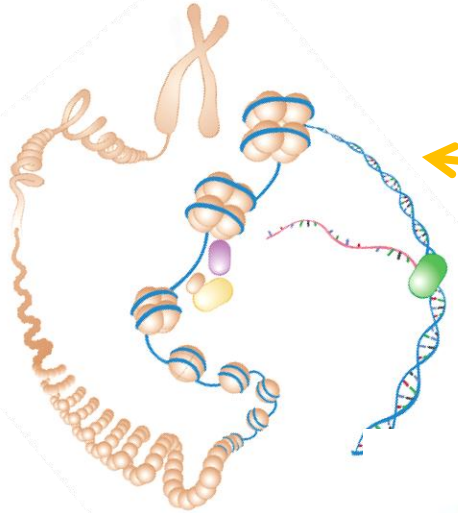
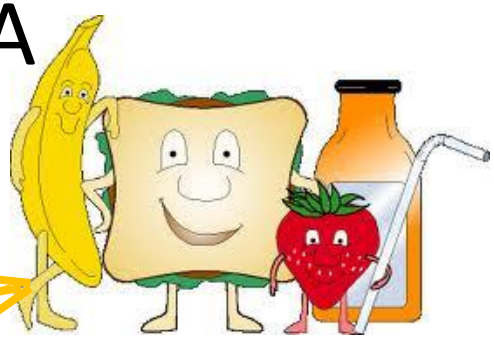
# NUTRIGENÓMICA



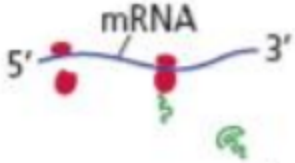


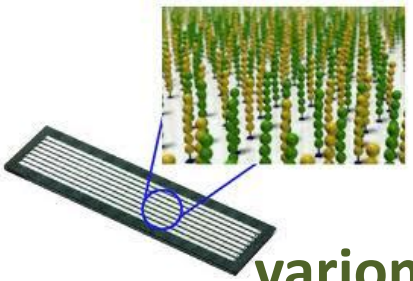
epigenoma

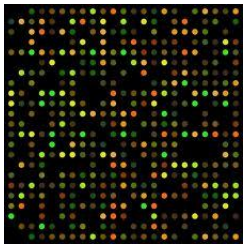
genoma

transcripción

traducción

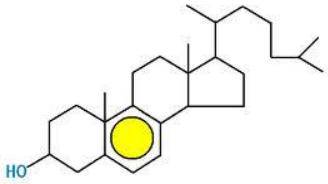


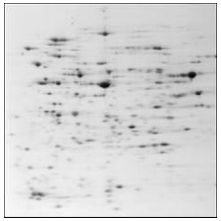





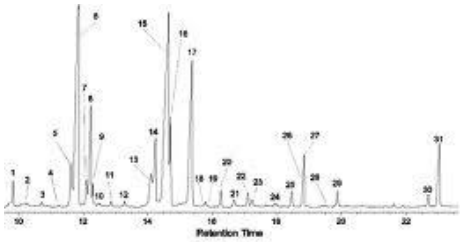
varioma

transcriptoma

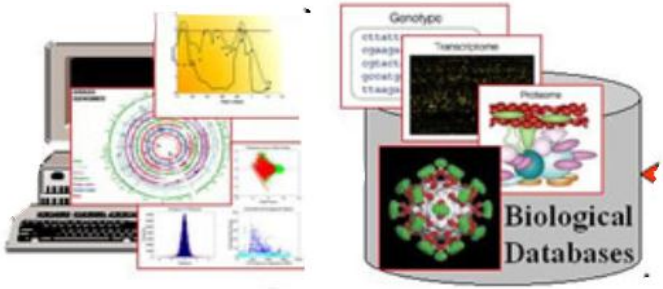


proteoma



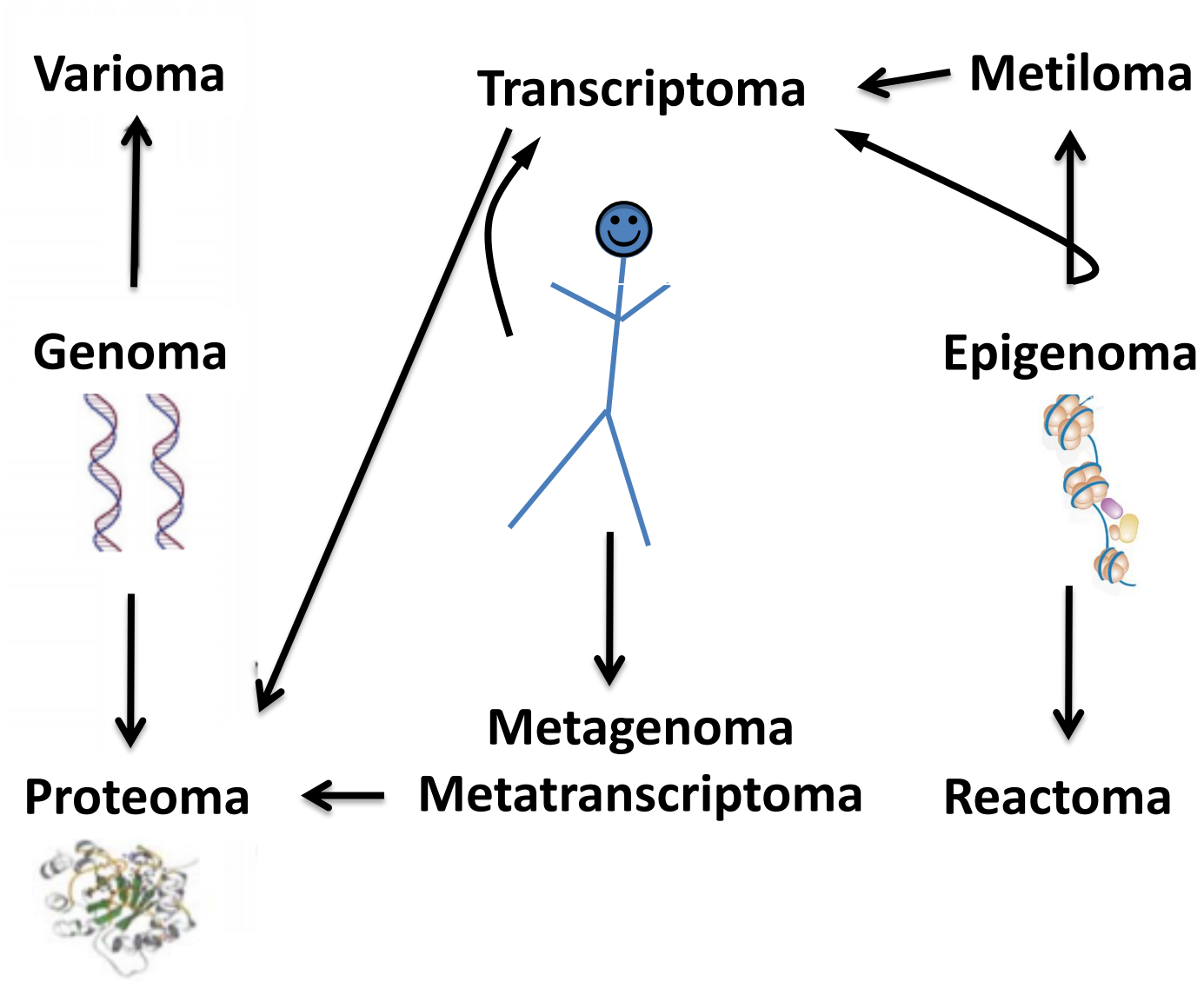
metaboloma



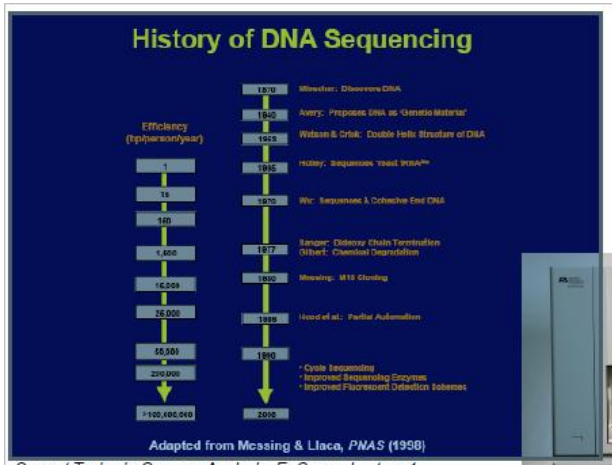

estadística

bioinformática

# OMICAS




Adaptación Slide “Omics” de M Caccamo




*Current Topics in Genome Analysis, E. Green, Lecture 1*

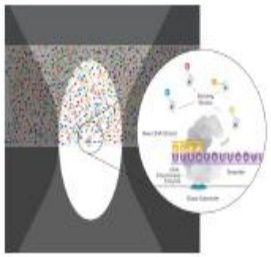
AB 3730 xl

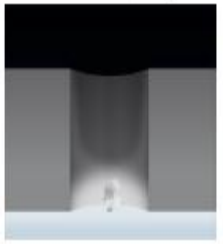
## Secuenciación EC

Helicos BioSciences Corporation

HeliScope

PACIFIC BIOSCIENCES





SMRT Technology

## Secuenciación de molécula simple

454

Pyrosequencing

Genome Analyzer

Reversible Terminator Chemistry

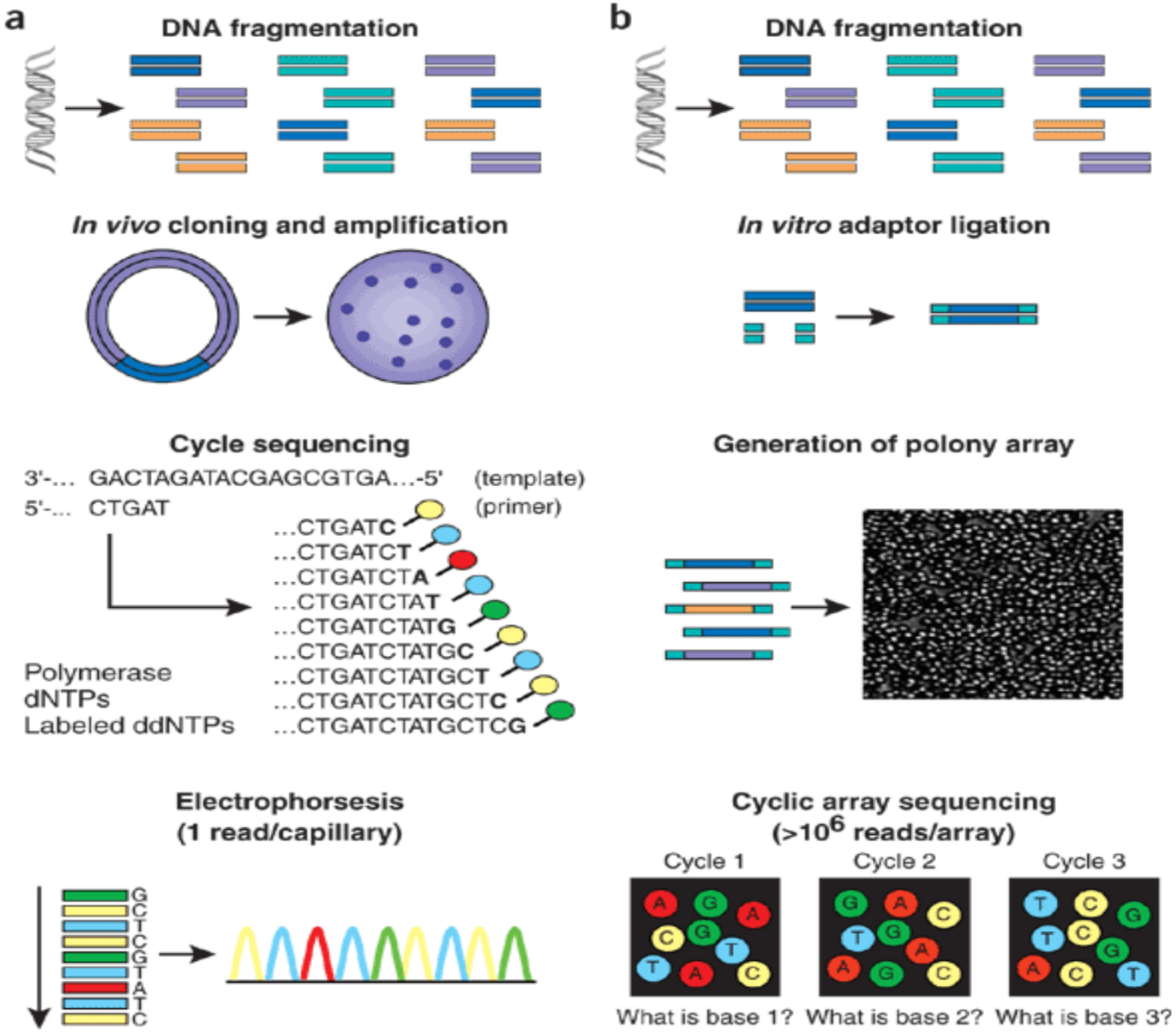
Applied Biosystems

SOLiD

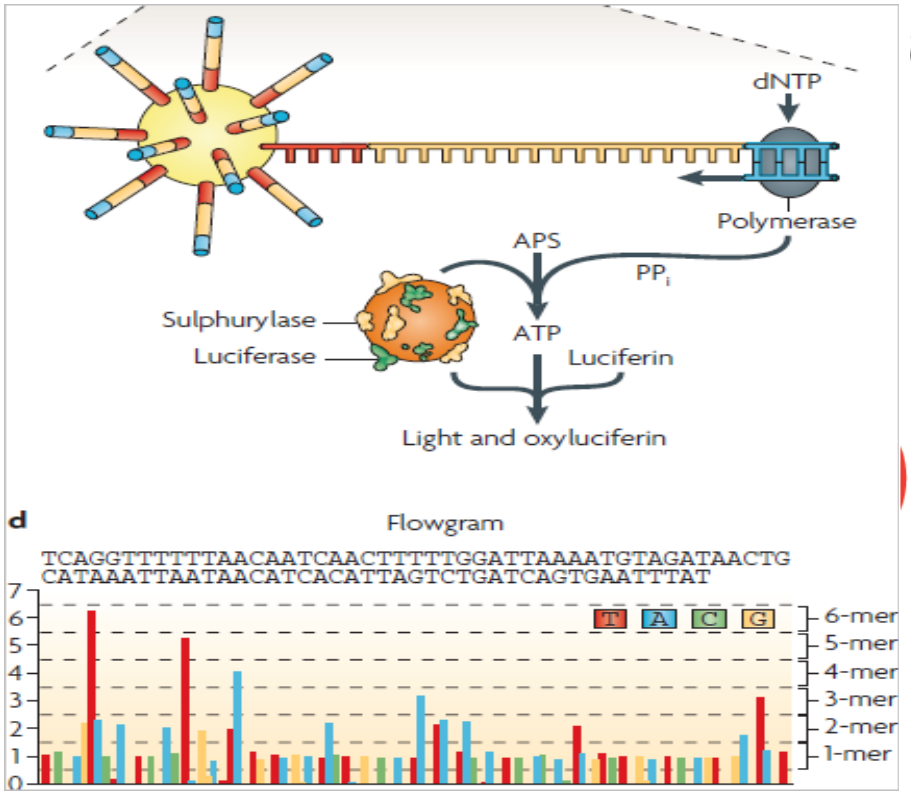
Ligation-based extension

## Secuenciación por síntesis o ligación

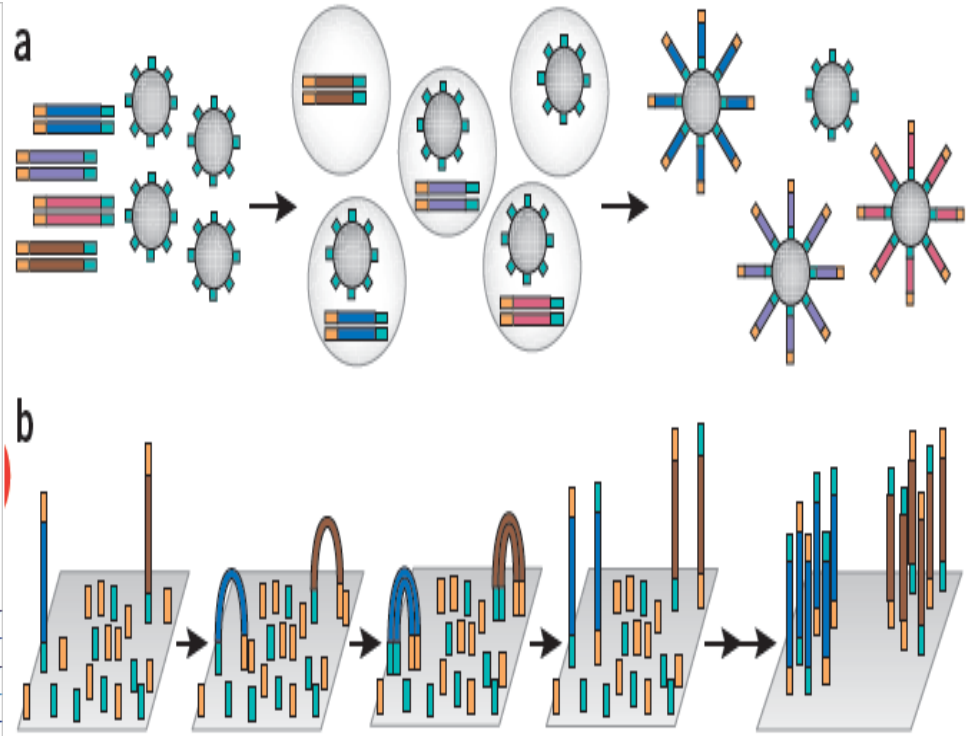
# TECNOLOGÍAS DE SECUENCIACION DE NUEVA GENERACIÓN



454 LIFE SCIENCES

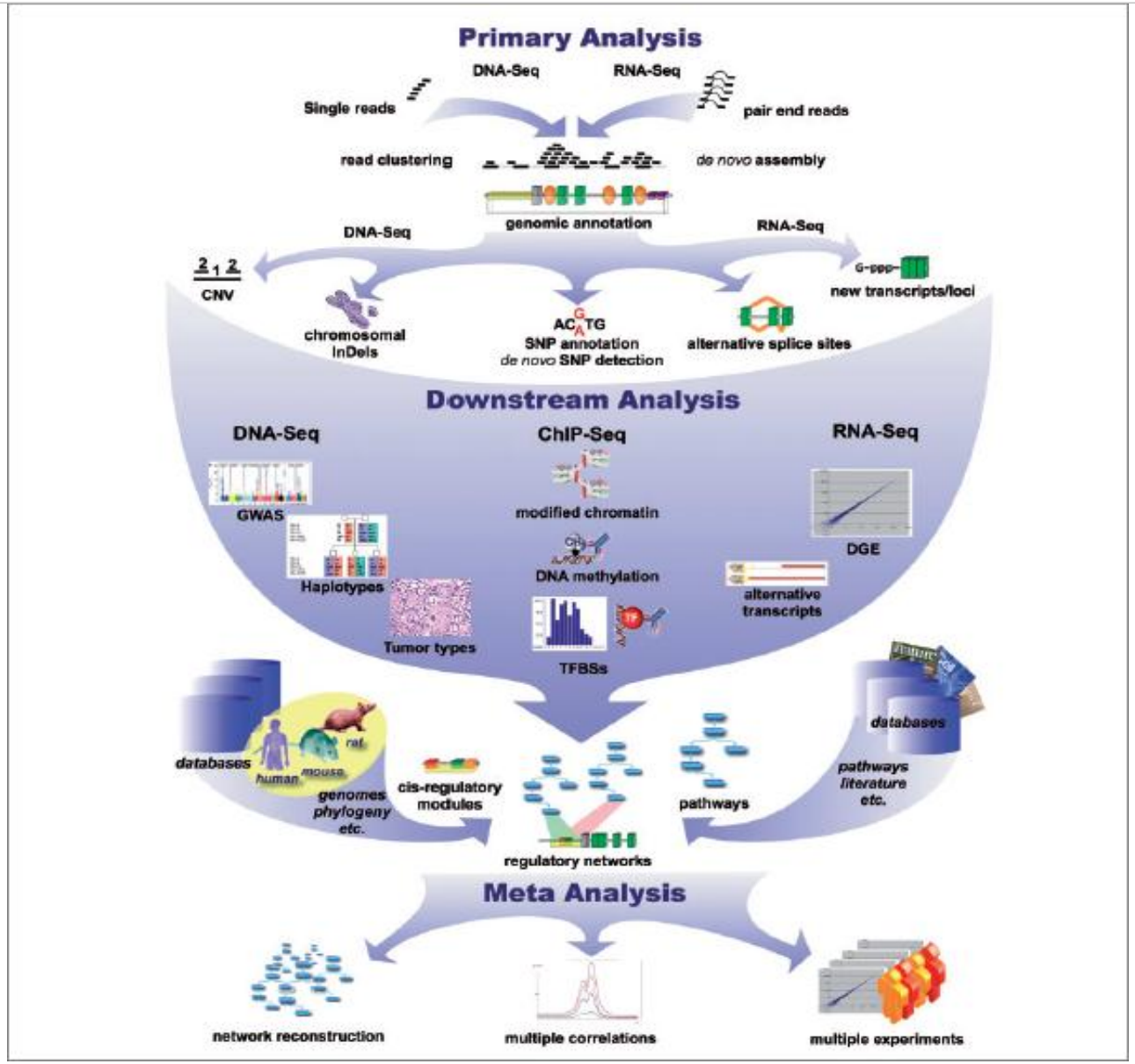



illumina®



# Next generation sequencing in functional genomics

*Thomas Werner*



# NUEVAS DEFINICIONES EN GENOMICA NUTRICIONAL

- The study of those positive and negative diet-genome interactions that over time, can affect health outcomes.
  - ✓ ***Nutrigenetics:*** Genetic variation (i.e., SNPs, CNVs, VNTRs) that can affect how nutrient and non-nutrient bioactives are assimilated, partitioned and utilized to impact metabolism and physiology
  - ✓ ***Nutrigenomics***: Diet-induced changes in gene expression that can influence network interactions and cellular information flow and
  - ✓ ***Nutritional epigenomics***: Diet-informed epigenetic modifications of chromatin (DNA methylation and histone acetylation) that can alter gene function and long term health outcomes

# NUTRIGENOMICS

## CONCEPTUAL BASES:

**1- Improper diets are risk factors for diseases**

**2- Dietary components alter gene expression and/or genome structure**

**3- Influence of diet on health depends upon na individual's genetic makeup**

**4- Genes regulated by diet play a role in chronic diseases**

**5- "Personalized nutrition" – diets based upon genotype, nutritional requirements and status prevents and mitigate chronic disease**

http://nutrigenomics.ucdavis.edu


*R Freitas-www.ilsi.org/Brasil/Documents/01%20Renata_pdf.pdf*

# 1- Improper diets are risk factors for diseases

## FACTS

Epidemiological studies show associations between some food/diet pattern and incidence and severity of diseases:

- CVD
- Obesity
- Type 2 Diabetes
- Cancer
- Other

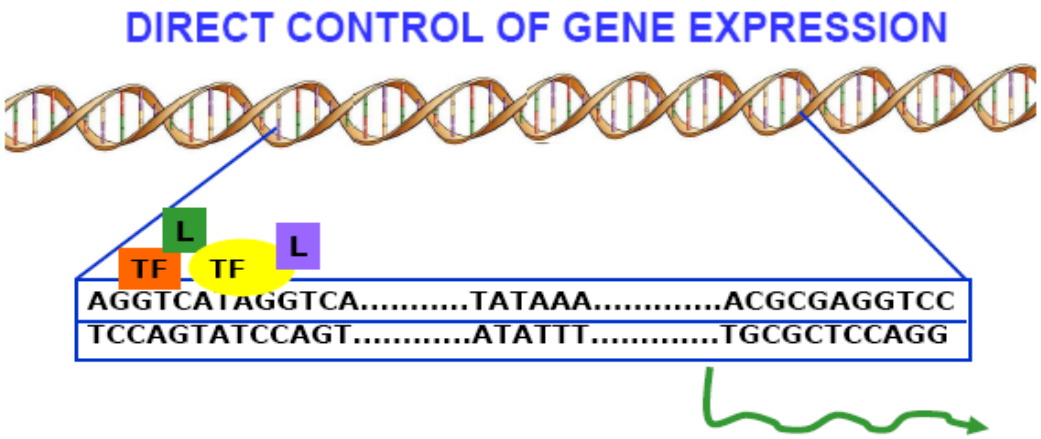
## PROBLEMS

Individuals respond differently to diet

Mechanisms are not fully understood

*R Freitas-www.ilsi.org/Brasil/Documents/01%20Renata_pdf.pdf*

**2- Dietary components alter gene expression and/or genome structure**




**Transcription-factor pathways mediating nutrient–gene interactions**

| Nutrient | Compound | Transcription factor |
|---|---|---|
| ***Macronutrients*** | | |
| Fats | Fatty acids<br>Cholesterol | PPARs, SREBPs, LXR, HNF4, ChREBP<br>SREBPs, LXRs, FXR |
| Carbohydrates | Glucose | USFs, SREBPs, ChREBP |
| Proteins | Amino acids | C/EBPs |
| ***Micronutrients*** | | |
| Vitamins | Vitamin A<br>Vitamin D<br>Vitamin E | RAR, RXR<br>VDR<br>PXR |
| Minerals | Calcium<br>Iron<br>Zinc | Calcineurin/NF-ATs<br>IRP1, IRP2<br>MTF1 |
| ***Other food components*** | | |
| | Flavonoids<br>Xenobiotics | ER, NFκB, AP1<br>CAR, PXR |

Müller & Kersten, Nature Rev. Gen., 4, 2003

*R Freitas-www.ilsi.org/Brasil/Documents/01%20Renata_pdf.pdf*

4- Genes regulated by diet play a role in chronic diseases

## PARADIGM OF NUTRITION GUIDES

Best information available

Dietary recomendations consider that all individuals are:

...culturally

...socio-economically

...physiologically

...genetically..... identical

"Nutrition is for real people. Statistical humans are of little interest."
R J Williams

*R Freitas-www.ilsi.org/Brasil/Documents/01%20Renata_pdf.pdf*

# HUMAN GENOME PROJECT

## Complex diseases genetic studies

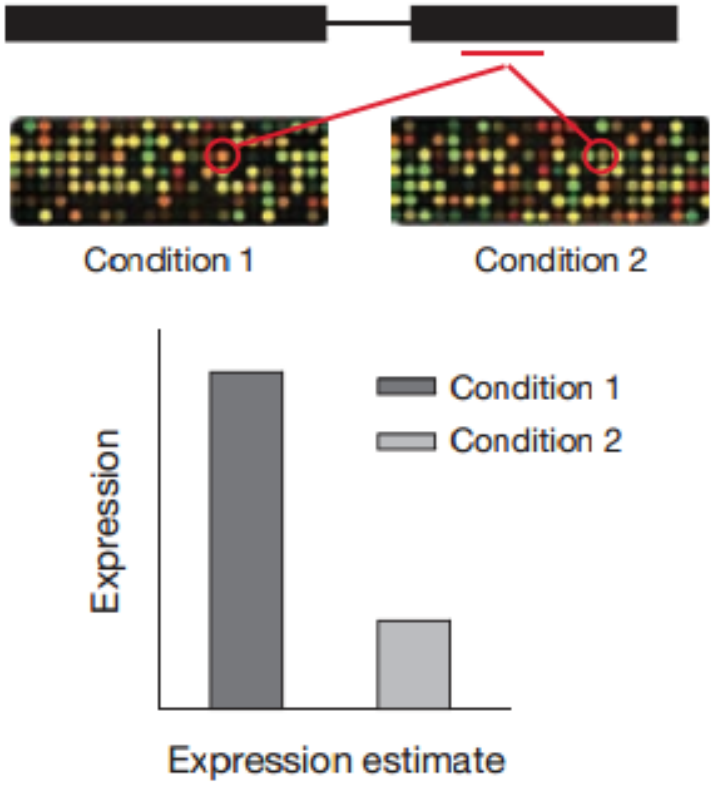
Genetic variants (polymorphisms) occuring in the genome structure/sequence with frequency > 1% in the general population (SNPs, insertions, deletions).

Functional polymorphisms – change molecules bioactivity/expression leading to variation in the response to diet/environmental factors.

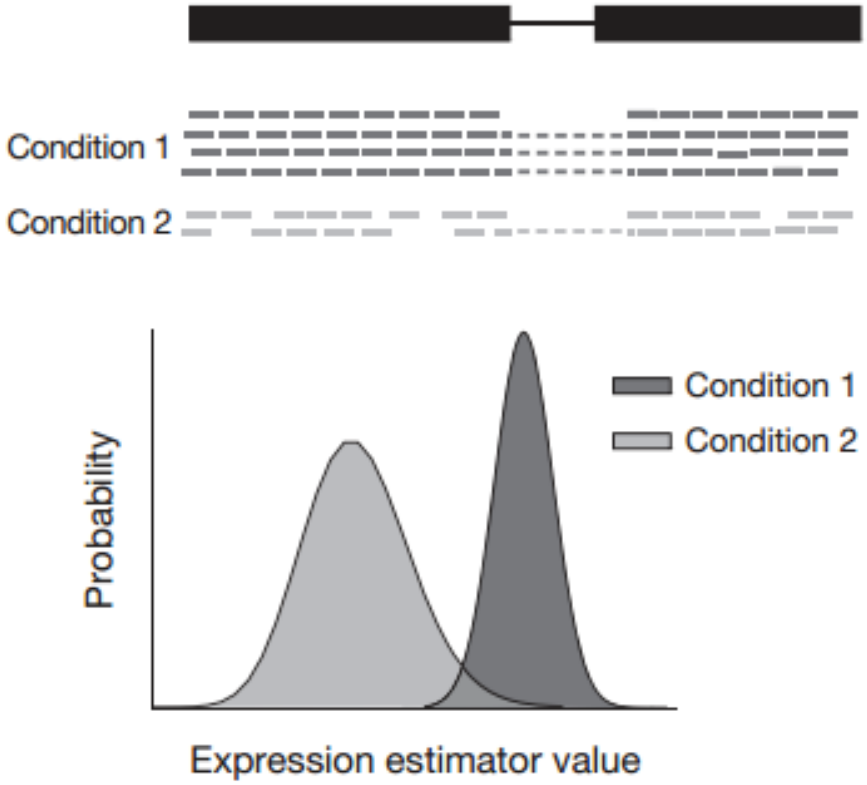
*R Freitas-www.ilsi.org/Brasil/Documents/01%20Renata_pdf.pdf*

# ANALISIS DE EXPRESIÓN DIFERENCIAL DE GENES

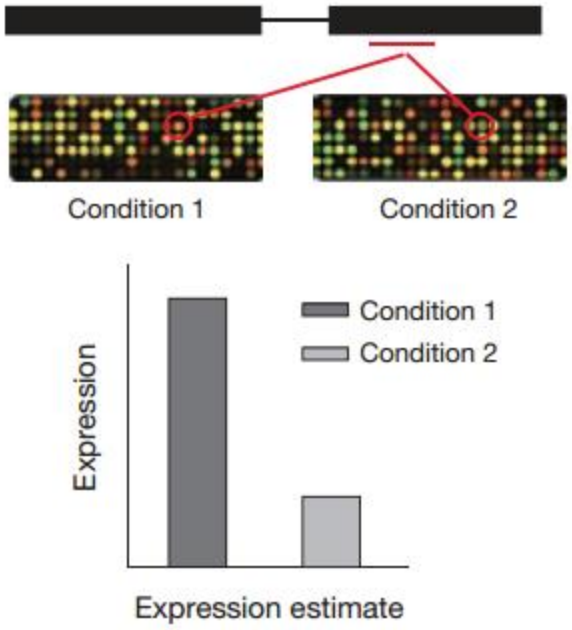
## Microarreglos de ADN




## RNA-Seq



# MICROARREGLOS DE ADN




*Critical Reviews in Food Science and Nutrition*, 50:693–698 (2010)

ISSN: 1040-8398
DOI: 10.1080/10408390903044156

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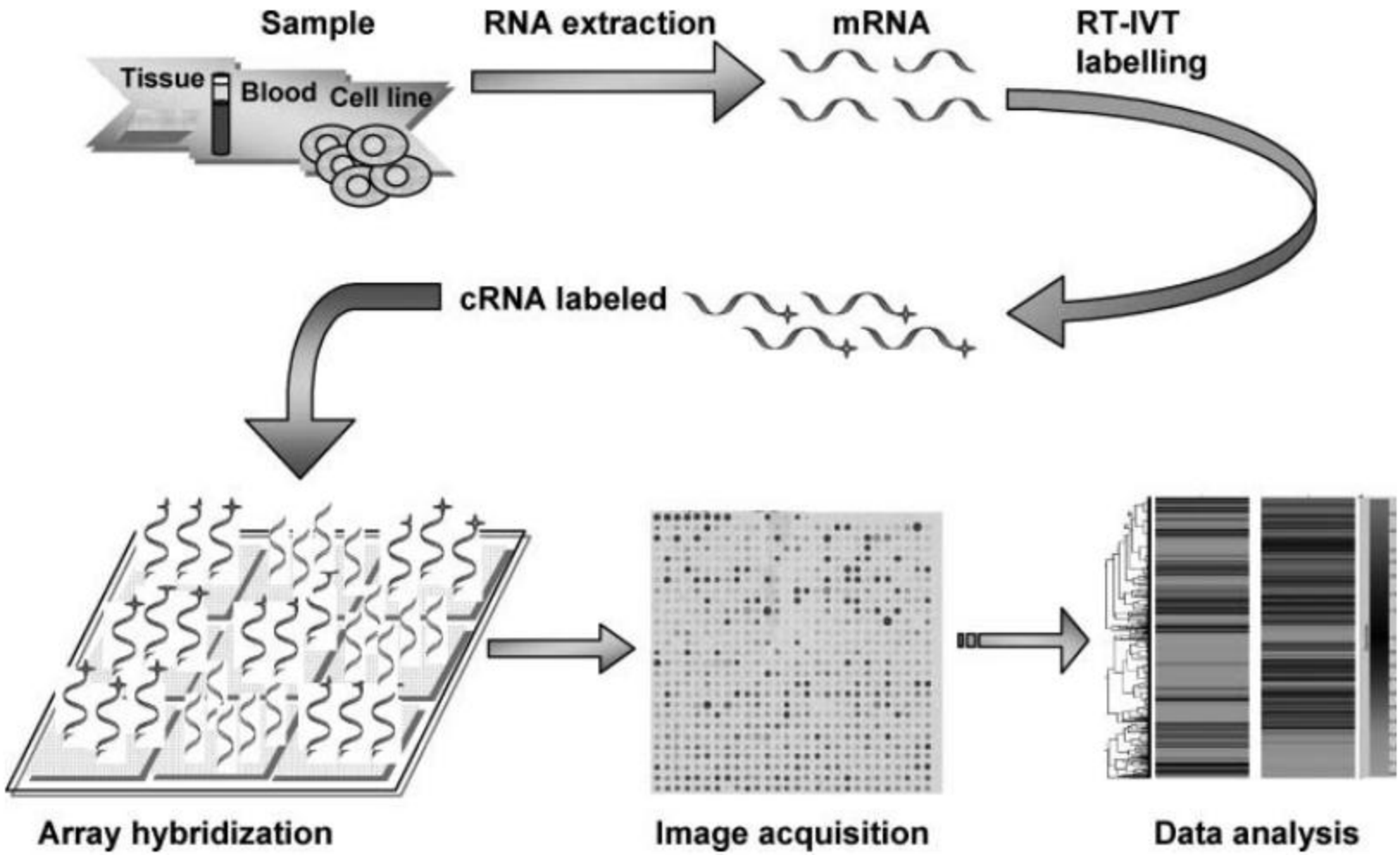
## Microarray Technology: A Promising Tool in Nutrigenomics

**ANDREA MASOTTI, LETIZIA DA SACCO, GIAN FRANCO BOTTAZZO, and ANNA ALISI**

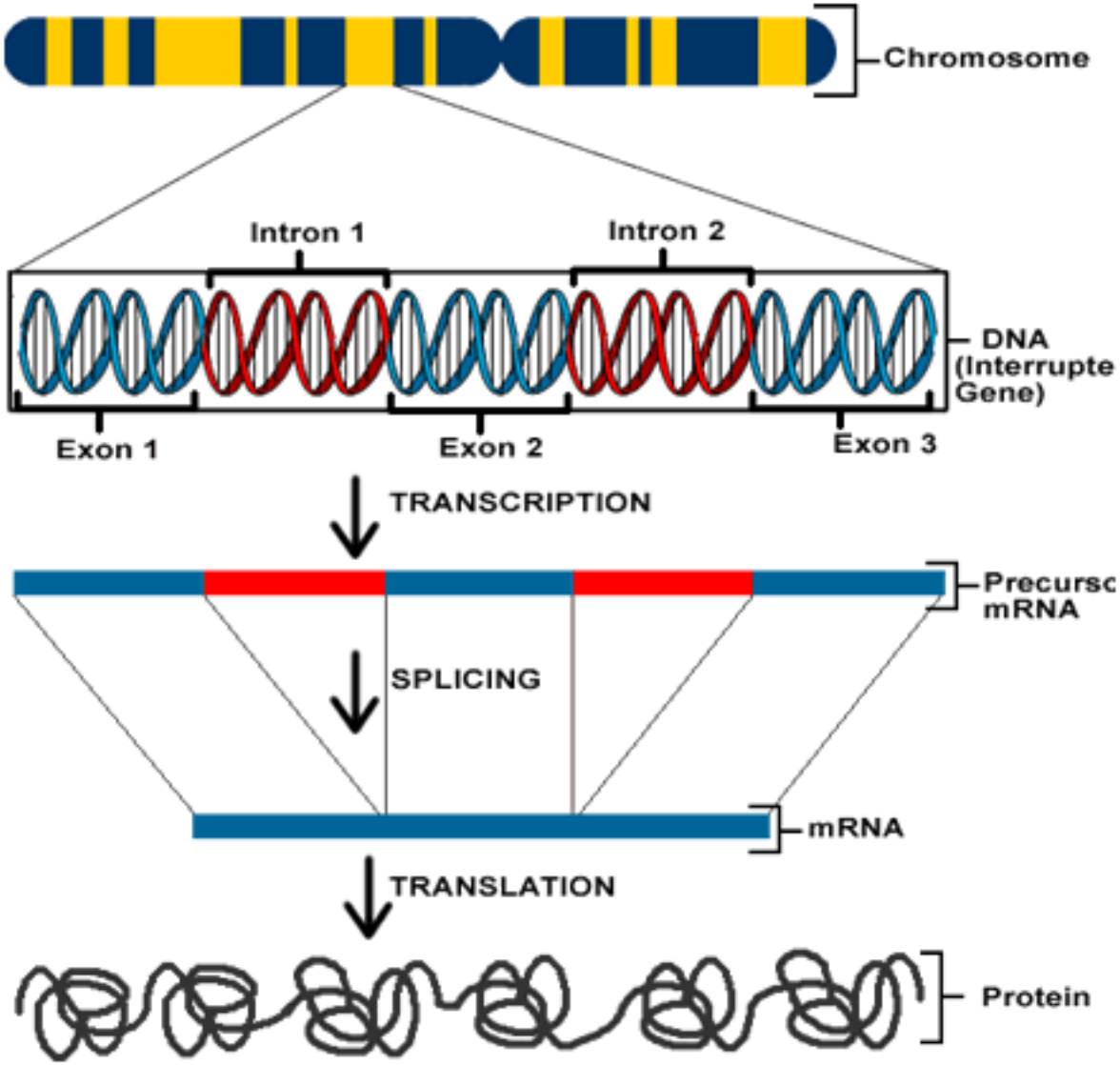
Bambino Gesù Children's Hospital, Research Institute (IRCCS), Rome, Italy

*Microarray technology is a powerful tool for the global evaluation of gene expression profiles in tissues and for understanding many of the factors controlling the regulation of gene transcription. This technique not only provides a considerable amount of information on markers and predictive factors that may potentially characterize a specific clinical picture, but also promises new applications for therapy. One of the most recent applications of microarrays concerns nutritional genomics. Nutritional genomics, known as nutrigenomics, aims to identify and understand mechanisms of molecular interaction between nutrients and/or other dietary bioactive compounds and the genome. Actually, many nutrigenomic studies utilize new approaches such as microarrays, genomics, and bioinformatics to understand how nutrients influence gene expression. The coupling of these new technologies with nutrigenomics promises to lead to improvements in diet and health. In fact, it may provide new information which can be used to ameliorate dietary regimens and to discover novel natural agents for the treatment of important diseases such as diabetes and cancer. This critical review gives an overview of the clinical relevance of a nutritional approach to several important diseases, and proposes the use of microarray for nutrigenomic studies.*

# MICROARREGLOS DE ADN



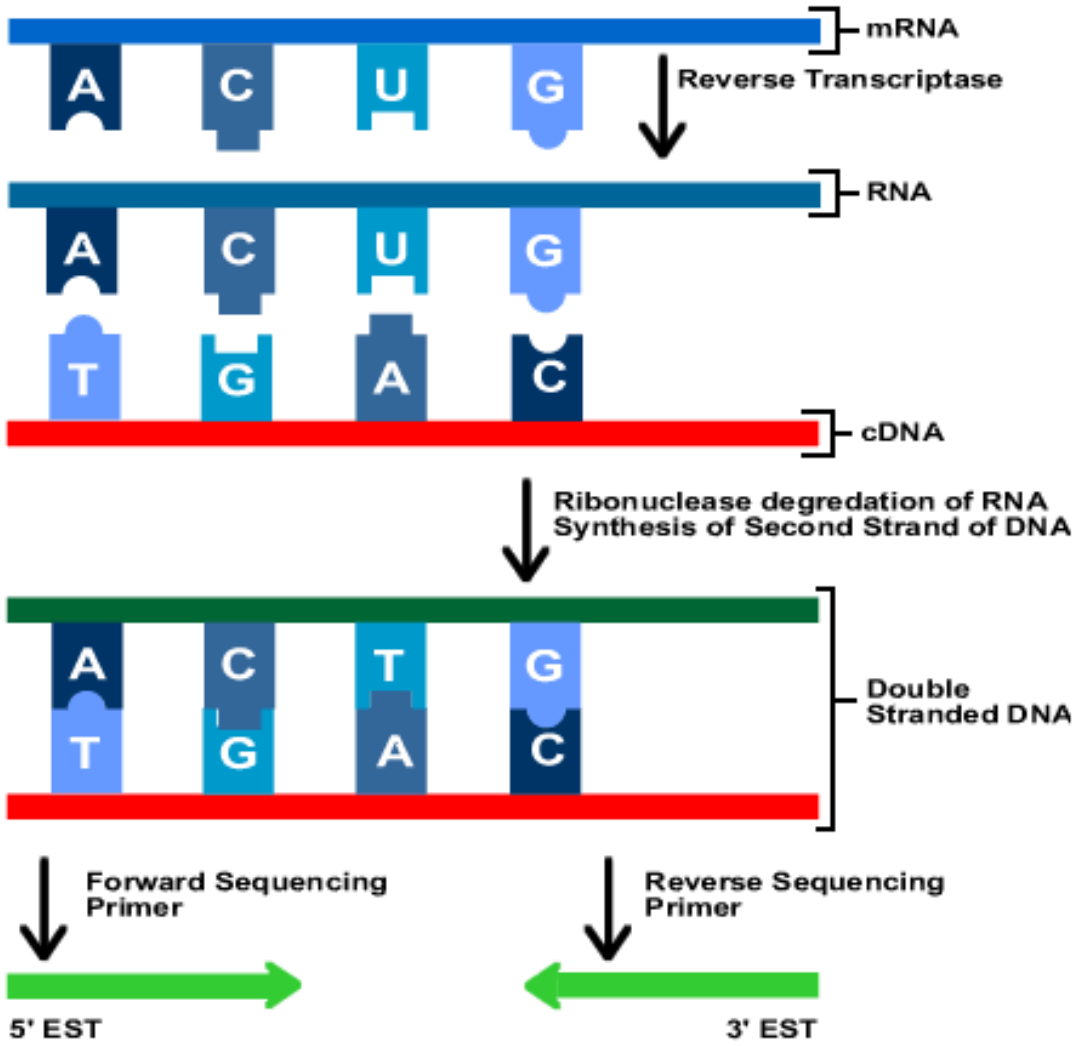
# ESQUEMA DEL PROCESO DE SINTESIS DE PROTEINAS



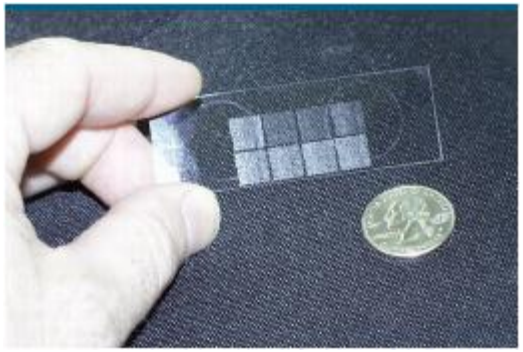

A Science Primer

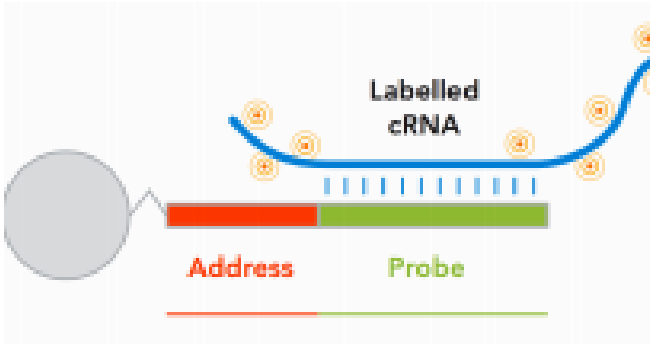
www.ncbi.nlm.nih.gov/About/primer/est.html

# ESQUEMA GENERAL DE OBTENCIÓN DE ESTs




www.ncbi.nlm.nih.gov/About/primer/est.html






# Laboratory Essentials

- Arrays
- Hybridization and Wash Equipment
- Scanner
- Software for processing array image
- Software for data analysis and display
- Bioinformatics collaborator

# MICROARREGLOS DE AND: diseño experimento

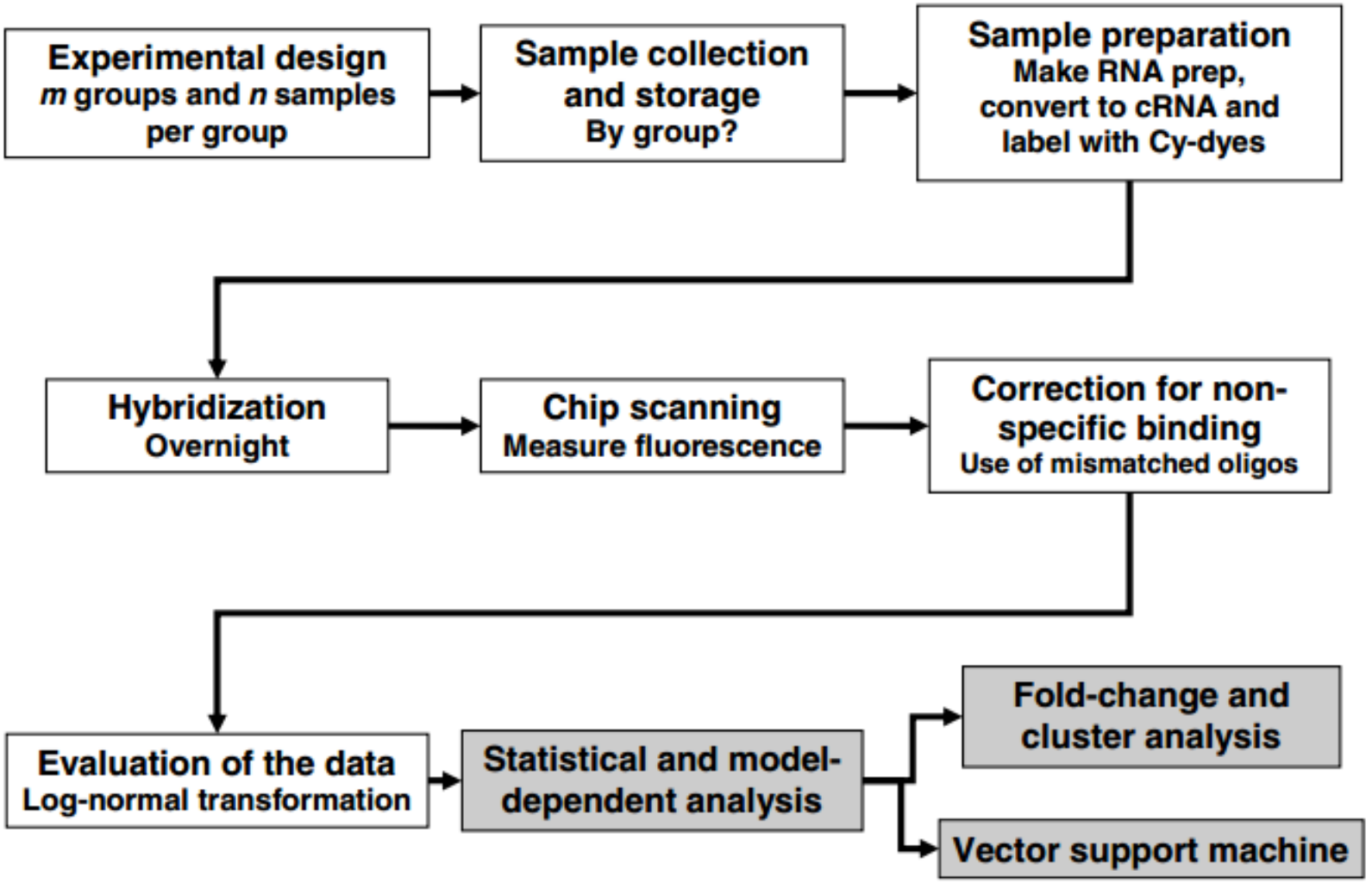



Figure 14.4. Steps in an experiment in DNA microarray analysis. This is the sequence of events used in most current methods reported in the literature.

*Nutritional Genomics: Discovering the Path to Personalized Nutrition*
Edited by Jim Kaput and Raymond L. Rodriguez 

# MICROARREGLOS DE AND: consideraciones estadísticas

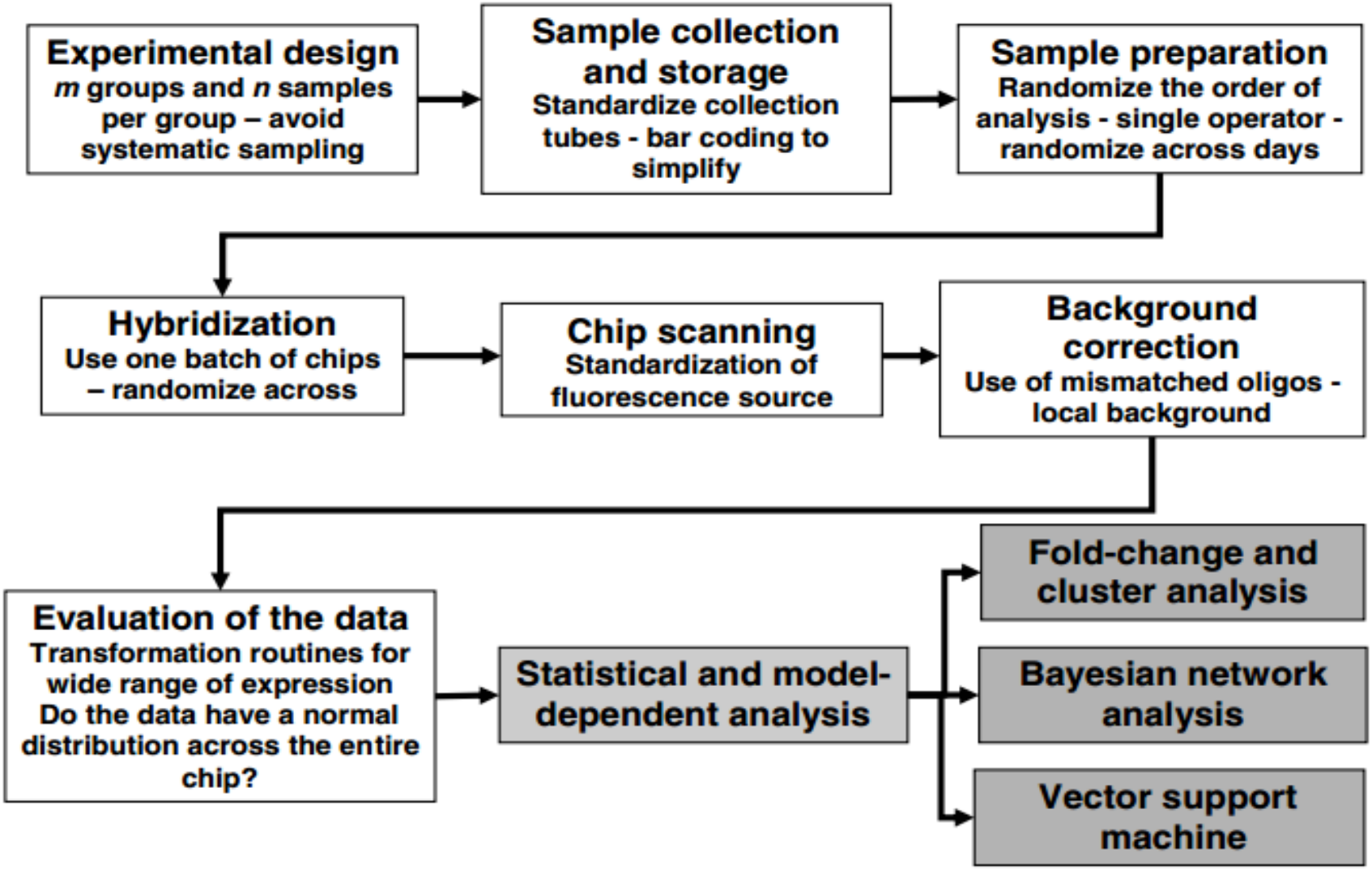



Figure 14.7. Optimizing the design of an experiment based on DNA microarray analysis. This is the suggested protocol for this type of analysis.

*Nutritional Genomics: Discovering the Path to Personalized Nutrition*
Edited by Jim Kaput and Raymond L. Rodriguez 

# Análisis de perfiles de expresión

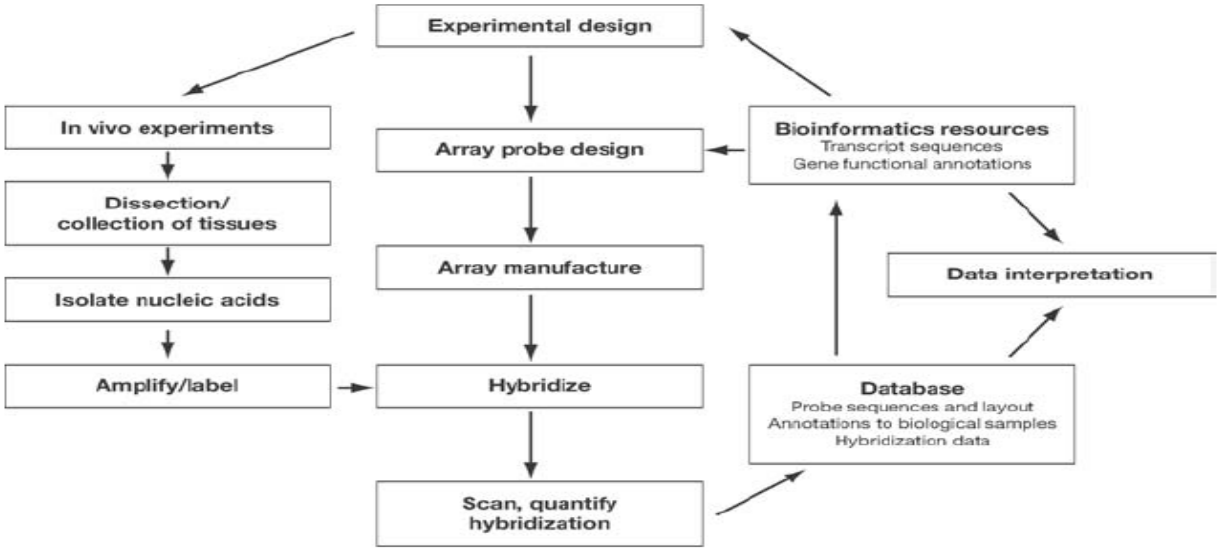



**Figure 2** Process flow for microarray experiments. Note that we have used the word "probe" to refer to the reporter sequence placed at a particular position on the microarray because it interrogates the sample for the presence of its reverse complement and also because the microarray market leader, Affymetrix, has adopted this definition. Historically probe has referred instead to the biological sample.

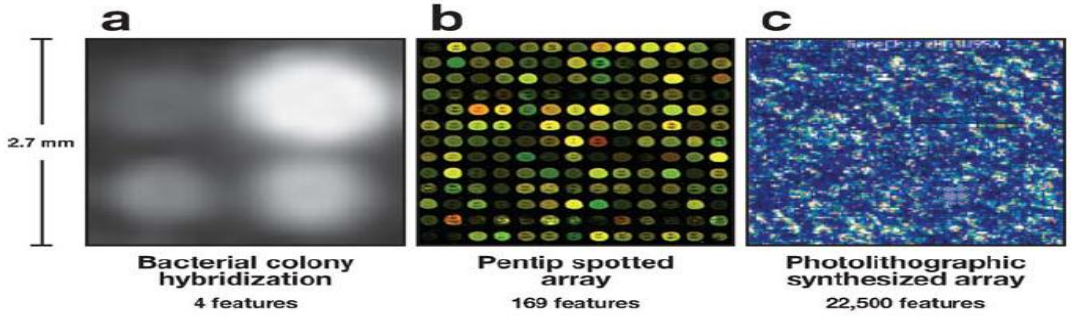



**Figure 3** Feature density of representative microarrays. Each image shows a 2.7 mm square subregion. (*a*) Bacterial colony spots on nylon from the 1980s. (*b*) Ink-jet in situ synthesized 60-mer oligo spots on glass. (*c*) Affymetrix human gene array with 18-$\mu$ features containing 25-mer oligos. Affymetrix chips now are available with 11-$\mu$ features.

Microarray Analysis, Paul Meltzer, NHGRI, Current Topics in Genome Analysis

Annu. Rev. Biochem. 2005. 74:53–82

# GENERACIÓN DE UNA COLECCIÓN DE UNIGENES

133,682 EST Genbank (release May 2009)
*Helianthus annuus L.*

↓

VecScreen
(http://www.ncbi.nlm.nih.gov/VecScreen/UniVec.html)

↓

Trimseq EMBOSS
(http://emboss.sourceforge.net/)

↓

28,089 singletons and 12,924 contigs = 41,013 unigenes
(CAP3 software: http://pbil.univ-lyon1.fr/cap3.php)

→

**Sunflower microarray**

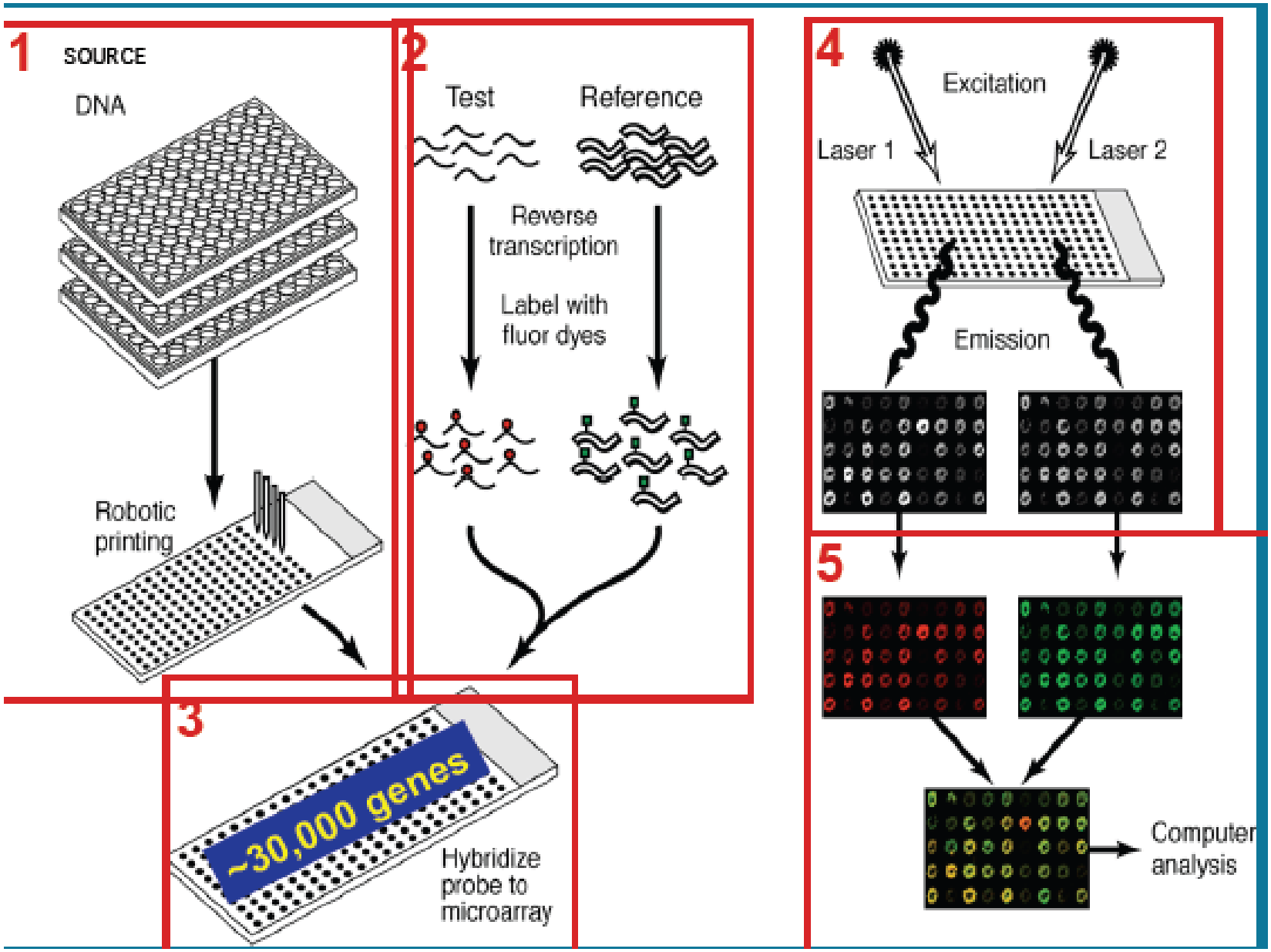
- 42,386 probes
- 74 specific control probes (10x: 740 controls)
- 1,417 Agilent controls

**OPA Assay**

- 384 SNP

↓

Functional annotation and KEGG mapping
(Blast2go software: www.blast2go.org)
20,352 unique sequences (~ 50% GO annotation)



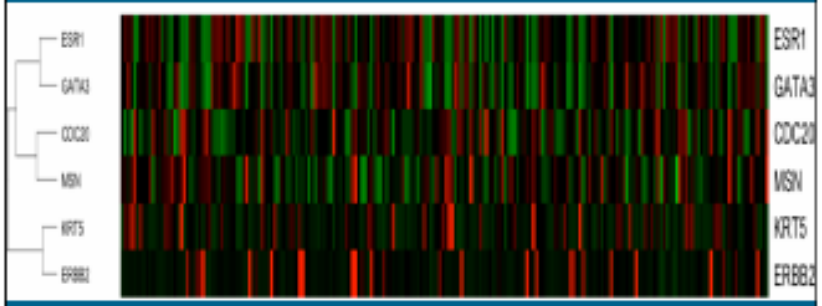

Microarray Analysis, Paul Meltzer, NHGRI, Current Topics in Genome Analysis

# EXPRESSION DATA ANALYSIS

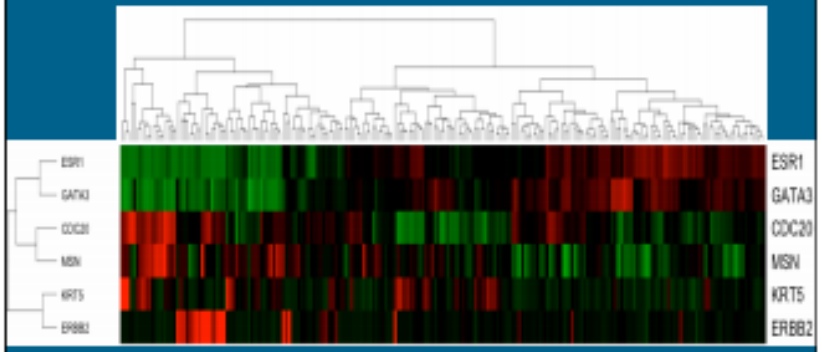
- Check quality of individual experiments
- **Preprocessing**
  - Normalization
  - Remove genes which are not accurately measured
  - Remove genes which are similarly expressed in all samples
- **Unsupervised Clustering**
  - How do genes and samples organize into groups?
  - Powerful method of data display.
  - Does not prove the validity of groups.
  - Clustered Samples Are Biologically Similar
  - Clusters of Co-expressed genes
    - May be functionally related
    - May be enriched for pathways

Microarray Analysis, Paul Meltzer, NHGRI, Current Topics in Genome Analysis

## CLUSTERING GENES ONLY



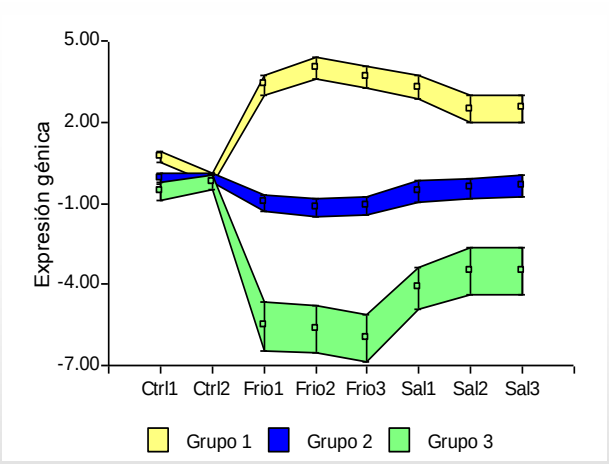

## CLUSTERING GENES AND SAMPLES



# Supervised Clustering

**What genes distinguish samples in selected groups from each other?**

- Choice of groups can be based on any known property of the samples.
- Many possible underlying methods: t-test or F-statistic frequently used.
- Output includes ranked gene list.
- Leads to the development of classifiers which can be applied to unknown samples.
- Must address the problem of false discovery due to multiple comparisons and discrepancy between sample/gene numbers.



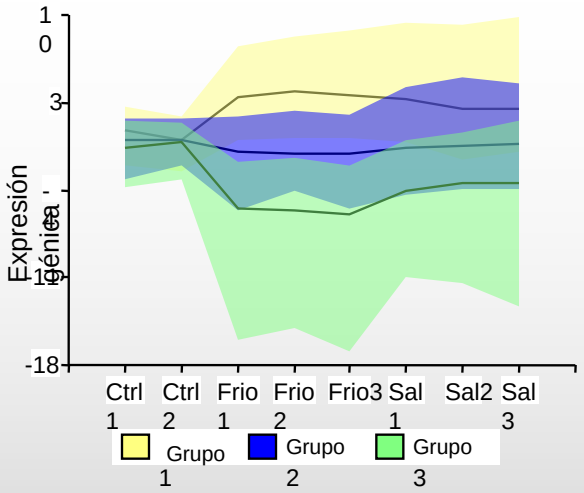




**Figura 1. Bandas del confianza al 95% (a) y bandas de predicción al 95% (b) para cada uno de tres grupos de genes agrupados por el algoritmo *k-centroides* de clasificación no supervisada aplicado a la matriz de expresiones génicas (CH1 y CH2 corresponden a las repeticiones biológicas del control, FH1, FH2 y FH3 las repeticiones del tratamiento con frío y SH1, SH2 y SH3 las correspondientes repeticiones del tratamiento salino).**

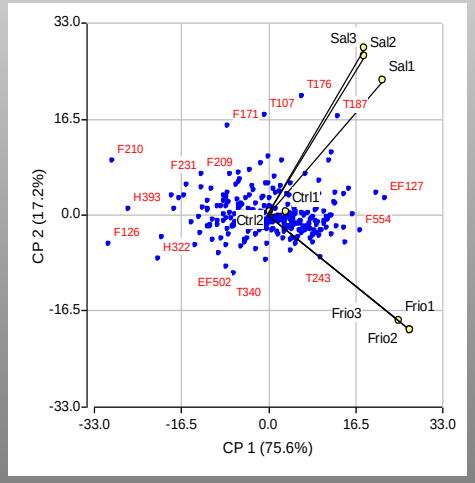
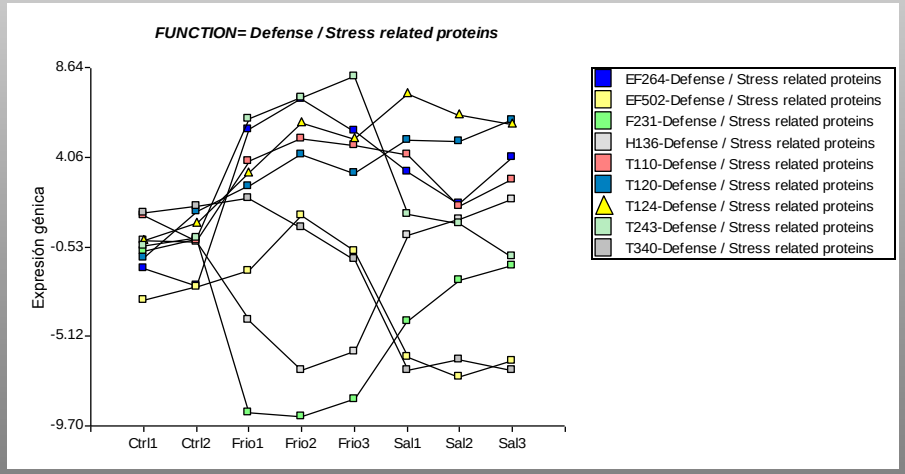



**Figura 2: Bi-plot mostrando los genes como puntos azules en el planto y las medias de tratamientos: Control (Ctrl), Frío (Frío) y Salinidad (Sal) conectadas al origen mostrando el sentido e intensidad relativa de la asociación con la expresión de los genes.**




Figuras xx – Perfiles de expresión por función génica hipotética

*Fernández y col. 2008, BMC Plant Biology, 8:11*

# MICROARREGLOS DE ADN

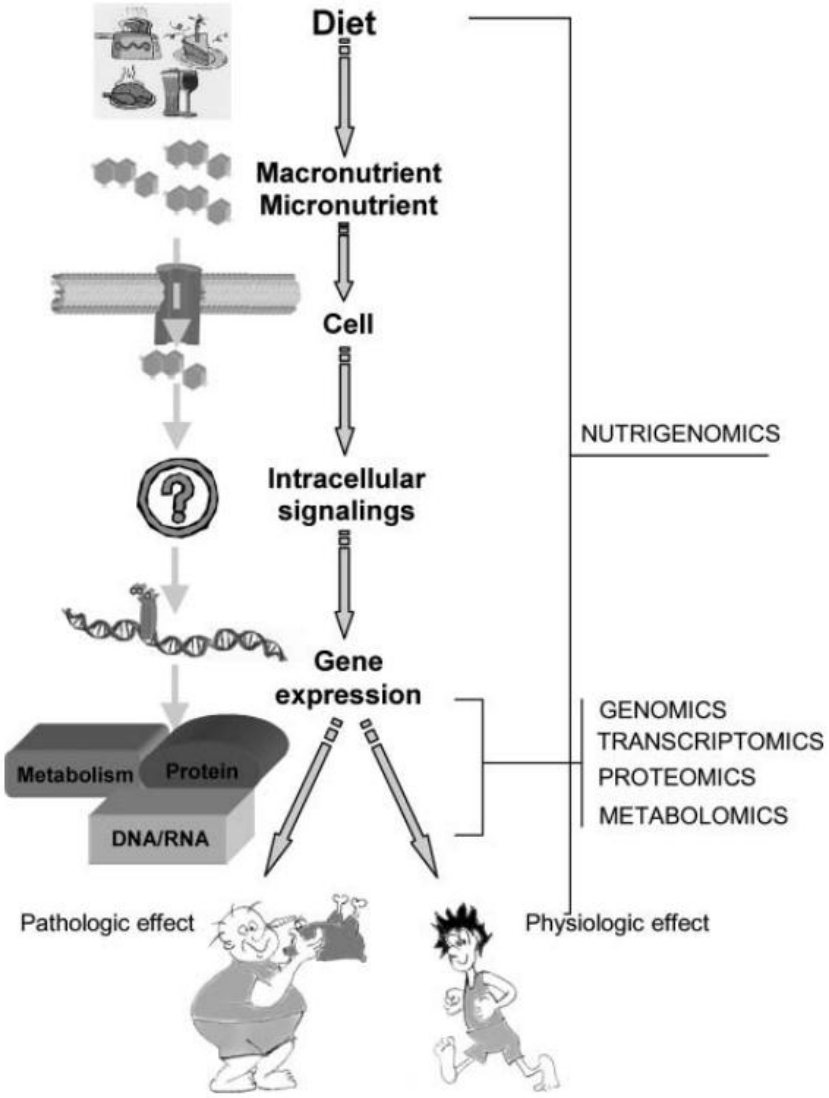
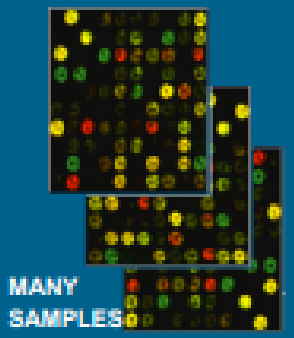
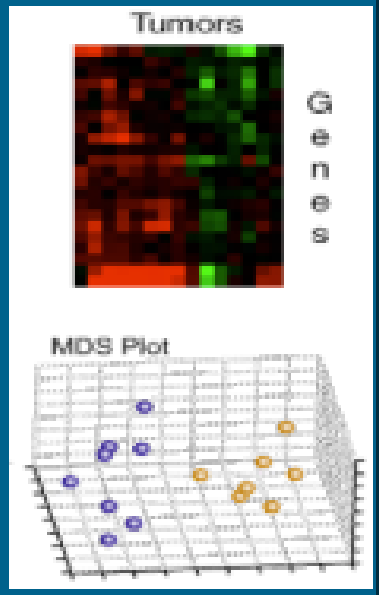



**Figure 2** Flow chart representing the different steps involved in gene expression, the stages at which diet can modulate these processes, the functional genomics techniques used to analyze each stage, and their effects on human health.

# GENOMICS FROM BENCH TO BEDSIDE

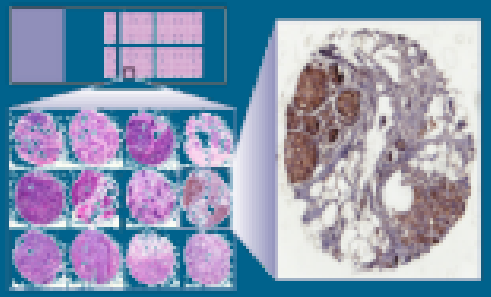
## WHOLE GENOME

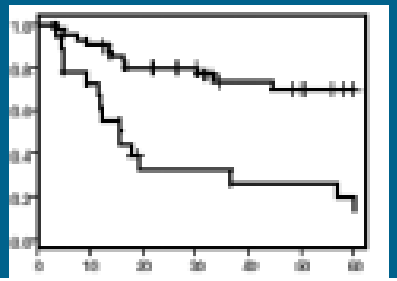



## GENE SELECTION

## GENE VALIDATION





## ASSAY DEVELOPMENT

## MICROARRAY STUDIES GENERATE ORGANIZED LIST OF GENES

- Often cryptic and hard to interpret.
- Hypothesis generating, but this is often rather subjective.
- Seldom provide strong evidence for a specific mechanism.
- Expression data is intrinsically limited.

## GETTING BEYOND GENE LISTS

- Optimal use of gene annotations.
  - Gene Ontology
    (http://david.abcc.ncifcrf.gov/)
- Optimizing use of public data.
  - GEO, ARRAY EXPRESS, ACADEMIC DATA
  - GENE SIGNATURE BASED METHODS (Gene Set Enrichment Analysis).

# Publishing Expression Data

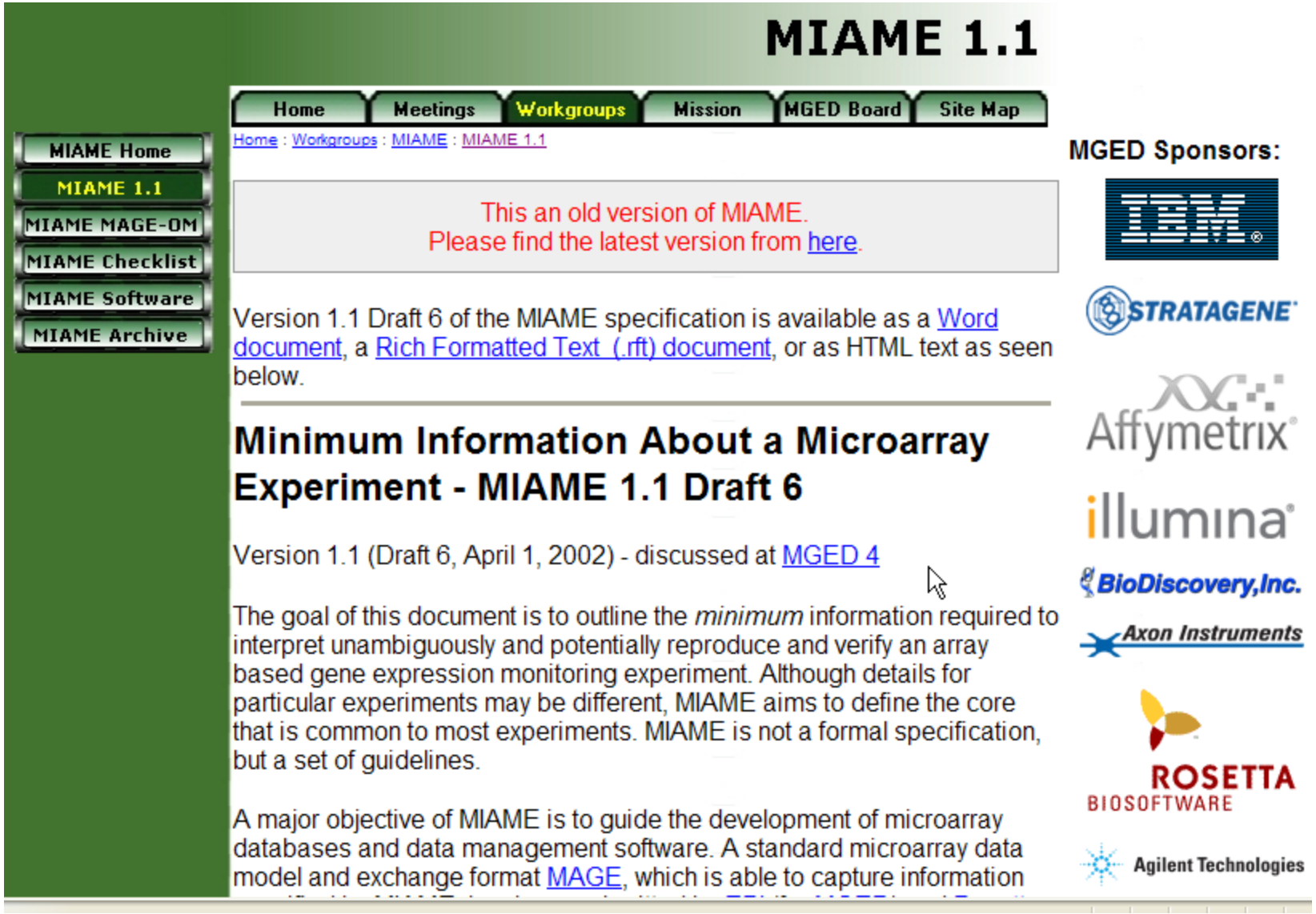
•MIAME standard

Minimum Information about a Microarray Experiment

- Format required by many journals
- Essential for database submissions

http://www.mged.org/Workgroups/MIAME/miame.html

# Protocolos Estandarizados




http://www.mged.org/Workgroups/MIAME/miame_1.1.html

# Accessing Expression Data

- Individual Lab and Journal Sites


# Accessing Expression Data

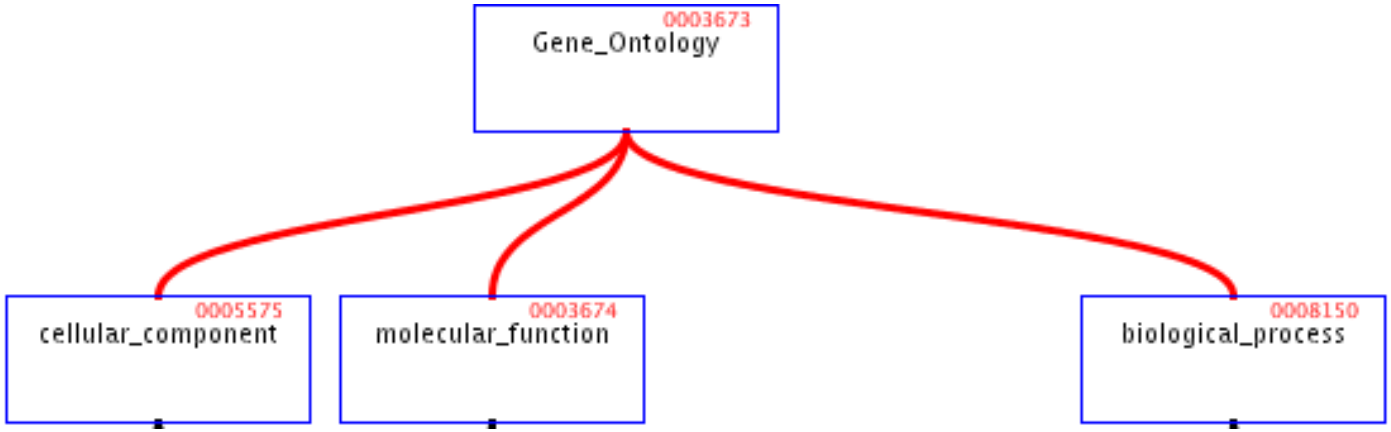
# GETTING BEYOND GENE LISTS

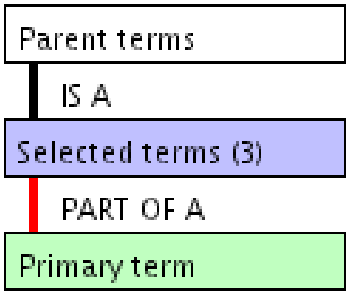
- Optimal use of gene annotations.
  - Gene Ontology
    (http://david.abcc.ncifcrf.gov/)
- Optimizing use of public data.
  - GEO, ARRAY EXPRESS, ACADEMIC DATA
  - GENE SIGNATURE BASED METHODS (Gene Set Enrichment Analysis).

# Gene Ontology (GO)

- El proyecto de Gene Ontology (GO) busca crear descripciones consistentes de productos de genes provenientes de diferentes bases de datos
- Se han desarrollado 3 ontologías (vocabularios controlados y estructurados):
  - Procesos biológicos
  - Funciones moleculares
  - Componentes celulares
- El uso de términos GO en diferentes bases de datos uniformiza las búsquedas en ellas
- Diferentes niveles

# Gene Ontology (GO)




- 3 ontologías
- 2 clases de relaciones

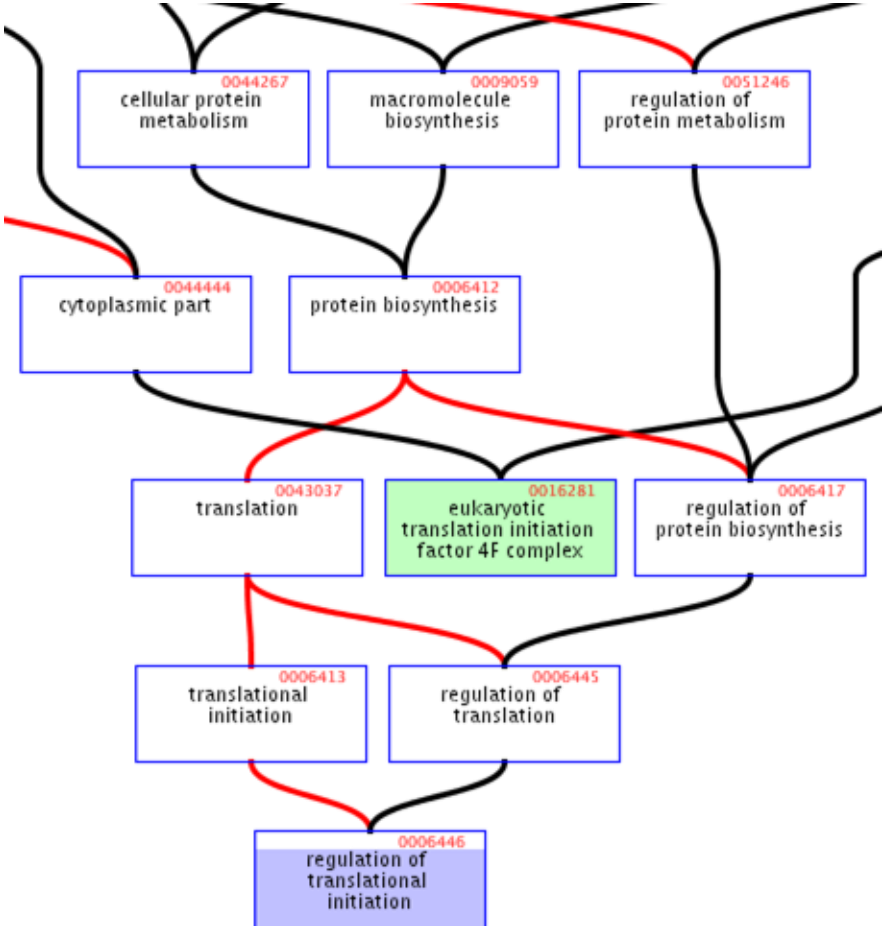
*is_a* represents an instance of
A mitotic chromosome *is_a* instance of a chromosome
*part_of*
A telomere is part_of a chromosome



**nature genetics • volume 25 • may 2000**

# Gene Ontology (GO)

- Diferentes relaciones
- Un nodo puede tener más de un padre
- Diferentes niveles de especificidad
- Un nodo puede encontrares en diferentes niveles al mismo tiempo



2008 International Conference on BioMedical Engineering and Informatics

# NutriGeneOntology: A Biomedical Ontology for Nutrigenomics Research

May 27-May 30
ISBN: 978-0-7695-3118-2

**Antonio Fabregat**
**Mar? Arregui**
**Elisabet Barrera**
**Olga Portol?**
**Dolores Corella**
**Oscar Coltell**

DOI Bookmark: http://doi.ieeecomputersociety.org/10.1109/BMEI.2008.315

## ABSTRACT

Currently, in Nutritional Genomics it is crucial to have computing models and solutions and technological platforms in order to support acquisition, storage, management and presentation of all the information generated. Our aim is to build a biomedical ontology in order to formalise and integrate genomic, environmental and phenotypic data applied to Nutritional Genomics research focused on cardiovascular diseases and related phenotypes. Four different food composition tables have been employed to estimate the amount of nutrients provided by the diet. Web engineering technologies have been applied for constructing the Web platform containing the ontology, which integrates three distinct ontologies offering the corresponding models and services: food composition table alignment, gene-environment interaction, and cardiovascular risk estimation

# RNA-seq

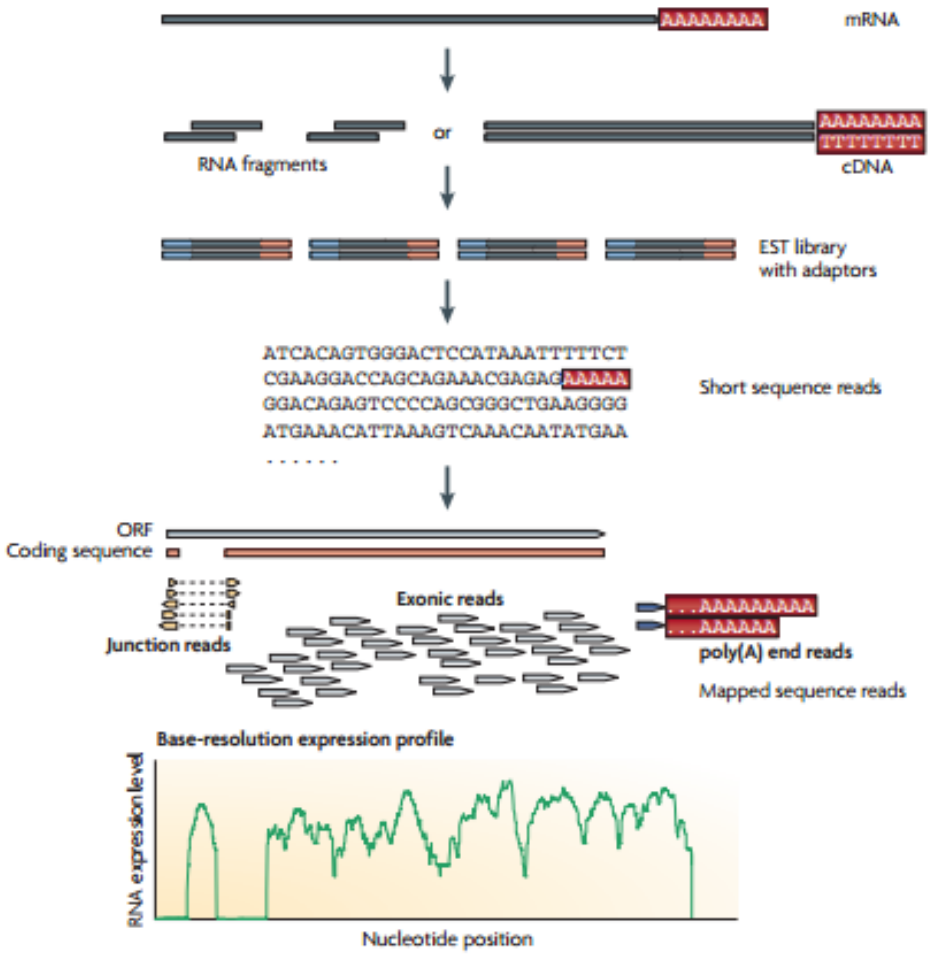
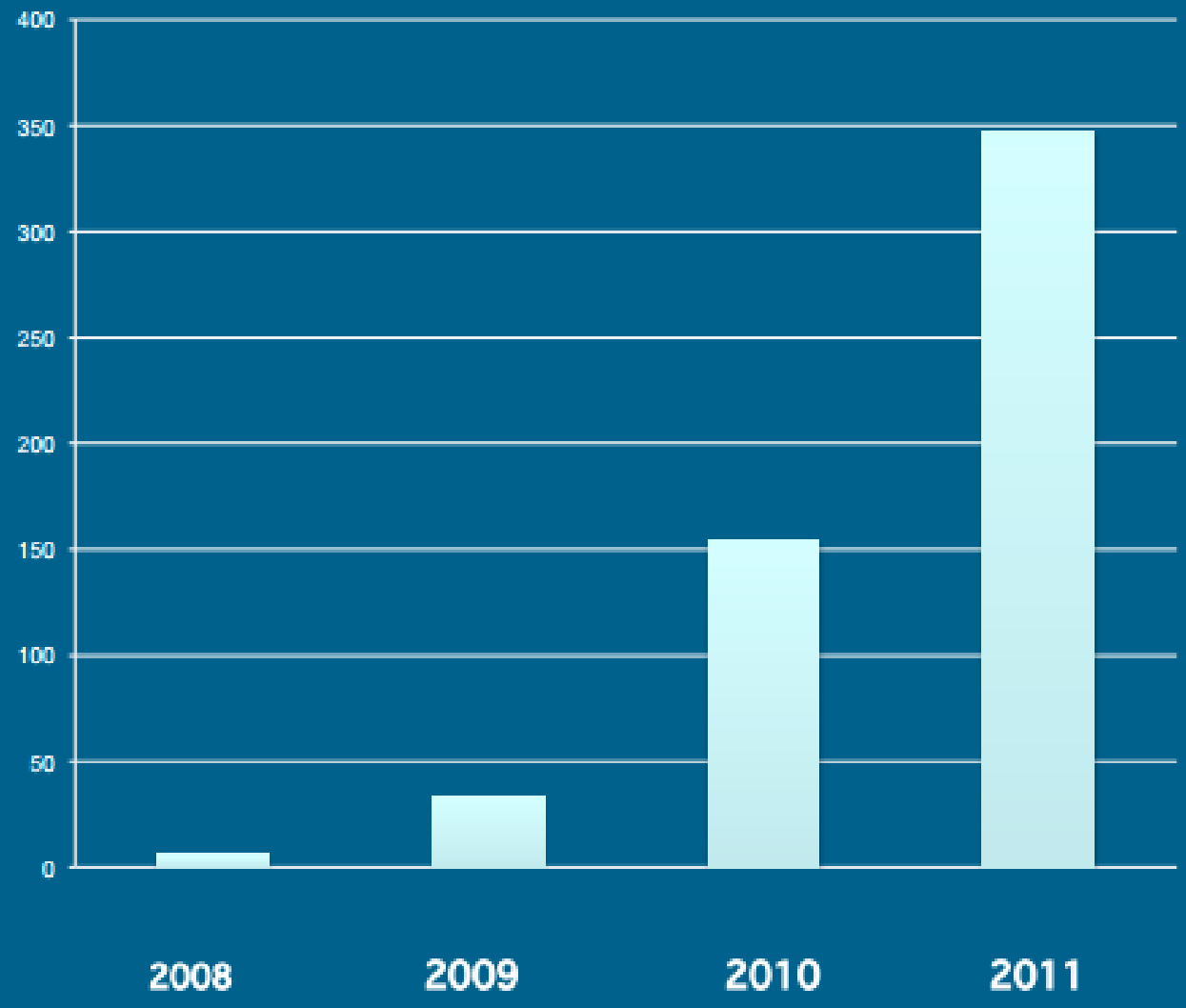



Figure 1 | **A typical RNA-Seq experiment.** Briefly, long RNAs are first converted into a library of cDNA fragments through either RNA fragmentation or DNA fragmentation (see main text). Sequencing adaptors (blue) are subsequently added to each cDNA fragment and a short sequence is obtained from each cDNA using high-throughput sequencing technology. The resulting sequence reads are aligned with the reference genome or transcriptome, and classified as three types: exonic reads, junction reads and poly(A) end-reads. These three types are used to generate a base-resolution expression profile for each gene, as illustrated at the bottom; a yeast ORF with one intron is shown.

# PubMed Citations for RNA-Seq



# ARRAYS VS. NEXT GENERATION SEQUENCING

## PROS

### MICROARRAYS

- READILY AVAILABLE MATURE TECHNOLOGY
- RELATIVELY INEXPENSIVE
- EFFECTIVE WITH VERY COMPLEX SAMPLES
- HUNDREDS OF SAMPLES PRACTICAL
- CAN TARGET SUBSET OF GENOME

### SEQUENCING

- WHOLE GENOME DATA
- RELATIVELY UNIFORM ANALYTICAL PIPELINE
- FREE OF HYBRIDIZATION ARTIFACTS
- POSSIBILITY OF ONE PLATFORM FOR ALL APPLICATIONS

## CONS

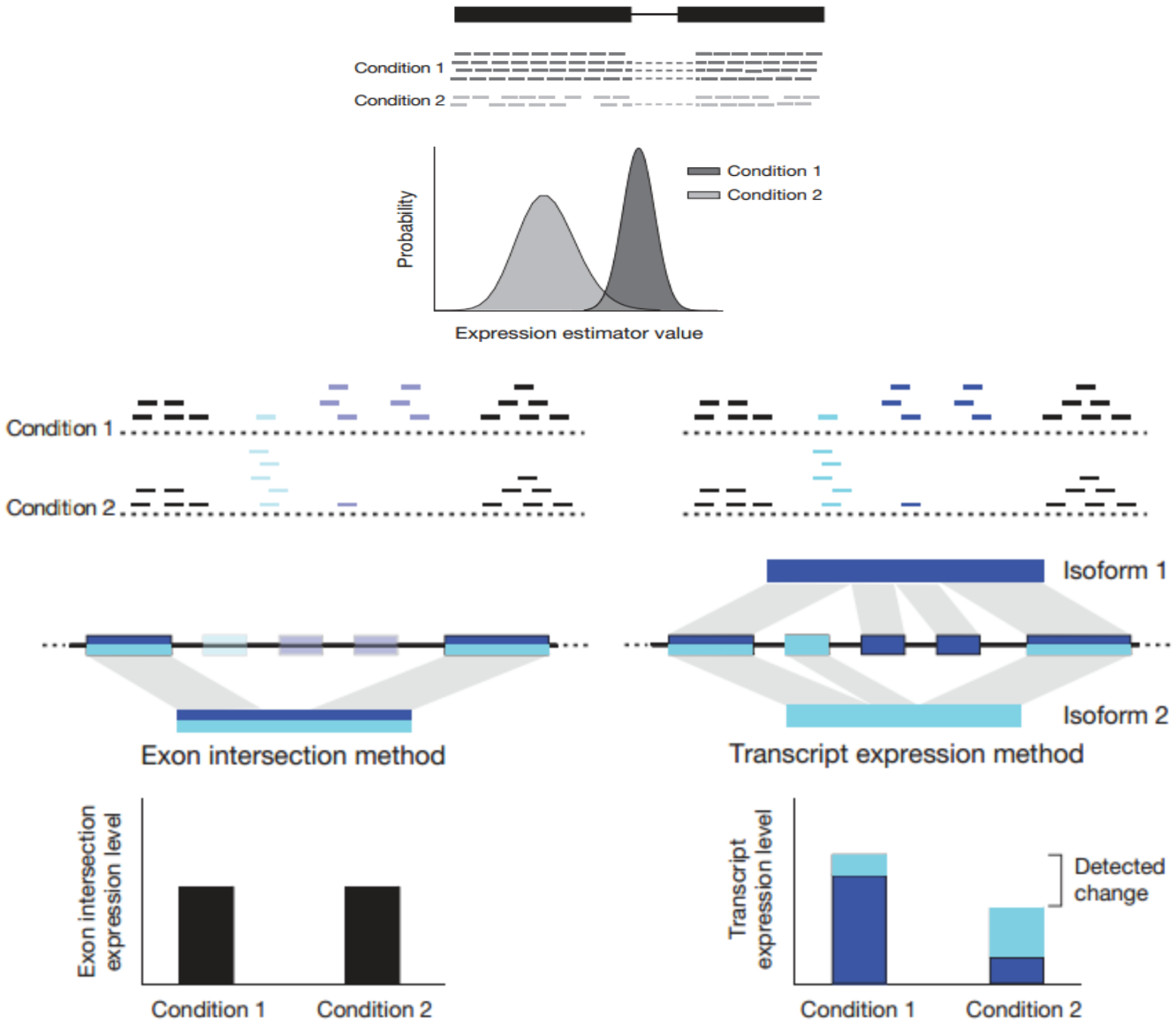
### MICROARRAYS

- REQUIRE PLATFORM AND APPLICATION SPECIFIC DATA PROCESSING
- PRONE TO PLATFORM SPECIFIC ARTIFACTS
- MANY SOURCES OF NOISE
- WHOLE GENOME STUDIES GENERALLY REQUIRE MANY ARRAYS, INCREASING SAMPLE REQUIREMENTS AND COMPLICATING ANALYSIS

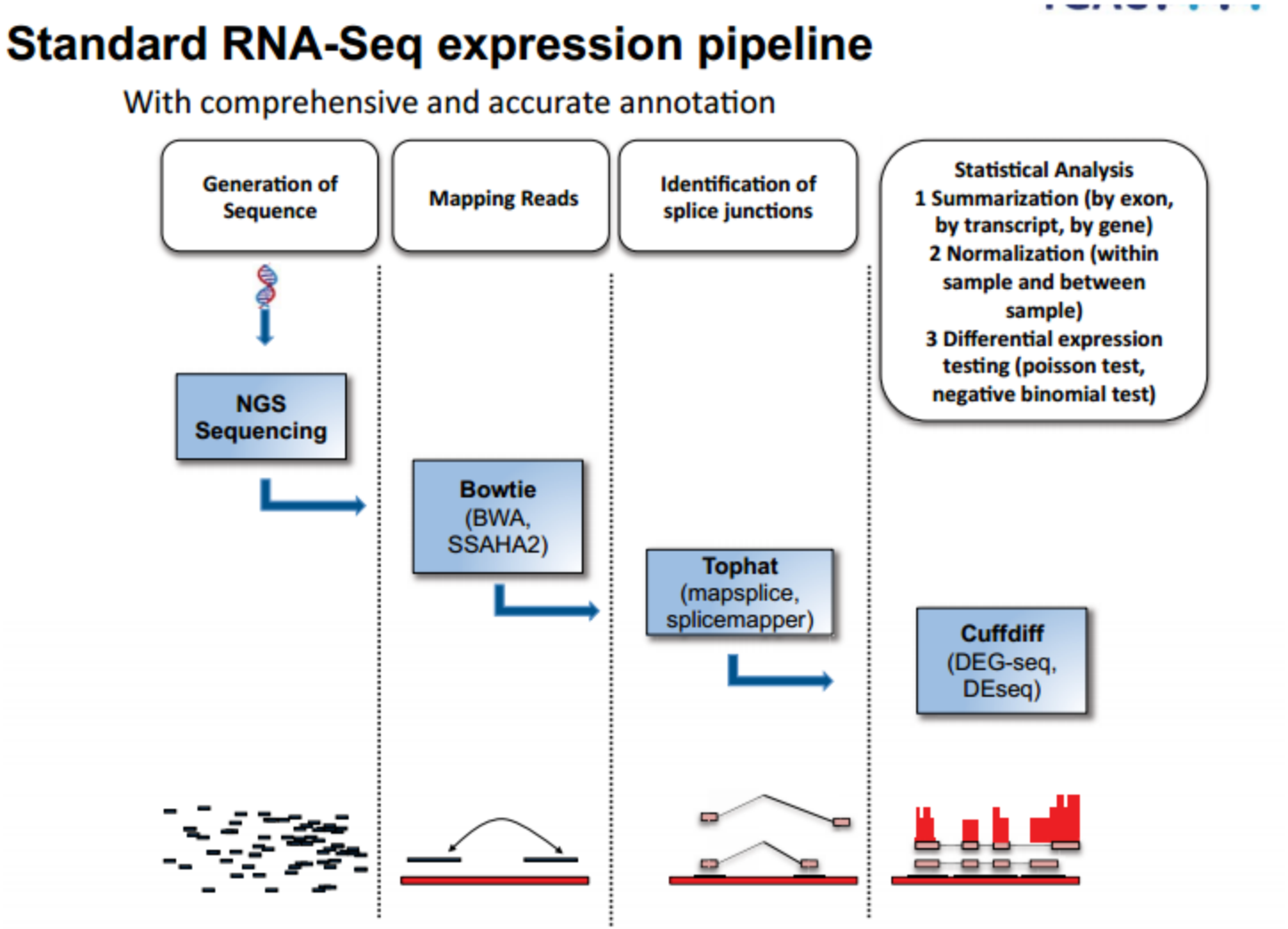
### SEQUENCING

- IMMATURE TECHNOLOGY
- TECHNOLOGY SPECIFIC ARTIFACTS
- RESOURCE INTENSIVE
- COMPUTATIONALLY INTENSIVE
- NO STANDARD ANALYSIS YET
- LOWER SAMPLE THROUGHPUT

# EXPRESION DIFERENCIAL DE GENES BASADOS EN NUEVAS TECNOLOGIAS DE SECUENCIACIÓN: RNA-SEQ



# RNA-seq


Standard RNA-Seq expression pipeline
With comprehensive and accurate annotation
Generation of Sequence
Mapping Reads
Identification of splice junctions
Statistical Analysis
1 Summarization (by exon, by transcript, by gene)
2 Normalization (within sample and between sample)
3 Differential expression testing (poisson test, negative binomial test)
NGS Sequencing
Bowtie (BWA, SSAHA2)
Tophat (mapsplice, splicemapper)
Cuffdiff (DEG-seq, DEseq)

# RNA-seq: technical variability and sampling

Lauren M McIntyre[1*], Kenneth K Lopiano[2], Alison M Morse[1], Victor Amin[1], Ann L Oberg[3], Linda J Young[2] and Sergey V Nuzhdin[4]

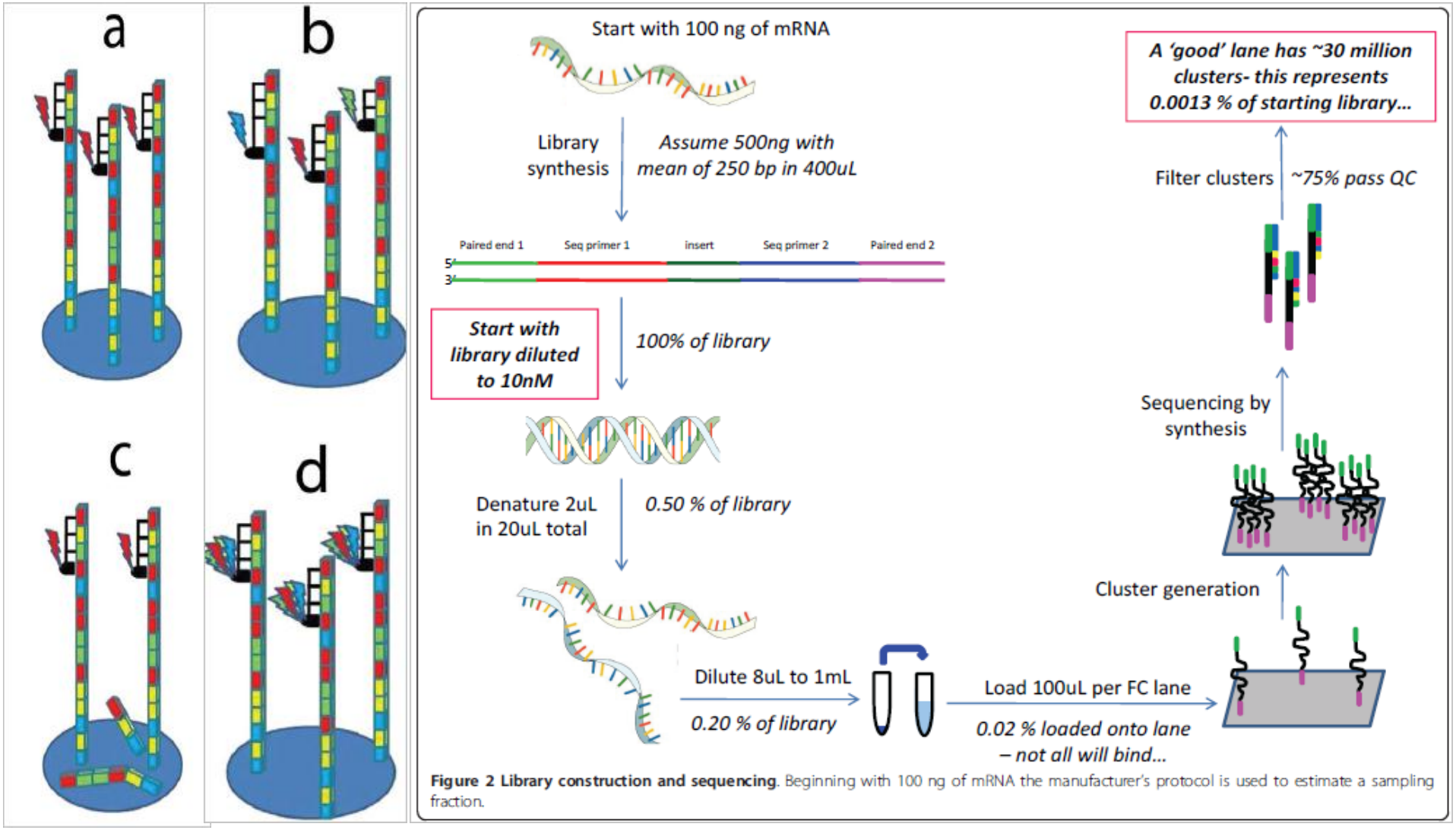



**Figure 2 Library construction and sequencing**. Beginning with 100 ng of mRNA the manufacturer's protocol is used to estimate a sampling fraction.

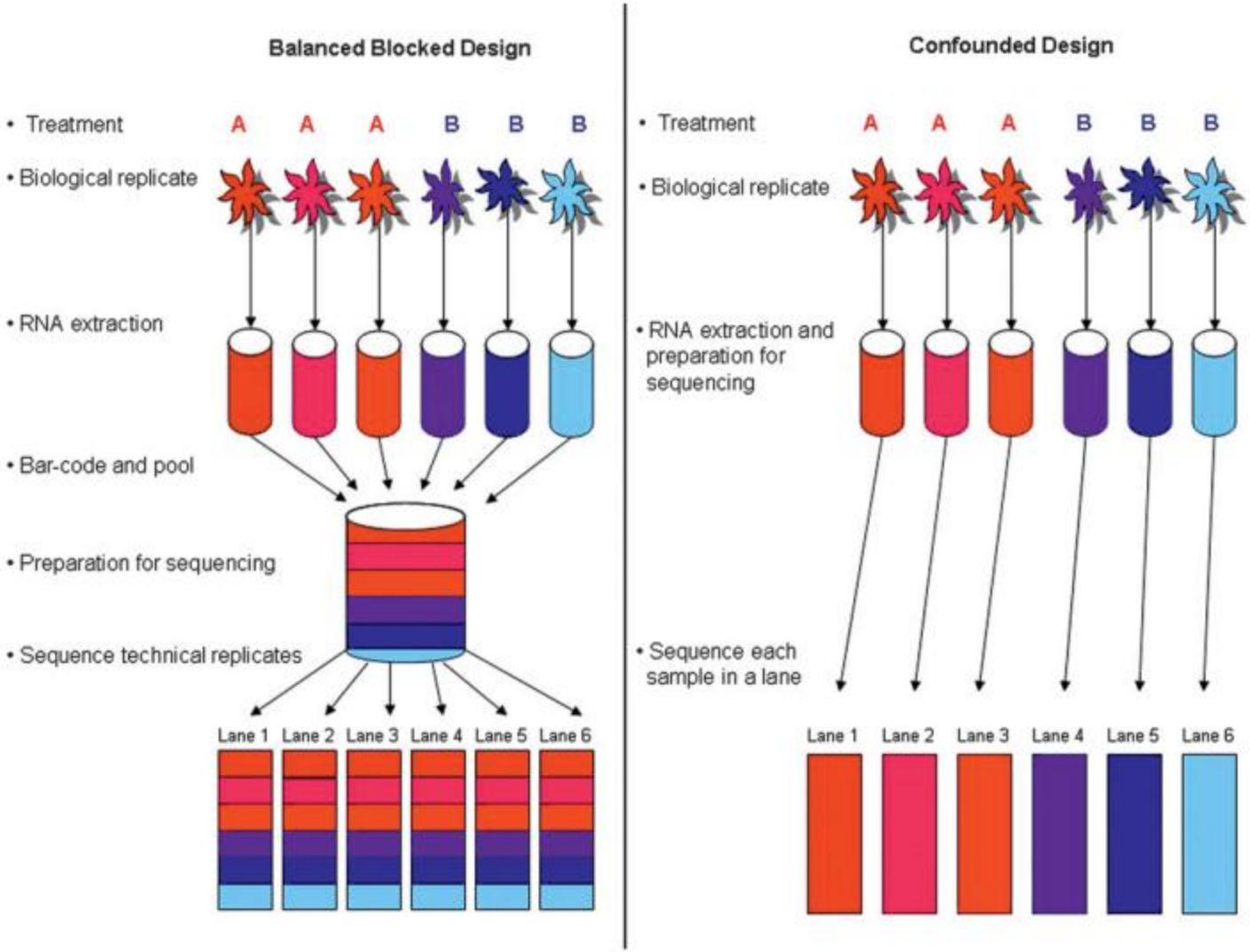
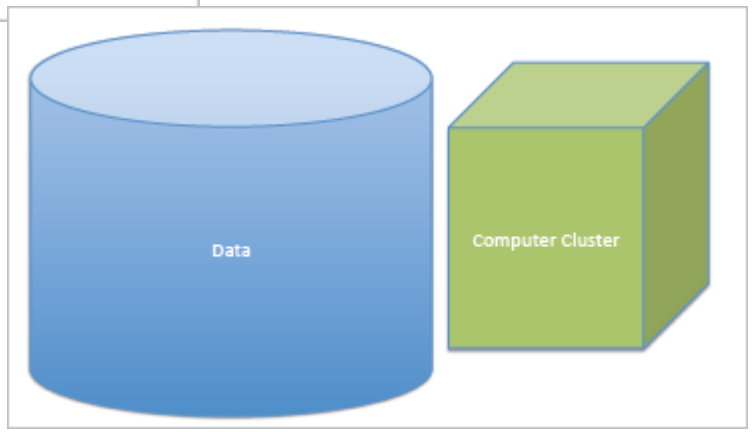



FIGURE 4.—Comparison of two designs for testing differential expression between treatments A and B. Treatment A is denoted by red tones and treatment B by blue tones. In the ideal balanced block design (left), six samples ($m = 6$) are bar coded, pooled, and processed together. The pool is then divided into six equal portions that are input to six lanes ($L = 6$) of the flow cell. Bar coding in the balanced block design results in six technical replicates ($T = 6$) of each sample, while balancing batch and lane effects and blocking on lane. The balanced block design also allows partitioning of batch and lane effects from the within-group biological variability. The confounded design (right) represents a typical RNA-Seq experiment and consists of the same six samples, with no bar coding, and does not permit partitioning of batch and lane effects from the estimate of within-group biological variability.

 DOI: 10.1534/genetics.110.114983

# ALMACENAMIENTO Y ANALISIS DE DATOS




THOMAS POROSTOCKY

# Nutrigenetics: The Relevance of Polymorphisms

*Susan E. McCann, Michelle R. Roberts, Mary E. Platek, and Christine B. Ambrosone*

**SNP Discovery by Massively Parallel Transcriptome Resequencing in Sunflower and Development of a Bioinformatic Pipeline and Database for Mining and Displaying SNPs in Next-Generation Sequence Assemblies**

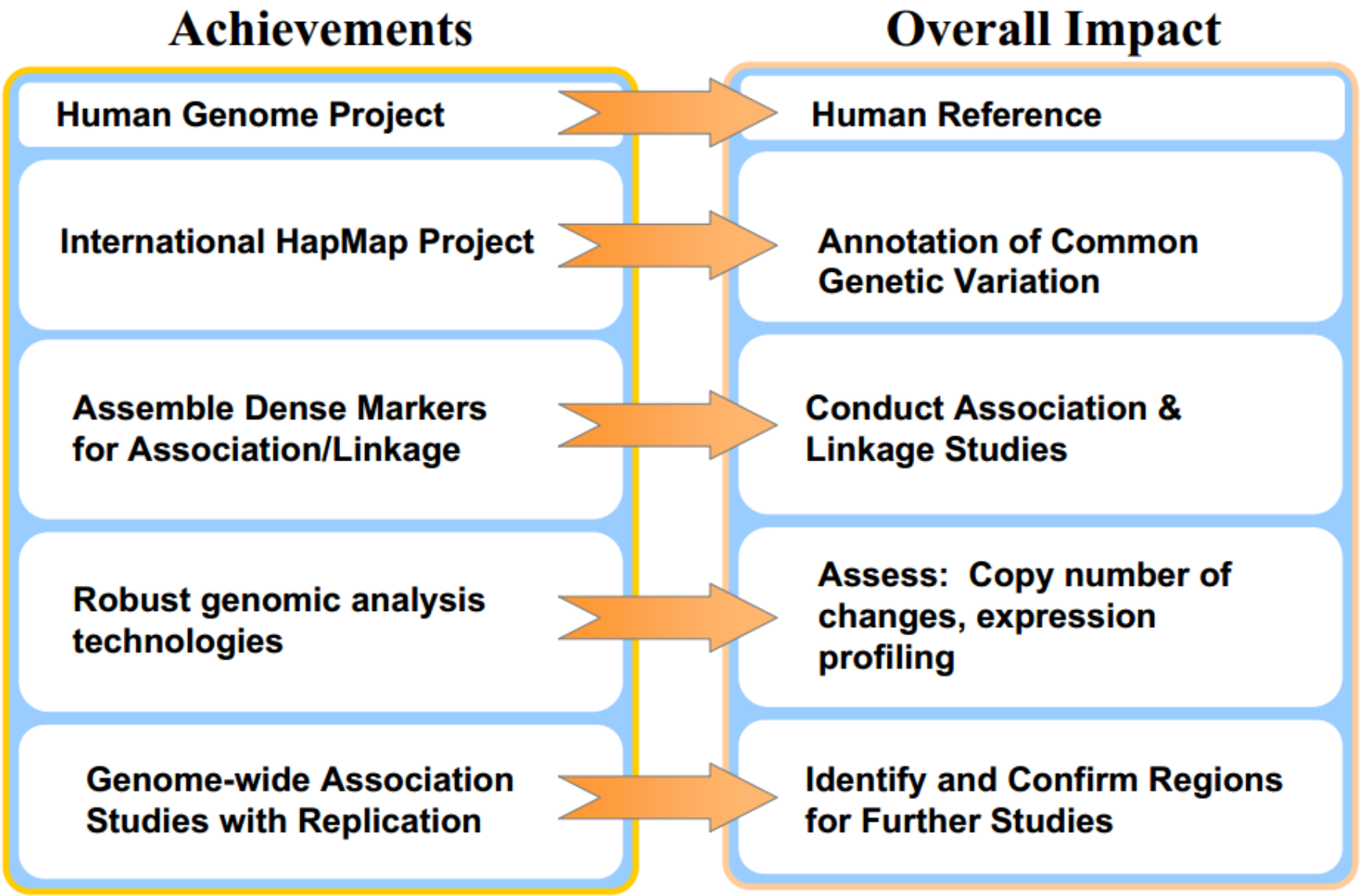
# Nutrigenetics: The Relevance of Polymorphisms

## Key Points

1. Nutrigenetics has been defined as "an integrated framework that simultaneously examines genetics and associated polymorphisms with diet-related diseases" and may lead to a better understanding of how diet may influence cancer risk.
2. Nutrigenetics enables us to better understand mechanisms of action of numerous food components in relation to cancer risk, and to better clarify risk relationships by focusing on those most likely to be impacted based upon genetics.
3. Single nucleotide polymorphisms (SNP) can change the structure, function, and cellular content of a specific protein. If the SNPs are harbored in genes involved in the metabolism of drugs, environmental agents, or dietary components, then they may greatly affect how an individual responds to specific exposures.
4. Fruits and vegetables are sources of many bioactive food components that possess anticarcinogenic properties, and the intake of specific bioactive components found in fruits and vegetables modulate the relationship between genetic variants and cancer risk.
5. Individuals with defective endogenous protection from oxidative stress may benefit from dietary antioxidants. Conversely, the intake of fruits and vegetables may have little impact on cancer risk in subjects with higher endogenous antioxidant potential.
6. It should be noted that regardless of one's genotype a balanced diet high in fruits, vegetables, and whole grains and low in meat and fats may be beneficial for overall health and well-being and prevention of numerous diseases other than cancer.

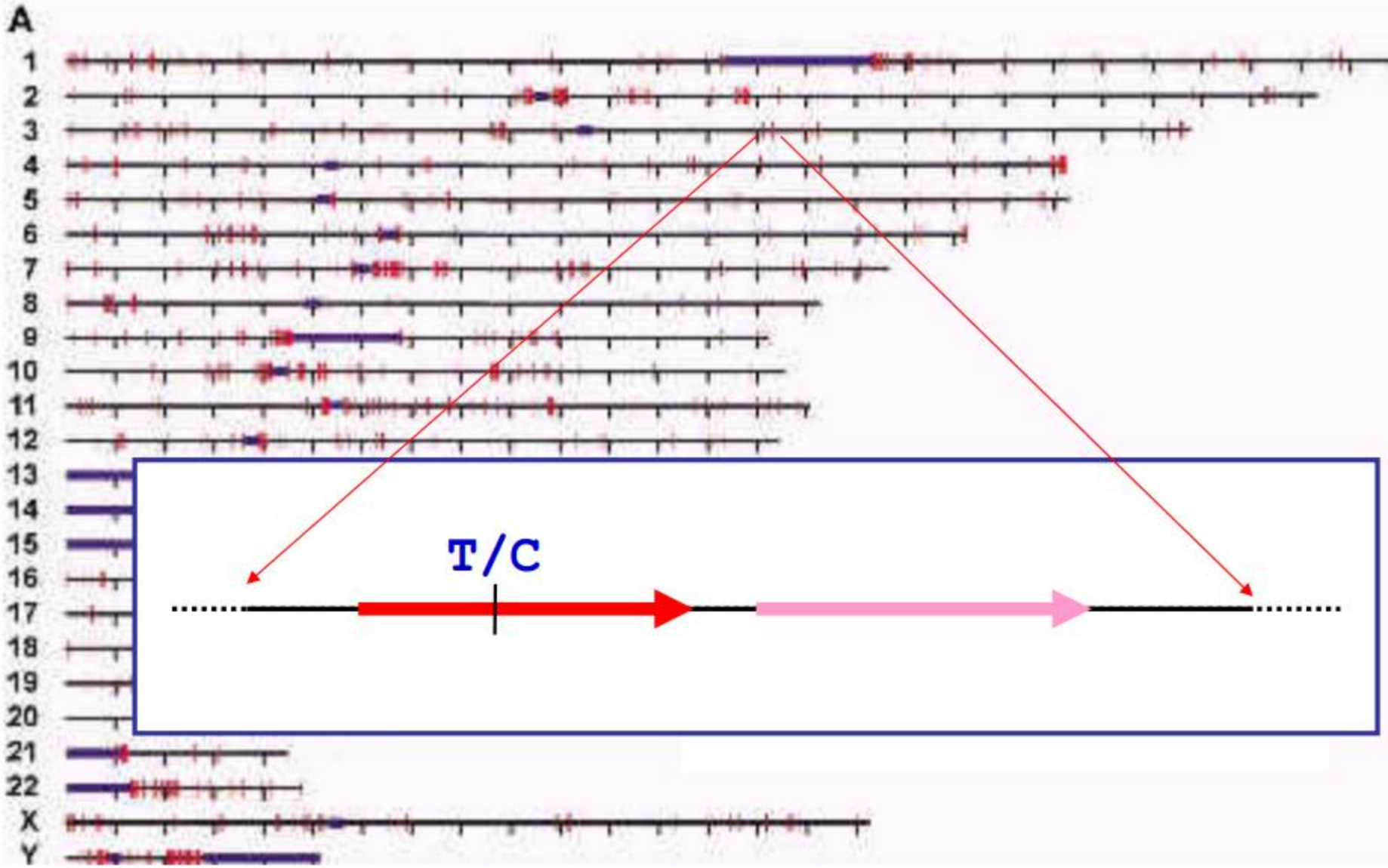
From: *Nutrition and Health: Bioactive Compounds and Cancer*
Edited by: J.A. Milner, D.F. Romagnolo, DOI 10.1007/978-1-60761-627-6_4,

# Milestones in Human Genomics & Disease Susceptibility

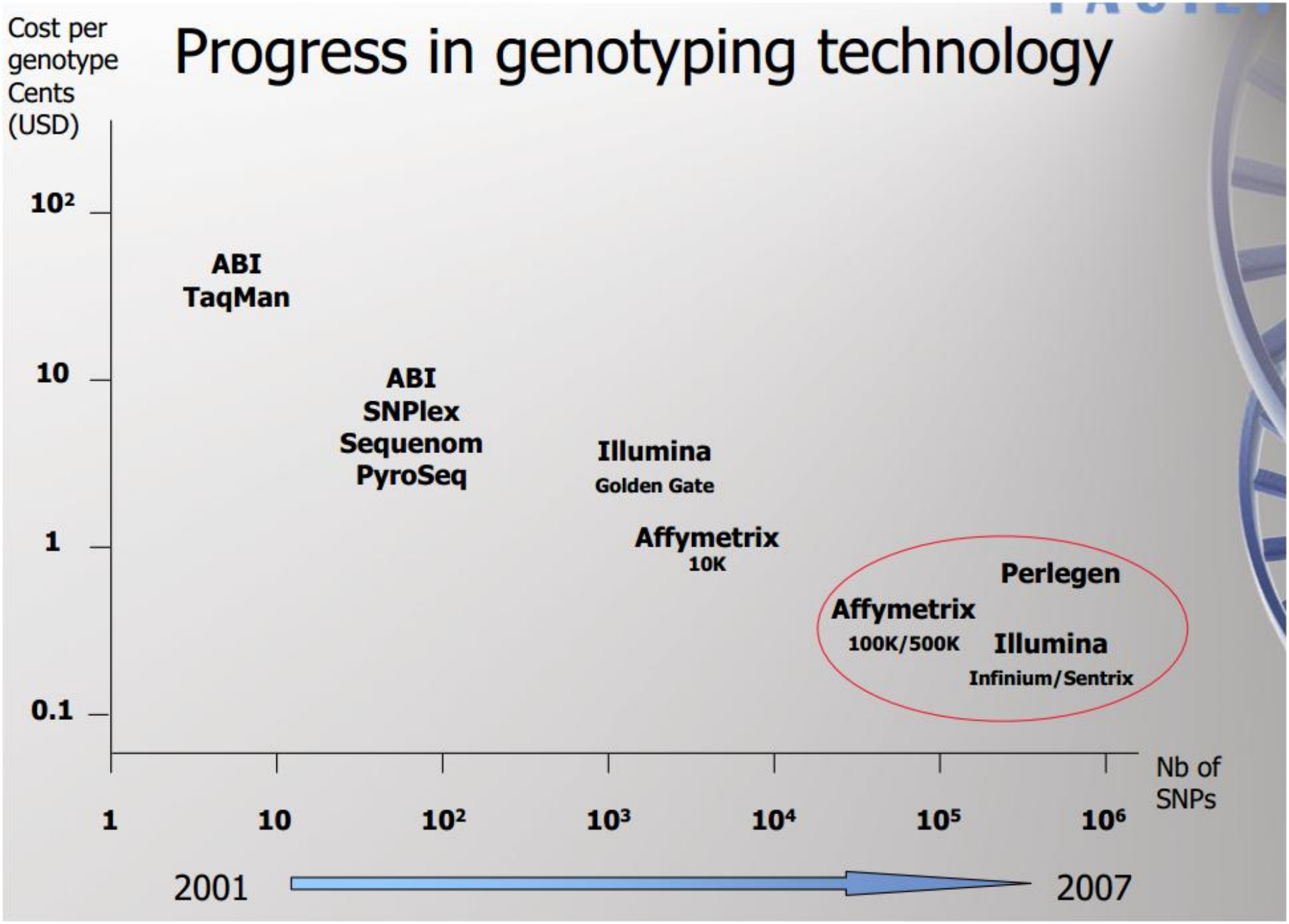



Stephen Chanock

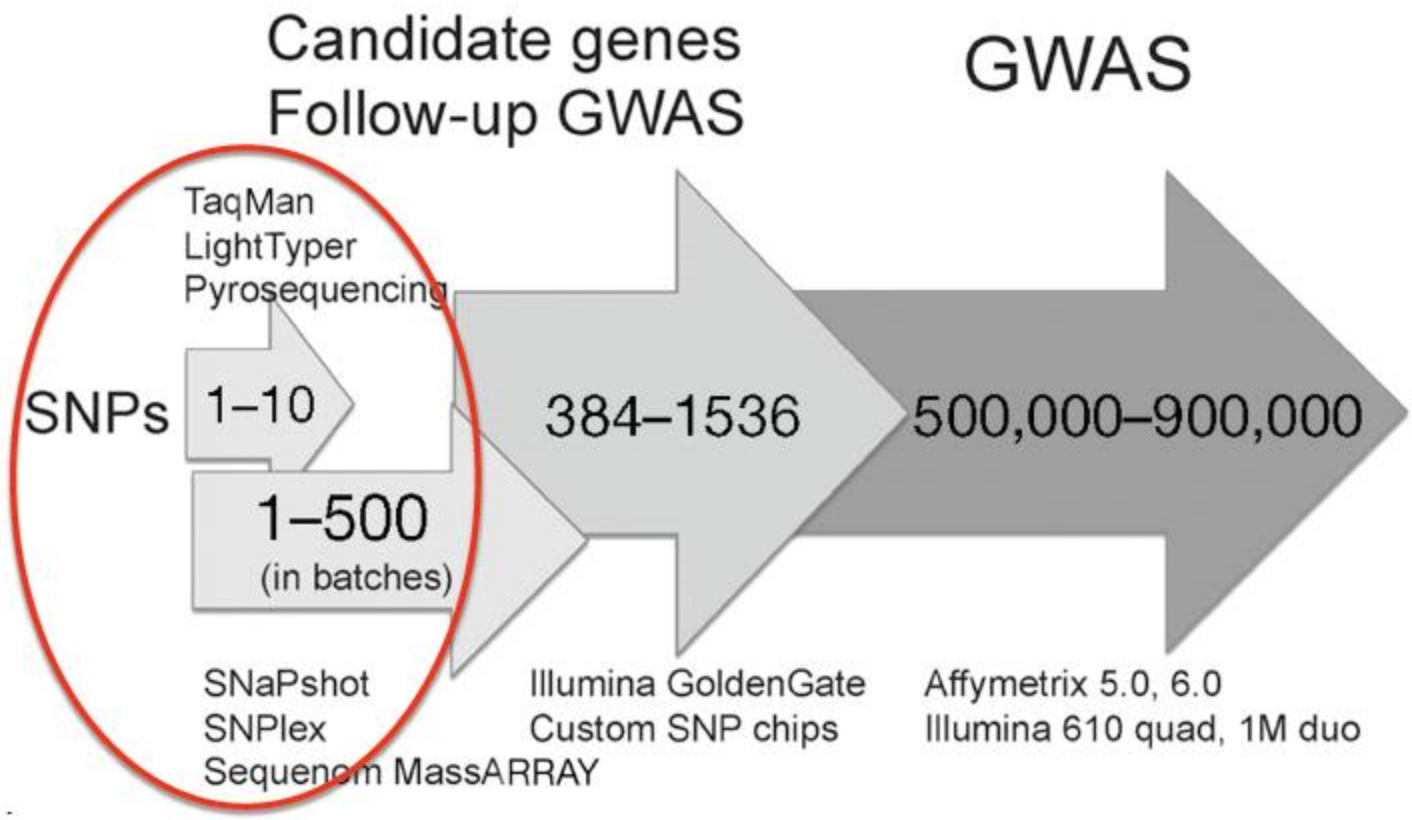
# SNP in Unique Sequence



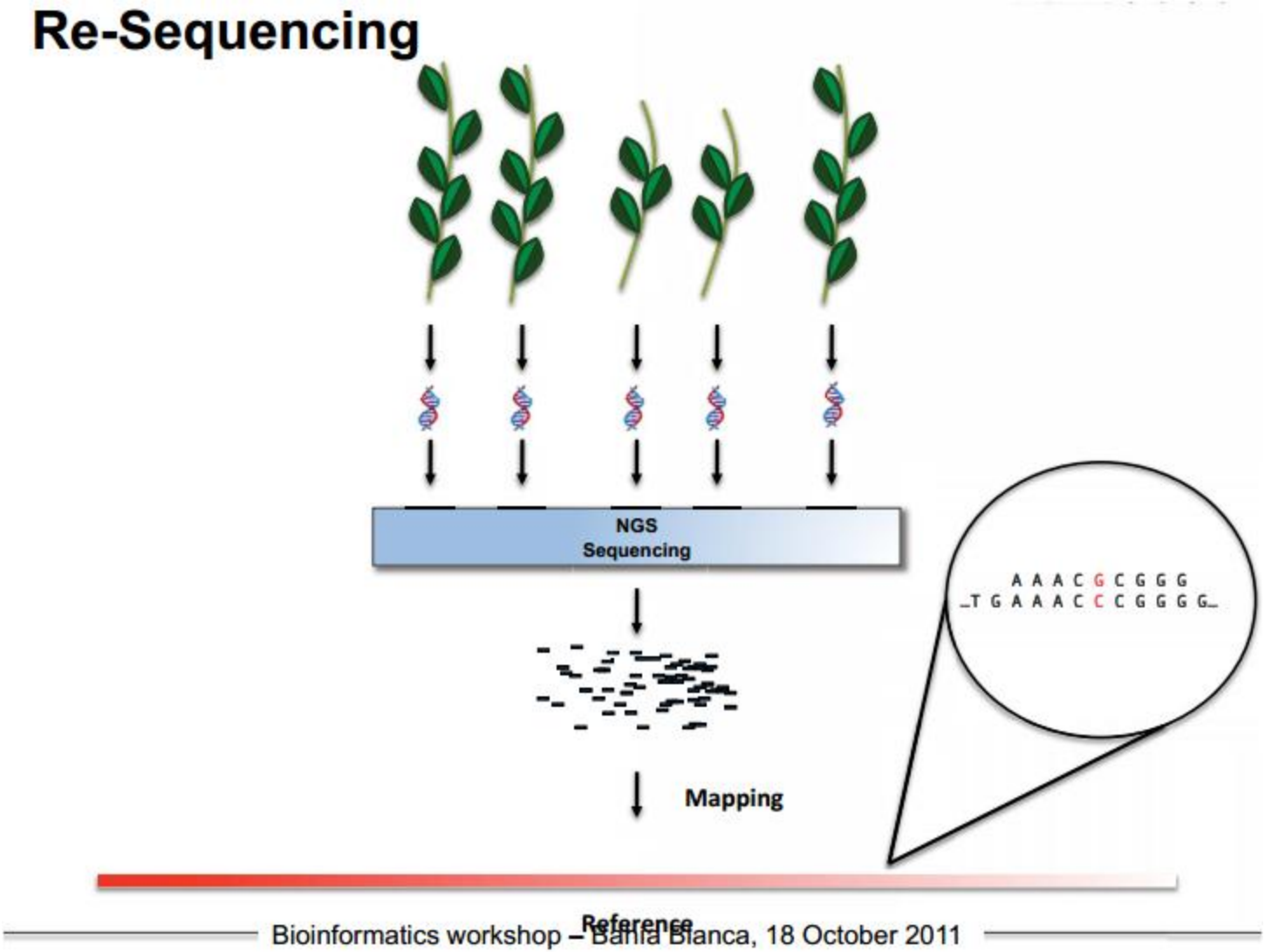
# Progress in genotyping technology

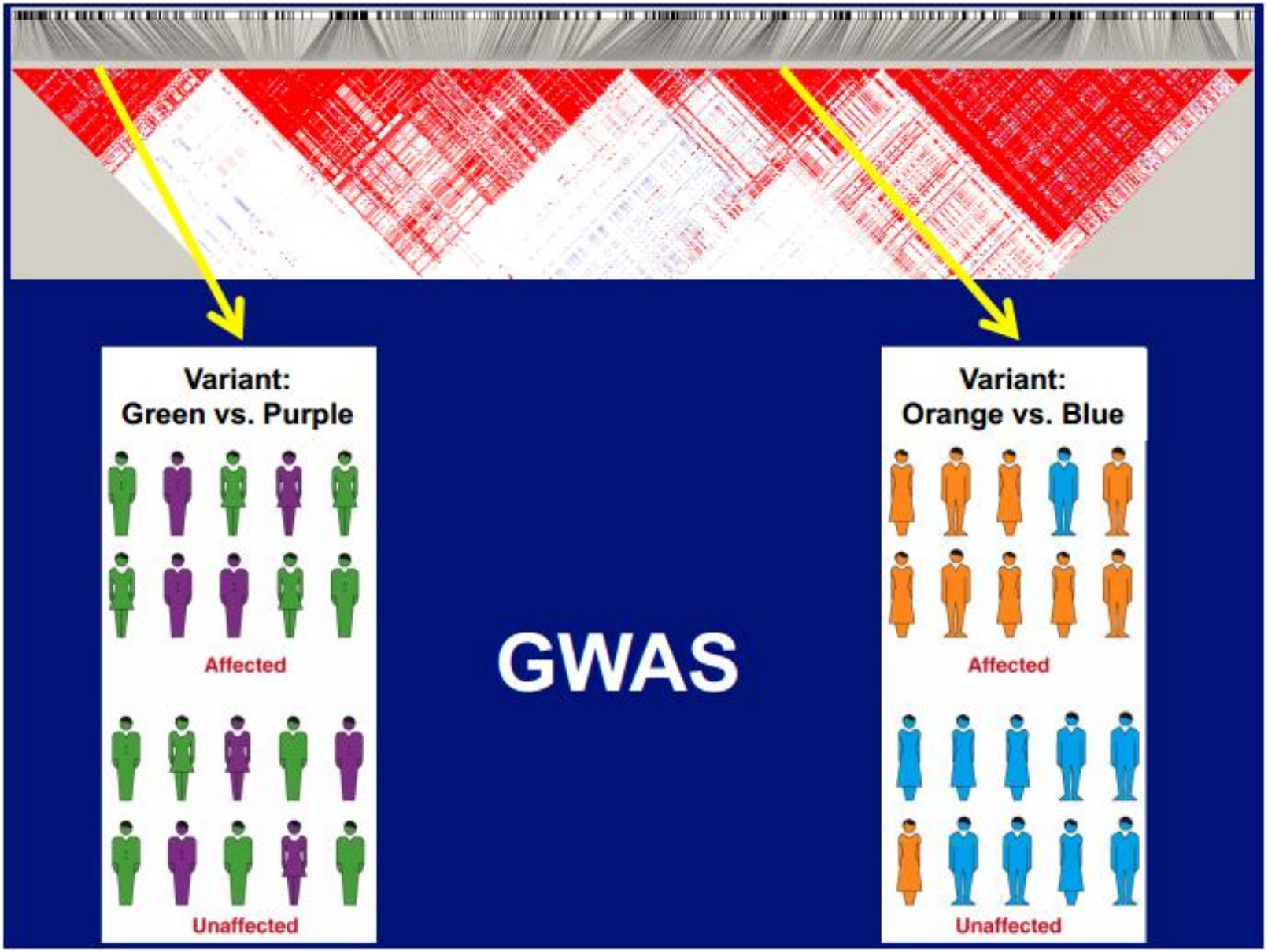


# SNP genotyping:
# Different technologies for different scales



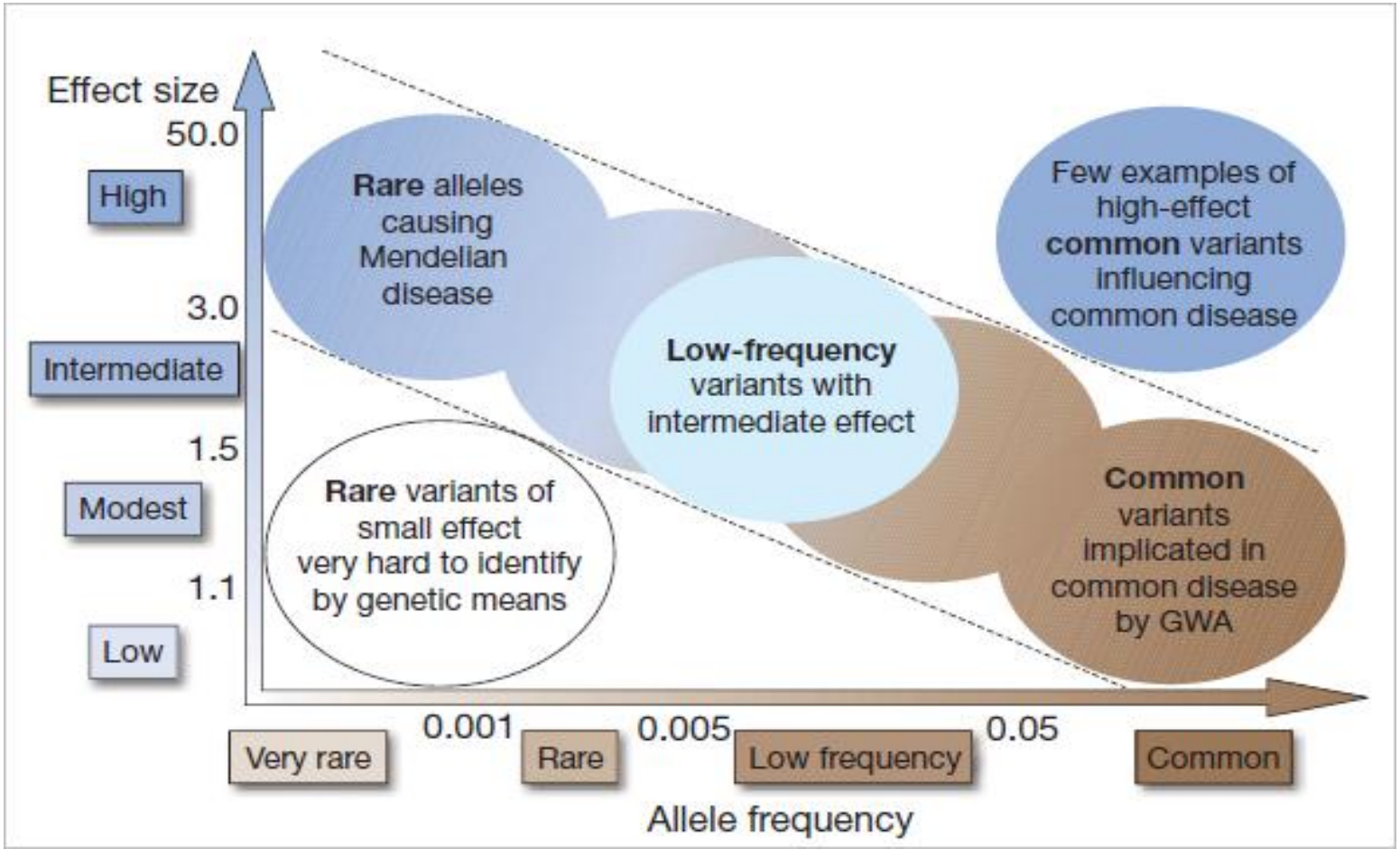
# GENOME WIDE ASSOCIATION STUDIES




Variant:
Green vs. Purple
Affected
Unaffected
GWAS
Variant:
Orange vs. Blue
Affected
Unaffected

# Finding the missing heritability of complex diseases

Vol 461|8 October 2009|doi:10.1038/nature08494

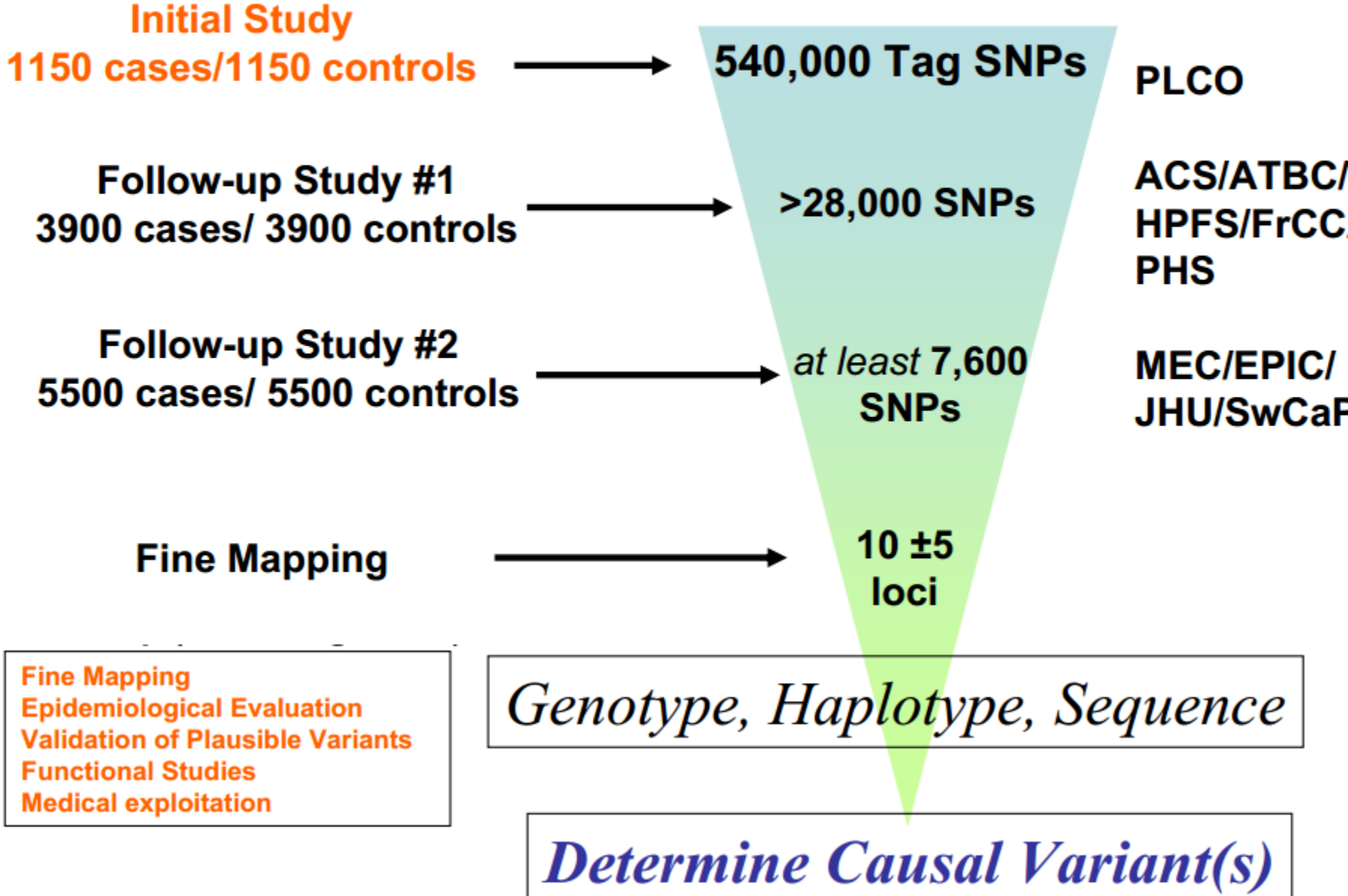



## Association studies for next-generation sequencing

Li Luo, Eric Boerwinkle and Momiao Xiong

*Genome Res.* 2011 21: 1099-1108 originally published online April 26, 2011

# General Strategy for Prostate GWAS



# GWAS Diagram Browser

Exploring Genome-wide Association Studies

National Human Genome Research Institute | EMBL-EBI

## Please take our short survey

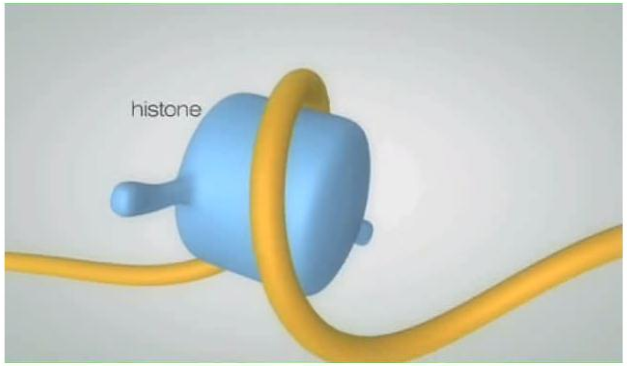
# The Promise of GWAS

- Discovery of Common Markers in the Genome
  - Represents a portion of the genetic contribution
- Opportunity to dissect genetic signal
- Establish genetic markers for:
  - Prevention
  - Intervention
- Explore genes/pathways
  - Etiology
  - Gene-Environment/Lifestyle Interactions
  - "Druggable" targets

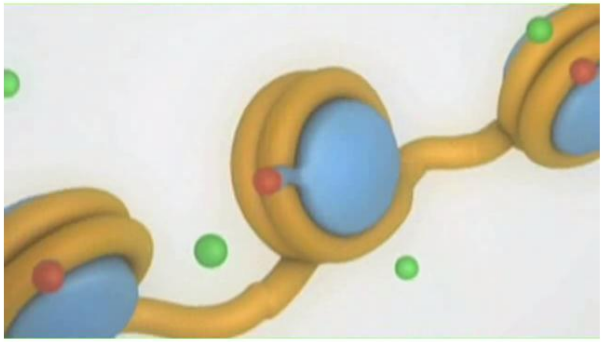

THOMAS POROSTOCKY

# EL EPIGENOMA

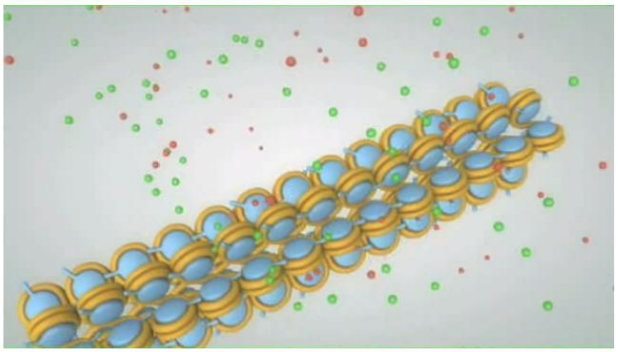
THE EPIGENOME AT A GLANCE

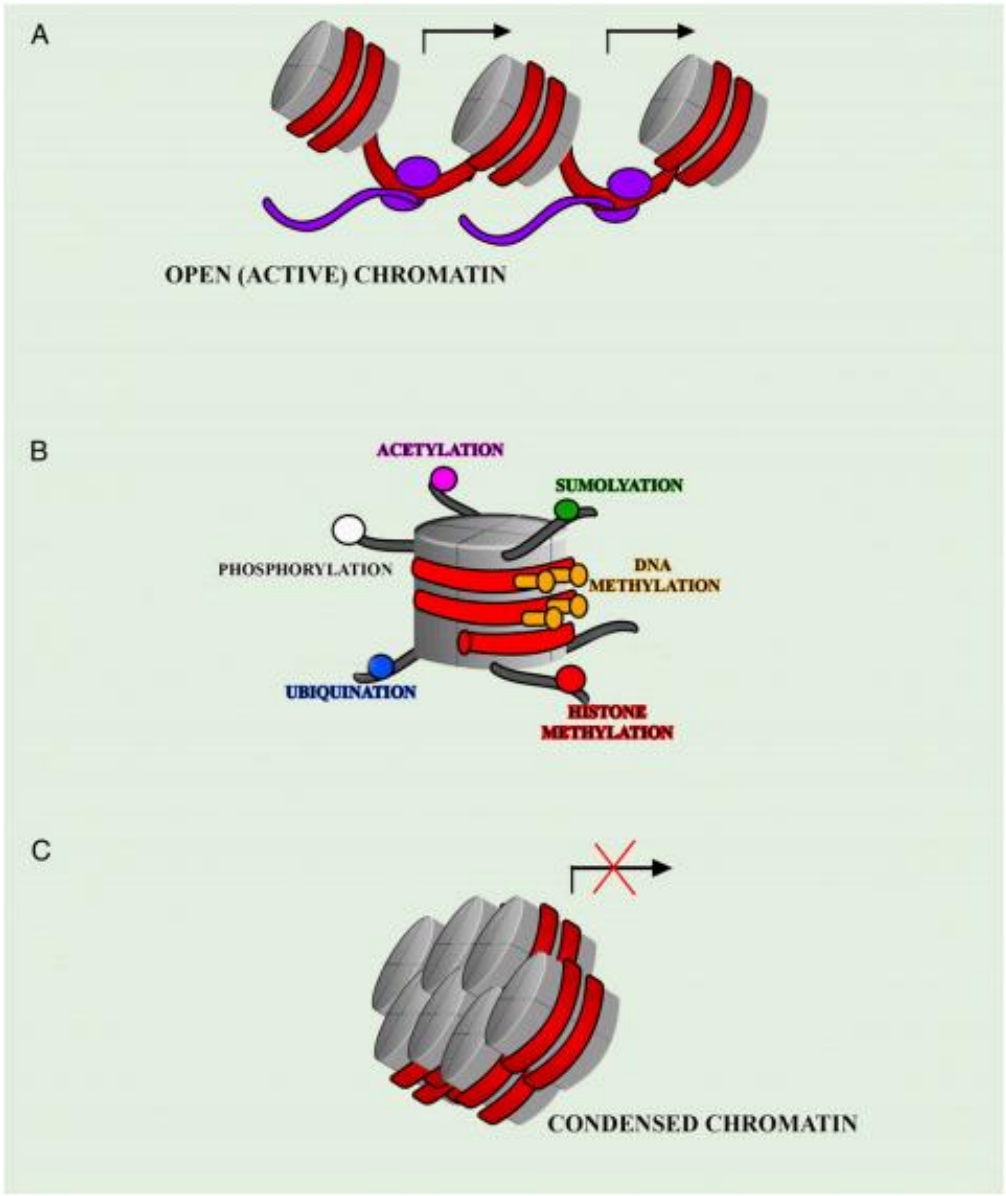



THE EPIGENOME AT A GLANCE



THE EPIGENOME AT A GLANCE





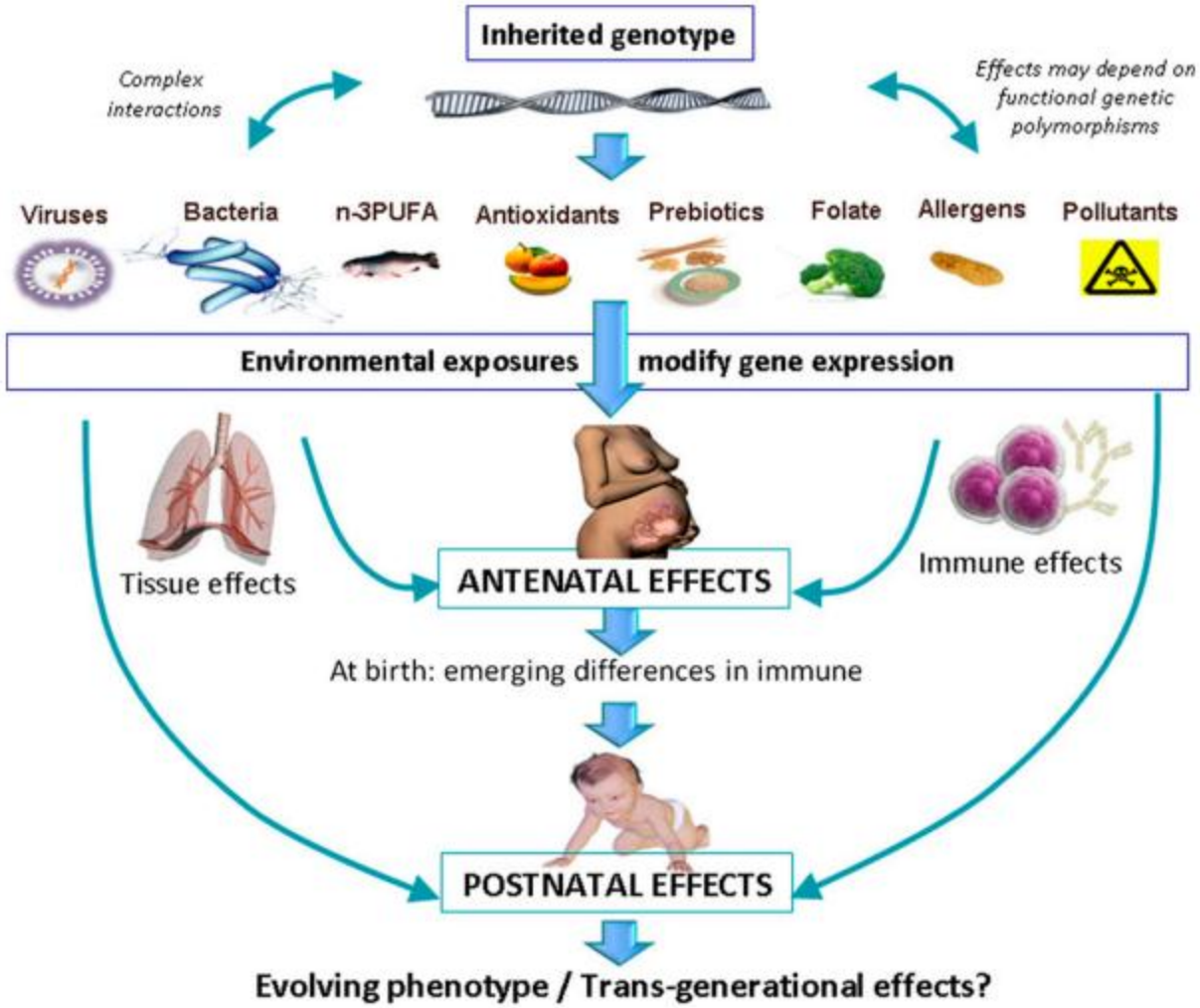



FIGURE 2. Complex gene-environmental interactions modify gene expression and phenotype during early development. PUFA = polyunsaturated fatty acid.

# Third-generation sequencing fireworks at Marco Island

David J Munroe & Timothy J R Harris

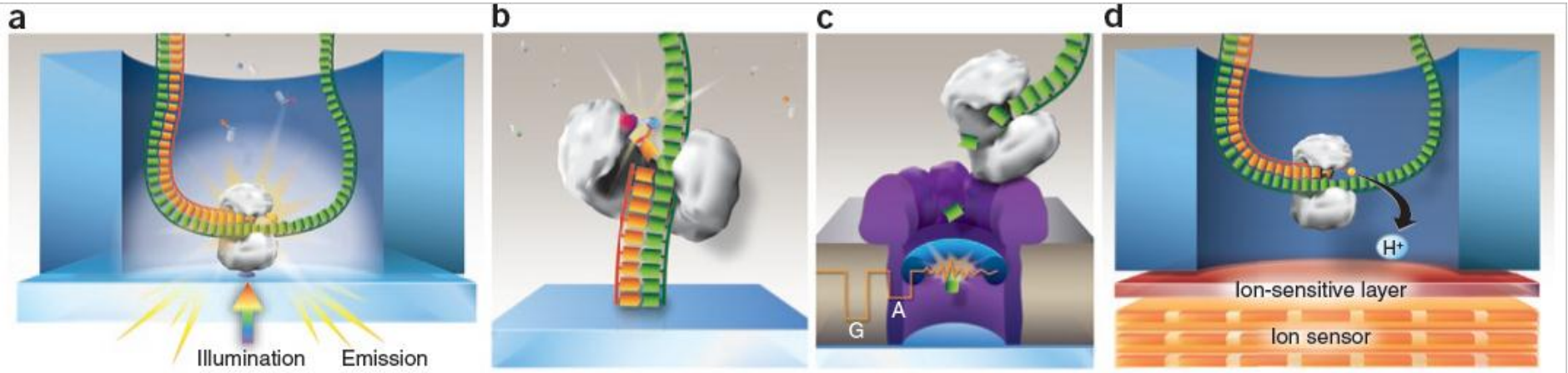



**Figure 1** Third-generation sequencing platforms. (**a**) Pacific Biosciences SMRT (single-molecule real-time) DNA sequencing method. The platform uses a DNA polymerase anchored to the bottom surface of a ZMW (pictured in cross section). Differentially labeled nucleotides enter the ZMW via diffusion and occupy the 'detection volume' (white translucent halo area) or microseconds. During an incorporation event, the labeled nucleotide is 'held' within the detection volume by the polymerase for tens of milliseconds. As each nucleotide is incorporated, the label, located on the terminal phosphate, is cleaved off and diffuses out of the ZMW. (**b**) Life Technologies FRET sequencing platform uses base fluorescent labeling technology, a DNA polymerase modified with a quantum dot and DNA template molecules immobilized onto a solid surface. During an incorporation event, energy is transferred from the quantum dot to an acceptor fluorescent moiety on each labeled base. Light emission can only emanate from labeled nucleotides as they are being incorporated. (**c**) The Oxford nanopore sequencing platform uses an exonuclease coupled to a modified $\alpha$-hemolysin nanopore (purple, pictured in cross section) positioned within a lipid bilayer. As sequentially cleaved bases are directed through the nanopore, they are transiently bound by a cyclodextrin moiety (blue), disturbing current through the nanopore in a manner characteristic for each base. (**d**) The Ion Torrent sequencing platform uses a semiconductor-based high-density array of microwell reaction chambers positioned above an ion-sensitive layer and an ion sensor. Single nucleotides are added sequentially, and incorporation is recorded by measuring hydrogen ions released as a by-product of nucleotide chain elongation.

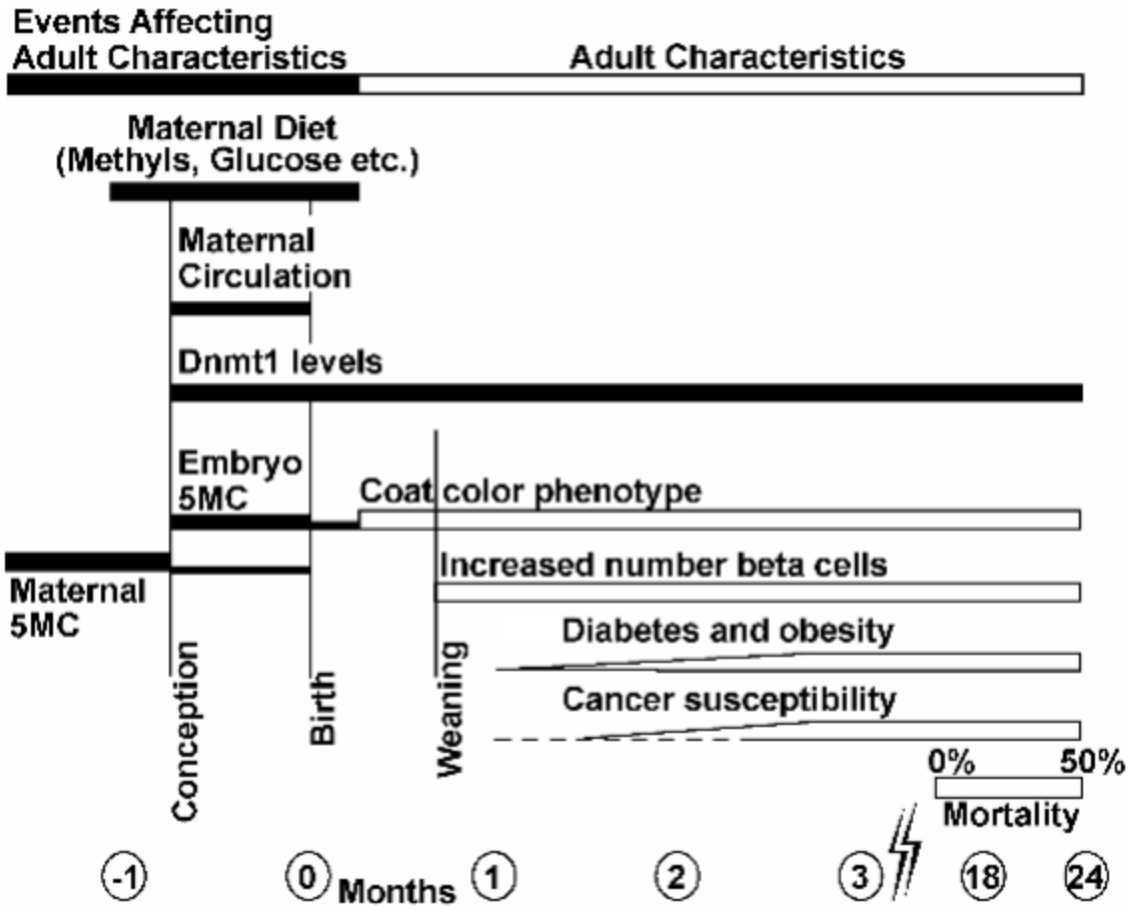



Figure 10.5. Time line of maternal effects and the phenotypic consequences.

Nutritional Genomics. Maternal Nutrition: Nutrients And Control Of Expression (2007)

# The exposome: from concept to utility

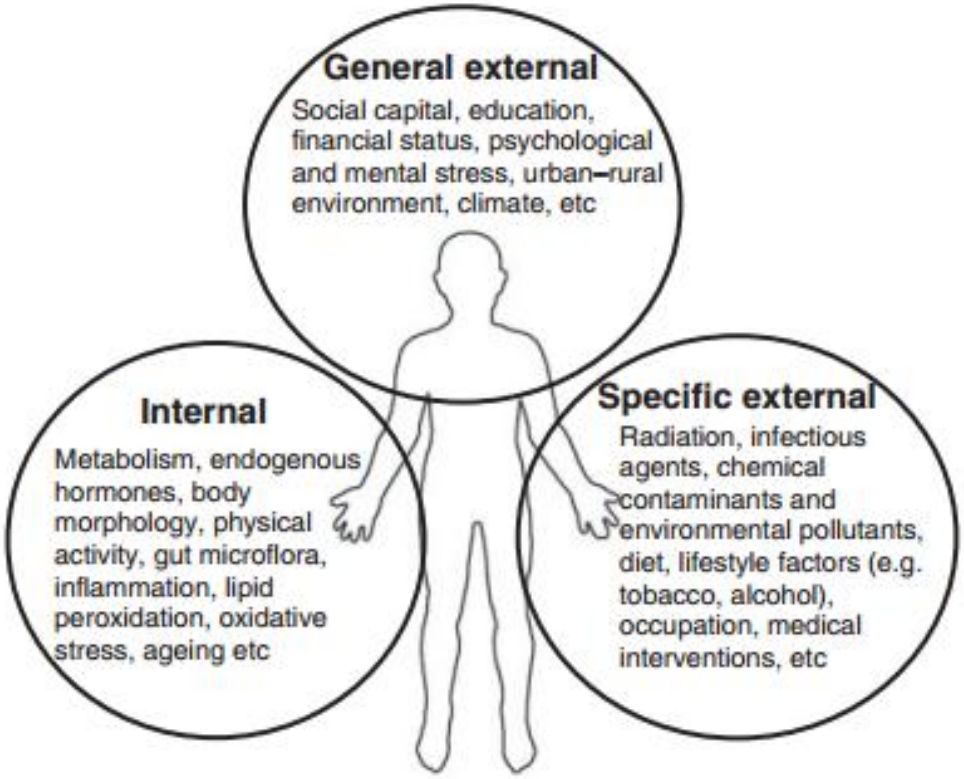



**Figure 1** Three different domains of the exposome are presented diagrammatically with non-exhaustive examples for each of these domains

*International Journal of Epidemiology* 2012;**41**:24–32

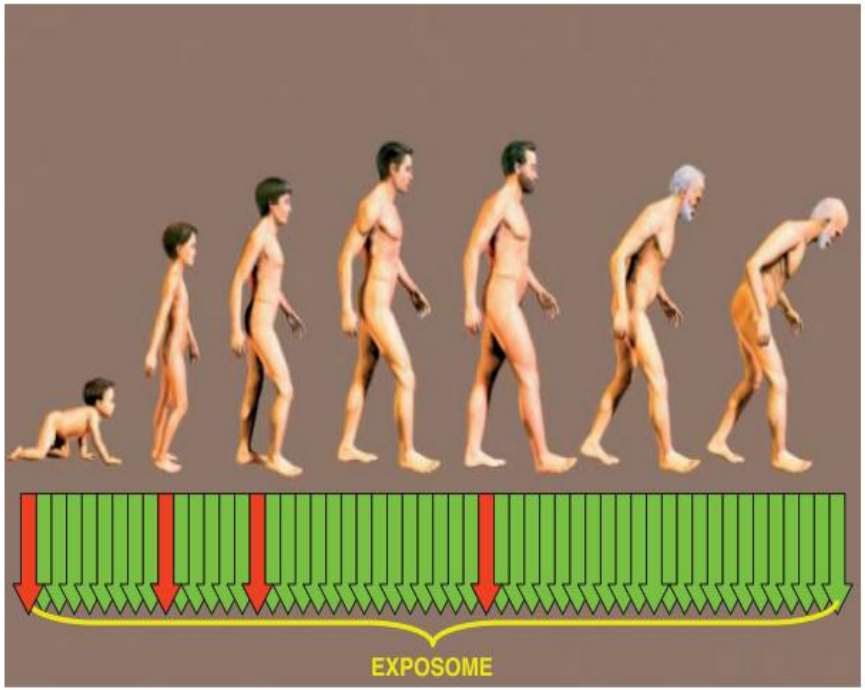



**Figure 2** The exposome would require measurement of exposures over time across the lifecourse of an indiv (*in utero* exposures are included but not represented on this schema). The darker arrows indicate possible time-p representative cross-sectional exposure assessments could be made in order to capture different key periods: *in u* childhood; adolescence; and adulthood

**Table 1** Some examples of approaches and tools to measure the exposome

| Approach | Tools |
|---|---|
| Biomarkers (omics) | |
| General | Genomics, transcriptomics, proteomics, metabolomics, epigenomics |
| Targeted | Adductomics, lipidomics, immunomics |
| Sensor technologies (including mobile phones) | Environmental pollutants, physical activity, stress, circadian rhythms, location [global positioning systems (GPS)] |
| Imaging (including mobile phones, video cameras) | Diet, environment, social interactions |
| Portable computerized devices (including palmtop computers) | Behaviour and experiences (ecological momentary assessment), stress, diet, physical activity |
| Improved conventional measurements (combined with environmental measures) | Job-exposure matrices; dietary recall (e.g. EPIC-Soft) |

IMPROVING THE HEALTH OF AMERICA'S CHILDREN

THE NATIONAL CHILDREN'S STUDY

HEALTH GROWTH ENVIRONMENT



## Study Locations

Find out more about active Study locations...Learn More

## In The Spotlight

Eleven abstracts from the National Children's Study Research Day (August 24, 2011) were accepted for publication by the *American Journal of Medical Genetics*. The abstracts appeared in the August 2012 online version of the Journal and will appear in the October 2012 print edition...Read More

Page last reviewed: 4/2/2012
Page last updated: 4/2/2012

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## What is the National Children's Study?

The National Children's Study will examine the effects of the environment, as broadly defined to include factors such as air, water, diet, sound, family dynamics, community and cultural influences, and genetics on the growth, development, and health of children across the United States, following them from before birth until age 21 years. The goal of the Study is to improve the health and well-being of children and contribute to understanding the role various factors have on health and disease. Findings from the Study will be made available as the research progresses, making potential benefits known to the public as soon as possible.

The National Children's Study is:

- data-driven
- evidence-based
- community and participant informed

Ultimately, the National Children's Study will be one of the richest research efforts geared towards studying children's health and development and will form the basis of child health guidance, interventions, and policy for generations to come. For more details on the Study, see the Study

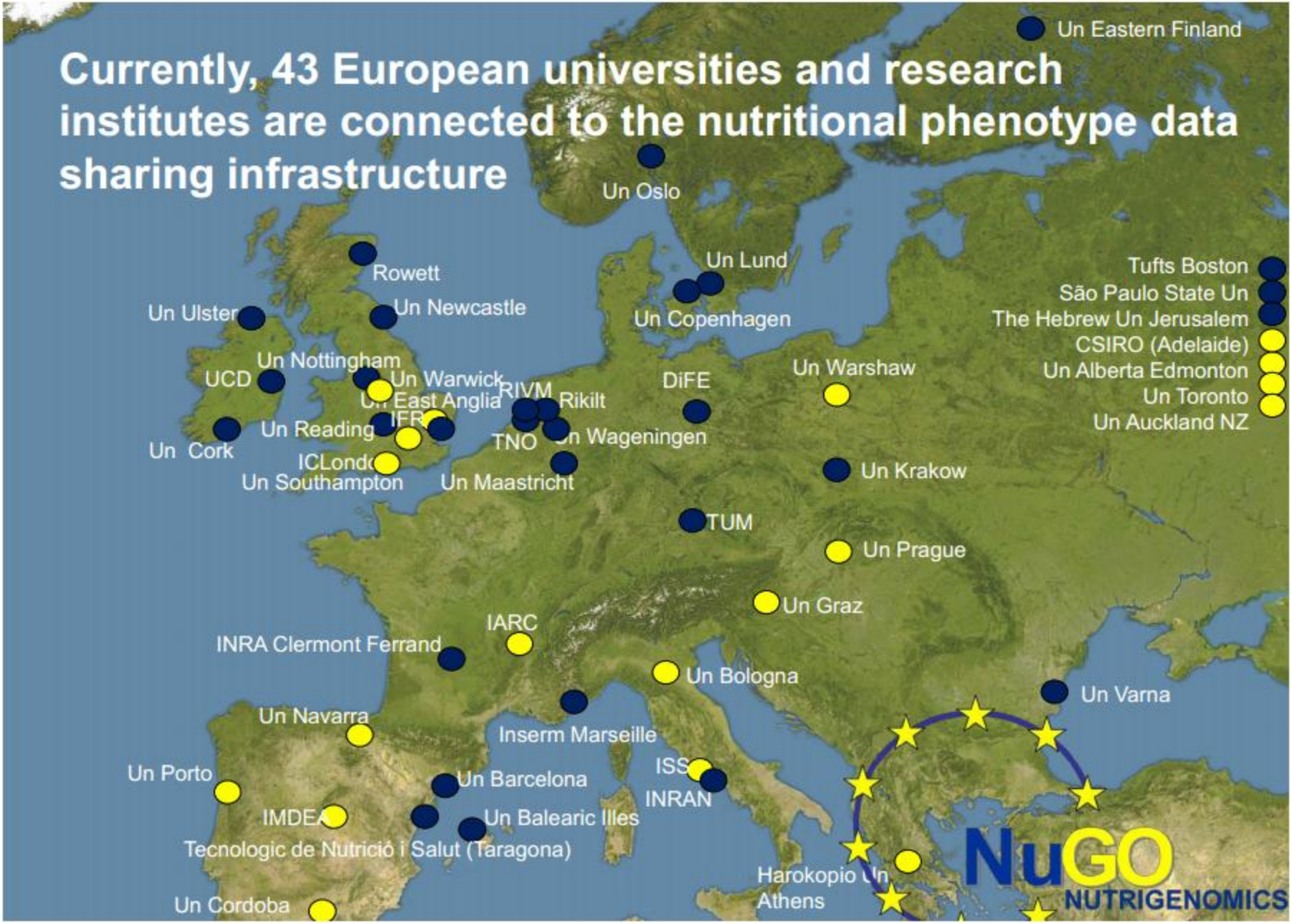
# About UK Biobank

UK Biobank is a major national health resource, and a registered charity in its own right, with the aim of improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses – including cancer, heart diseases, stroke, diabetes, arthritis, osteoporosis, eye disorders, depression and forms of dementia. UK Biobank recruited 500,000 people aged between 40-69 years in 2006-2010 from across the country to take part in this project. They have undergone measures, provided blood, urine and saliva samples for future analysis, detailed information about themselves and agreed to have their health followed. Over many years this will build into a powerful resource to help scientists discover why some people develop particular diseases and others do not.

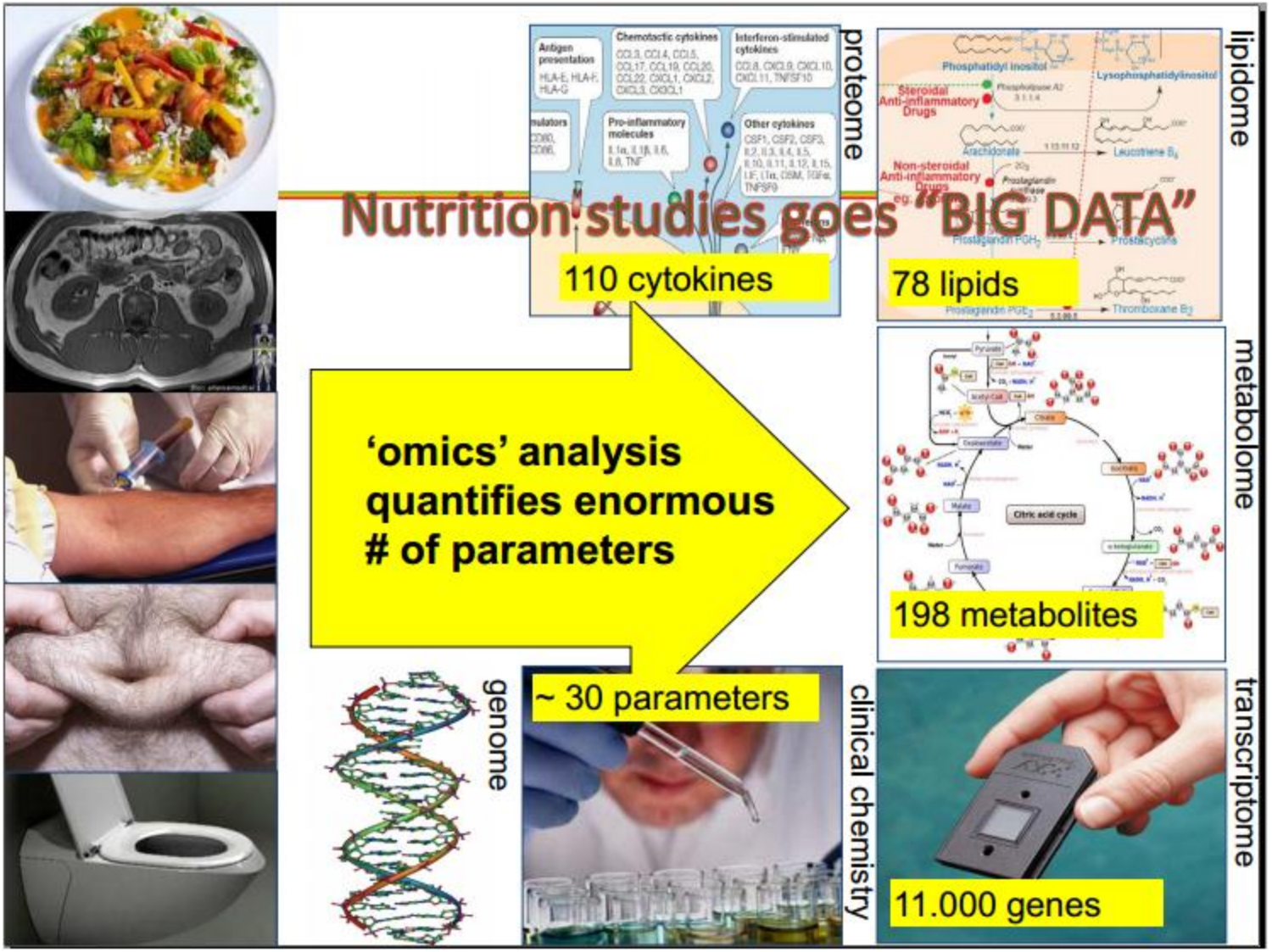
# UK Biobank diet questionnaire ends

The online UK Biobank diet questionnaire is now complete. More than 210,000 people took the time to undertake around 450,000 questionnaires. UK Biobank would like to thank all those people who have participated. They have helped to make UK Biobank even more useful to health scientists from around the world.

Combining the dietary information with the analyses of specific nutrients in blood, urine and saliva samples will help further. This will assist scientists to improve their understanding of the link between particular aspects of diet and diseases like particular types of cancer and heart disease.

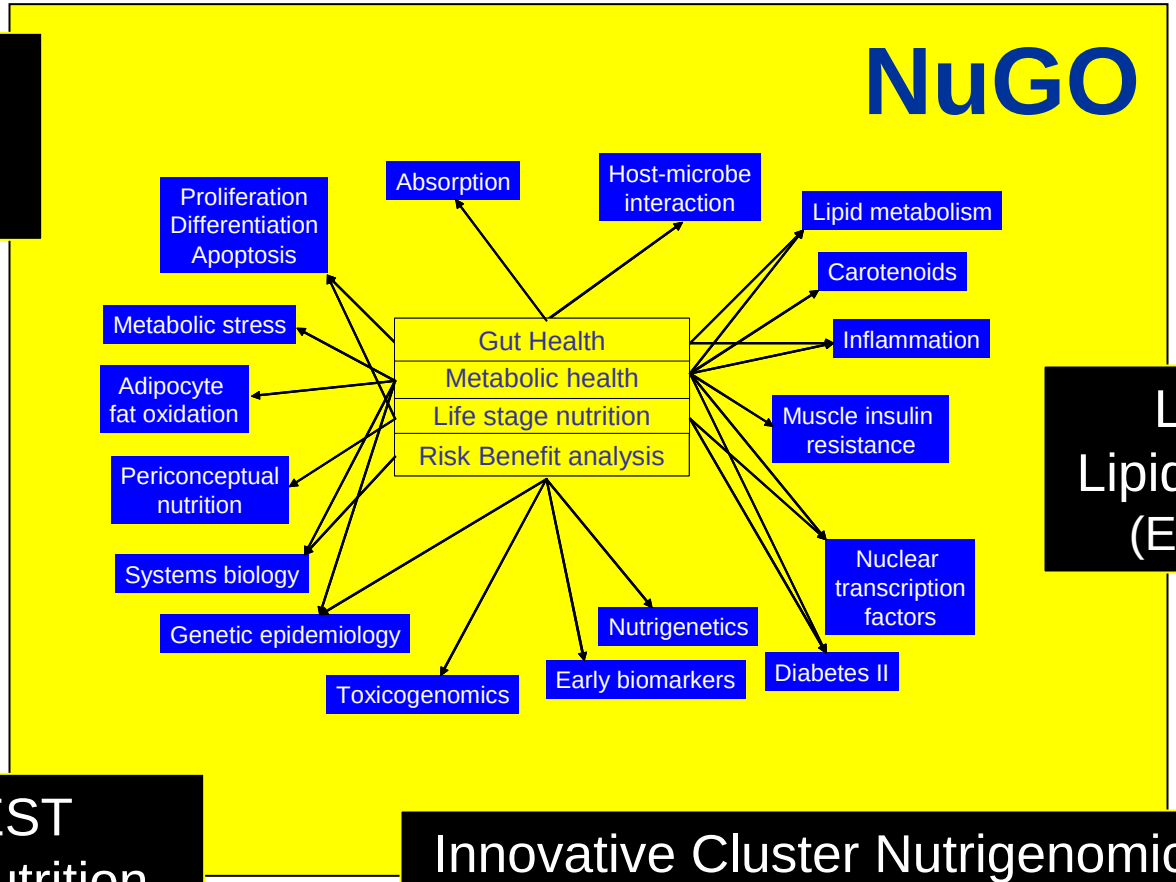



http://www.nugo.org/everyone/24017/5/0/30


Nutrition studies goes "BIG DATA"
'omics' analysis quantifies enormous # of parameters
proteome
110 cytokines
lipidome
78 lipids
metabolome
198 metabolites
genome
~ 30 parameters
clinical chemistry
transcriptome
11.000 genes

# Linking to other EU programs

DIOGENES
obesity
(EU, 12M€)




LIPGEN
Lipids & genes
(EU, 14M€)

EARNEST
early life nutrition
(EU, 14M€)

Innovative Cluster Nutrigenomics
Chronic metabolic stress
(Dutch, 21M€)

# Various researchers have performed intervention studies that might profit from each other

Partner 1:
Olive oil Intervention study

Partner 2:
Fish oil intervention study

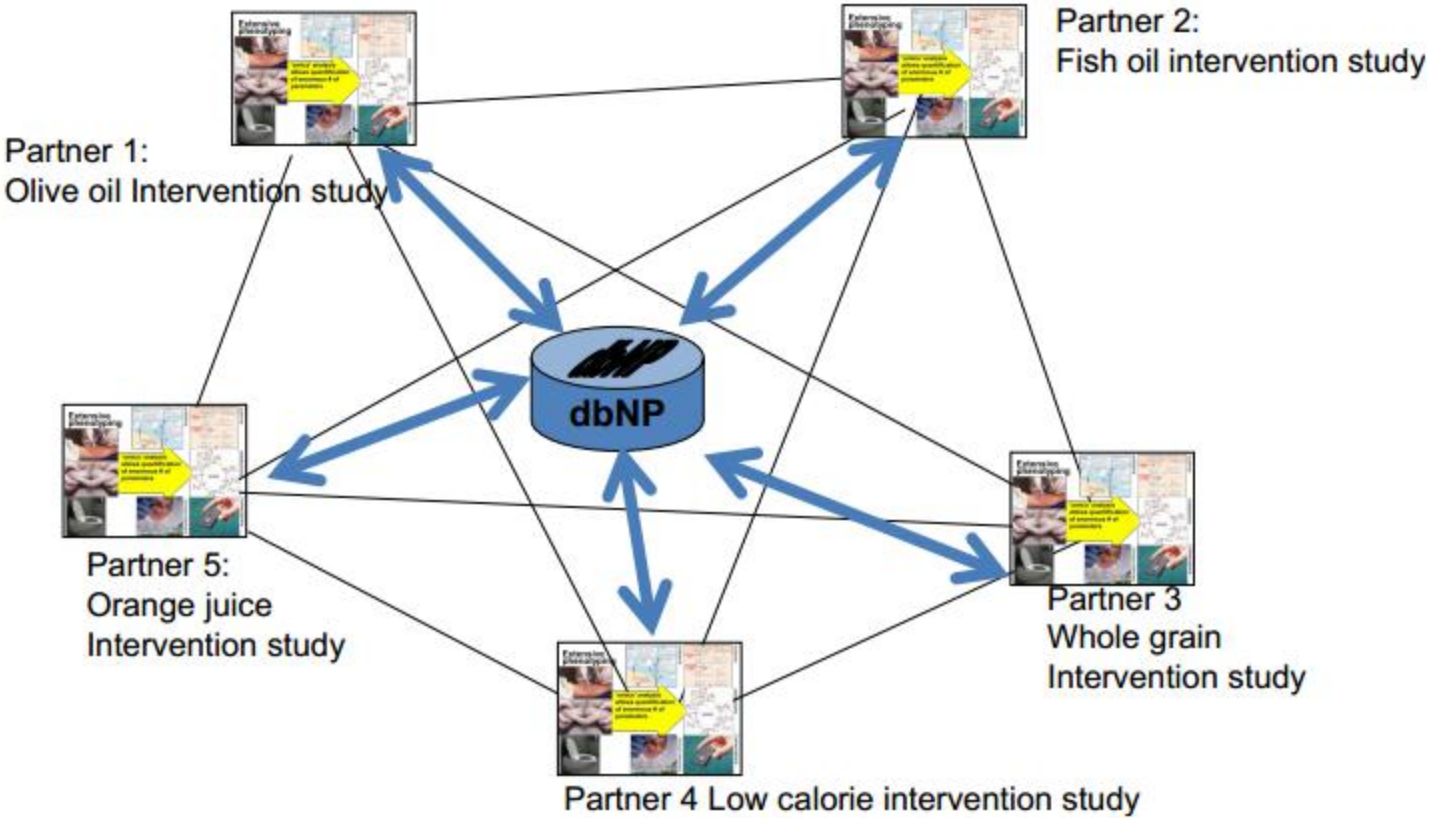
All diets are CVD- protective.
What are joint mechanisms, biomarkers, …

Partner 5:
Orange juice
Intervention study

Partner 3
Whole grain
Intervention study

Partner 4 Low calorie intervention study

# Are all partners allowed to dig into the joint study data pool?



# Sooner or later, all study data will become available to everyone