

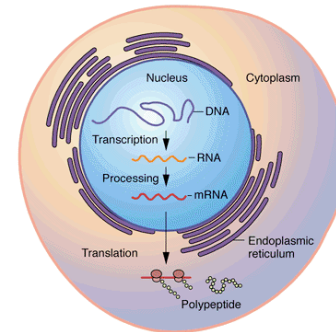
Overview of Functional genomics

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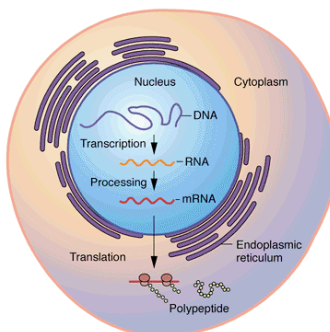
The central dogma of molecular biology:
how genotype becomes phenotype



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how genotype becomes phenotype



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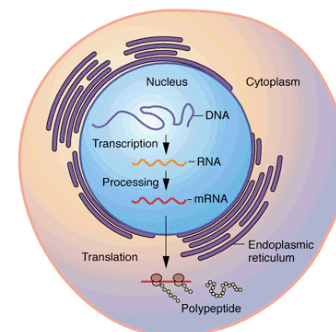
On a genome-wide scale:

Genome=21,000 genes
(same for all cells)

↓
Transcriptome
(cell type-specific)

↓
Proteome
(cell type-specific)

The central dogma of molecular biology:
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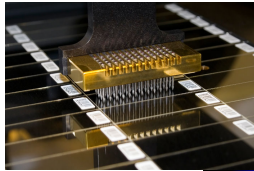
On a genome-wide scale:

Genome=22,000 genes
(same for all cells)

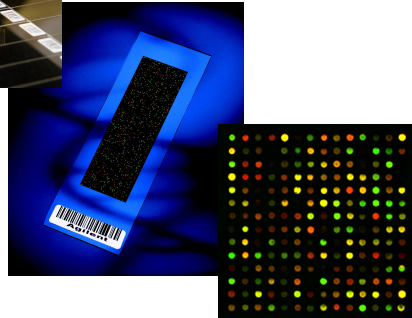
↓
Transcriptome
(cell type-specific)

↓
Proteome
(cell type-specific)

Microarrays measure mRNA expression on a genome-wide scale



All 21,000 human genes are printed on a glass slide



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'Omic' assays provide information on a genome-wide scale

Genome

- Array comparative genomic hybridization (copy number)
- SNP arrays (detect polymorphisms)
- Ultradeep sequencing (sequence)

Methylome

- Array-based methylation profiling (epigenetic DNA modification)
- ChIP-seq

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'Omic' assays provide information on a genome-wide scale

Transcriptome

- Dual channel cDNA microarrays
- Single channel oligonucleotide arrays
- Serial Analysis of Gene Expression (SAGE)
- Ultradeep sequencing, a.k.a. RNA-seq
- Available for mRNA, total RNA, miRNA, ssRNA, dsRNA,...

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'Omic' assays provide information on a genome-wide scale

Proteome

- Antibodies microarrays
- Mass spectrometry

Interactome

- Two-hybrid (protein-protein interactions)
- ChIP-seq (protein-DNA interactions)

More...

- tissues microarray
- mutant screens
- Etc., the only limit is your resources and imagination

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Why it is a technological revolution

Genotypes & phenotypes are considered in their

- globality, and
- diversity

Primary data are easily stored and exchanged

Globality + storage = reusable *in silico* assay

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Why it is a technological revolution

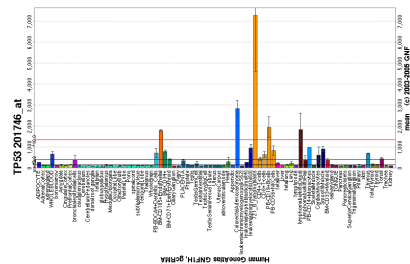
The size of omic data sets makes statistics and machine learning unescapable tools

Overall the omic revolution contributes to make biology a more quantitative science

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Example: the Novartis normal tissue expression atlas

Hybridize mRNA from all human, mouse and rat organs on whole genome microarrays, put data online (biogps.org)



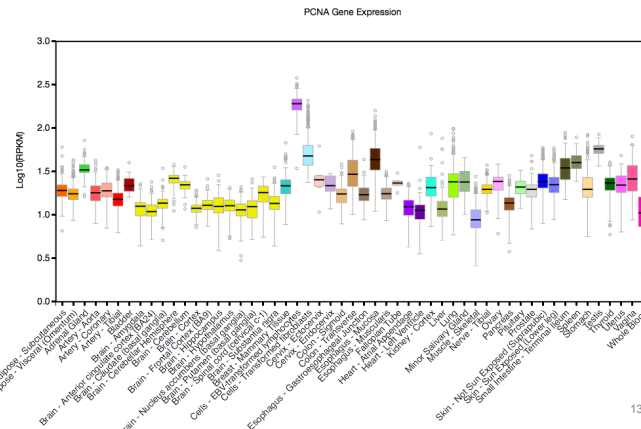
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Example: GTEx, diversity of gene expression across the organs of 900 individuals

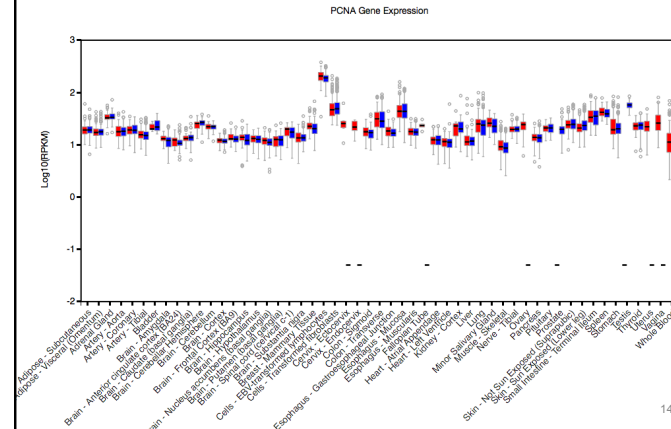
- The GTEx consortium collects samples of 50 the organs of 900 'normal' individuals
- They profiled mRNA expression of each organs of each individuals
- All individuals have been genotyped with SNP array, and a subset with exome-seq and WGS
- It's available to all, for free at www.gtexportal.org
- It's ongoing, currently 578 individuals, 8550 mRNA profiles

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Example: GTEx, diversity of gene expression across the organs of 900 individuals



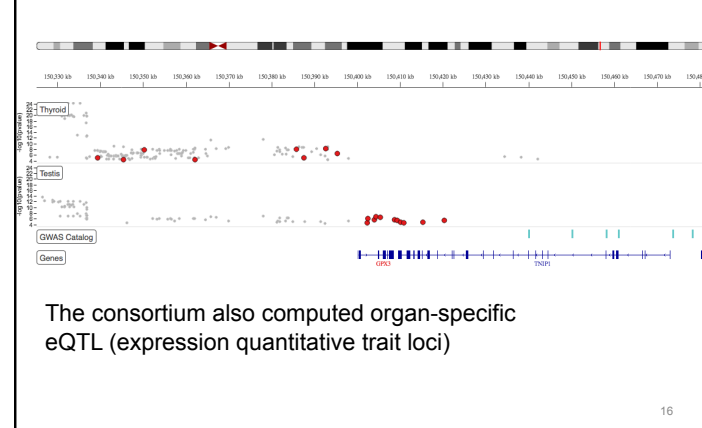
Example: GTEx, diversity of gene expression across the organs of 900 individuals



Example: GTEx, diversity of gene expression across the organs of 900 individuals



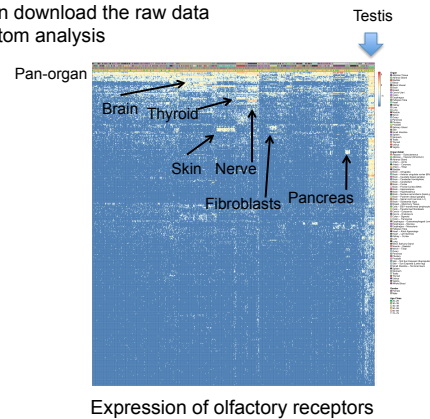
Example: GTEx, diversity of gene expression across the organs of 900 individuals



The consortium also computed organ-specific eQTL (expression quantitative trait loci)

Example: GTEx, diversity of gene expression across the organs of 900 individuals

You can download the raw data for custom analysis



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This course

- Focuses on mRNA expression
- Examples drawn from oncology, mostly
- Focuses on the biology as much as on the computational techniques
- Presents cutting edge research in all its uncertainties and hectics (i.e. *not* a clean textbook view)

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