



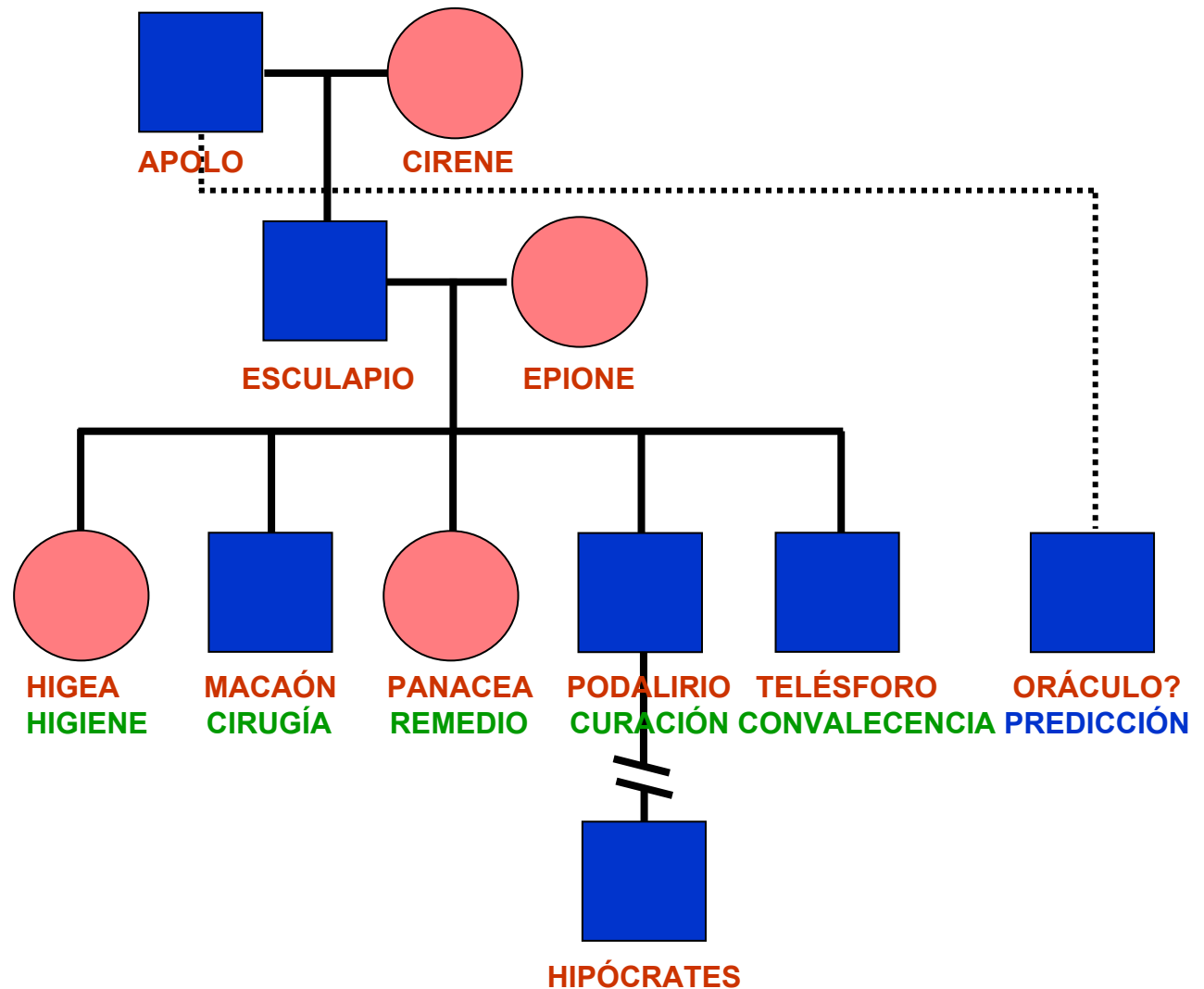
IDENTIFICACIÓN DE MARCADORES PROTEICOS Y GENÉTICOS PARA EL CÁNCER DE PRÓSTATA

Augusto Rojas y cols.

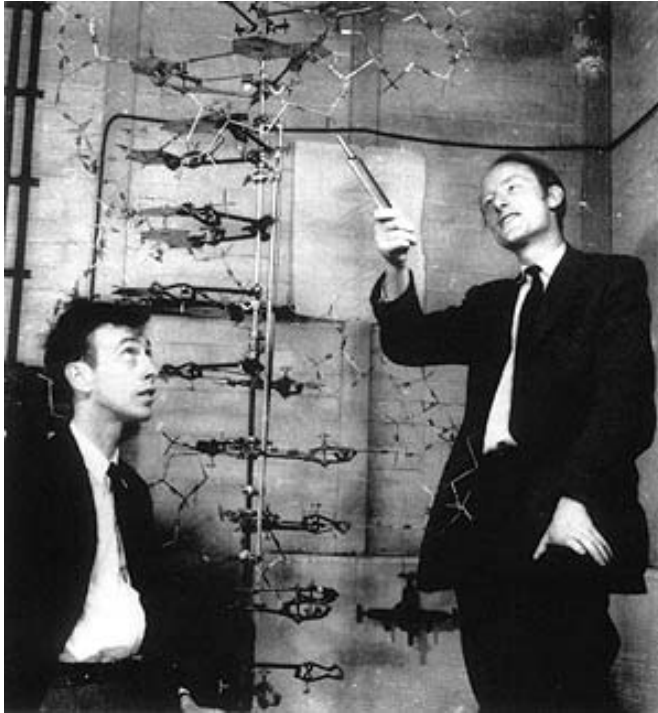
arojas@fm.uanl.mx

*Universidad Autónoma de Nuevo León y
University of Texas Health Science Center
at San Antonio*

Origen de la Medicina



Evolución del Concepto de Enfermedad



DNA



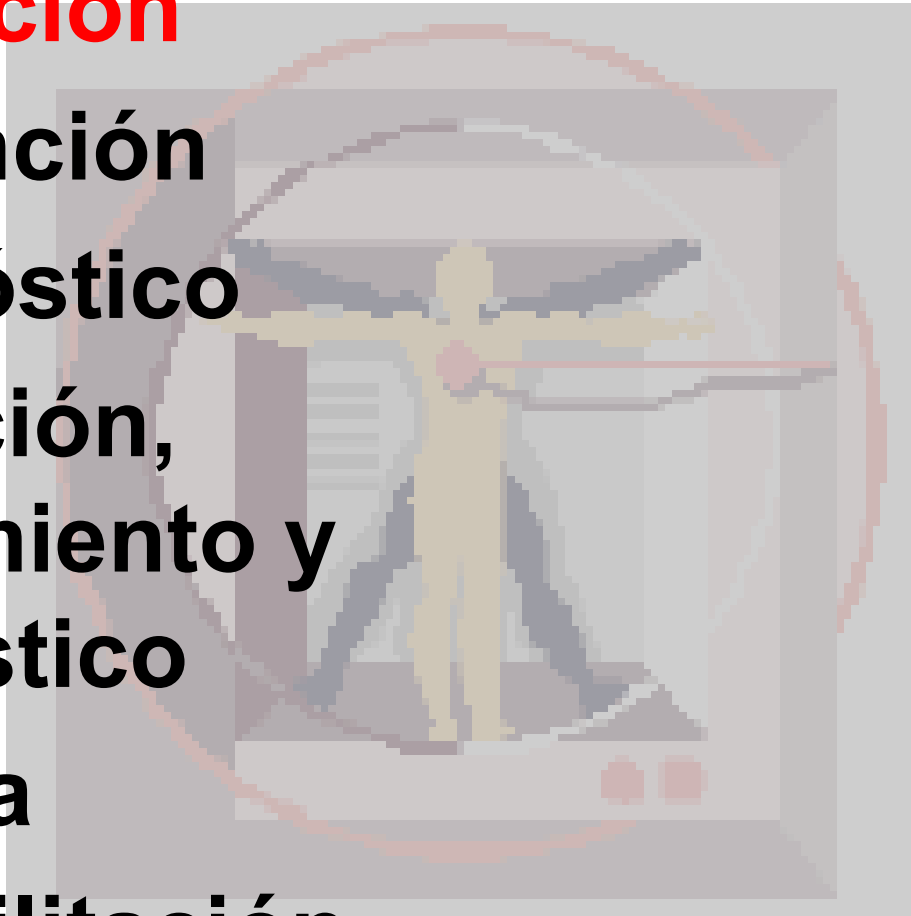
GENOMA HUMANO



EL ARTE ACTUAL DE LA MEDICINA



- **Predicción**
- **Prevención**
- **Diagnóstico**
- **Evolución,
seguimiento y
pronóstico**
- **Terapia**
- **Rehabilitación**



La Salud y la Enfermedad Hoy



GENÉTICA



MEDIO AMBIENTE

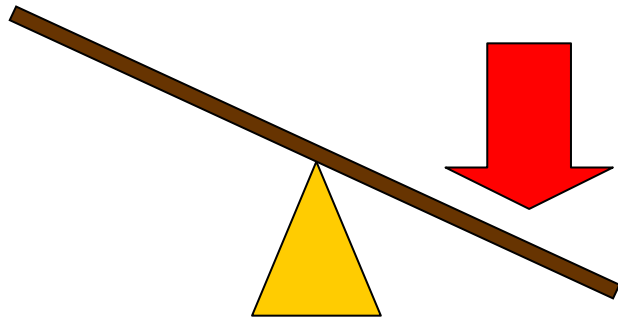
La Genómica: Disecando una de las porciones



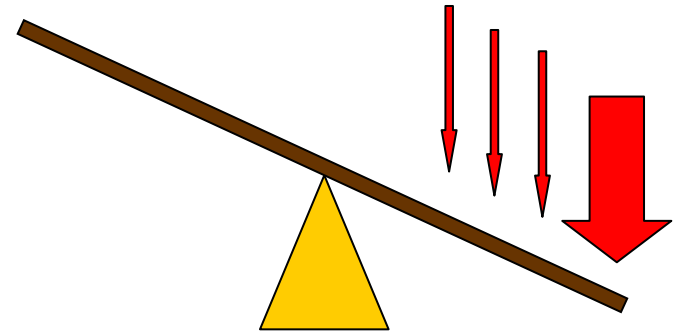
GENÉTICA



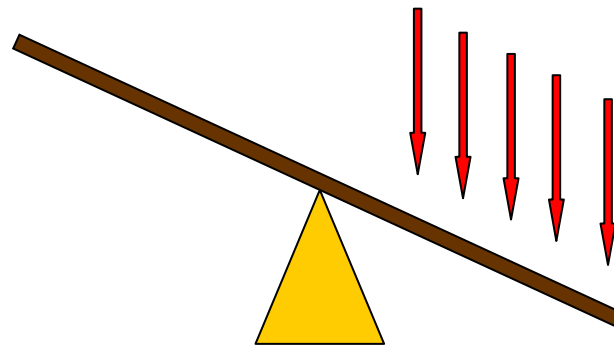
PESO DE LOS GENES EN LA ENFERMEDAD



ENFERMEDAD MONOGÉNICA

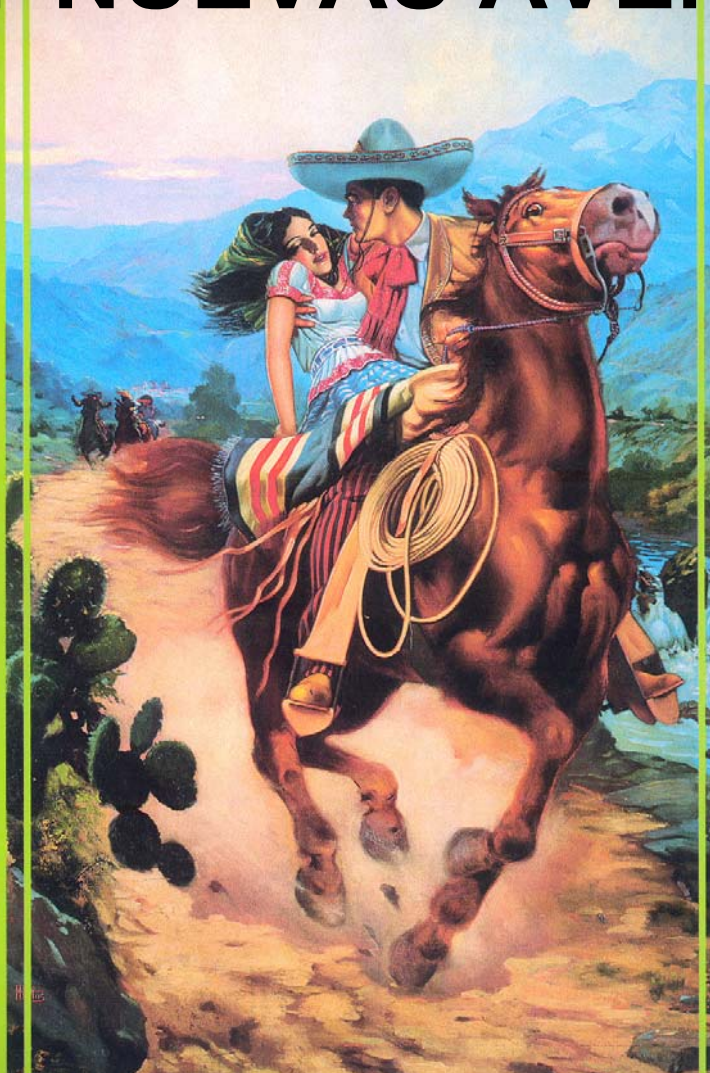


GEN MAYOR



ENFERMEDAD POLIGÉNICA (MULTIFACTORIAL)

CIENCIAS GENÓMICAS: NUEVOS VIAJES Y NUEVAS AVENTURAS





Las Enfermedades Complejas

Características Epidemiológicas de México: Primeras 10 causas de mortalidad en el 2002*

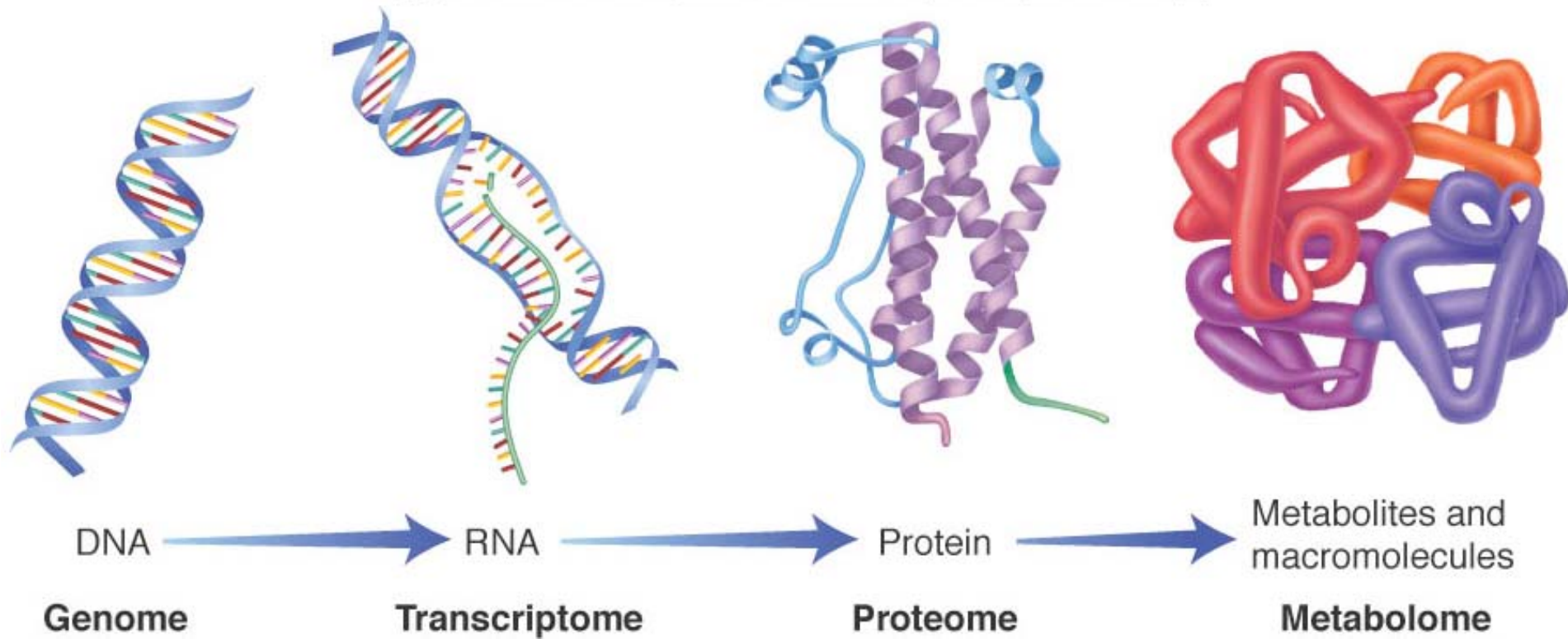
| CAUSA (CIE) | DEFUNCIONES |
|---|---------------|
| ■ Enfermedades del corazón | 74,325 |
| ■ CÁNCER (PULMÓN, ESTÓMAGO, HÍGADO, CERVICAL, PRÓSTATA Y MAMA) | 58,599 |
| ■ Diabetes mellitus | 54,952 |
| ■ Accidentes | 35,639 |
| ■ Hepatopatías | 28,449 |
| ■ Enfermedades cerebrovasculares | 26,538 |
| ■ Ciertas afecciones perinatales | 18,582 |
| ■ EPOC | 12,016 |
| ■ Influenza, neumonía | 11,706 |
| ■ Agresiones | 10,088 |

* Cuaderno No.20. Estadísticas del Sector Salud y Seguridad Social 2003.
INEGI. Aguascalientes, MX, 2004

TODO ES UN PROBLEMA DE MANEJO DE INFORMACIÓN



El Dogma Central: La Base



Welcome to the Entrez cross-database search page

- | | |
|---|--|
| PubMed: biomedical literature citations and abstracts | Books: online books |
| PubMed Central: free, full text journal articles | OMIM: online Mendelian Inheritance in Man |
| Site Search: NCBI web and FTP sites | OMIA: online Mendelian Inheritance in Animals |
| Nucleotide: sequence database (GenBank) | UniGene: gene-oriented clusters of transcript sequences |
| Protein: sequence database | CDD: conserved protein domain database |
| Genome: whole genome sequences | 3D Domains: domains from Entrez Structure |
| Structure: three-dimensional macromolecular structures | UniSTS: markers and mapping data |
| Taxonomy: organisms in GenBank | PopSet: population study data sets |
| SNP: single nucleotide polymorphism | GEO Profiles: expression and molecular abundance profiles |
| Gene: gene-centered information | GEO DataSets: experimental sets of GEO data |
| HomoloGene: eukaryotic homology groups | Cancer Chromosomes: cytogenetic databases |
| PubChem Compound: unique small molecule chemical structures | PubChem BioAssay: bioactivity screens of chemical substances |
| PubChem Substance: deposited chemical substance records | GENSAT: gene expression atlas of mouse central nervous system |
| Genome Project: genome project information | Probe: sequence-specific reagents |
| Journals: detailed information about the journals indexed in PubMed and other Entrez databases | MeSH: detailed information about NLM's controlled vocabulary |
| NLM Catalog: catalog of books, journals, and audiovisuals in the NLM collections | |

Go to GEO DataSets Search Page



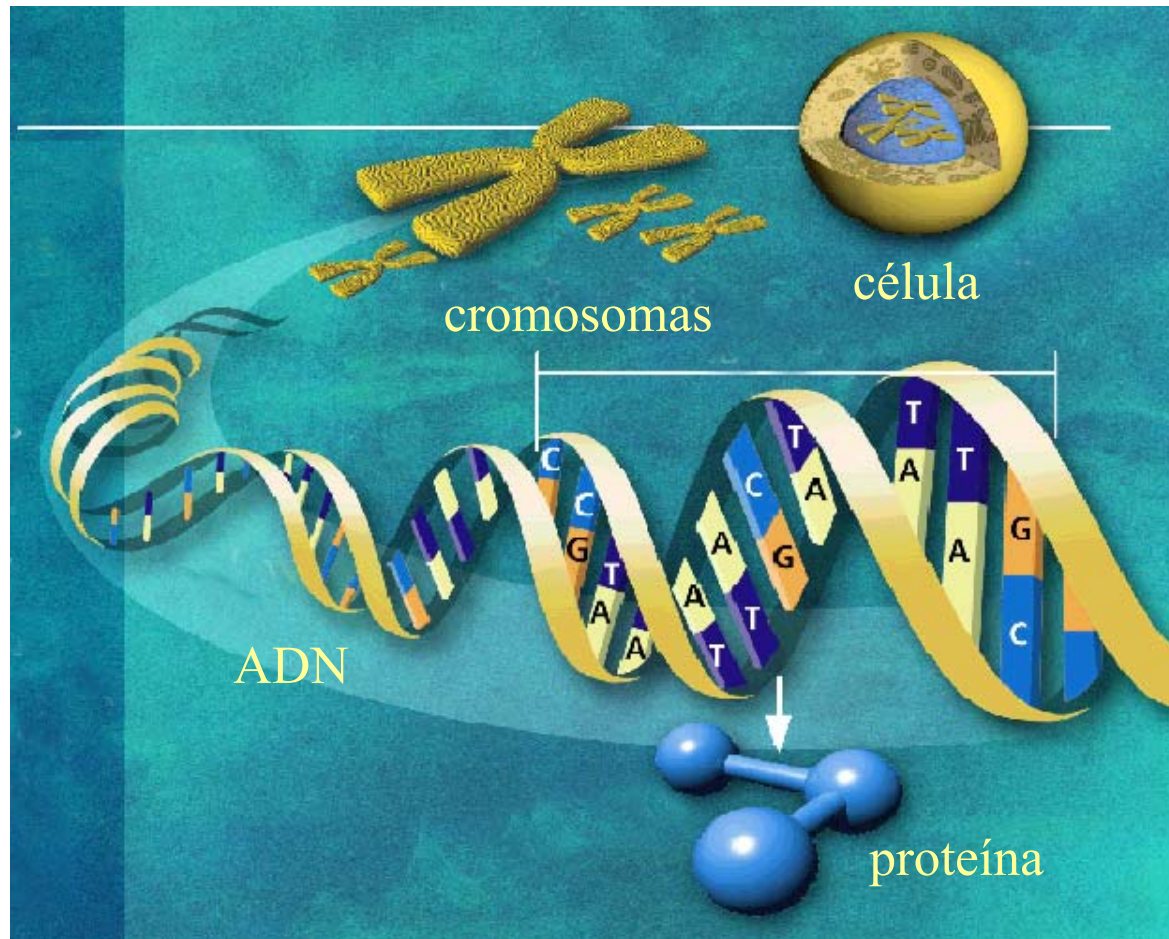
El Genoma Humano

-23 cromosomas humanos

-1 m de DNA

-3 mil millones de subunidades de DNA (las bases A, T, C, G)

-Aprox. 30,000 genes



AL CHANGARRO, A TRABAJAR!



Laboratorios de Genómica



International Human Genome Sequencing Consortium

Celera Genomics



Genome Sequencing Centres (Listed in order of total genomic sequence contributed, with a partial list of personnel. A full list of contributors at each centre is available as Supplementary Information.)

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Max Planck Institute for Molecular Genetics: Juliane Ramser²³, Hans Lehrach²³ & Richard Reinhardt²³

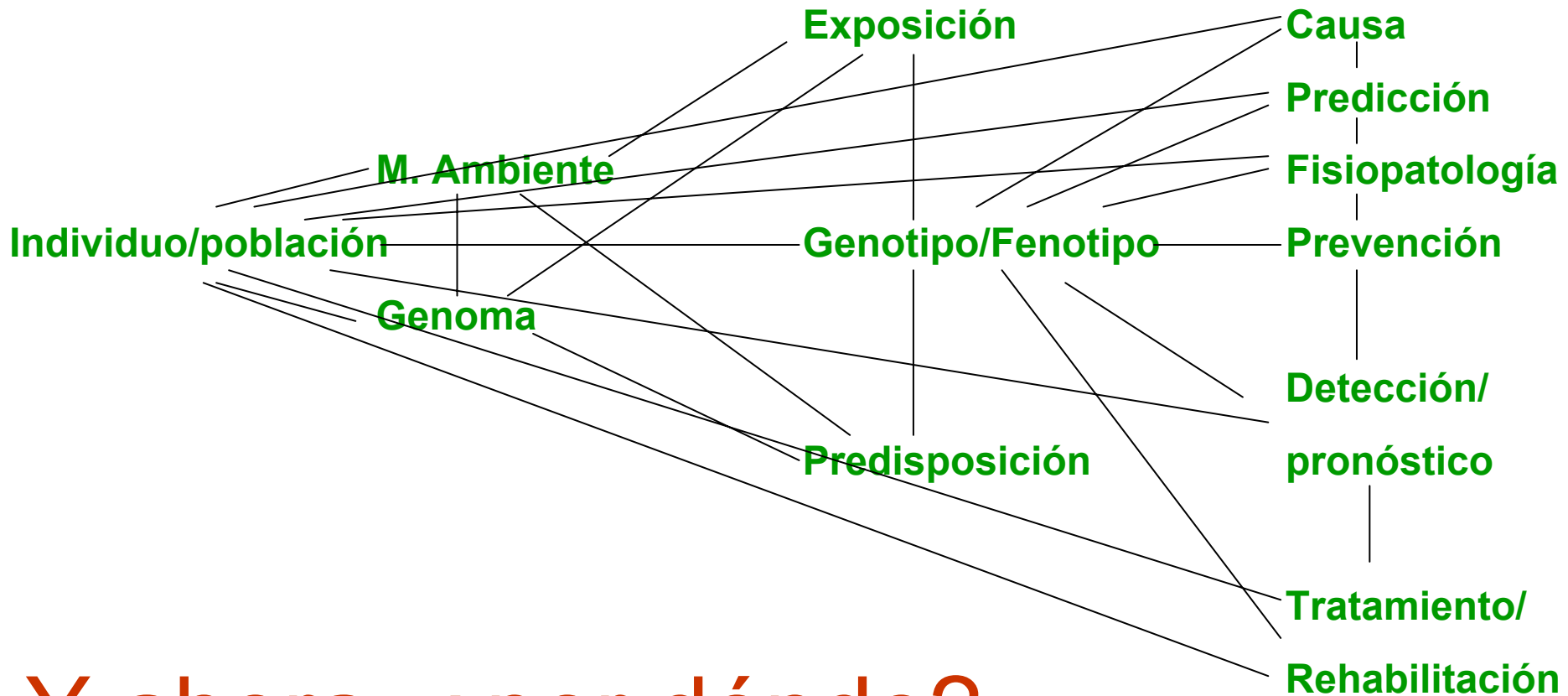
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GBF—German Research Centre for Biotechnology: Helmut Blöcker²⁵, Klaus Hornischer²⁵ & Gabriele Nordtsiek²⁵

* **Genome Analysis Group (listed in alphabetical order, also includes individuals listed under other headings):** Richa Agarwala²⁶, L. Aravind²⁶, Jeffrey A. Bailey²⁷, Alex Bateman², Serafim Batzoglou¹, Ewan Birney²⁸, Peer Bork^{29,30}, Daniel G. Brown¹, Christopher B. Burge³¹, Lorenzo Cerutti²⁸, Hsiu-Chuan Chen²⁶, Deanna Church²⁶, Michele Clamp², Richard R. Copley³⁰, Tobias Doerks^{29,30}, Sean R. Eddy³², Evan E. Eichler²⁷, Terrence S. Furey³, James Galagan¹, James G. R. Gilbert², Cyrus Harmon³⁴, Yoshihide Hayashizaki³⁵, David Hausler³⁶, Henning Hermjakob²⁸, Karsten Hokamp³⁷, Wonhee Jang²⁶, L. Steven Johnson³², Thomas A. Jones³², Simon Kasif³⁸, Arek Kasprzyk²⁸, Scot Kennedy³⁹, W. James Kent⁴⁰, Paul Kitts²⁶, Eugene V. Koonin²⁶, Ian Korf³, David Kulp³⁴, Doron Lancet⁴¹, Todd M. Lowe⁴², Aoife McLysaght⁴³, Tarjei Mikkelsen³⁶, John V. Moran⁴³, Nicola Mulder²⁸, Victor J. Pollara¹, Chris P. Ponting⁴⁴, Greg Schuler²⁶, Jörg Schultz³⁰, Guy Slaten²⁸, Arian F. A. Smit⁴⁵, Elia Stupka²⁸, Joseph Szustakowicz³⁸, Danielle Thierry-Mieg²⁶, Jean Thierry-Mieg²⁶, Lukas Wagner²⁶, John Wallis³, Raymond Wheeler³⁴, Alan Williams³⁴, Yuri I. Wolf²⁶, Kenneth H. Wolfe³⁷, Shiw-Pyng Yang³ & Ru-Fang Yeh³¹

Scientific management: National Human Genome Research Institute, US National Institutes of Health: Francis Collins⁴⁶, Mark S. Guyer⁴⁶, Jane Peterson⁴⁶, Adam Felsenfeld⁴⁶, & Kris A. Wetterstrand⁴⁶; **Office of Science, US Department of Energy:** Aristides Patrinos⁴⁷; **The Wellcome Trust:** Michael J. Morgan⁴⁸

Ahora, todo parece más claro...



Y ahora, ¿por dónde?

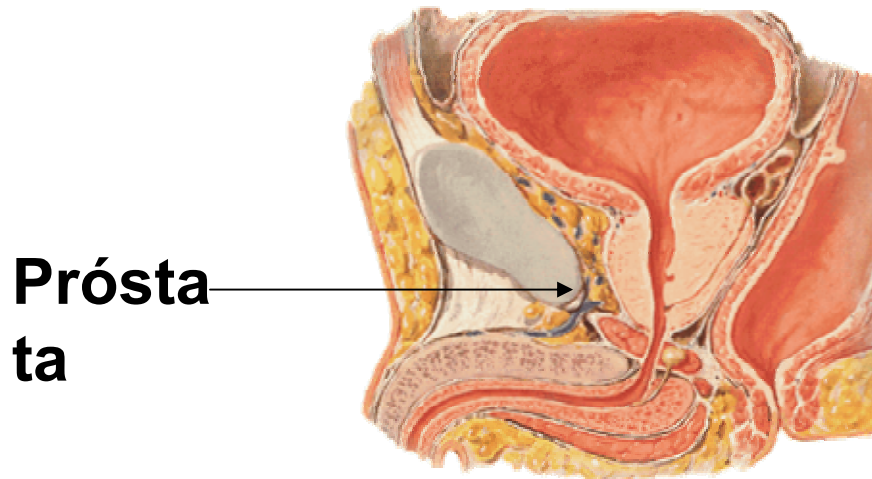
Depende de la araña



S. ANTONIO/MONTERREY

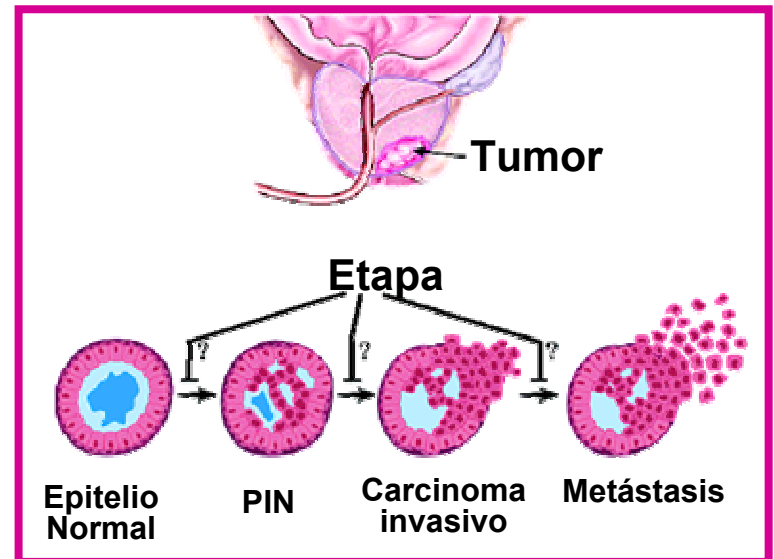


EL CÁNCER DE PRÓSTATA



Se distinguen 3 zonas:

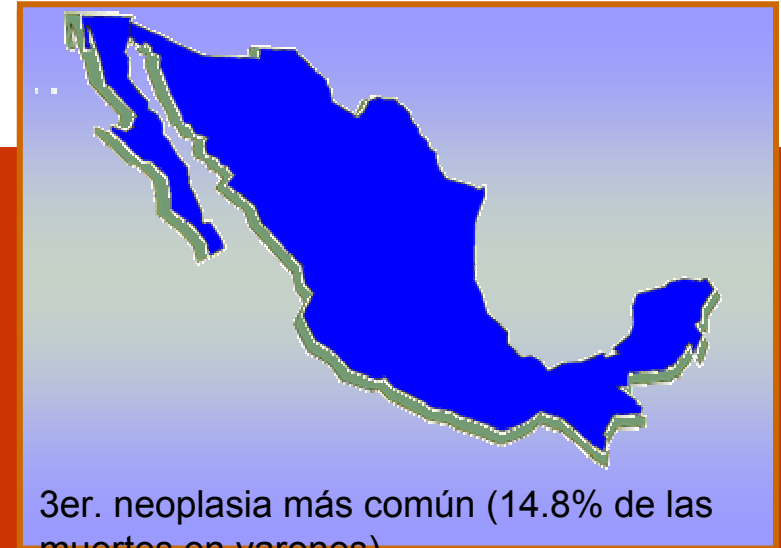
- 1). Central (25%).
- 2). Transicional (5%).
- 3). Periférica (70%).



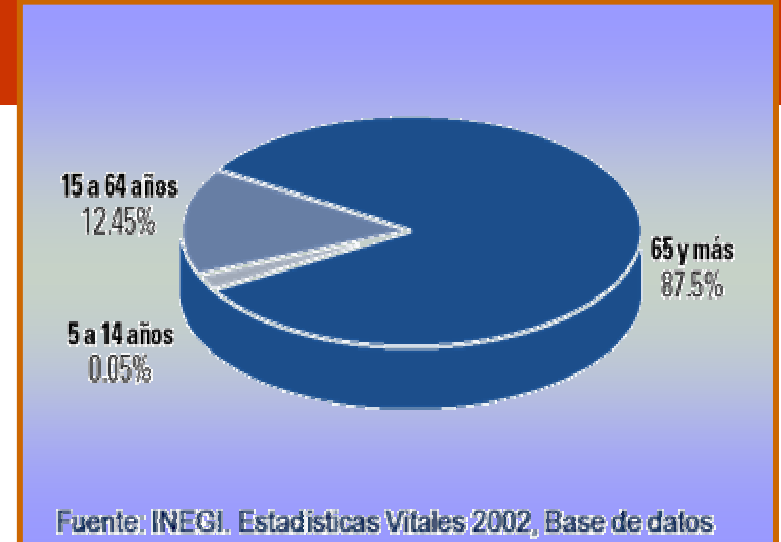
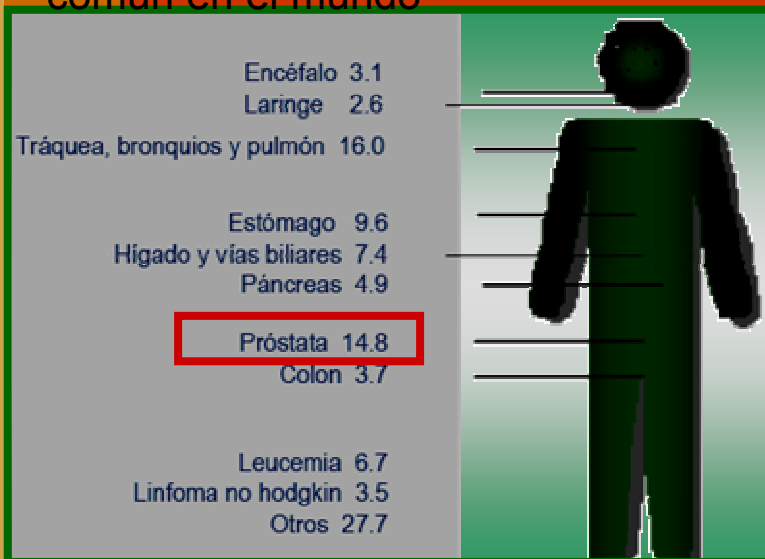
CÁNCER DE PRÓSTATA



Segundo tipo de neoplasia más común en el mundo



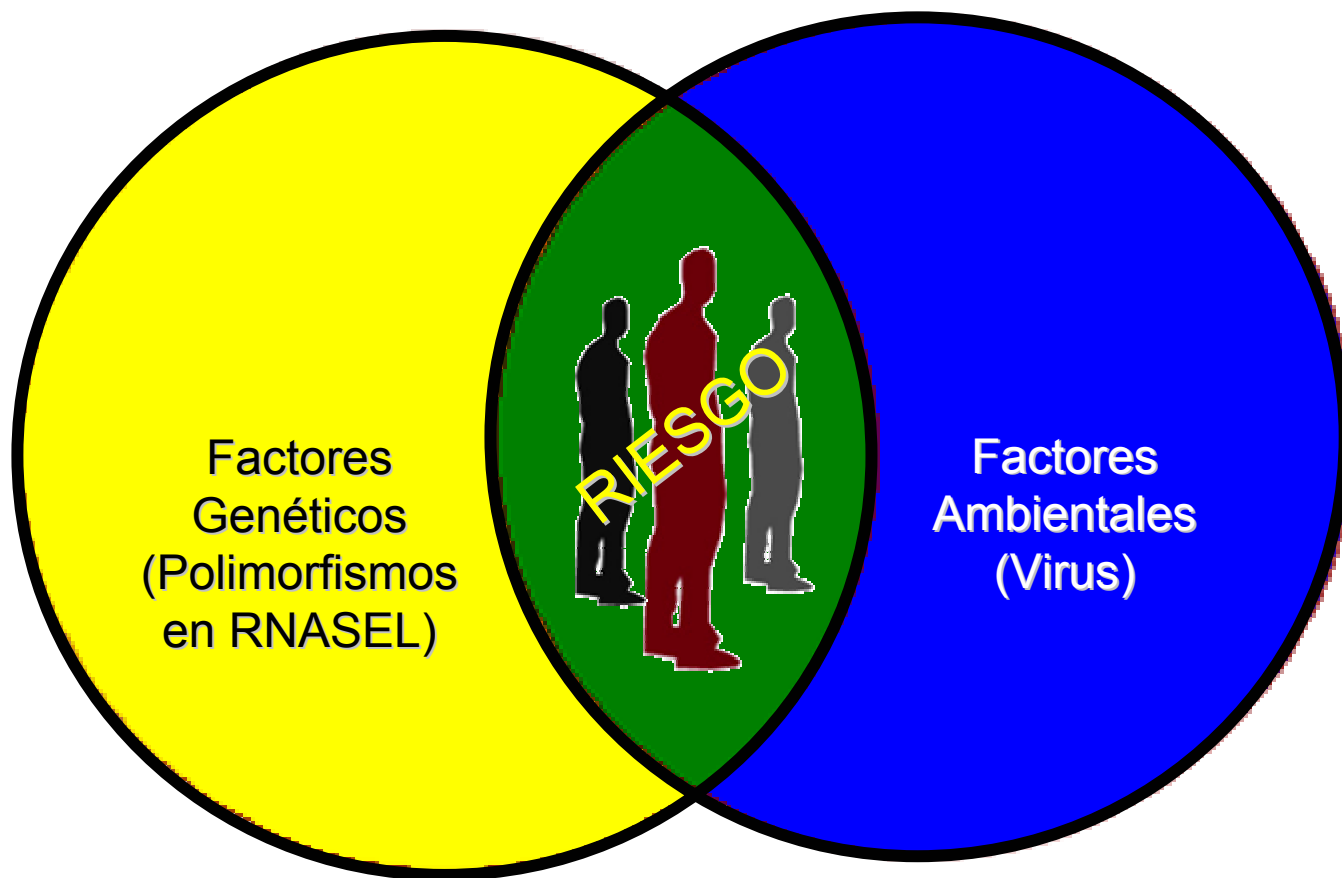
3er. neoplasia más común (14.8% de las muertes en varones).



Fuente: INEGI. Estadísticas Vitales 2002, Base de datos

FACTORES DE RIESGO

- **Edad**
- **Grupo étnico**
- **Factores alimenticios**
- **Historia familiar y polimorfismos genéticos**
- **Enfermedades de transmisión sexual (virus)**

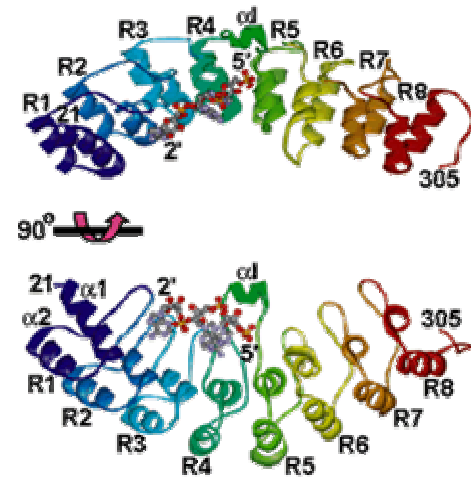
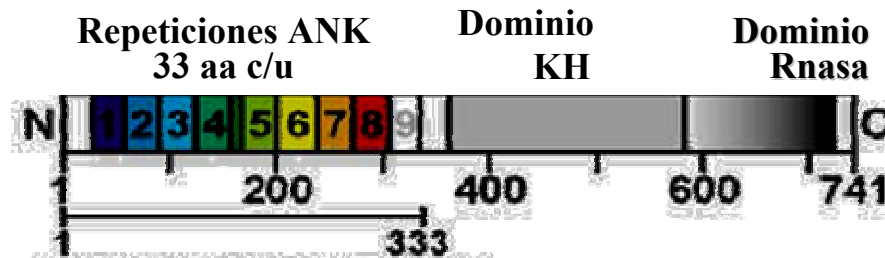


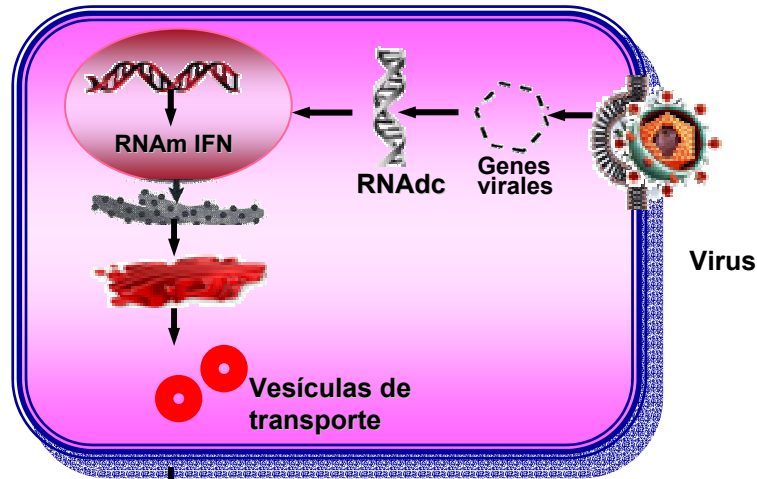
Loci de susceptibilidad para CaP: estudios de ligamiento genético

| LOCI | UBICACIÓN | HLOD |
|----------------------------------|------------------|-------------|
| Región PCAP | 1q42.2-43 | 2.2 |
| Región HPC1 (RNaseI) | 1q23-25 | 5.43 |
| Región HPCX | Xq27-28 | 3.85 |
| Región CAPB | 1p36 | 3.65 |
| Región HPC20 | 20q13 | 1.08 |
| MSR1 | 8p22-23 | 1.84 |
| Región HPC2 (ELAC) | 17p | 4.3 |

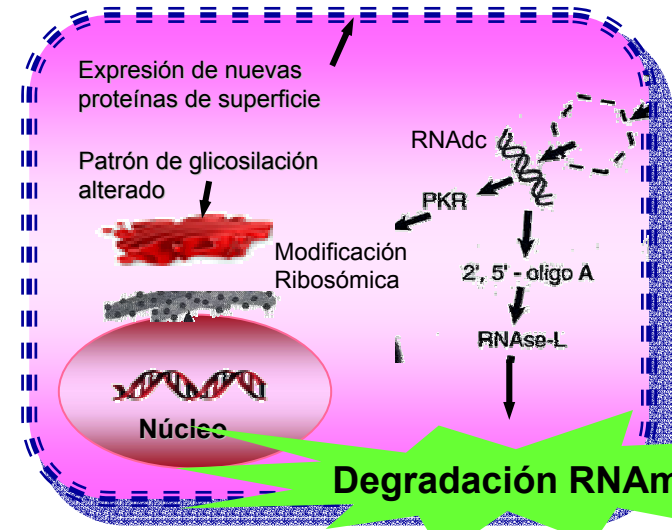
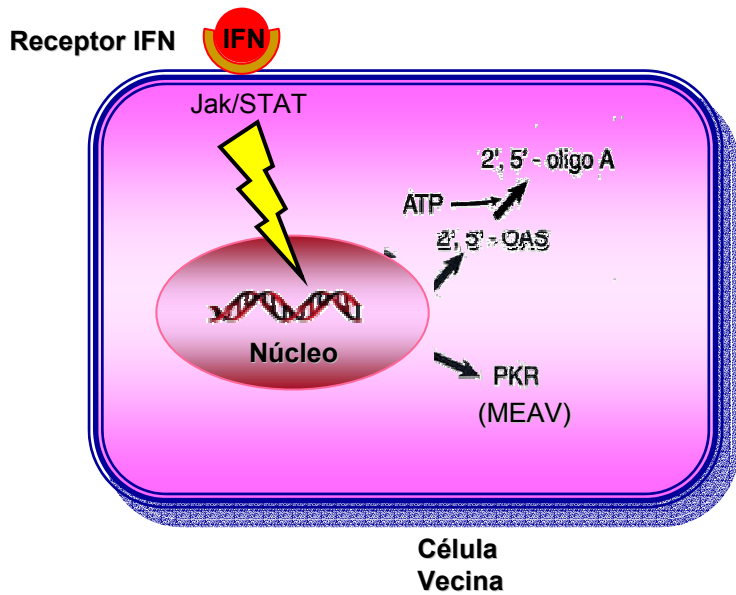
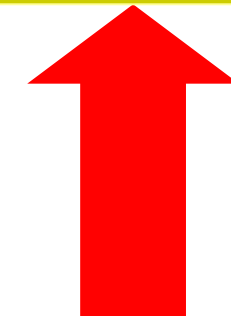
"RNAsa L"

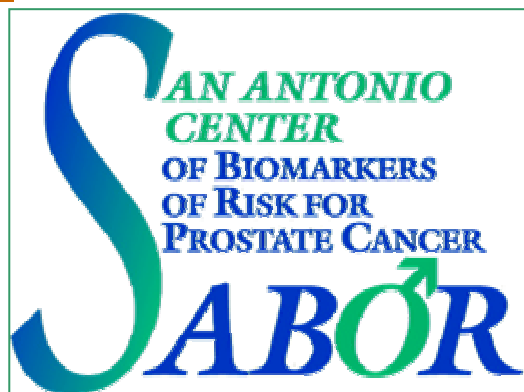
Es una endorribonucleasa que media las actividades antiproliferativas y apoptóticas del sistema 2-5A inducible por el interferón





Cáncer..??





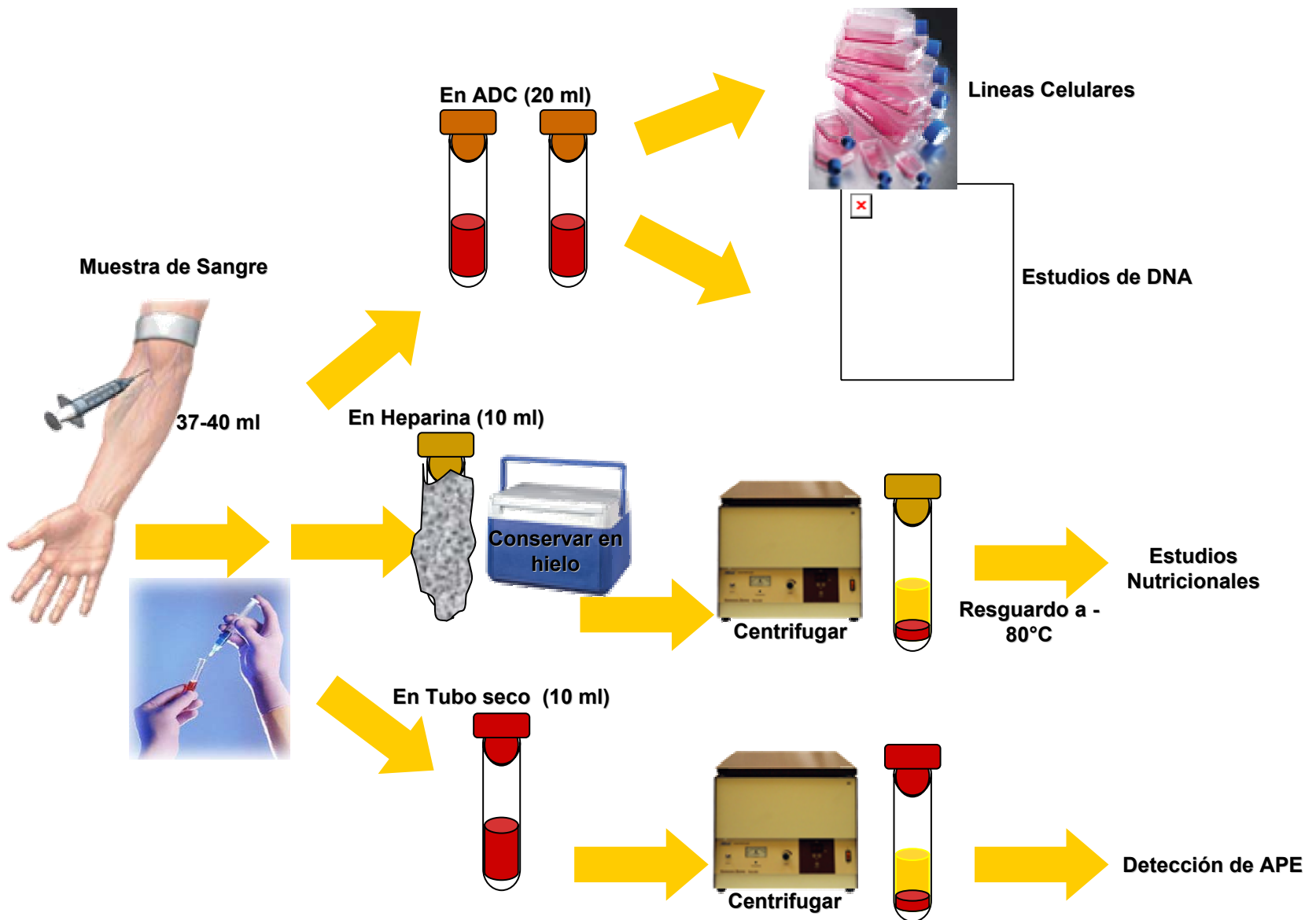
Banco de Muestras de CaP: Sangre y Tejidos

- ~ 850 muestras de tejido tumoral embebido en parafina
- ~ 330 muestras de tejido tumoral tanto en parafina como tejido fresco congelado.

| | |
|--------------|-------------|
| Total | 1025 |
|--------------|-------------|

- ~ 100 Tejido no tumoral.

MANEJO DE MUESTRAS

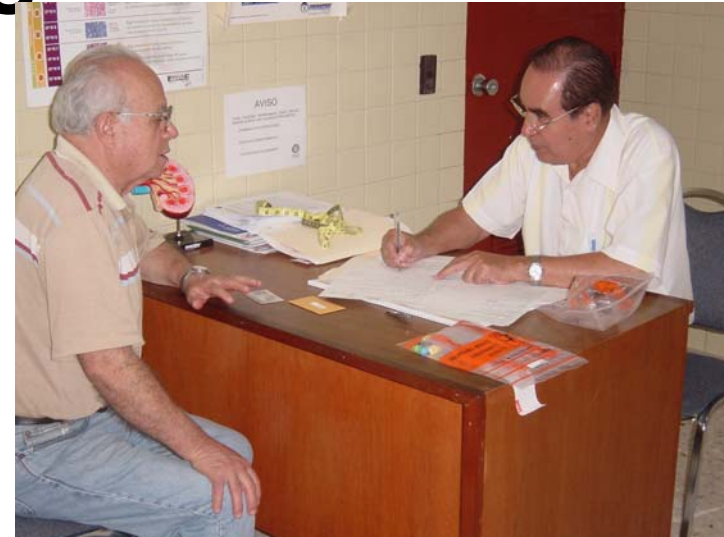


MUESTRA DE PACIENTES

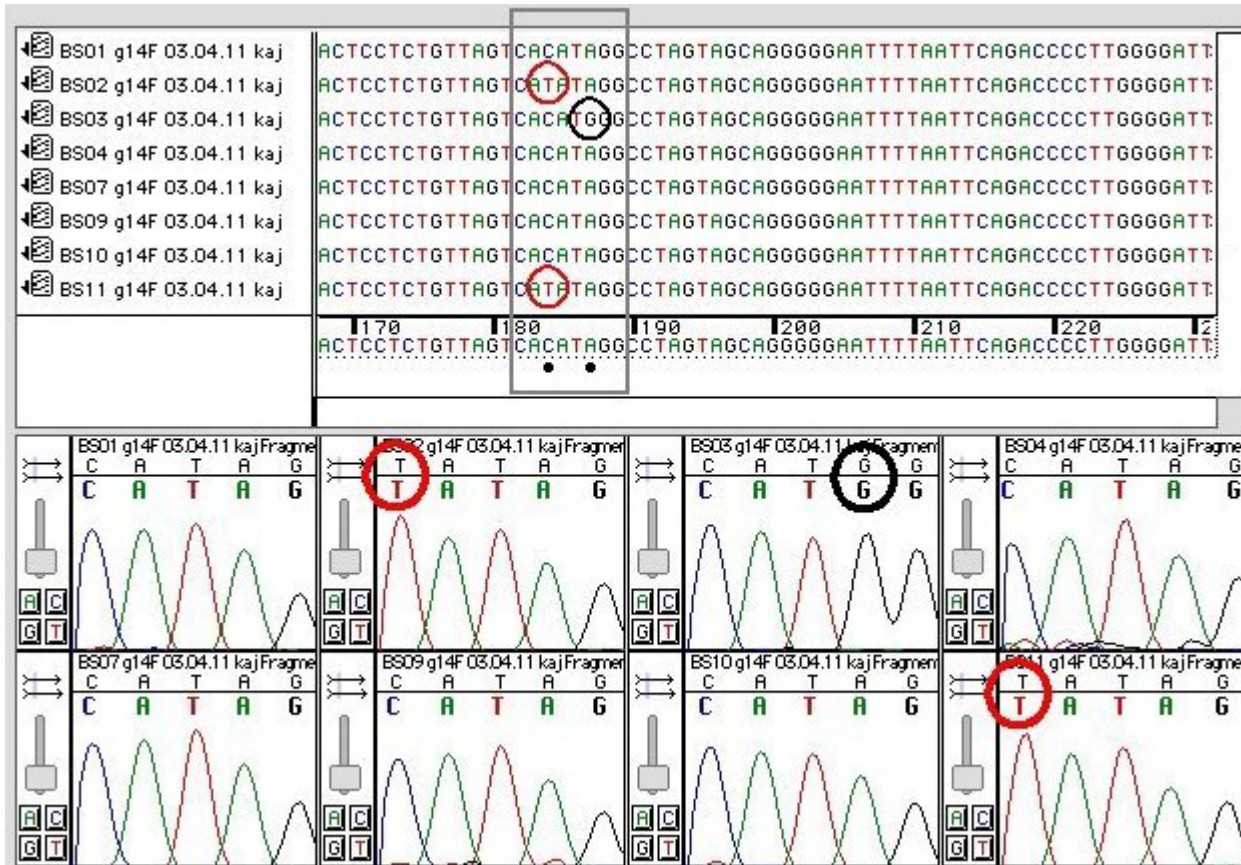
**TOTAL DE PACIENTES:
973**

**PACIENTES BIOPSIADOS:
68**

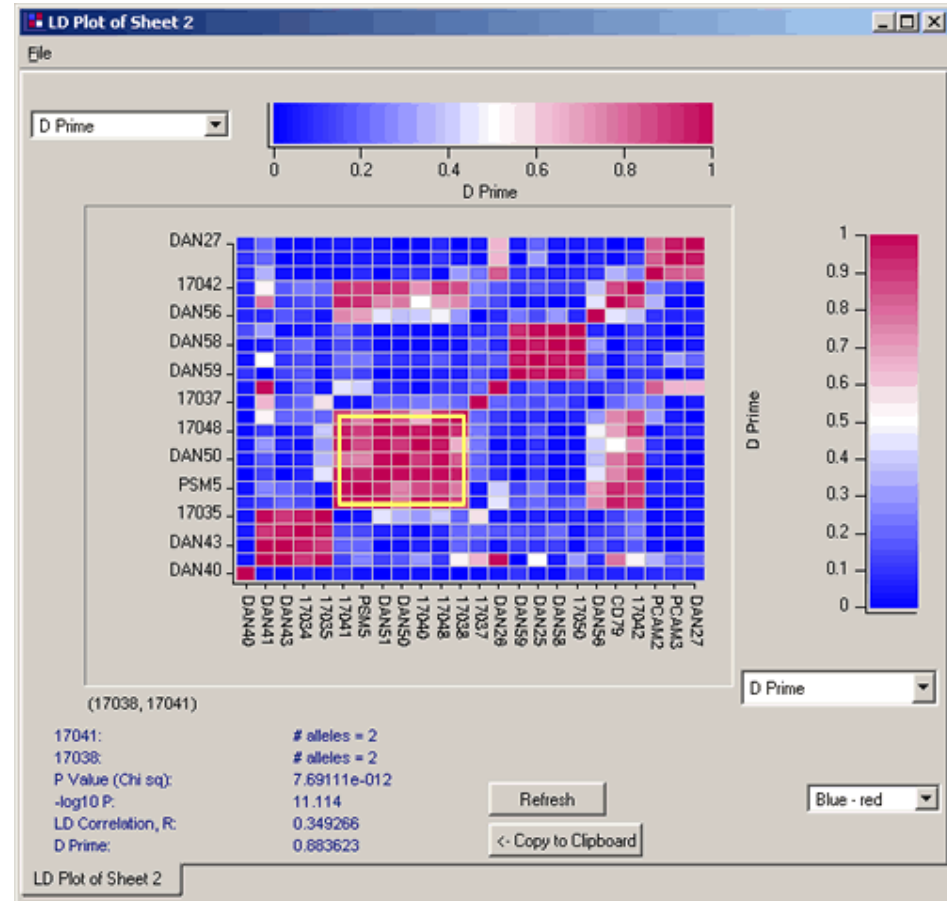
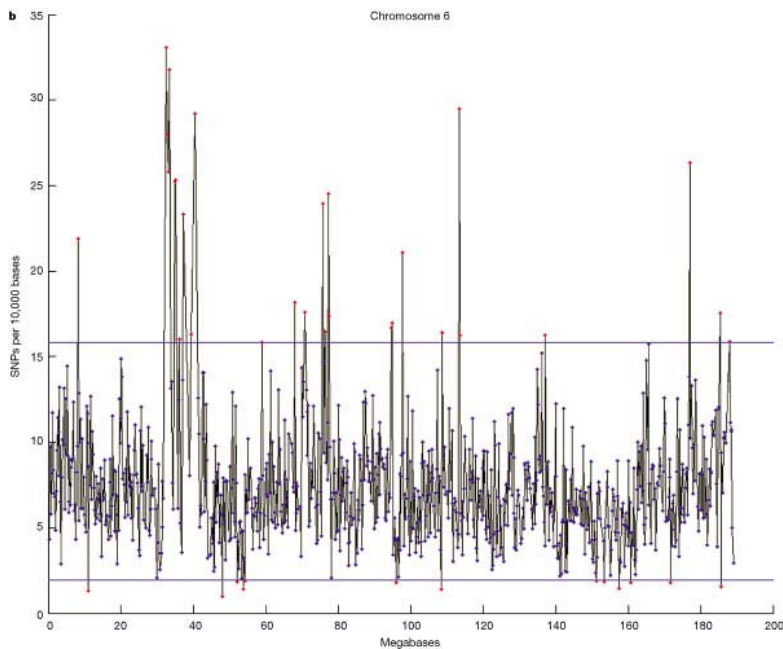
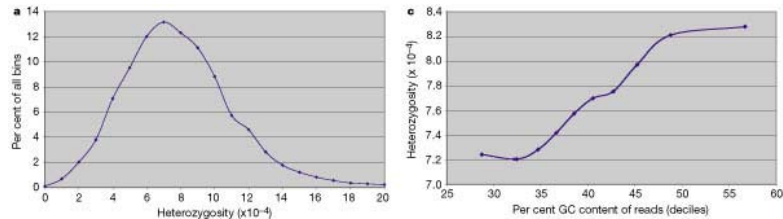
**BIOPSIAS POSITIVAS PARA
CÁNCER: 19**



SNPs

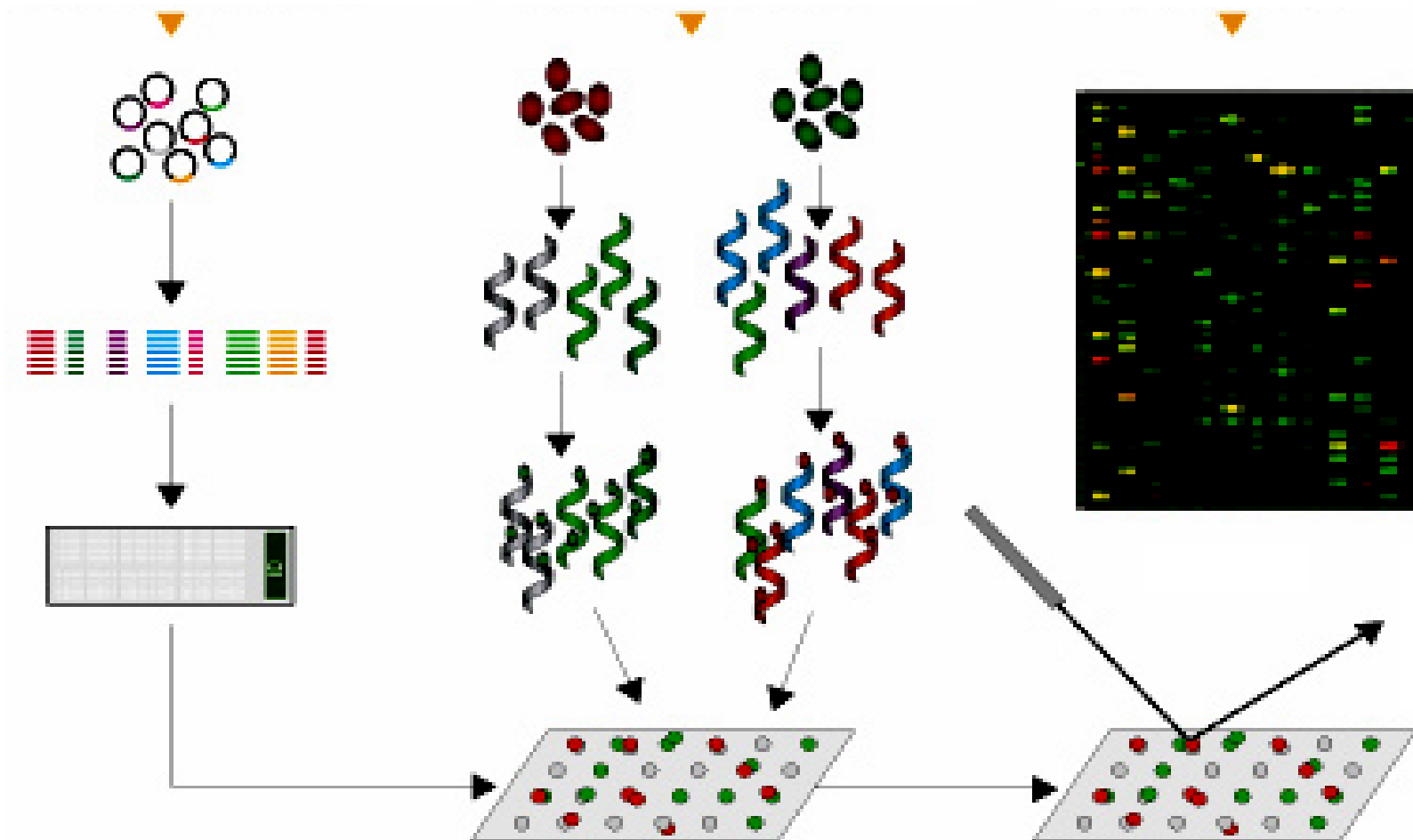


SNPs y ligamiento genético



Microarreglos-Microchips

Para análisis global de la expresión de genes



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GRACIAS!

