

# WHAT IS FUNCTIONAL GENOMICS?

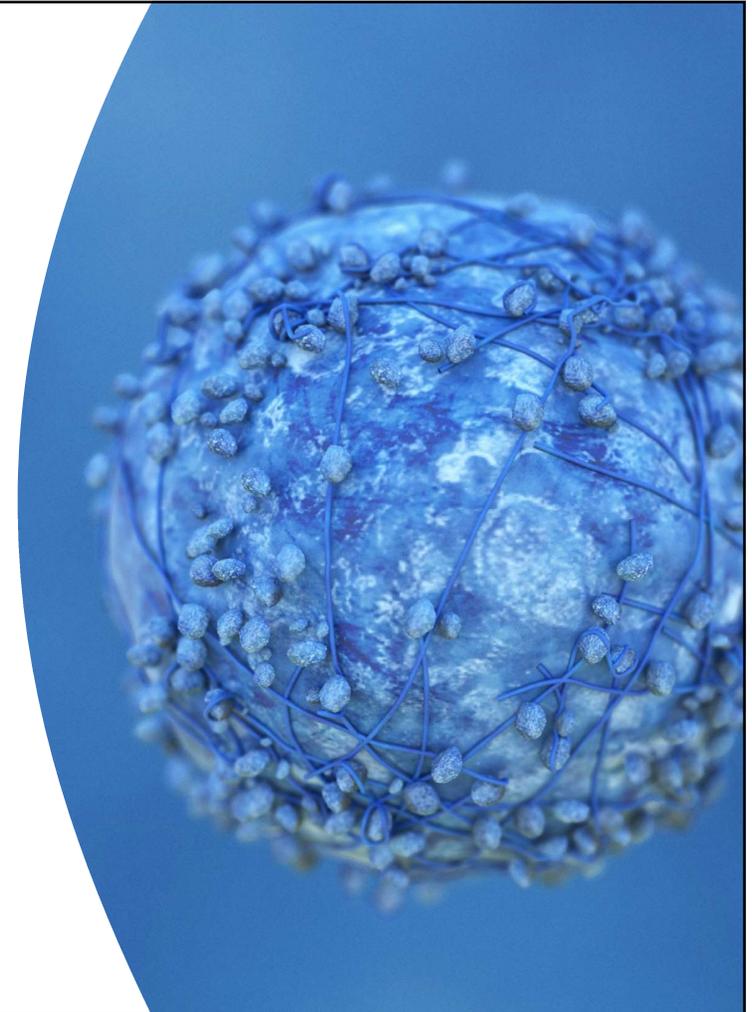
Rory Stark

CRUK Bioinformatics Summer School

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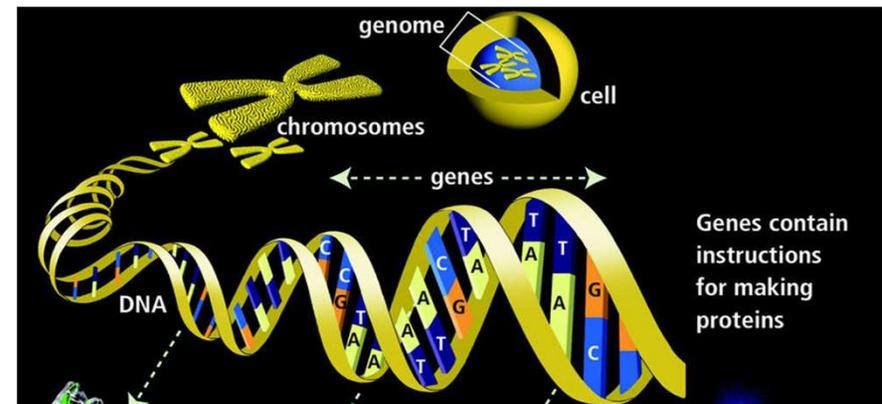


Together we will beat cancer



## What is functional genomics?

Determination of the relationship between an organism's **genome** and its **phenotype**



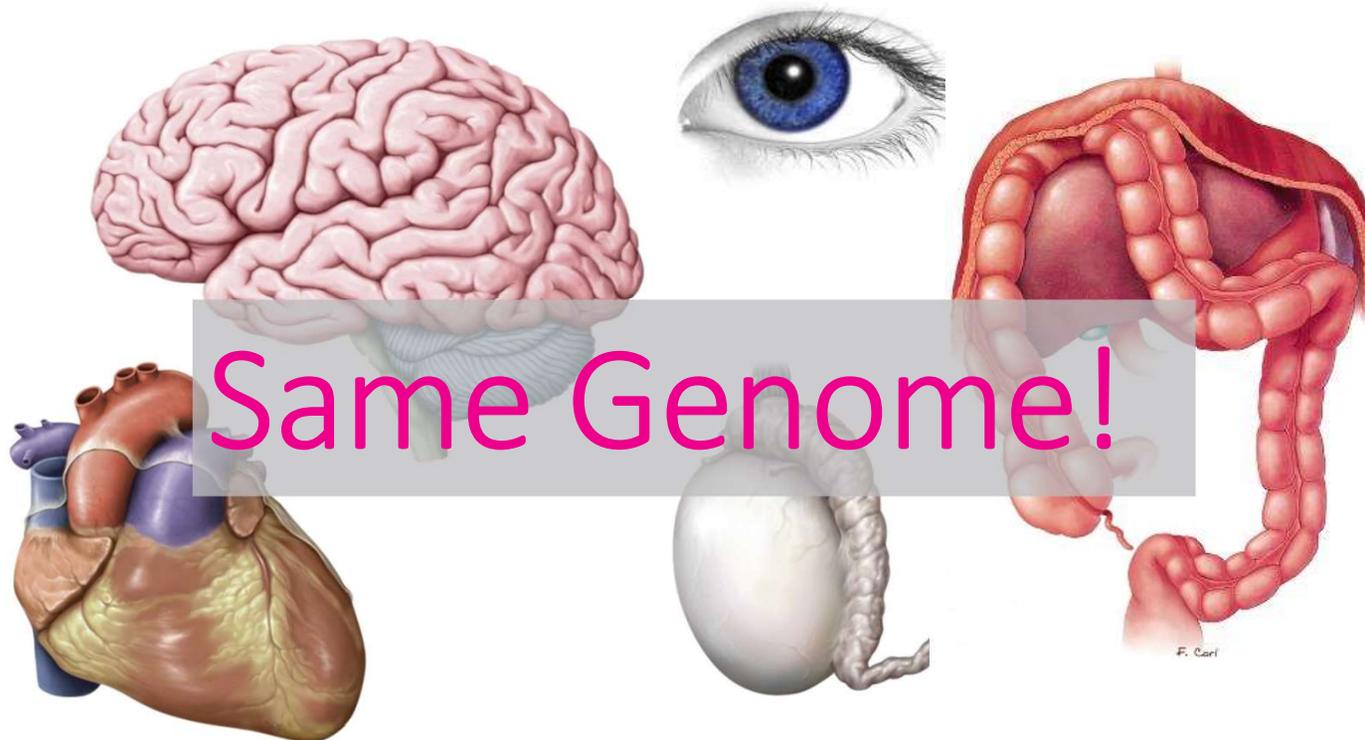
- Each cell contains a complete copy of the genome, distributed along chromosomes (compressed and entwined DNA)
- $3 \times 10^9$  (3Gb) base pairs in human DNA: 5-6 meters in each cell!
- Encodes blueprint for all cellular structures and activities and which cells go where (somehow...)

## What accounts for differences in phenotype?



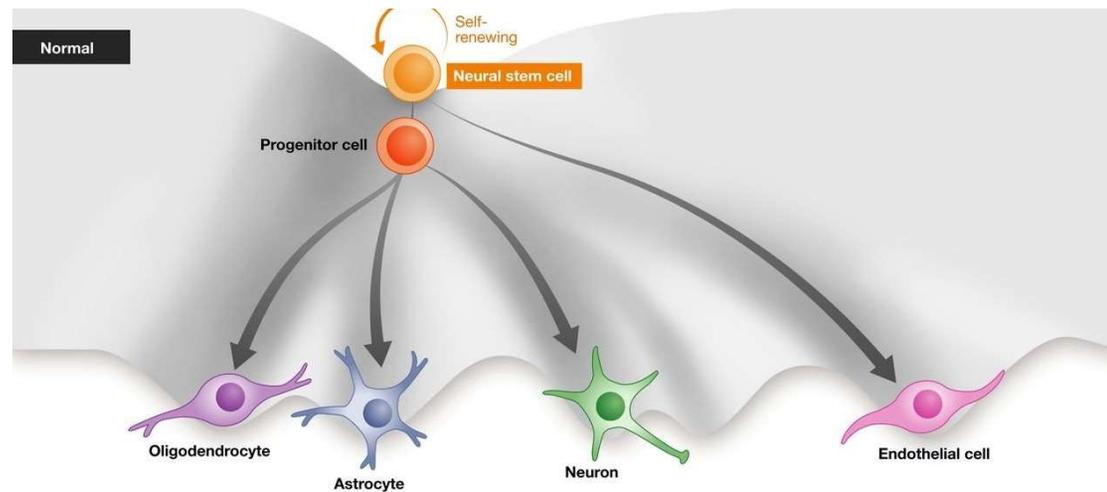
Different Genome!

What accounts for differences in phenotype?

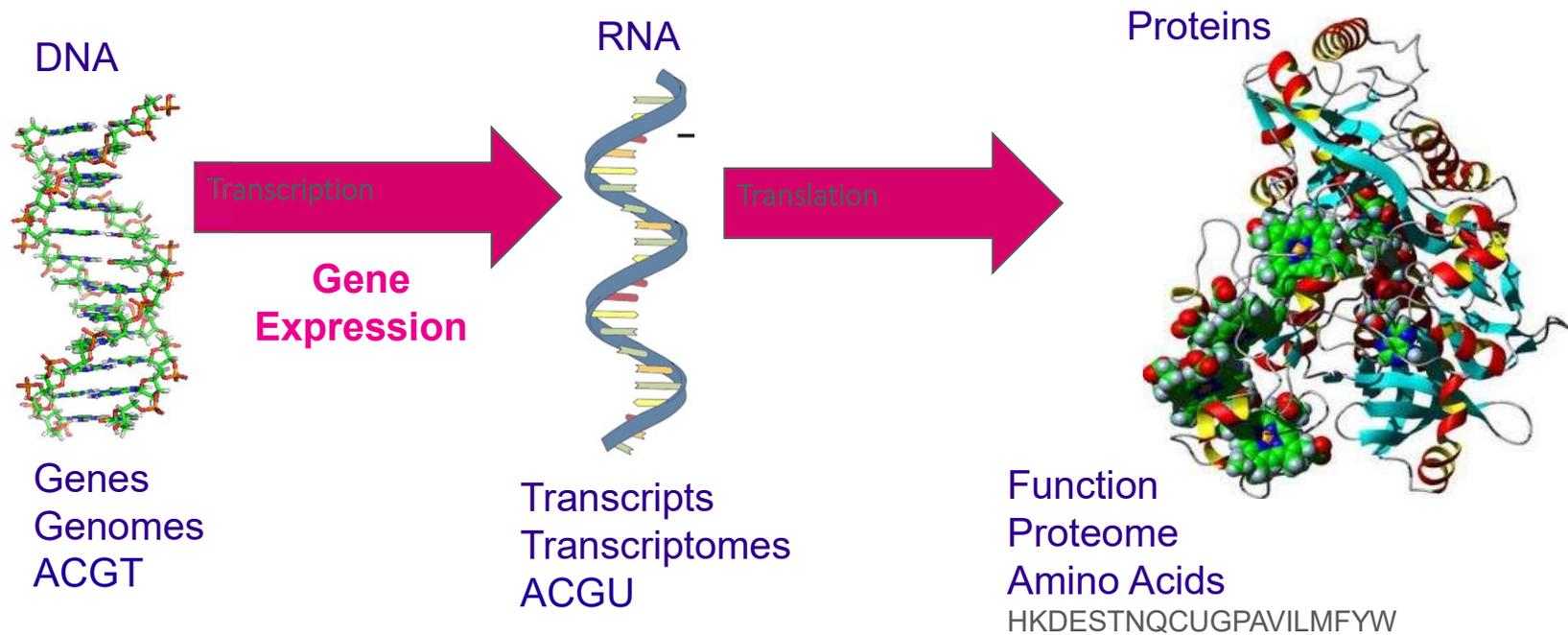


# What is functional genomics?

Determination of the relationship between an organism's genome and its phenotype

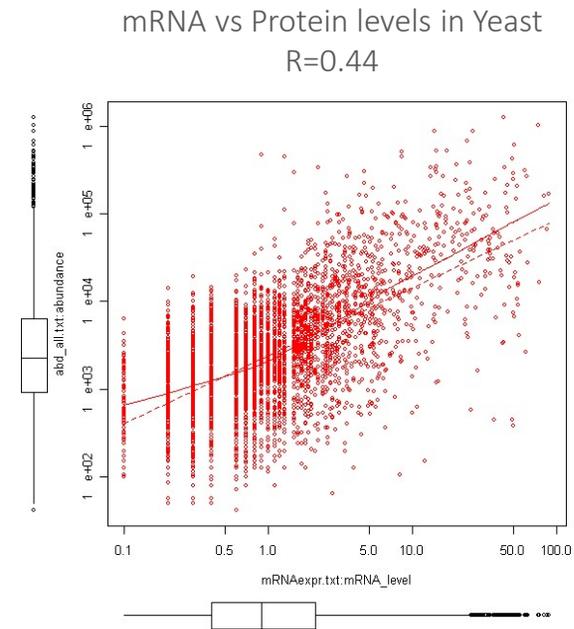


# How do genomes determine function?



## Gene expression

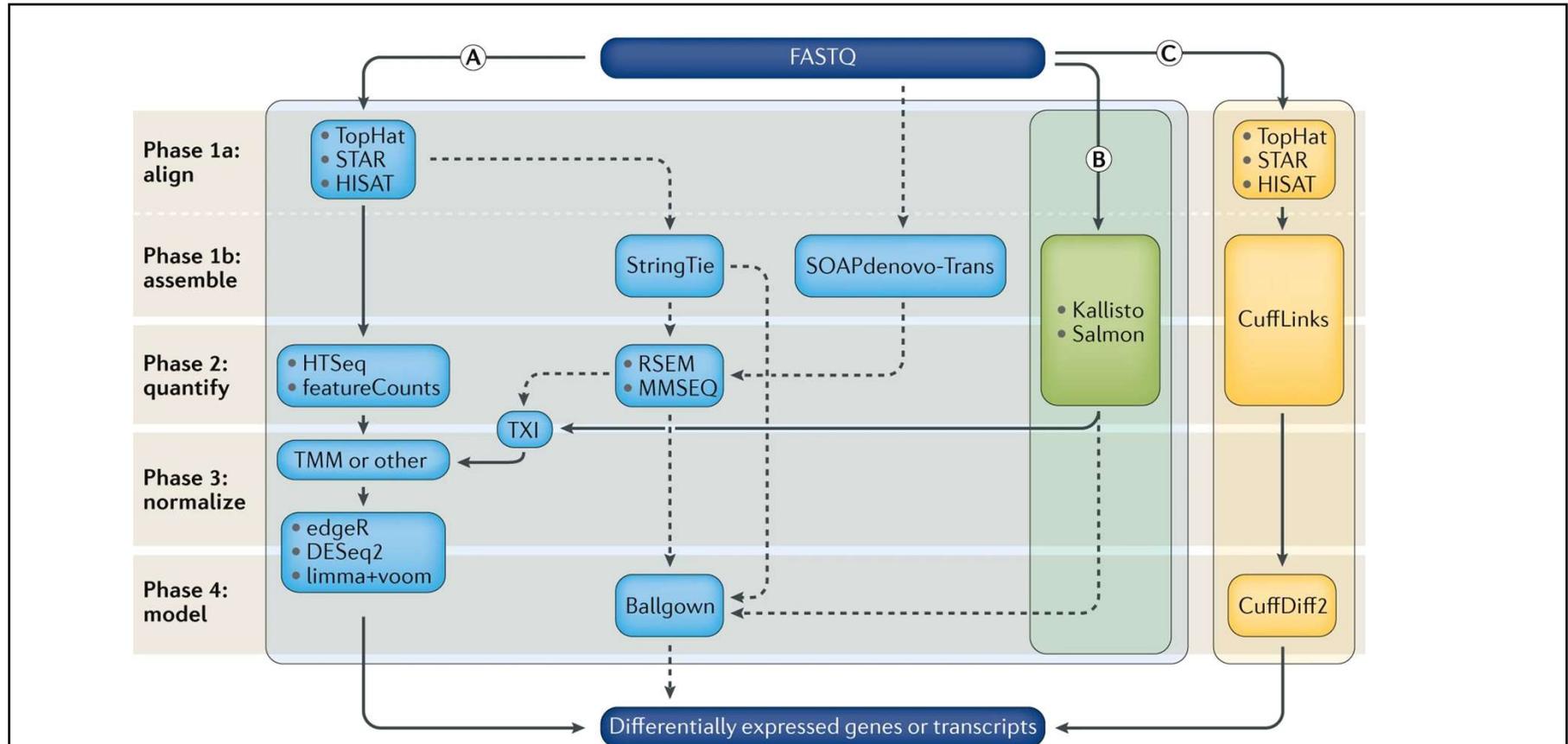
- Ideally, we'd measure all protein levels
- Instead, use mRNA (“transcript”) levels as a proxy for protein levels
- Measure the **expression** levels of many genes in parallel
- Analyses:
  - Expression levels
  - **Differences in expression levels (DE)**
  - Patterns of expression
  - Splicing and isoforms



*Ghaemmaghami et al Nature 2003*

## Comparing gene expression (DE)

- Different **tissues**, same organism
  - human brain/human liver
- Same tissue, different **organism**
  - human liver/mouse liver
  - wt/ko/CRISPR
- Same tissue, same organism, different **condition**
  - benign/tumour
  - treated/untreated
- Time course
- *In vivo* vs *In vitro*
- ...



# Bulk (RNA-seq) vs single-cell (scRNA) analysis

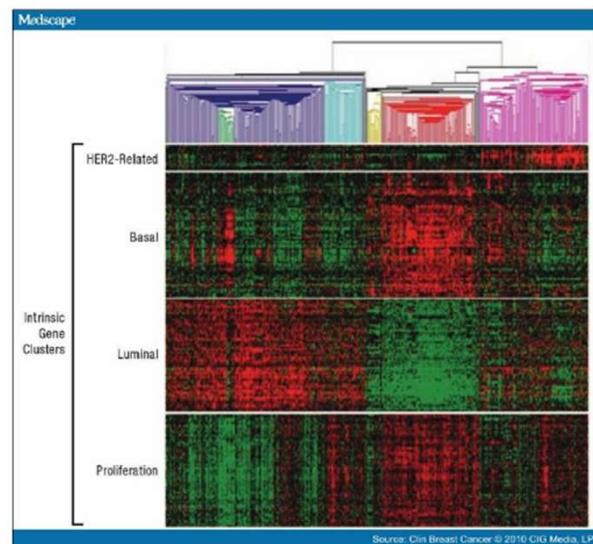
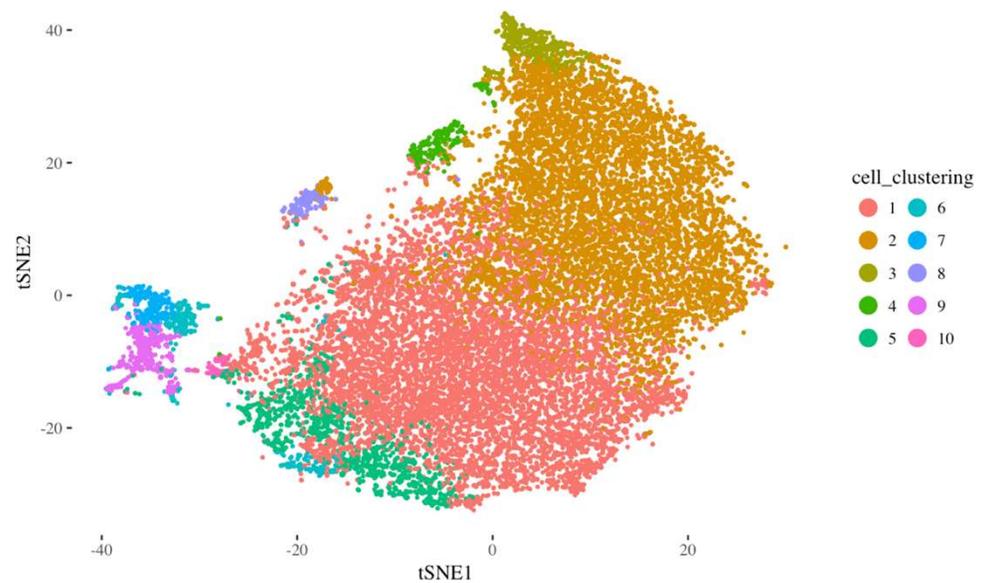
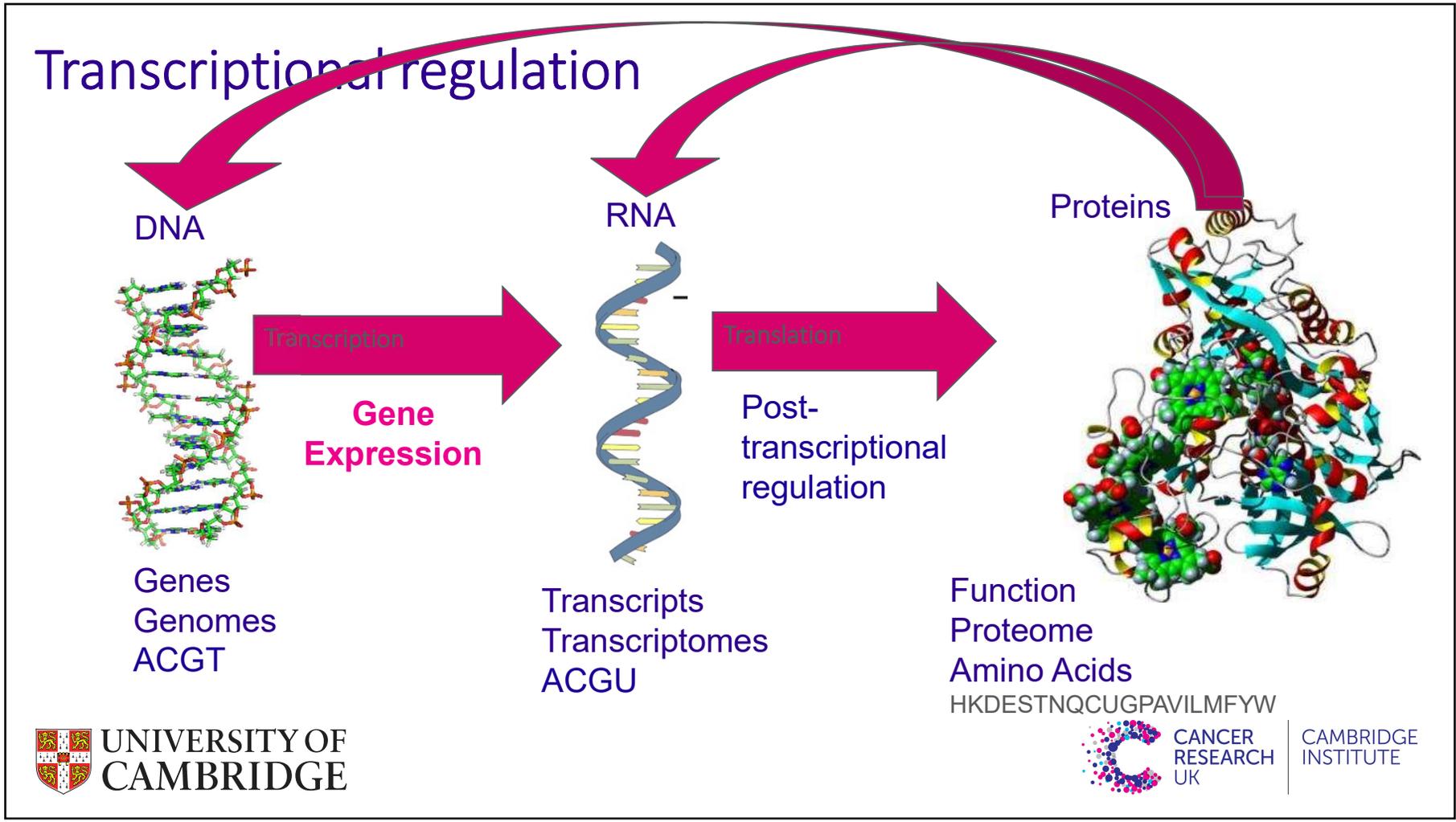
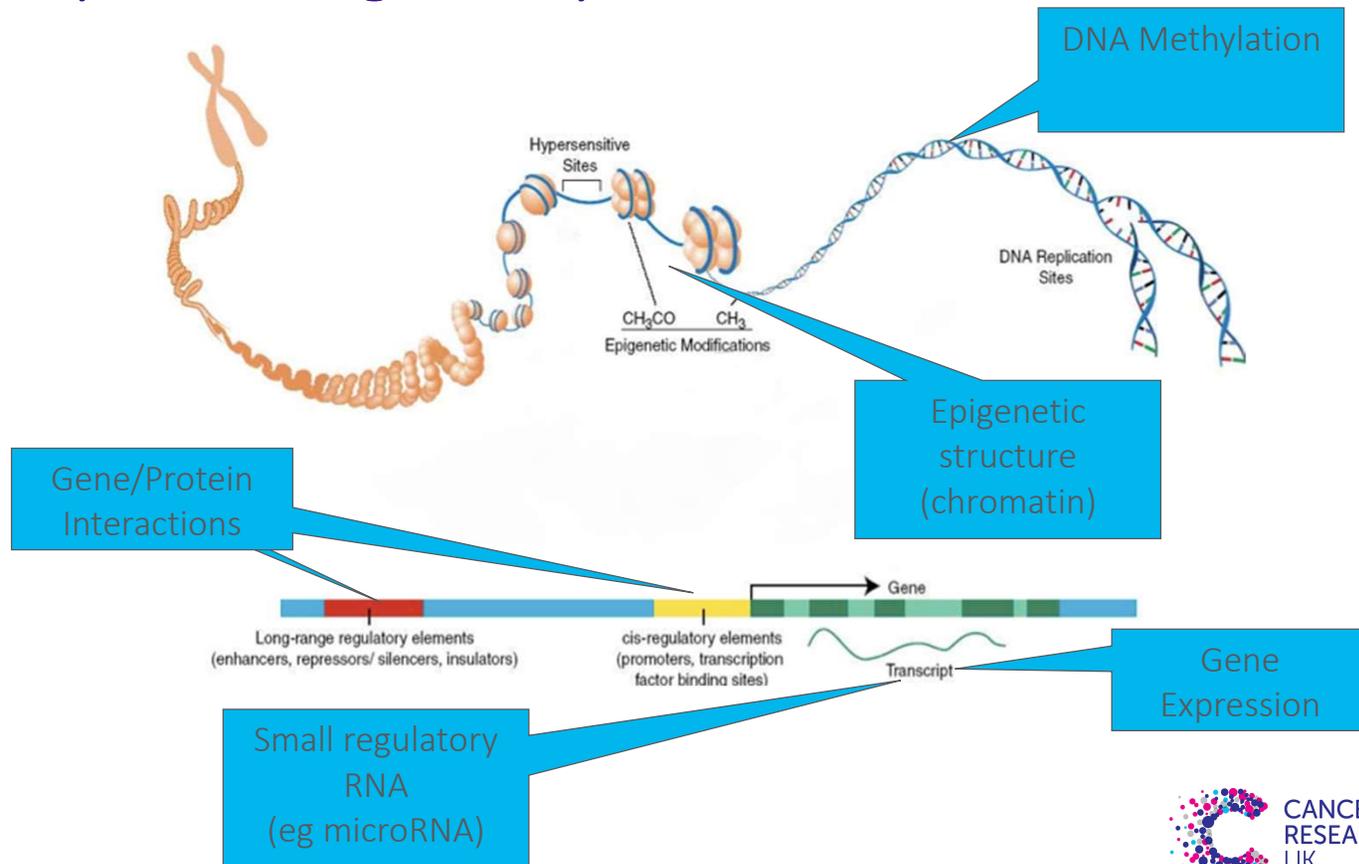


Figure 1.  
**Semi-Unsupervised Gene Expression Array Analysis of a Cohort of Breast Cancers Identifies Several Intrinsic Subtypes**  
 Shown are luminal A (outlined in dark blue), luminal B (pale blue), HER2-enriched (pink), basal-like (red), claudin-low (yellow), and normal-like (green) tumors. Heat map courtesy of CM Perou.





# Transcriptional regulatory elements



# Transcriptional regulatory elements

## Transcription Factors

- CHIP

## Histone marks

- CHIP

## DNA Methylation

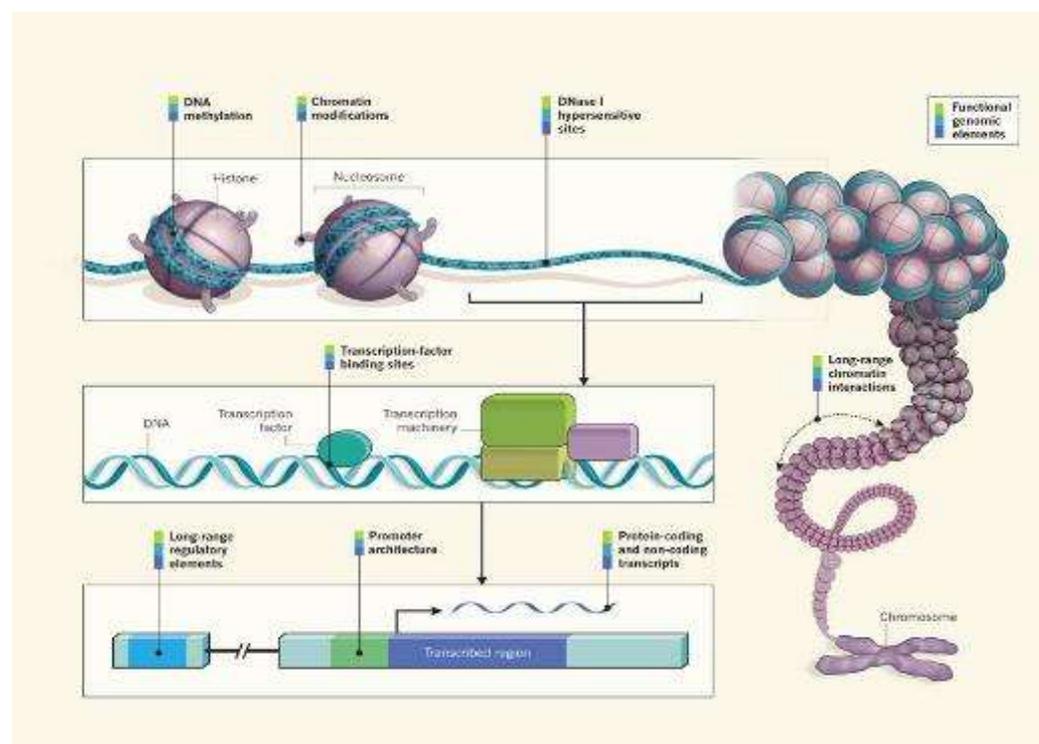
- RRBS
- MeDIP

## Open chromatin

- ATAC

## Chromatin structure

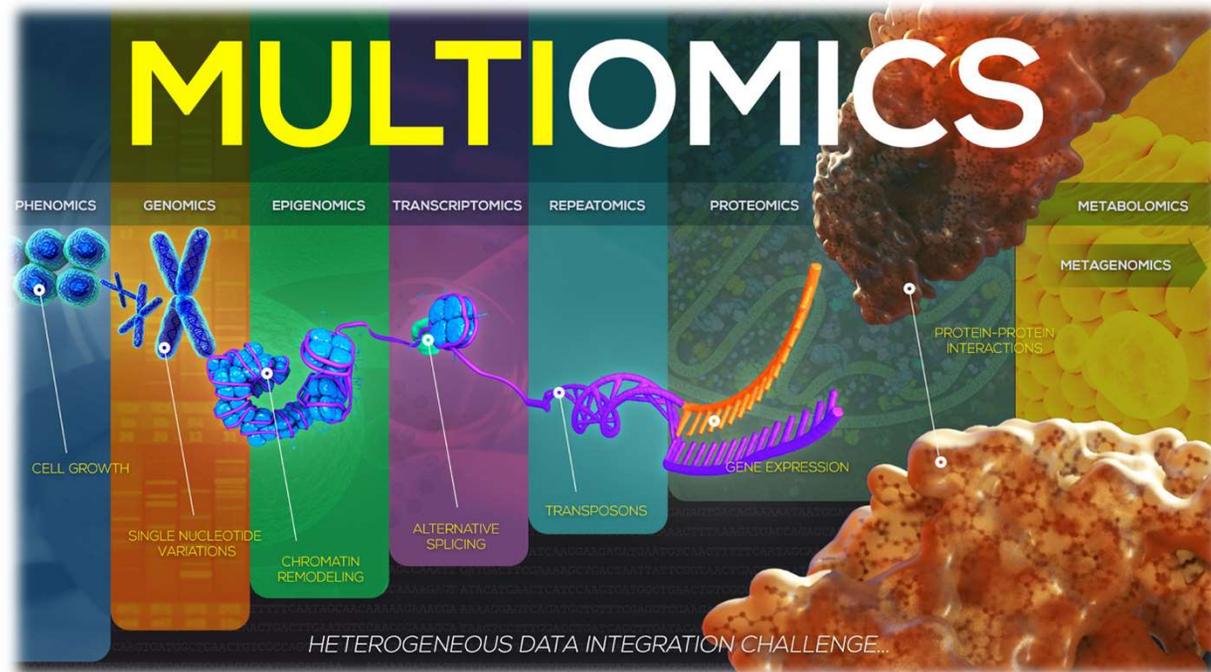
- HiC
- RNA Polymerase
- Pol II ChIP



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# Functional genomics: the ultimate challenge



# ACKNOWLEDGEMENTS

## Historical contributions to slides

Benilton S Carvalho  
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