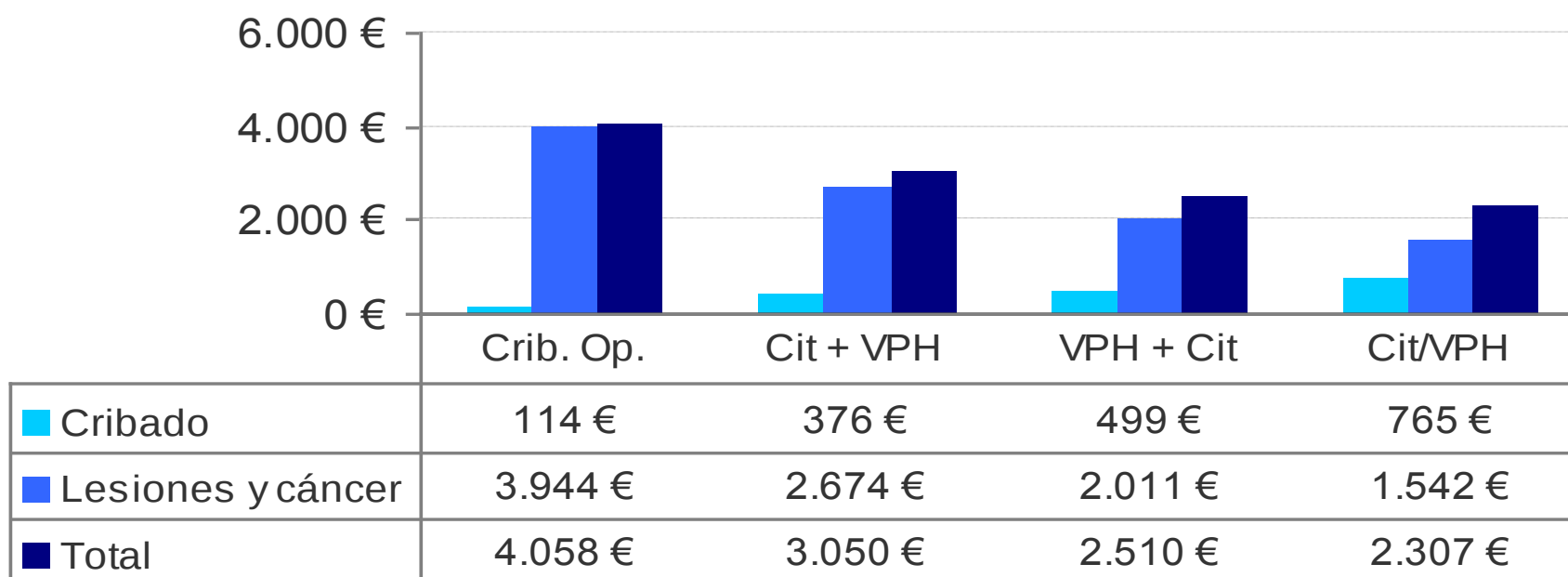
**Años de Vida Ajustados por Calidad (AVAC)
(promedio por paciente)**

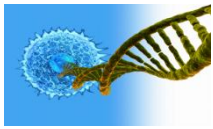


Modelización Económica del Cribado de Cáncer Cervical

Resultados del modelo - Costos

Coste Total (promedio por paciente, €)

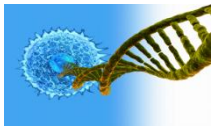




Ejemplo 2:

Biomarcadores Oncológicos y Medicina Personalizada

Historia de la Genómica: El proyecto Genoma Humano



1990

Human Genome Project (HGP) launched in the U.S.



Ethical, Legal, and Social Implications (ELSI) programs founded at NIH and DOE

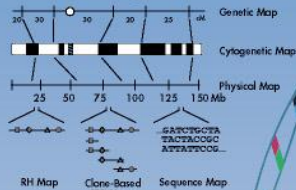


First gene for breast cancer (BRCA1) mapped



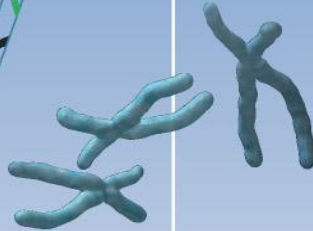
1991

First U.S. Genome Centers established



1992

Second-generation human genetic map developed



Rapid data release guidelines established by NIH and DOE

1993

New five-year plan for the HGP in the U.S. published



Sanger Centre founded (later renamed Wellcome Trust Sanger Institute)



The Wellcome Trust

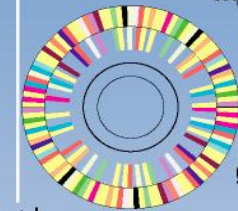
1994

HGP's human genetic mapping goal achieved



1995

HGP's human physical mapping goal achieved



First bacterial genome (*H. influenzae*) sequenced

U.S. Equal Employment Opportunity Commission issues policy on genetic discrimination in the workplace

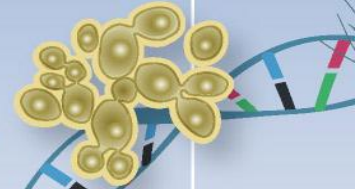
1996

First human gene map established

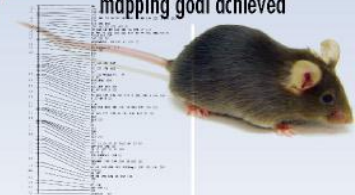
Pilot projects for human genome sequencing begin in U.S.

First archaeal genome sequenced

Yeast (*S. cerevisiae*) genome sequenced

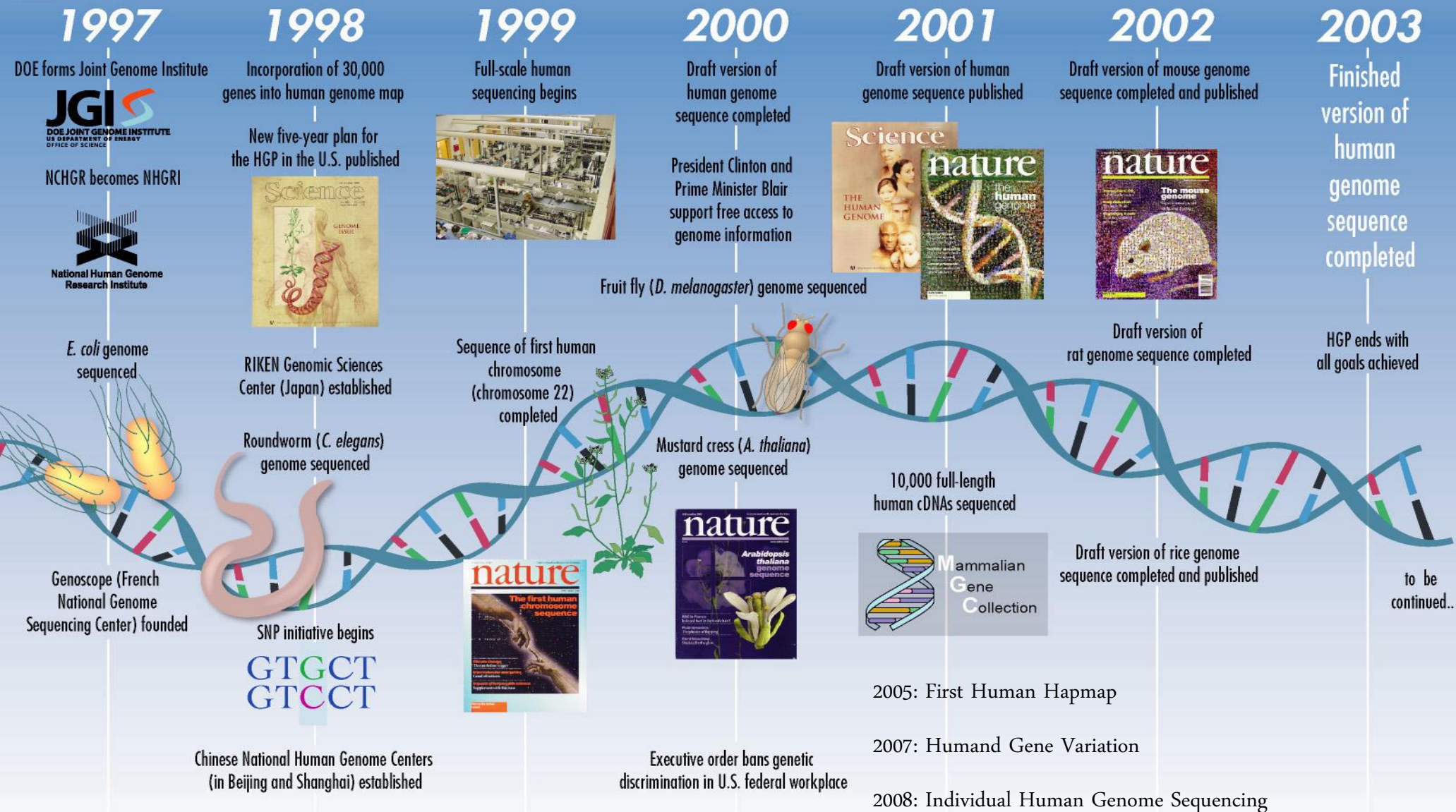
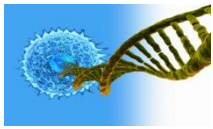


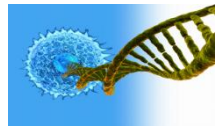
HGP's mouse genetic mapping goal achieved



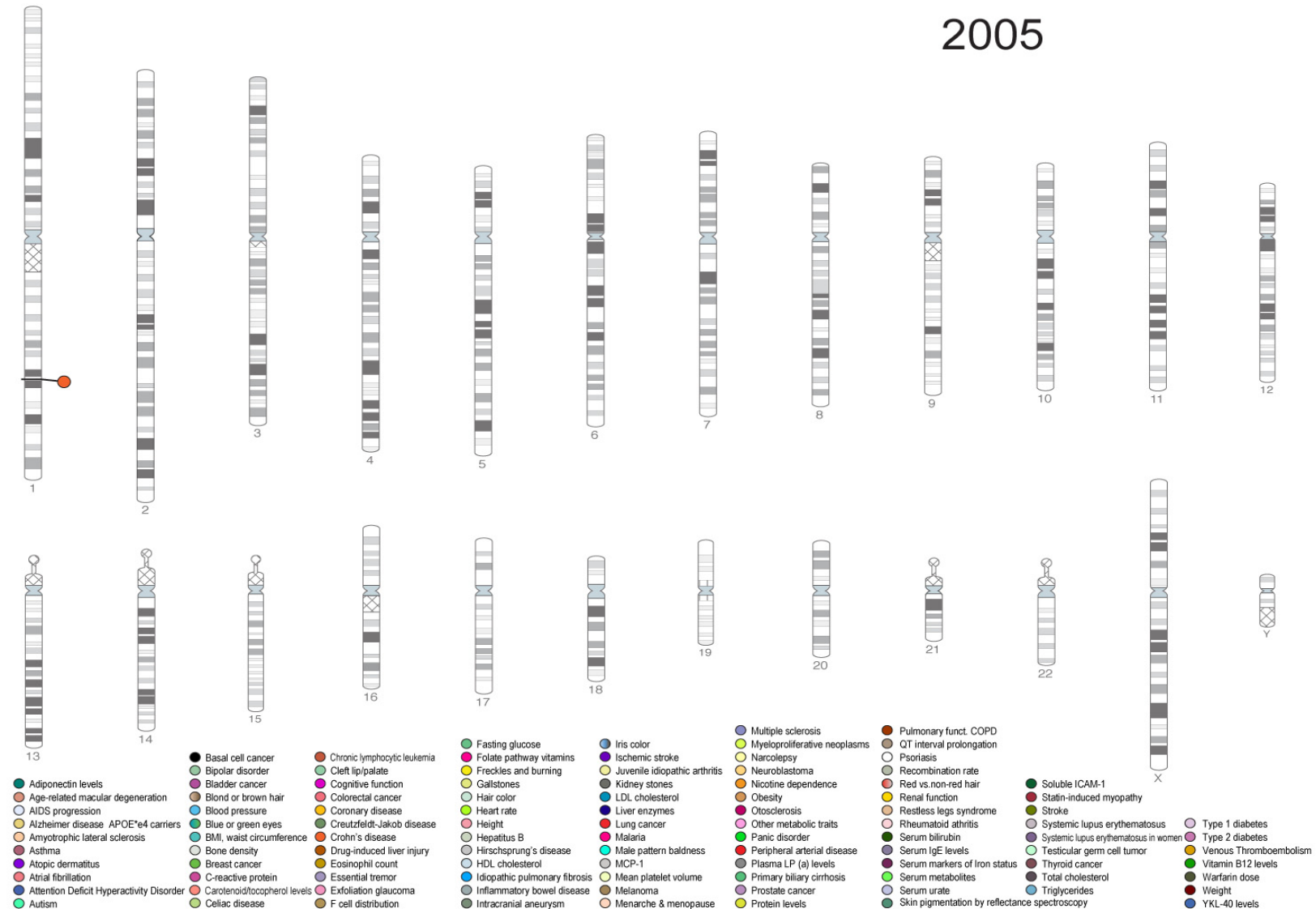
Bermuda principles for rapid and open data release established

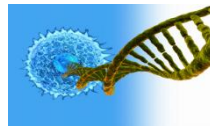
Historia de la Genómica: El proyecto Genoma Humano



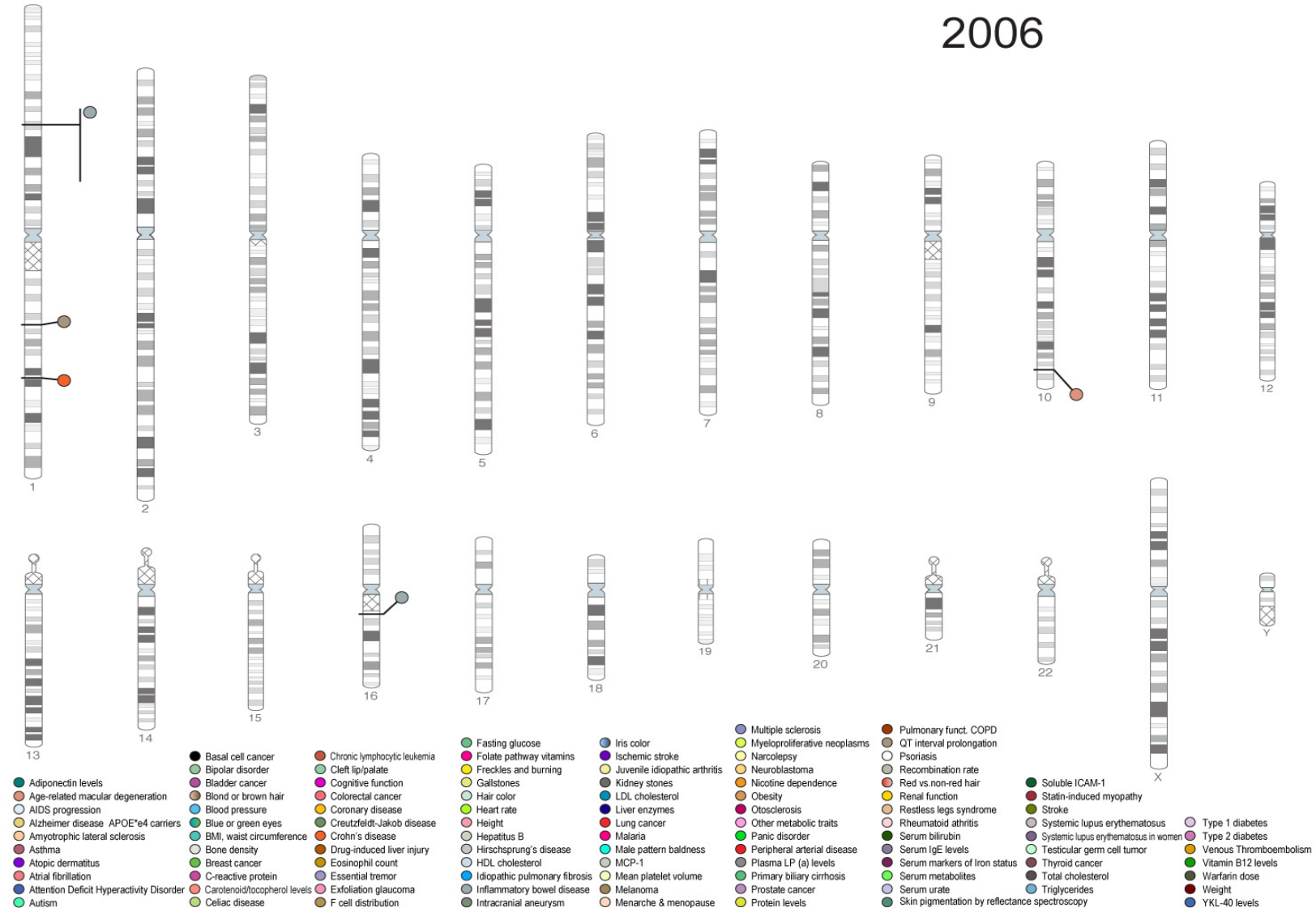


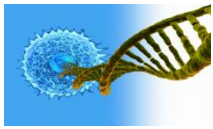
2005



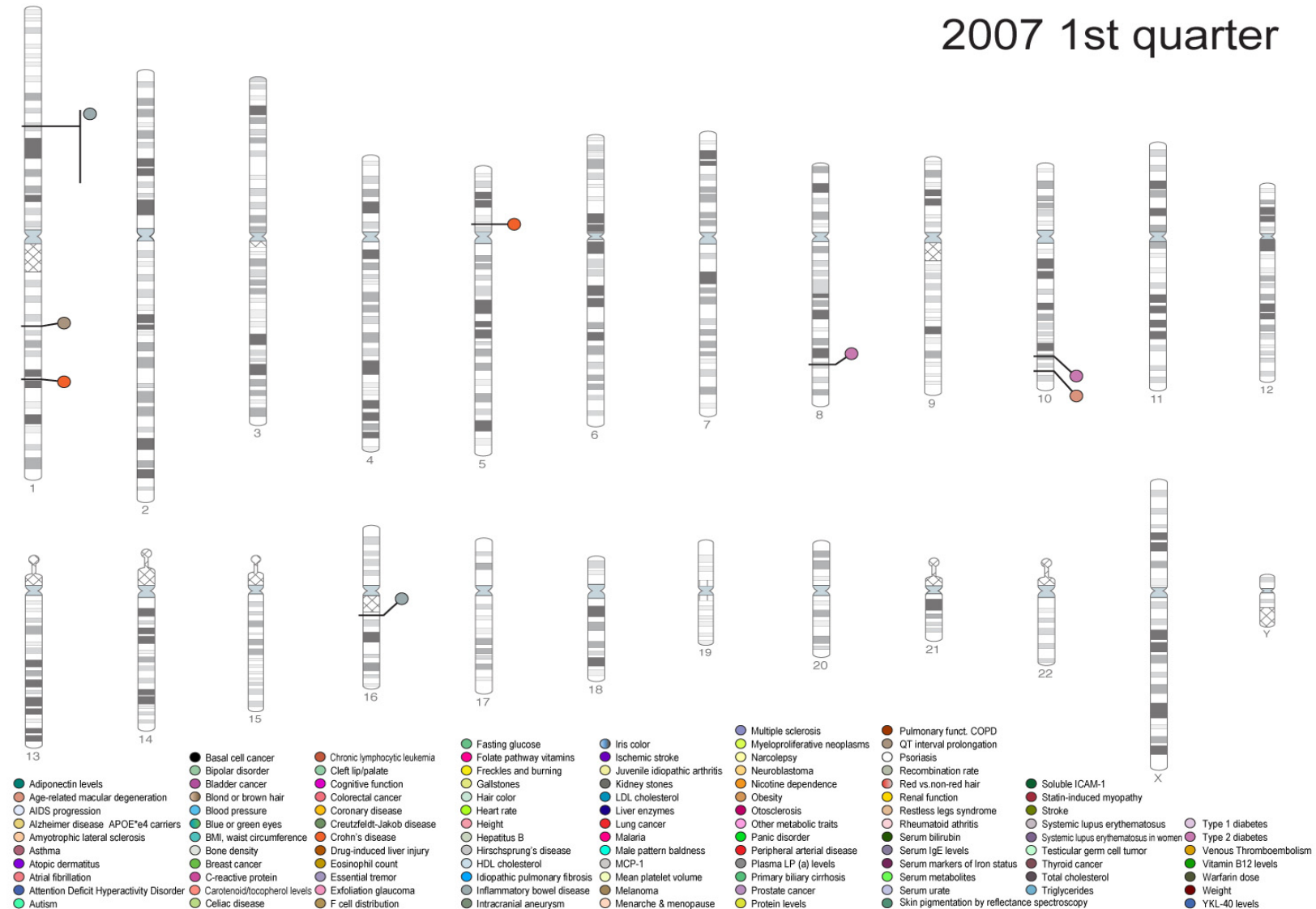


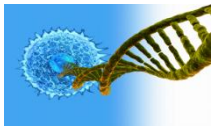
2006



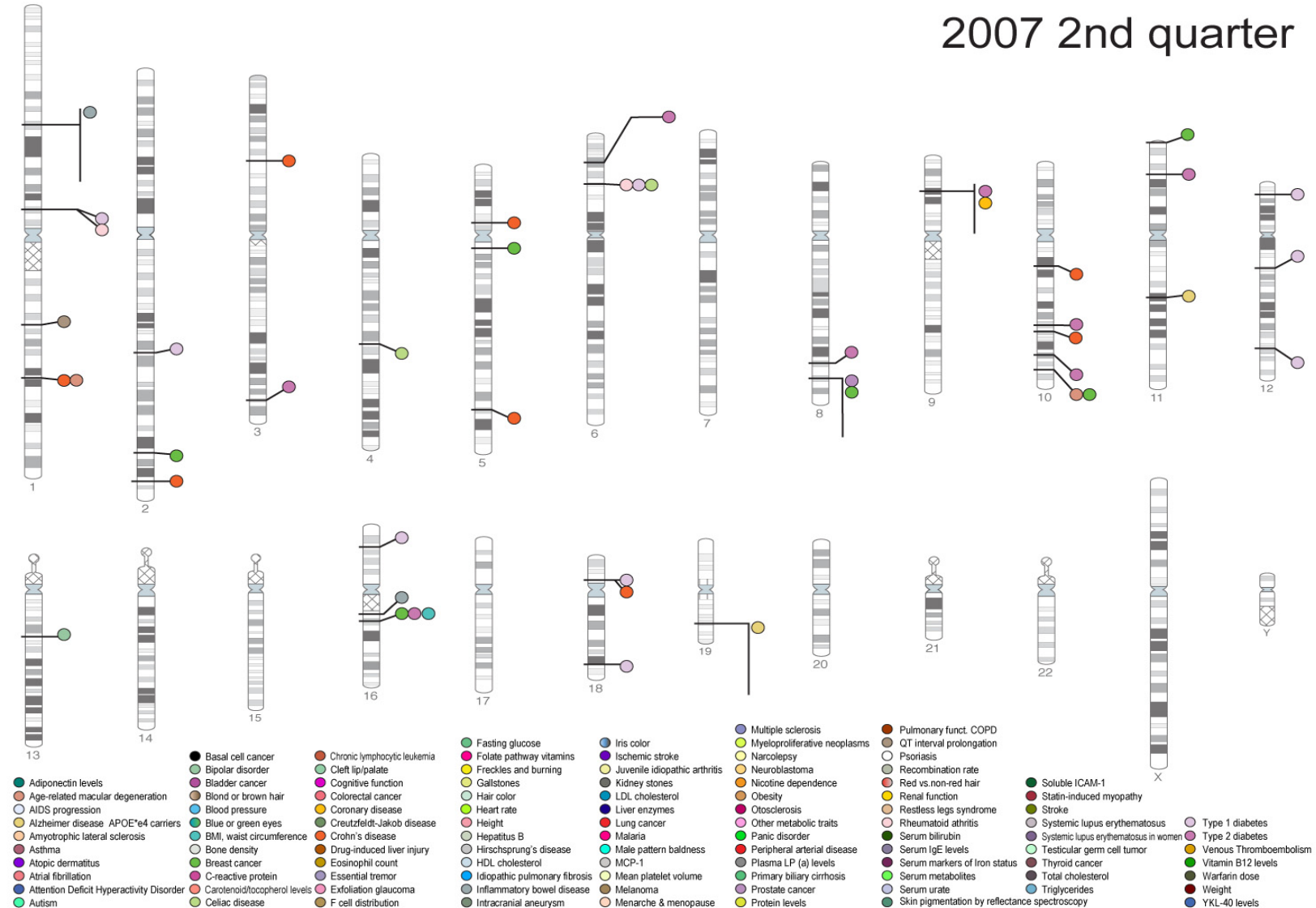


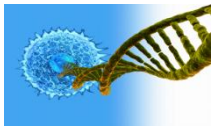
2007 1st quarter



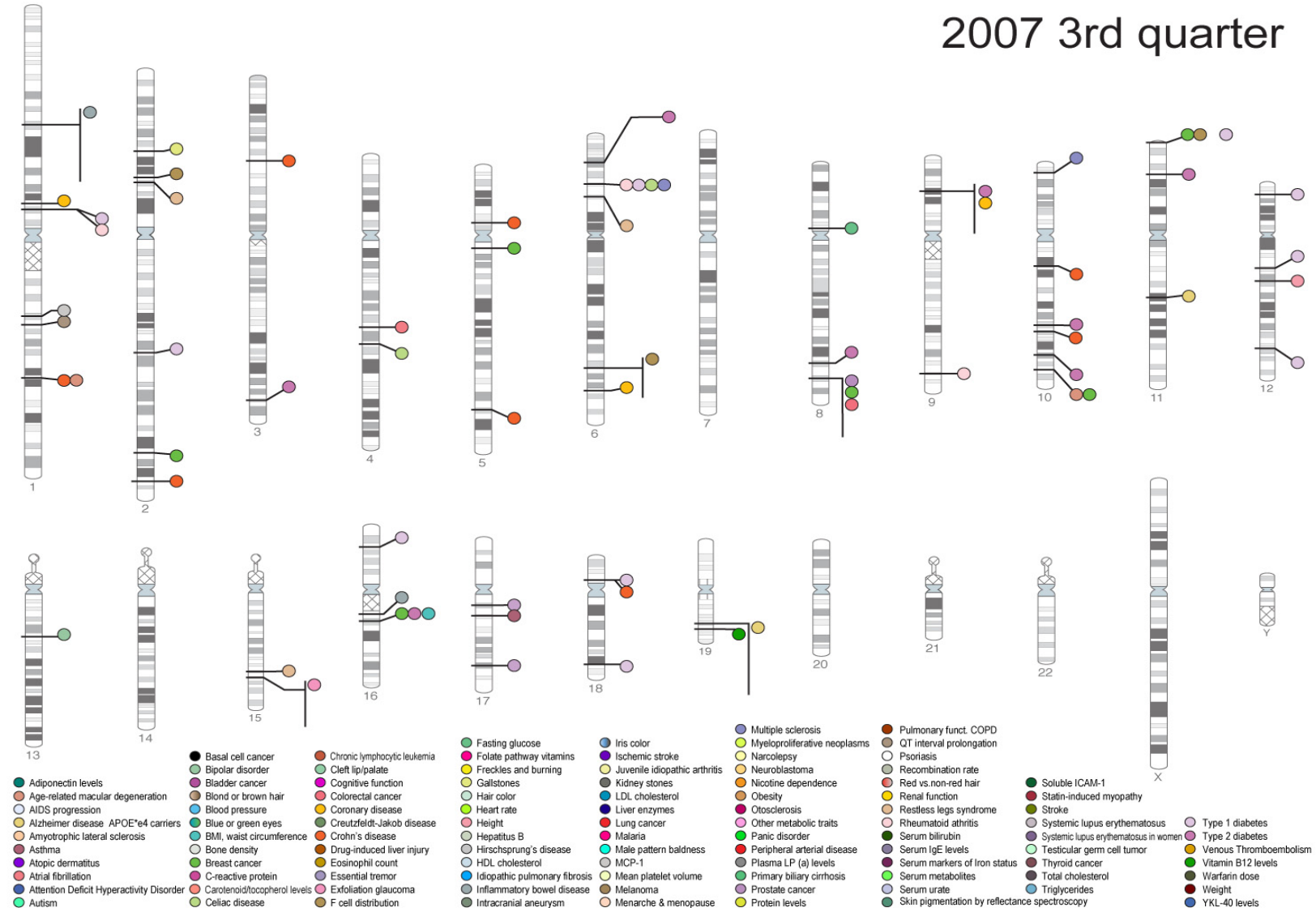


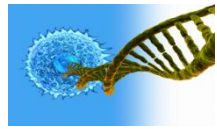
2007 2nd quarter



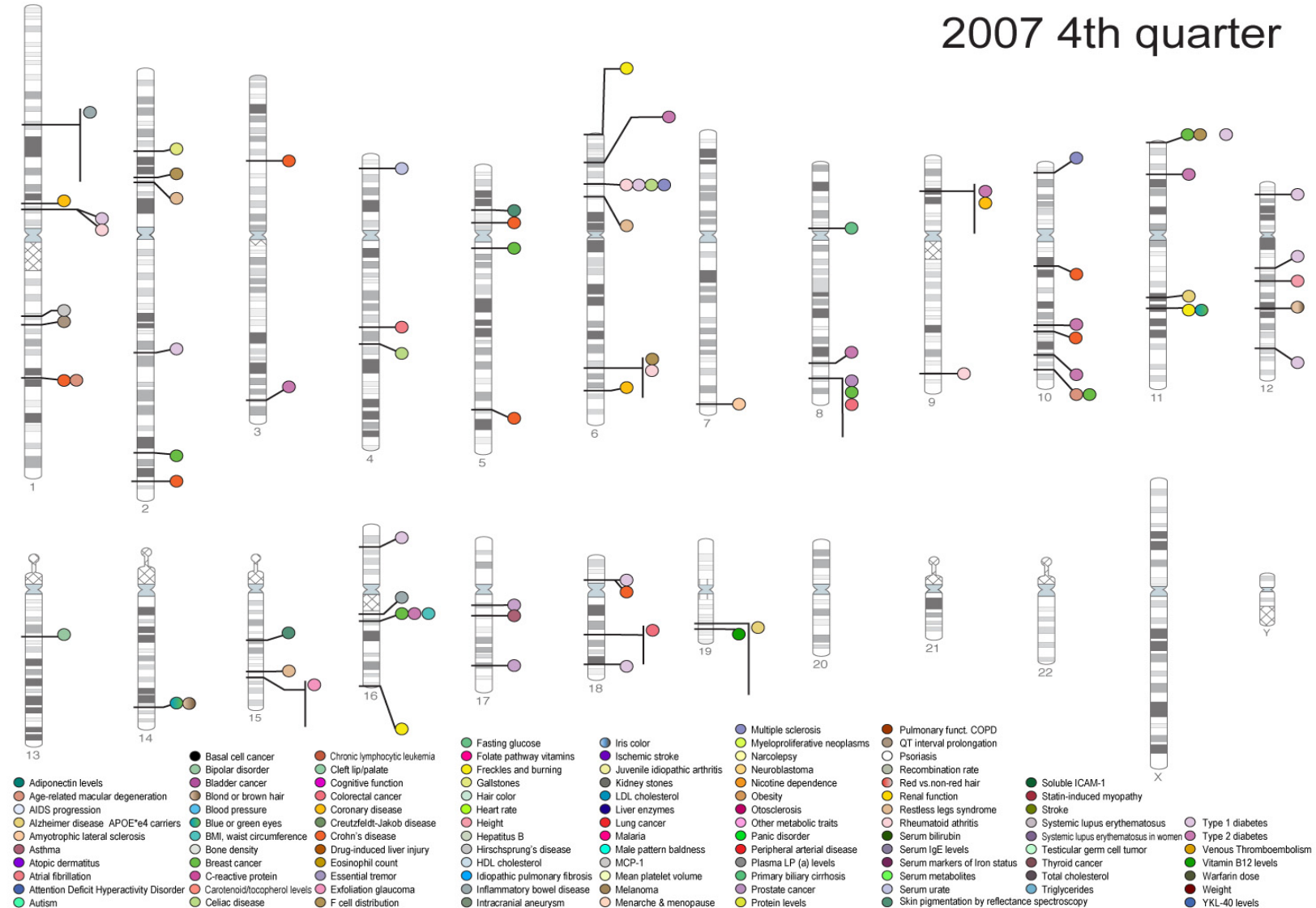


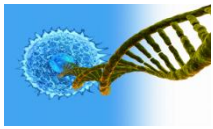
2007 3rd quarter



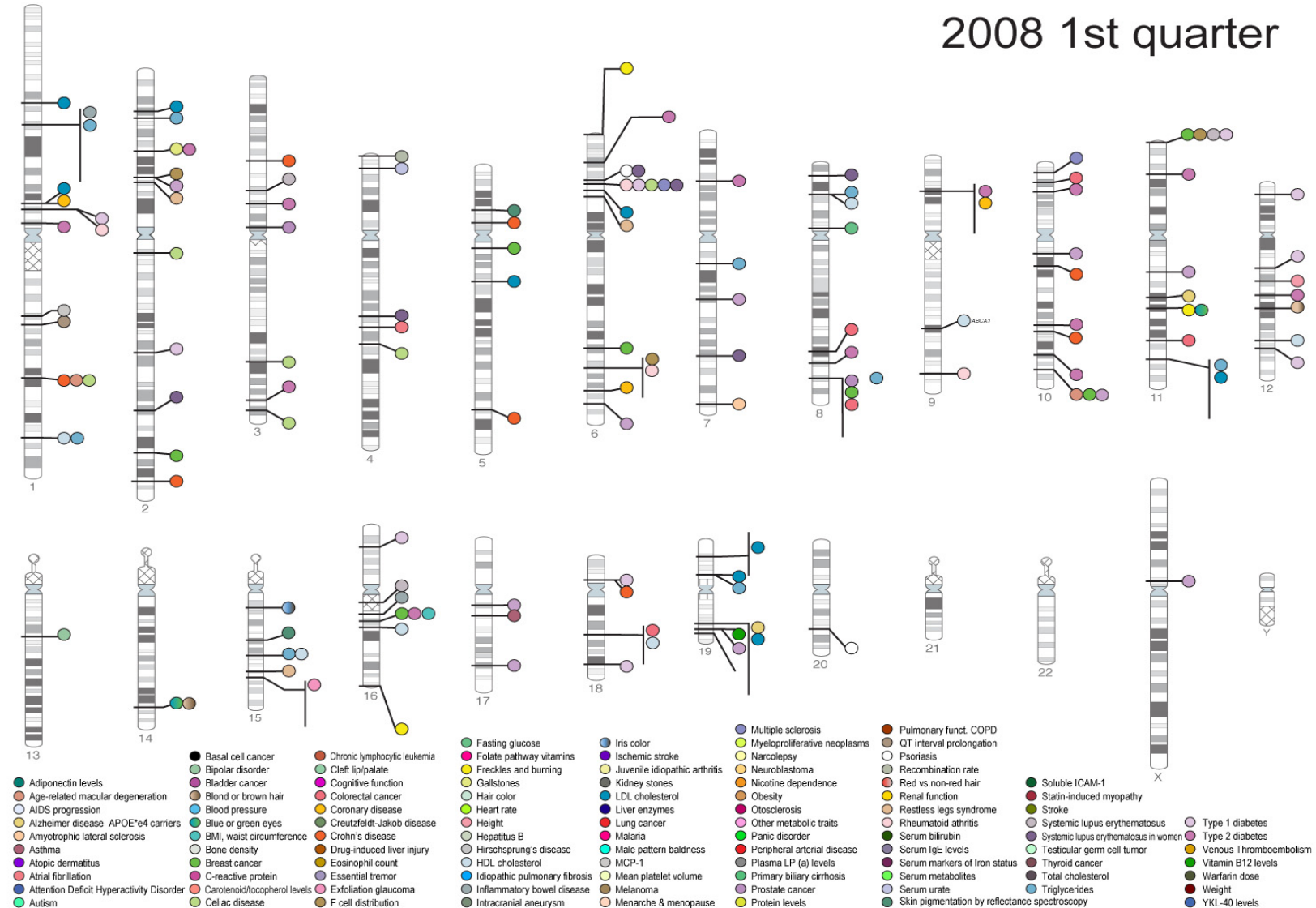


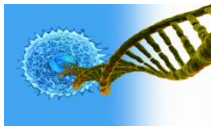
2007 4th quarter



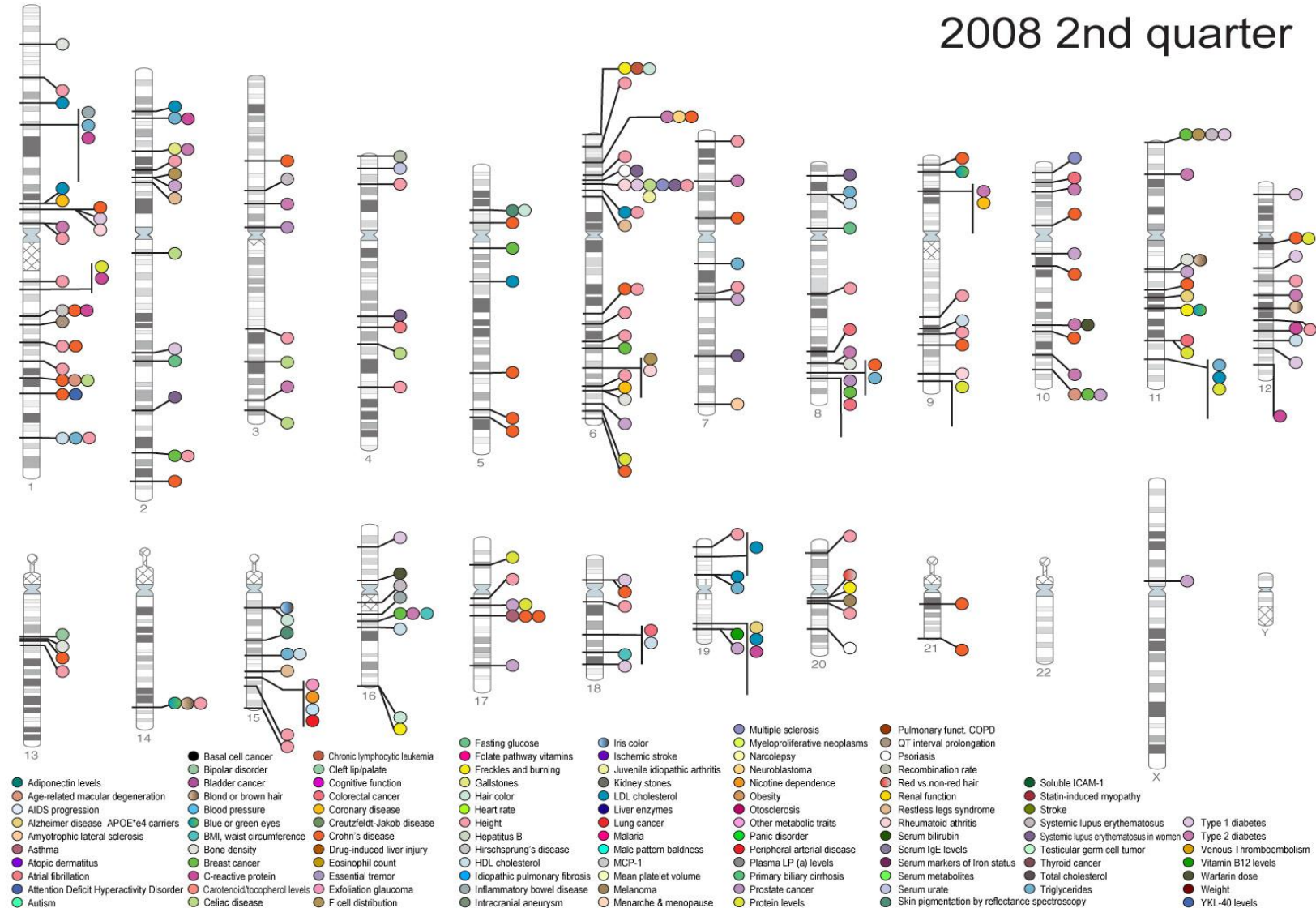


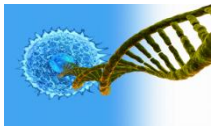
2008 1st quarter



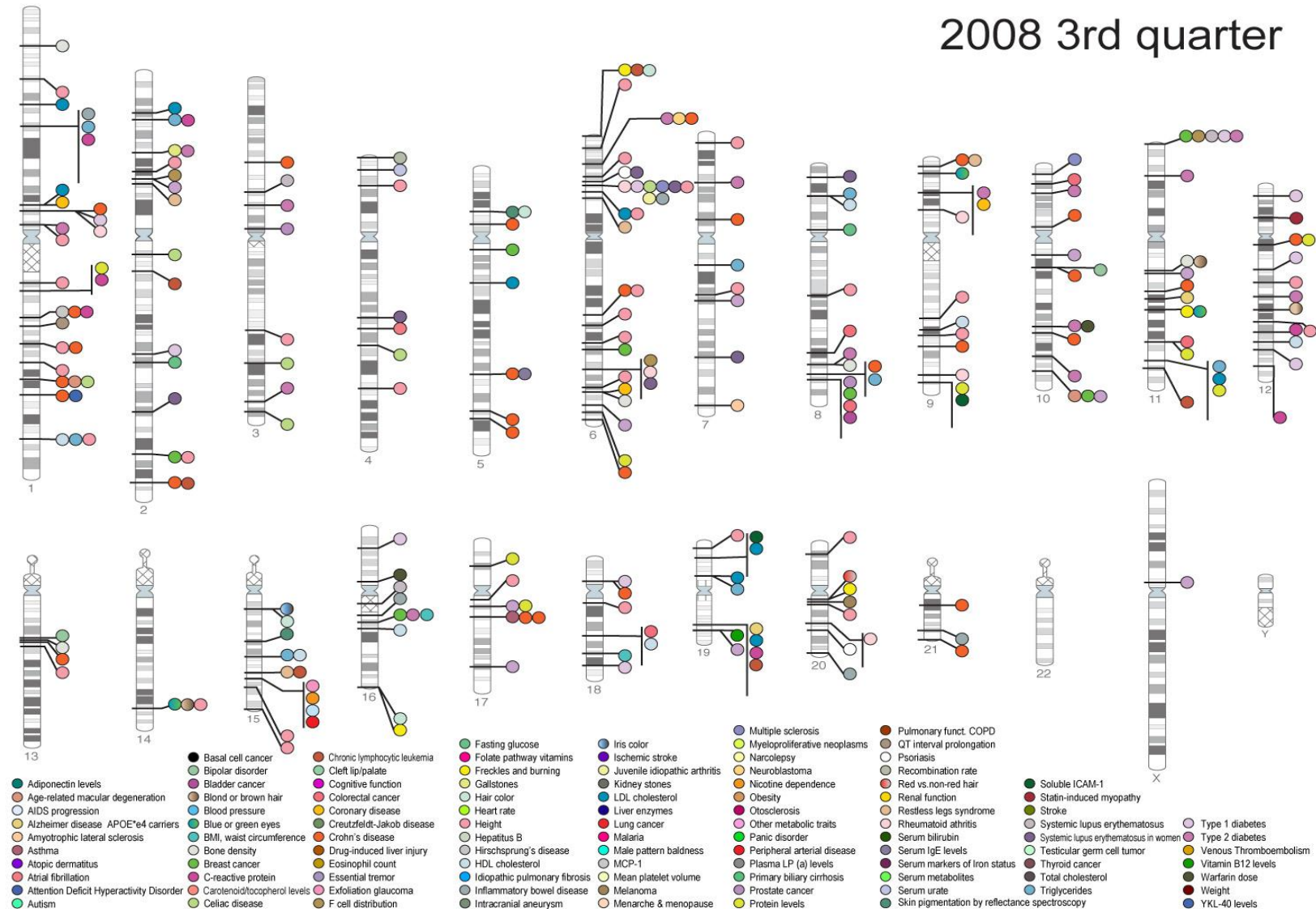


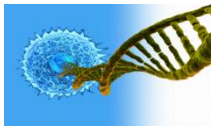
2008 2nd quarter



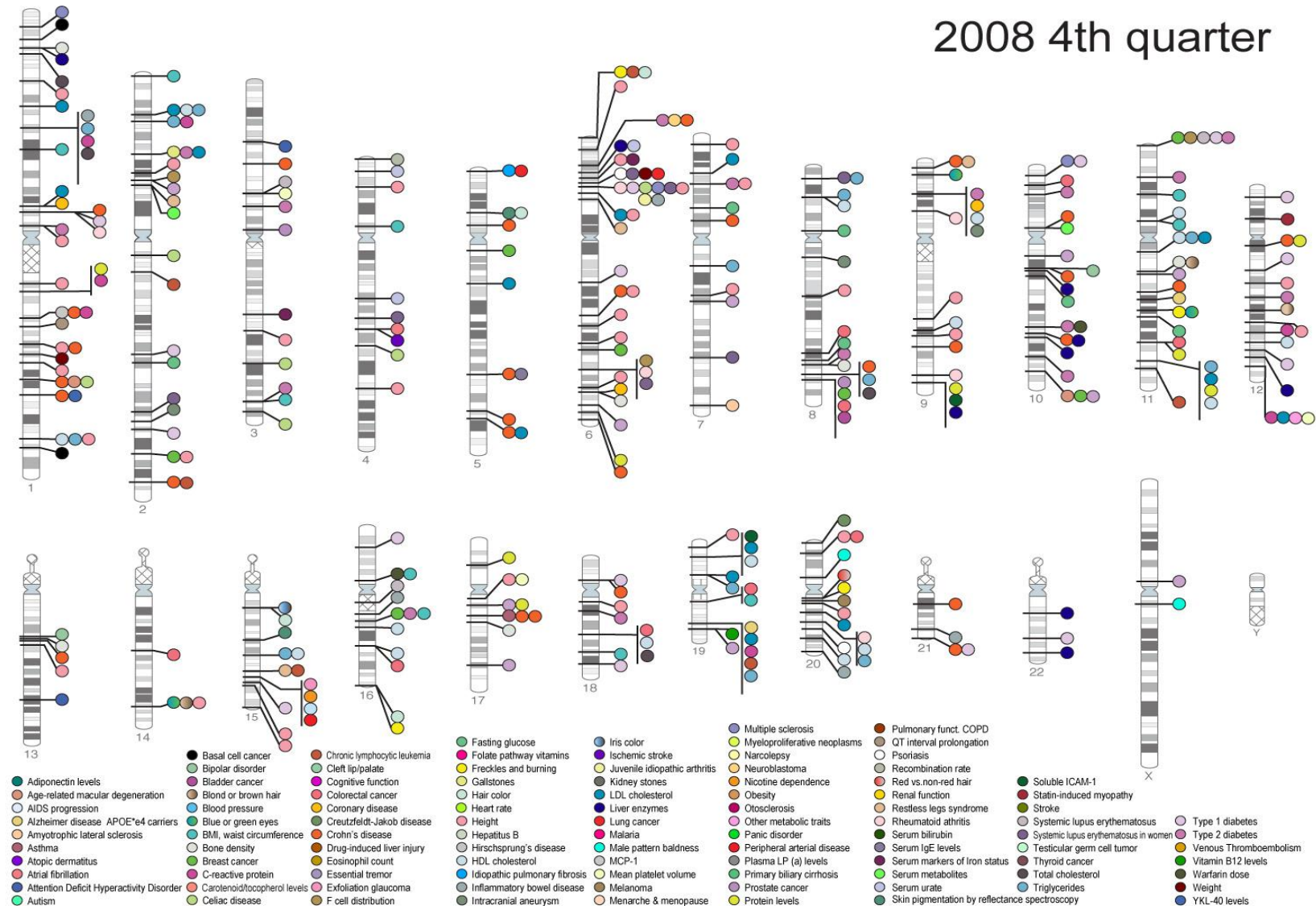


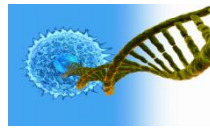
2008 3rd quarter



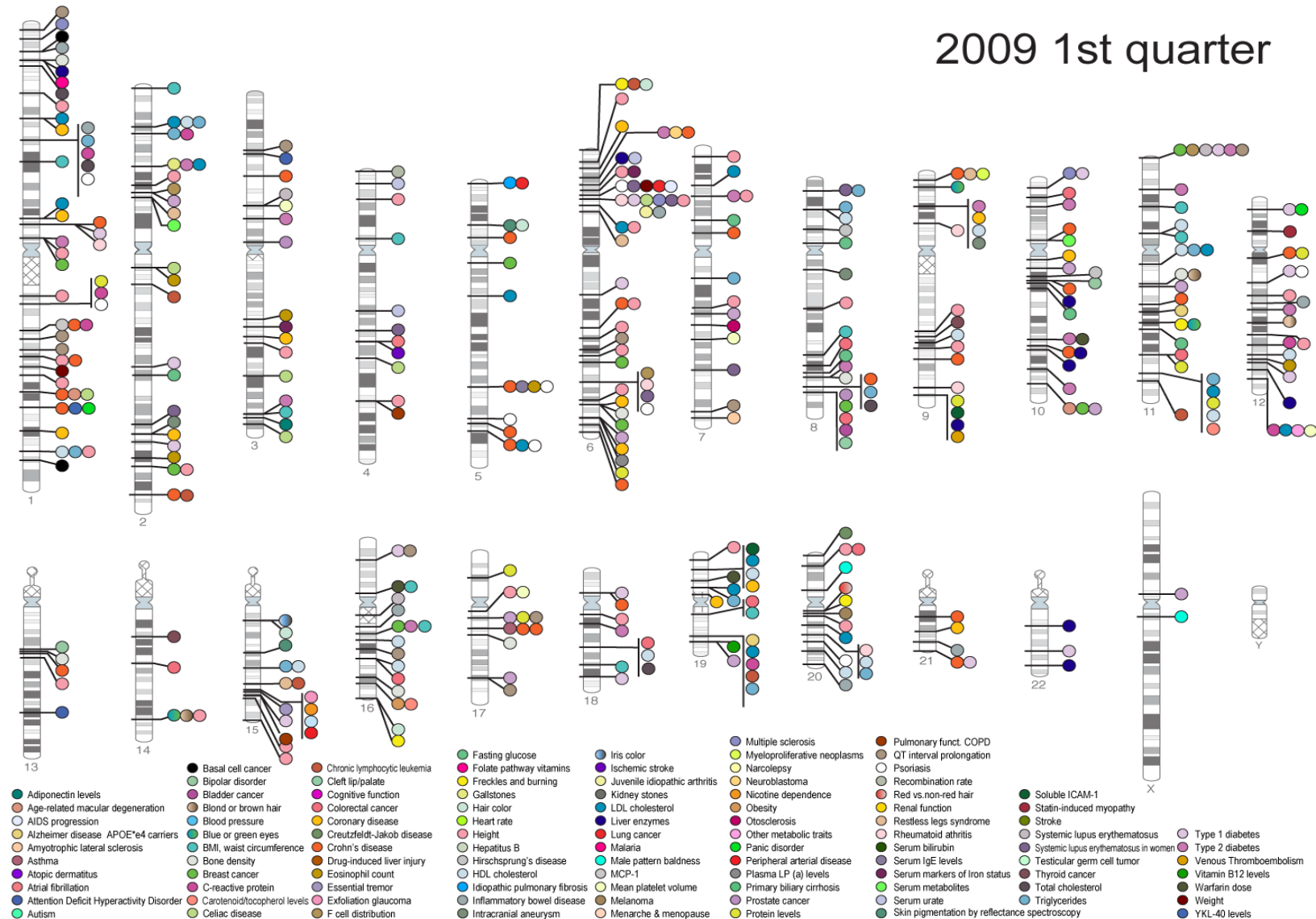


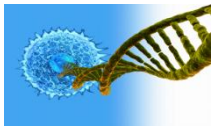
2008 4th quarter



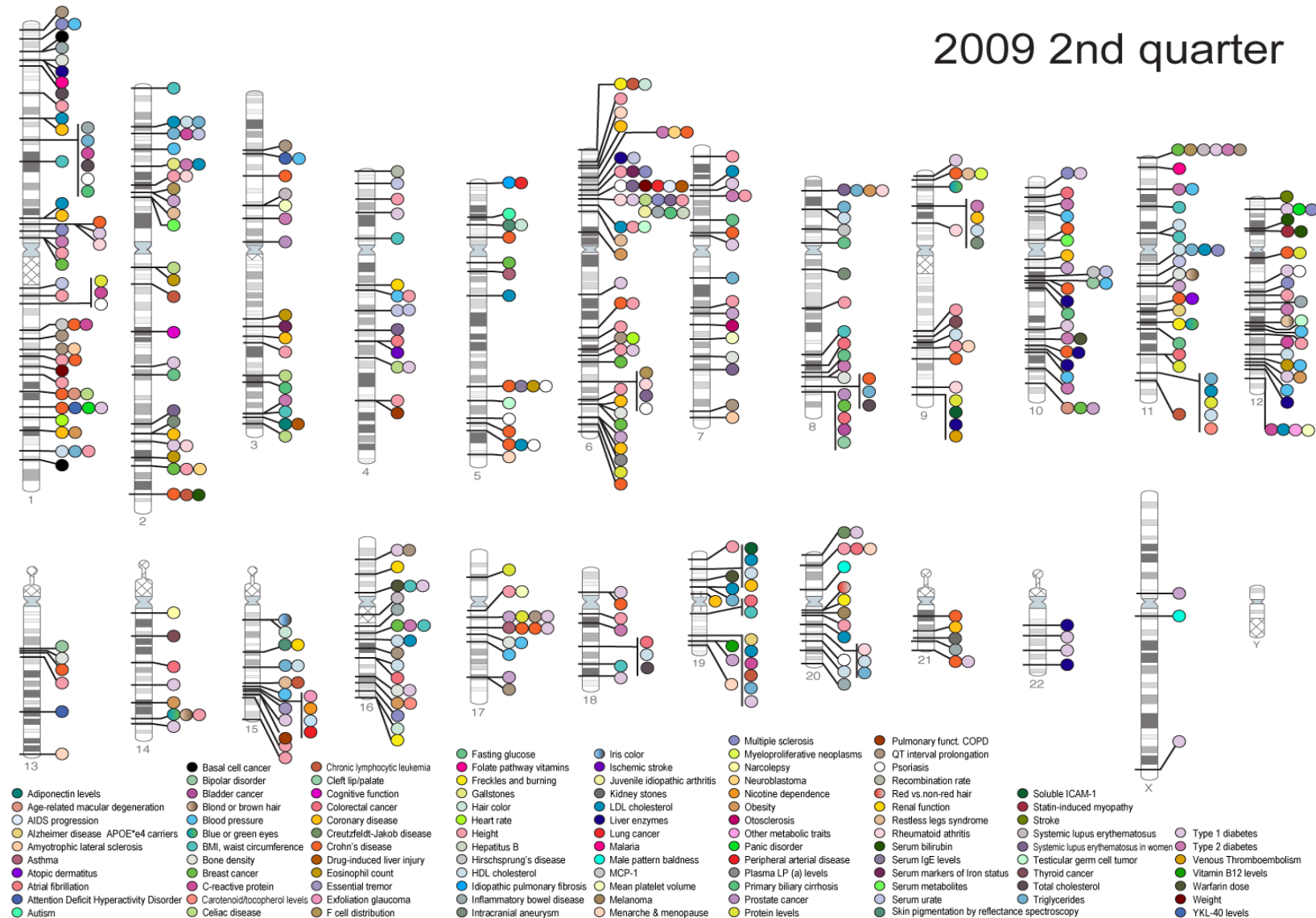


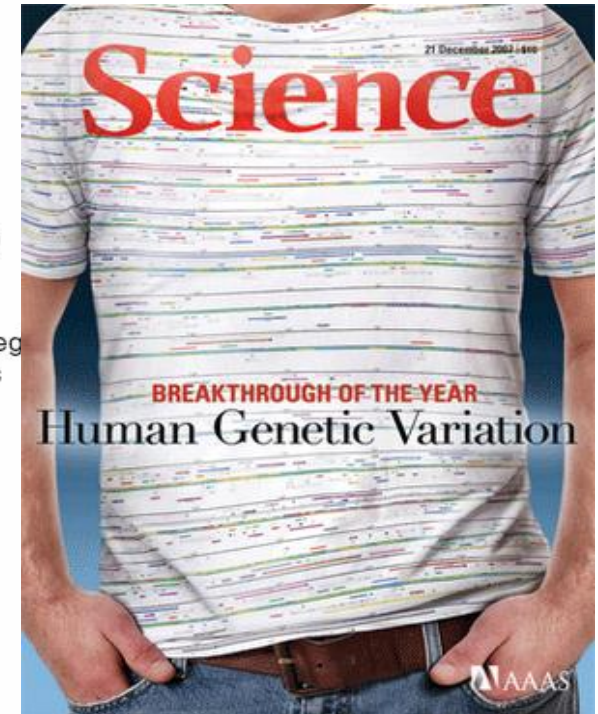
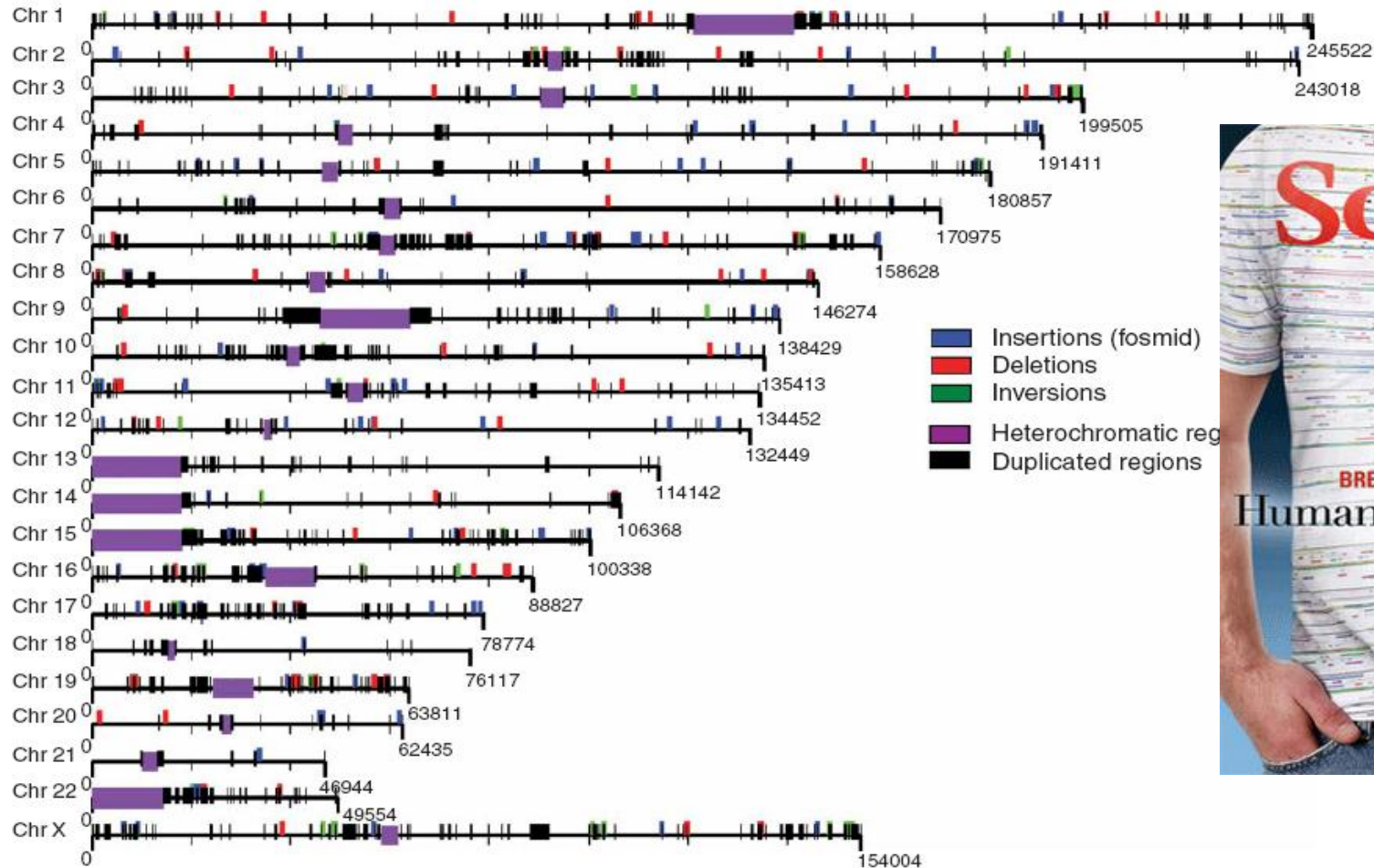
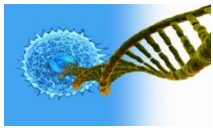
2009 1st quarter



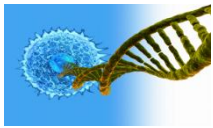


2009 2nd quarter

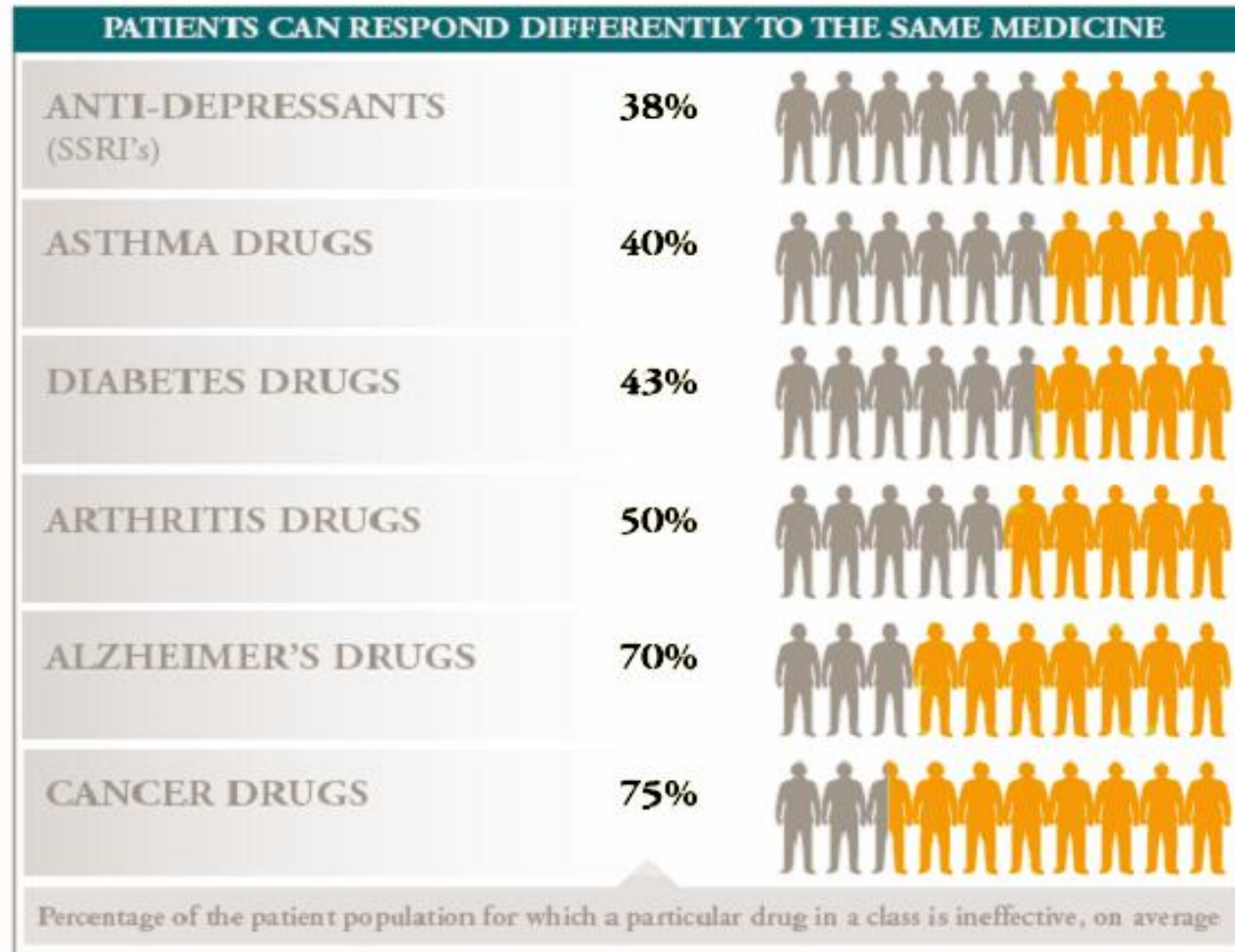




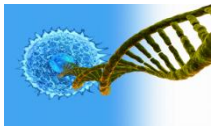
2007



Limitaciones en la eficacia de los tratamientos actuales son el motor de la medicina personalizada

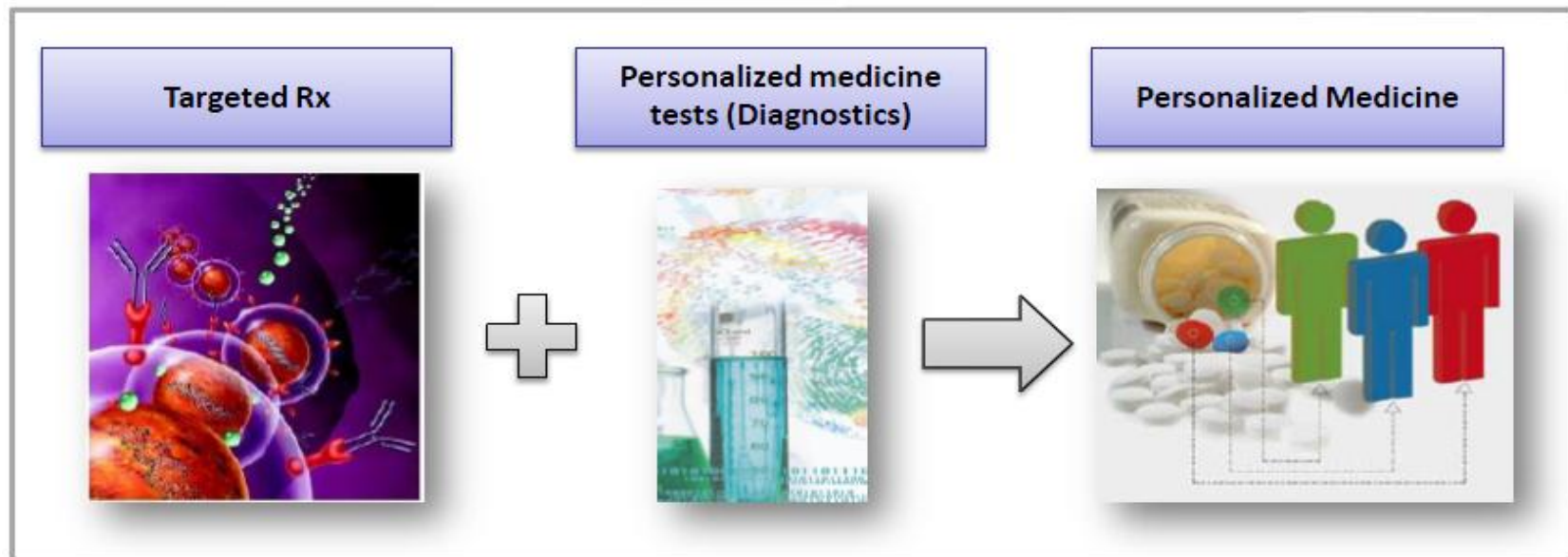


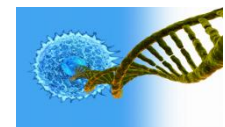
Source of data: Brian B. Spear, Margo Heath-Chiozzi, Jeffrey Huff, "Clinical Trends in Molecular Medicine, Volume 7, Issue 5, 1 May 2001, Pages 201-204.



The Right Therapy for the Right Patient, at the Right Time

La mejor respuesta a la terapia significa usar test de diagnostico molecular o biomarcadores para seleccionar y ajustar la terapia y así conseguir maximizar la eficacia y minimizar las reacciones adversas.



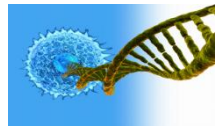


Eleven Drugs Requiring Biomarker Testing Prior to Deciding on Drug Use

Drug	Drug Marketer	Test Requirement	Indication
Ziagen (abacavir)	GlaxoSmithKline	Screening for carriage of the HLA-B*5701 allele should be performed in any HIV-infected patient. Abacavir should not be used in patients known to carry the HLA-B*5701 allele, unless no other therapeutic option is available in these patients, based on the treatment history and resistance testing.	Infectious Diseases
Epitol / Tegretol (carbamazepine)	Novartis	Patients of Han Chinese and Thai origin should be screened for HLA-B*1502 as this allele strongly predicts the risk of severe carbamazepine-associated Stevens Johnson syndrome.	Neuropsychiatric Diseases
Herceptin (trastuzumab)	Genentech/Roche	Susceptibility to the therapy is determined by the analysis for HER2/neu over-expression.	Cancer
Tasigna (nilotinib)	Novartis	Patients with imatinib-resistant Ph+ chronic myeloid leukemia.	Cancer
Sprycel (dasatinib)	Bristol-Myers Squibb	Patients with imatinib-resistant Ph+ chronic myeloid leukemia.	Cancer
Trisenox (arsenic trioxide)	Cephalon	PML/RAR alpha gene+ [or t(15;17) translocation] acute promyelocyticleukemia.	Cancer
Erbix (cetuximab)	Bristol-Myers Squibb, ImClone Systems, Merck	EGFR+ metastatic colorectal cancer after failure of irinotecan; KRAS wild-type metastatic colorectal cancer.	Cancer
Tarceva (erlotinib)	Genentech/Roche	Advanced non-small cell lung carcinoma; no clinically relevant effects demonstrated for patients with EGFR- tumours.	Cancer
Vectibix (panitumumab)	Amgen	EGFR+, non-mutated KRAS, metastatic, previously treated colorectal cancer – Conditional Marketing Authorisation.	Cancer
Tykerb / Tyverb (lapatinib)	GlaxoSmithKline	In combination with capecitabinefor Her2+ breast cancer after failure of taxanesand trastuzumab – Conditional Marketing Authorisation.	Cancer
Iressa (gefitinib)	AstraZeneca, Teva	For the treatment of patients with locally advanced or metastatic non-small cell lung carcinoma with activating mutations of EGFR-TK.	Cancer

Source: Data extracted from the presentation by Dr. Marisa Papaluca Amati, Deputy Head, Sector Safety and Efficacy of Medicines, EMEA, at the SGPPH Spring Conference, London, 3 June 2009

Note: This presentation of testing requirements by the EMEA is different from the FDA table as it starts with the drug for which there is a biomarker testing requirement rather than starting with the biomarker which needs to be tested for.



Beneficios de adoptar la medicina personalizada

Compañías farmacéuticas

- Potencial de mejorar precios debido a mayor eficacia
- Permite enfocar clinical trials en grupos menores por menor tiempo y mejores resultados
- DX facilita la entrada y expansión en el mercado

Compañías Diagnósticas

- Creación de nuevas compañías DX
- Avances den investigación y descubrimiento de biomarcadores se trasladan directamente a test diagnósticos.

Pacientes y Médicos

- La medicina personalizada reduce terapias innecesarias y generan menos efectos adversos.

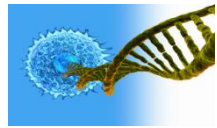
Reguladores

- Una mayor integración entre Terapia y Dx hacen más eficientes y seguros los clinical trials.
- Incremento de vigilancia en la aprobación de drogas.
- Incremento de aprobación de test genómicos que influyen en la seguridad y eficacia de las drogas.

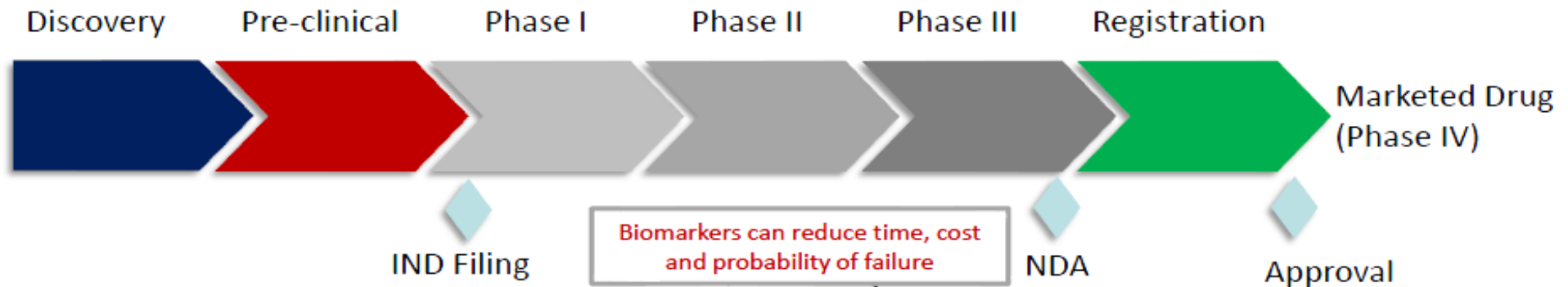
Pagadores

- Reducción general en los gastos de salud por la integración Rx-Dx
- Pago por rendimiento o resultado.





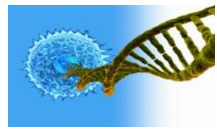
Biomarkers pueden reducir tiempo, riesgo y dinero en el desarrollo de fármacos..



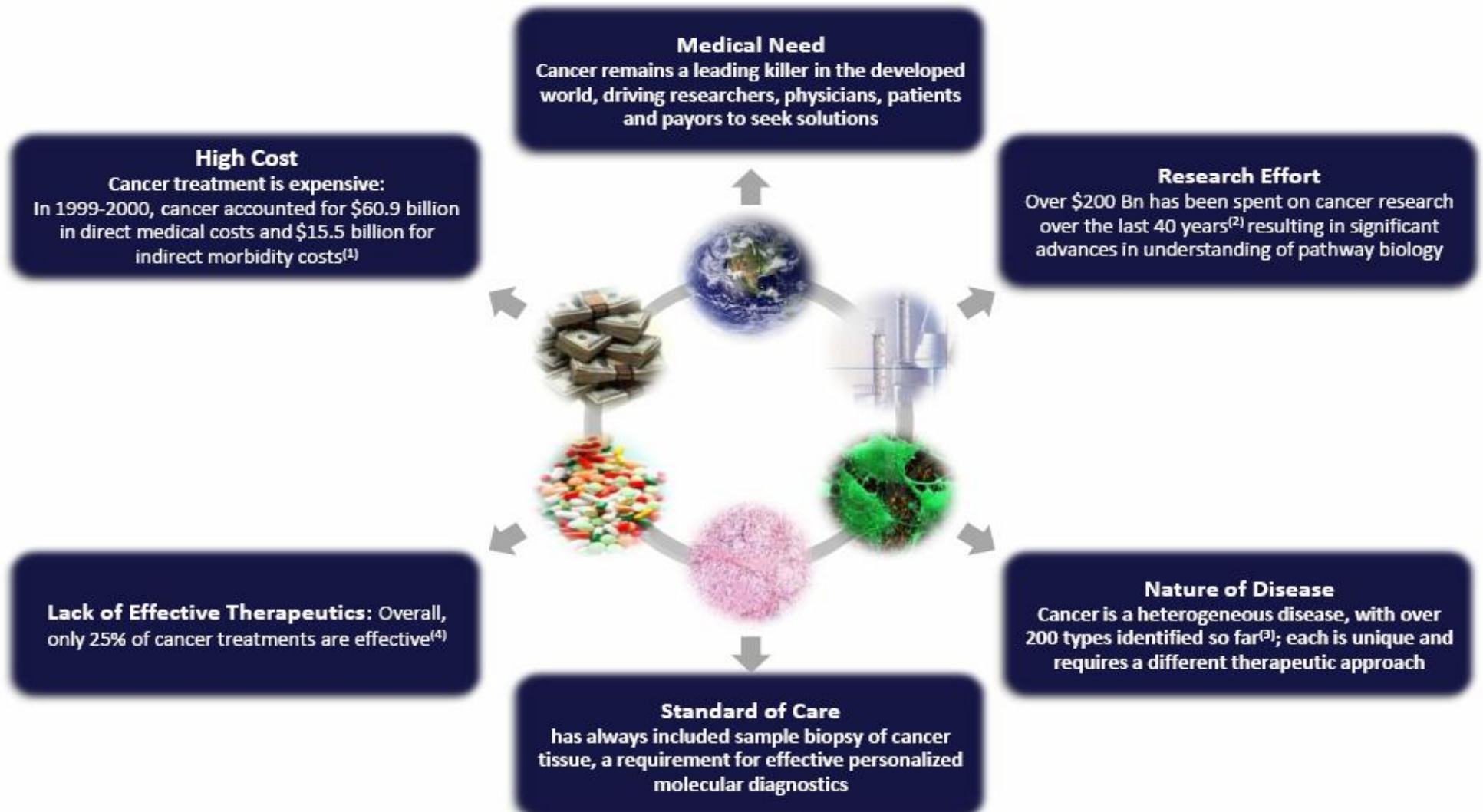
	Discovery	Pre-clinical	Phase I ¹	Phase II	Phase III	Registration	Cumulative (candidate to approval)
Time (~years)²	-	1	1	2	3	1	~8
P(success)³	-	0.40	0.70	0.47	0.80 ²	0.80 ²	0.084
Cost, \$M⁴	22	9	20	30	100	40	~200 ⁵

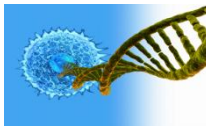
Notes: IND = Investigational New Drug; NDA = New Drug Application; (1) Phase I cost includes parallel animal studies; (2) simplifying assumptions, time in each phase is variable; (3) probability of entering the next phase; (4) direct costs only, not discounted or risk-adjusted, from 1990s data; current direct costs are likely to be higher; (5) Total pipeline costs per candidate from discovery to approval, probability adjusted and discounted to account for cost of capital is estimated to be over \$800 Million (DiMasi et al, 2003).

Sources: Di Massi et al., 2003; FDA, Center for Drug Education and Research; Boston Consulting Group; Scientia Analysis.



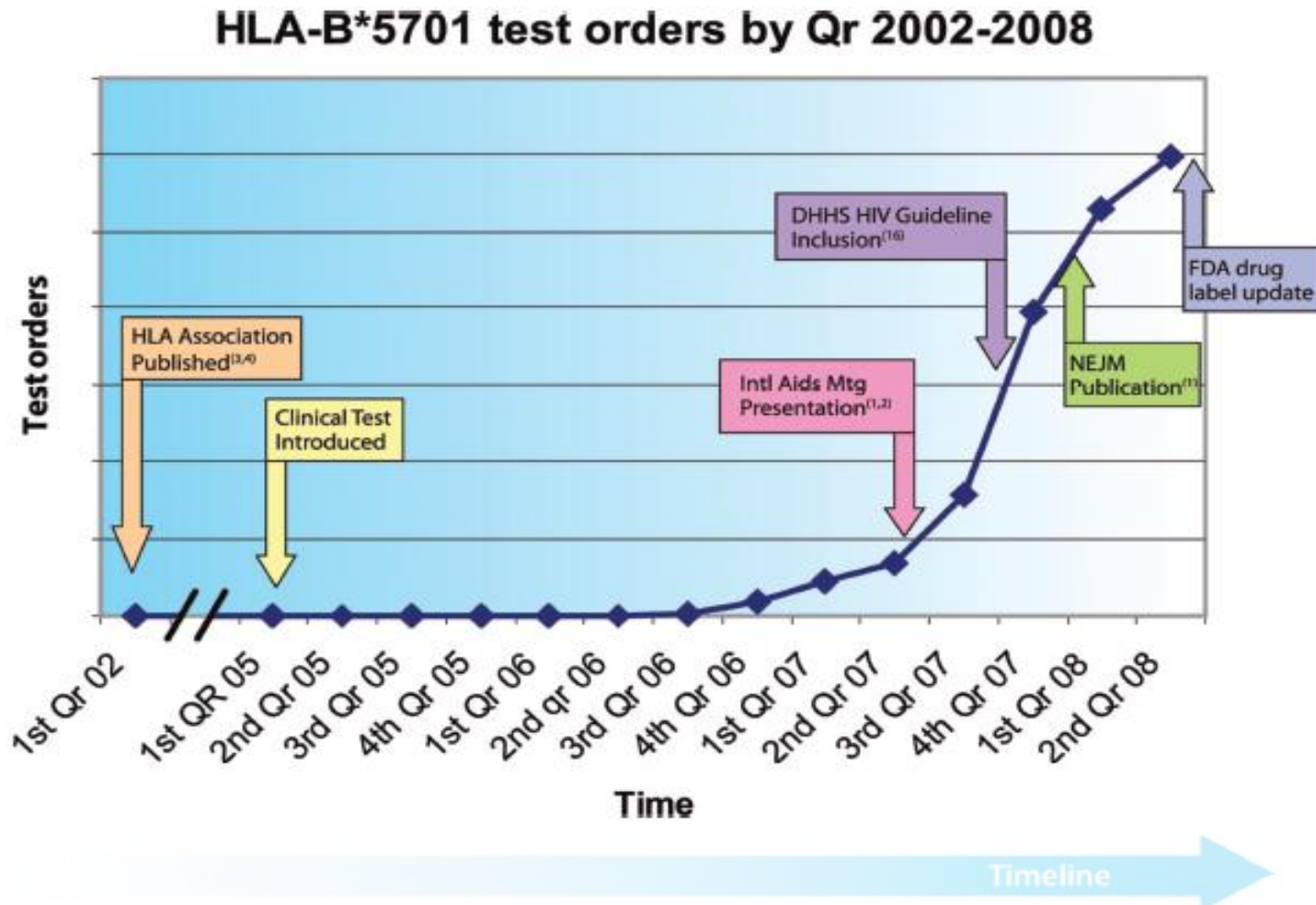
Oncología ha sido el “early adopter” de la MP por múltiples factores.

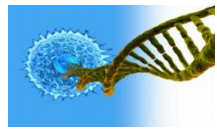




Companion Diagnostics- Hipersensibilidad al Abacavir (HIV terapia)

New Test Adoption Curve





La democratización de la genómica personalizada.

1. The Retail DNA Test - TIME's Best Inventions of 2008 - TIME - Windows Internet Explorer

http://www.time.com/time/specials/packages/article/0,28804,1852747_1854493,00.html

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TIME's Best Inventions of 2008

Invention of the Year

1. The Retail DNA Test

By Anita Hamilton

Before meeting with Anne Wojcicki, co-founder of a consumer gene-testing service called 23andMe, I know just three things about her: she's pregnant, she's married to Google's Sergey Brin, and she went to Yale. But after an hour

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Here's what you do:

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3. Our CLIA-certified lab analyzes your DNA in 2-4 weeks.
4. Log in and start exploring your genome.

Trace your roots back to the dawn of humanity.

Get the highest resolution view into your maternal and paternal lineages.

23andMe Ancestry Edition (\$399) also includes:

- **Relative Finder:** Find people who share DNA with you.
- **Your Global Origins:** Ancestry Painting and Global Similarity.

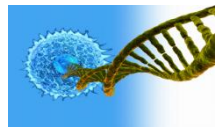
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A comprehensive view into your ancient past.

Immerse yourself in the lives of your ancestors.

Explore the details of your ancestors' migrations and accomplishments. Did they paint bison in the caves of northern Spain? Invent agriculture in the Middle East? Find out which unique pieces of history are part of your lineage.

See the history passed on from generation to generation.



La democratización de la genómica personalizada.

<http://www.decodeme.com/>



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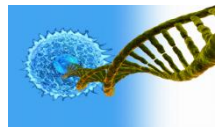
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Navigenics - Using the power of genetic testing to help you take control of your health - Microsoft Internet Explorer

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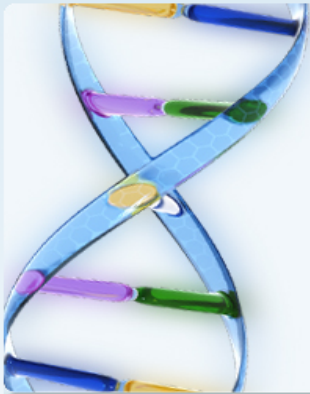
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Success Stories



Navigenics testimonial success story entrepreneur
Aaron
Internet entrepreneur

"We hear a lot of different – and sometimes conflicting – opinions about how to take care of our health. I'm very excited about receiving only the most relevant information to me, based on my DNA."

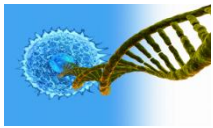
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http://www.navigenics.com/visitor/what_we_offer/success_stories/aaron/ Internet



La democratización de la genómica personalizada.



Example Results This is an example Navigenics Health Compass report.

Your estimated lifetime risk



Click anywhere on the colored boxes below to access in-depth information about each predispositions, what you can do, your specific genetic markers, and much more.

0 - 1%

Brain aneurysm
You: 0.91%
Avg: 0.90%

Macular degeneration
You: 0.78%
Avg: 3.1%

Sarcoidosis
You: 0.55%
Avg: 1.0%

Glaucoma
You: 0.47%
Avg: 2.4%

Multiple sclerosis
You: 0.28%
Avg: 0.77%

Crohn's disease
You: 0.12%
Avg: 0.54%

>1 - 10%

Alzheimer's disease
You: 10%
Avg: 17%

Lung cancer
You: 5%
Avg: 6%

Deep vein thrombosis
You: 4.2%
Avg: 3.6%

Colon cancer
You: 4.1%
Avg: 5%

Psoriasis
You: 2.5%
Avg: 4.0%

Rheumatoid arthritis
You: 1.7%
Avg: 3.3%

>10 - 25%

Breast cancer
You: 20%
Avg: 13%

Atrial fibrillation
You: 19%
Avg: 23%

>25 - 50%

Diabetes, type 2
You: 36%
Avg: 30%

Heart attack
You: 26%
Avg: 25%

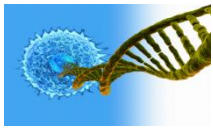
Osteoarthritis
You: 26%
Avg: 47%

Obesity
You: 25%
Avg: 32%

>50 - 100%

You have no results in this range

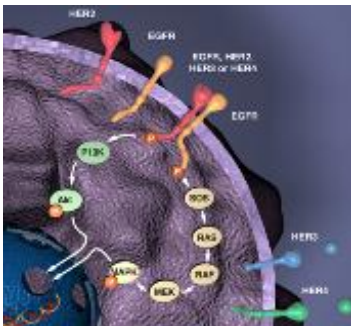
Conclusiones



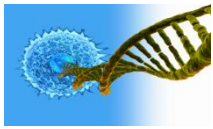
Foco de la Investigación en un área de aplicación cuyo mercado sea atractivo



Demostrar el valor médico de la innovación



Construir un modelo de costo efectividad aplicable a la realidad local



Gracias por su atención...

Dr. Andrés Araya

Fundador Biotecom

andres.araya@biotecom.cl