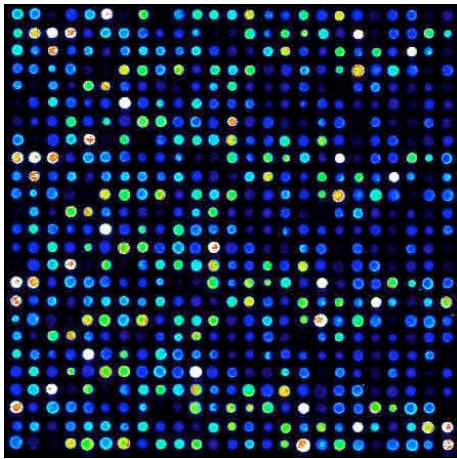


What is a Microarray?

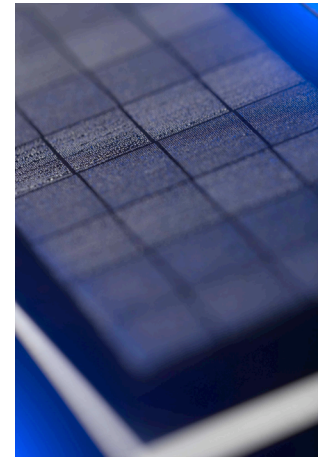


Introduction To:
Discovering Genomic Variation
Seminar Series

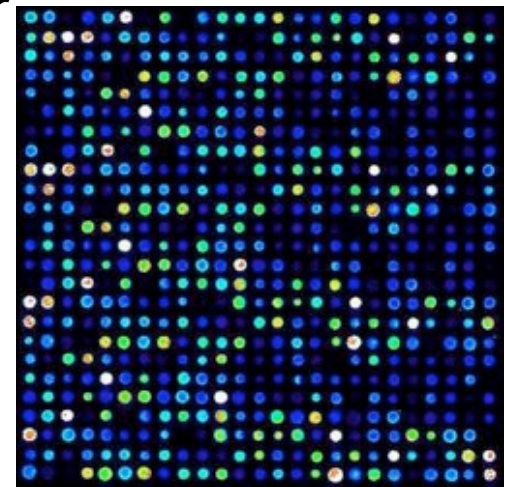
What is a microarray?

- Microarrays (DNA chips) are glass slides with miniature grids of thousands of DNA probes
- DNA microarrays have revolutionised genomic studies - genome sequence resource
- Used to analyse genome variation (DNA & RNA) and the influence on gene function
- Different types of microarray used depending on the research question
- Typically interrogate thousands of DNA probes in one experiment
- High-throughput “massively parallel” and cost effective

Before use...

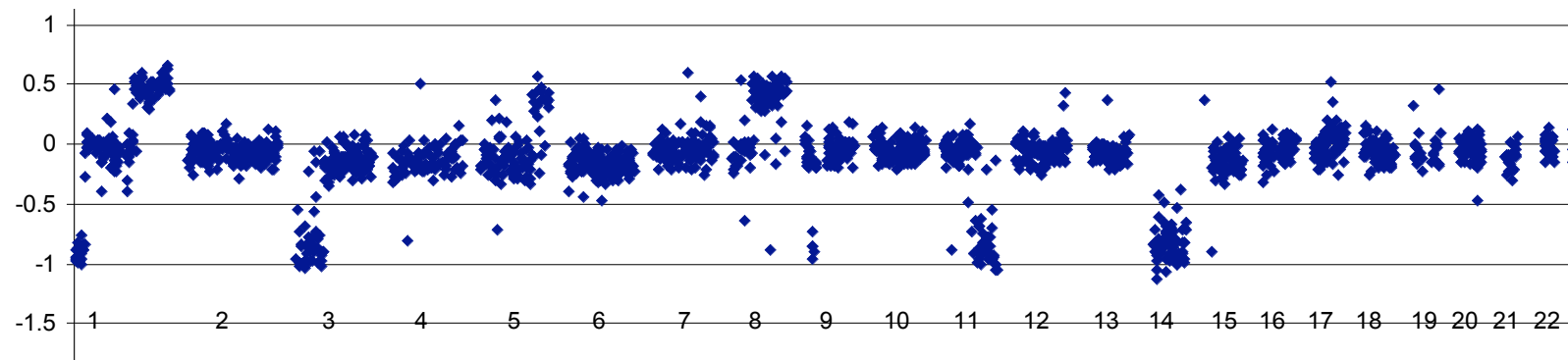


***Magnified
image after
use...***



APPLICATIONS

- Differences (mutations and natural variation) in single DNA bases (SNP genotyping)
- Gene activity levels
- DNA amplification or loss (copy number variation)



- **GENE FUNCTION** - environmental interactions = **risk factors for disease**

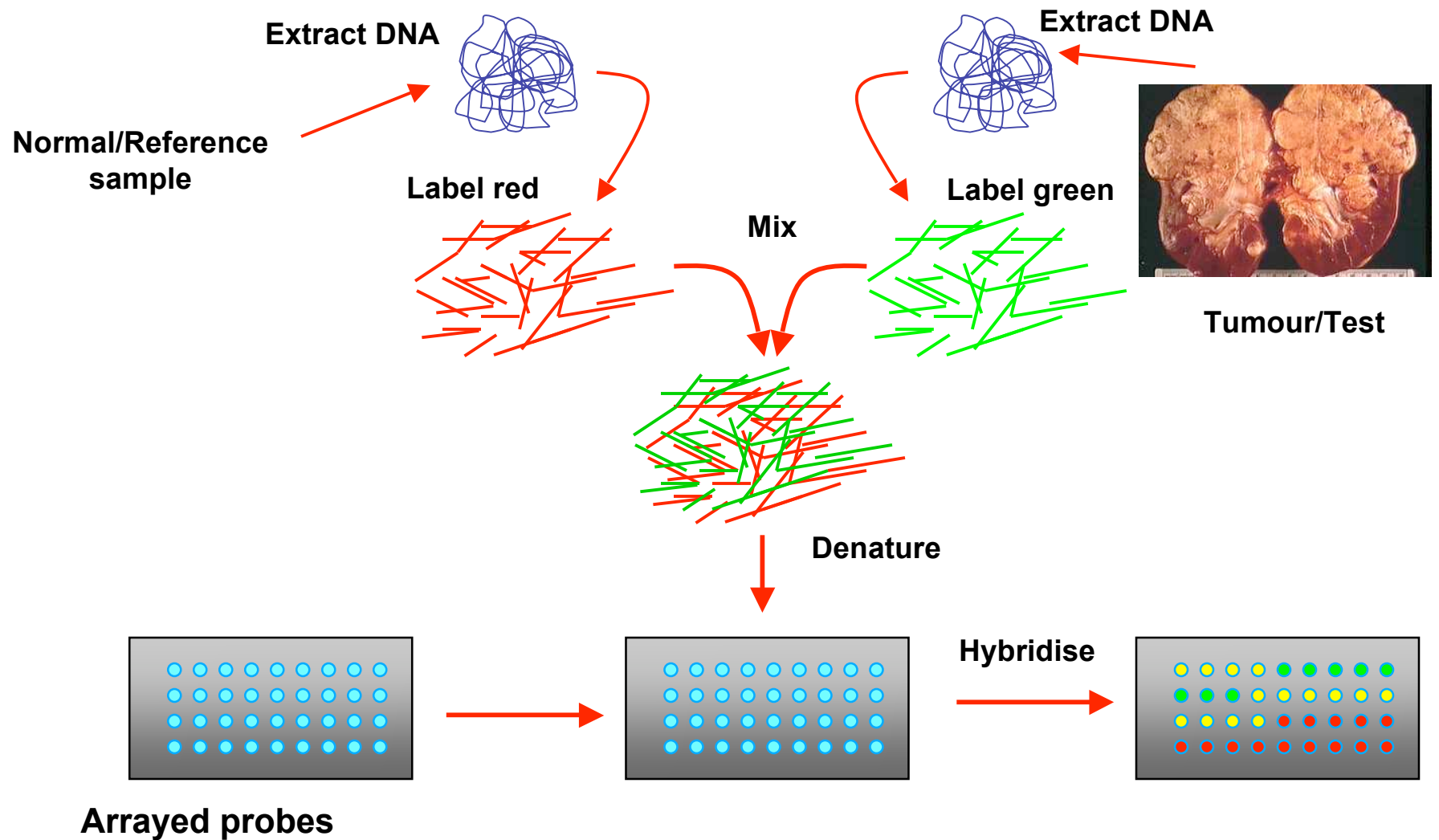
The Art of Hybridisation (1)

- Your Genome (animation)
- Microarrays rely on the nature of DNA
- Double-stranded molecule with complementary bases
- High temperature splits the strands apart (denaturation)
- At lower temperatures the complementary strands re-join (re-anneal)

The Art of Hybridisation (2)

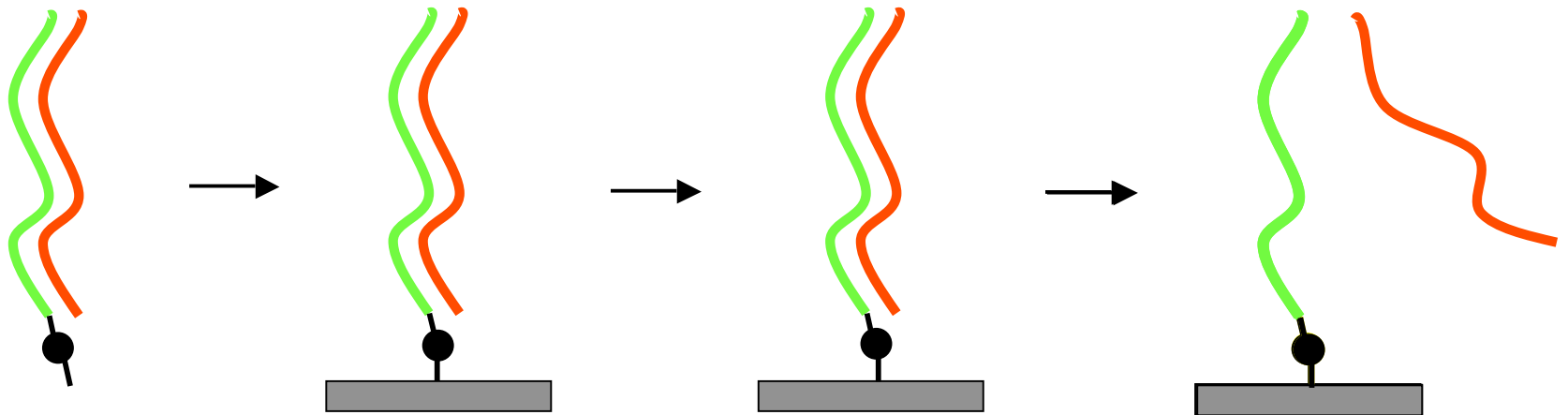
- Microarrays rely on the nature of DNA
- DNA spots are denatured and are single-stranded
- DNA/RNA sample for analysis is denatured
- Mixed together at the correct temperature
- DNA/RNA sample will re-anneal (hybridise) to the DNA spot - as long as sequences are complementary
- Use fluorescence and laser scanners to report the results

Typical Microarray Experiment

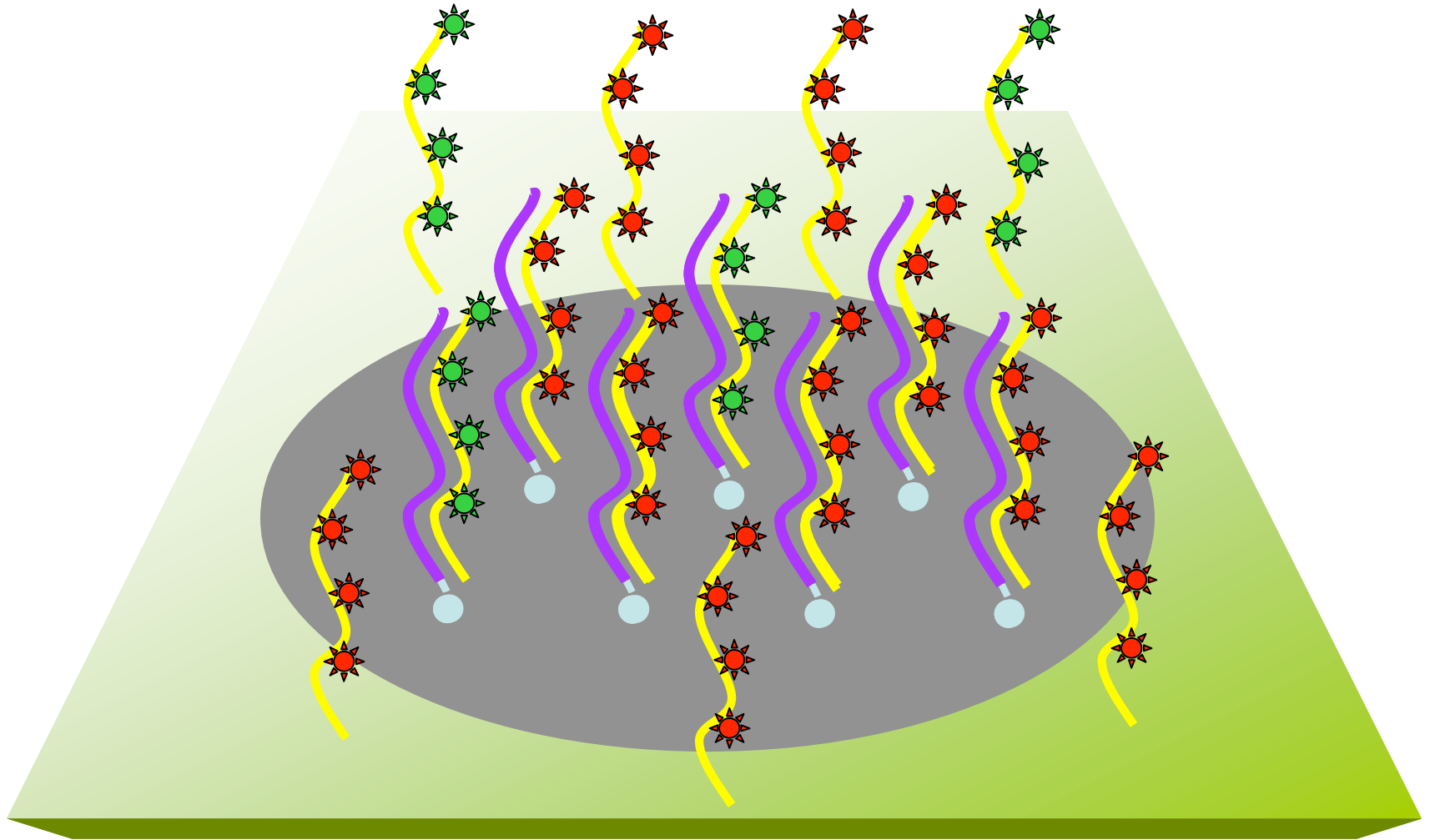


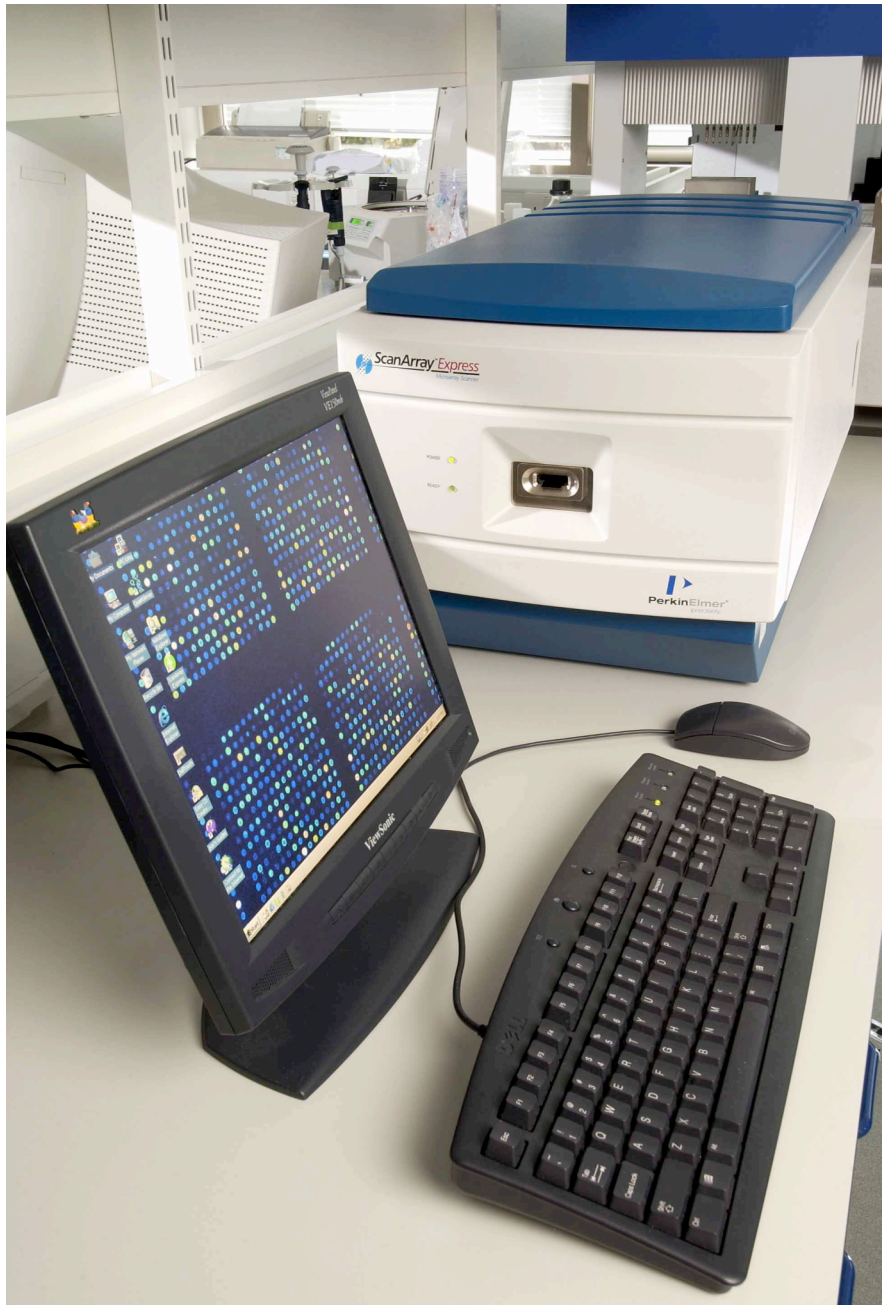
DNA Probe Attachment

- Double-stranded DNA probe chemically bound to slide
- Robotically spotted onto surface
- Single-stranded probes can be made after attachment



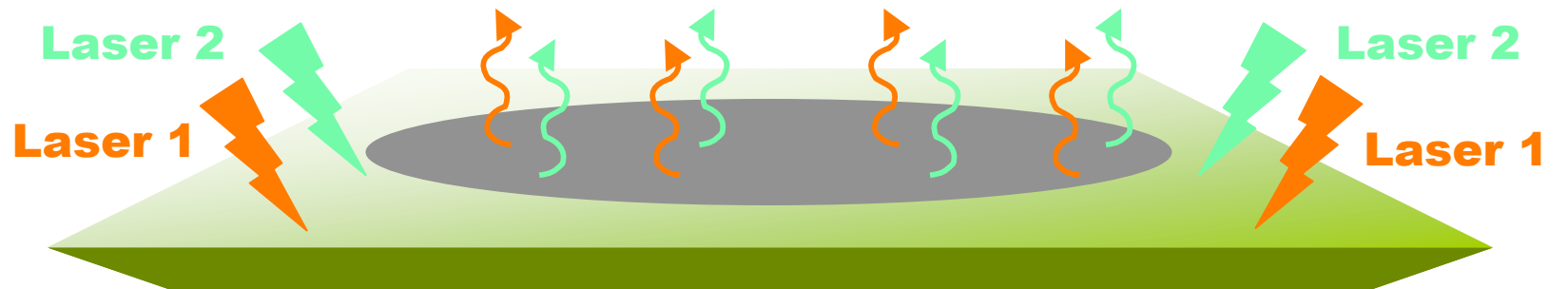
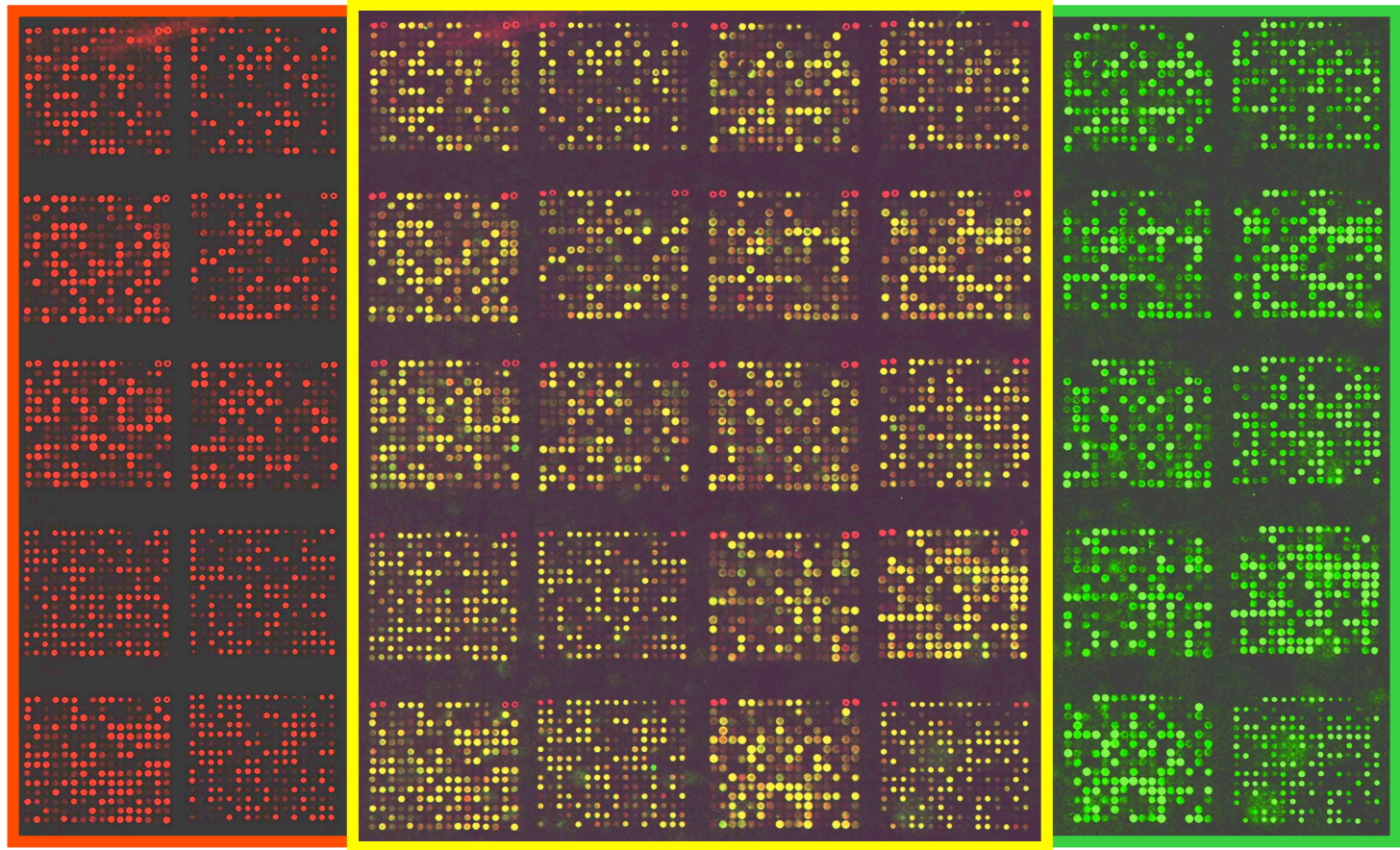
Hybridisation



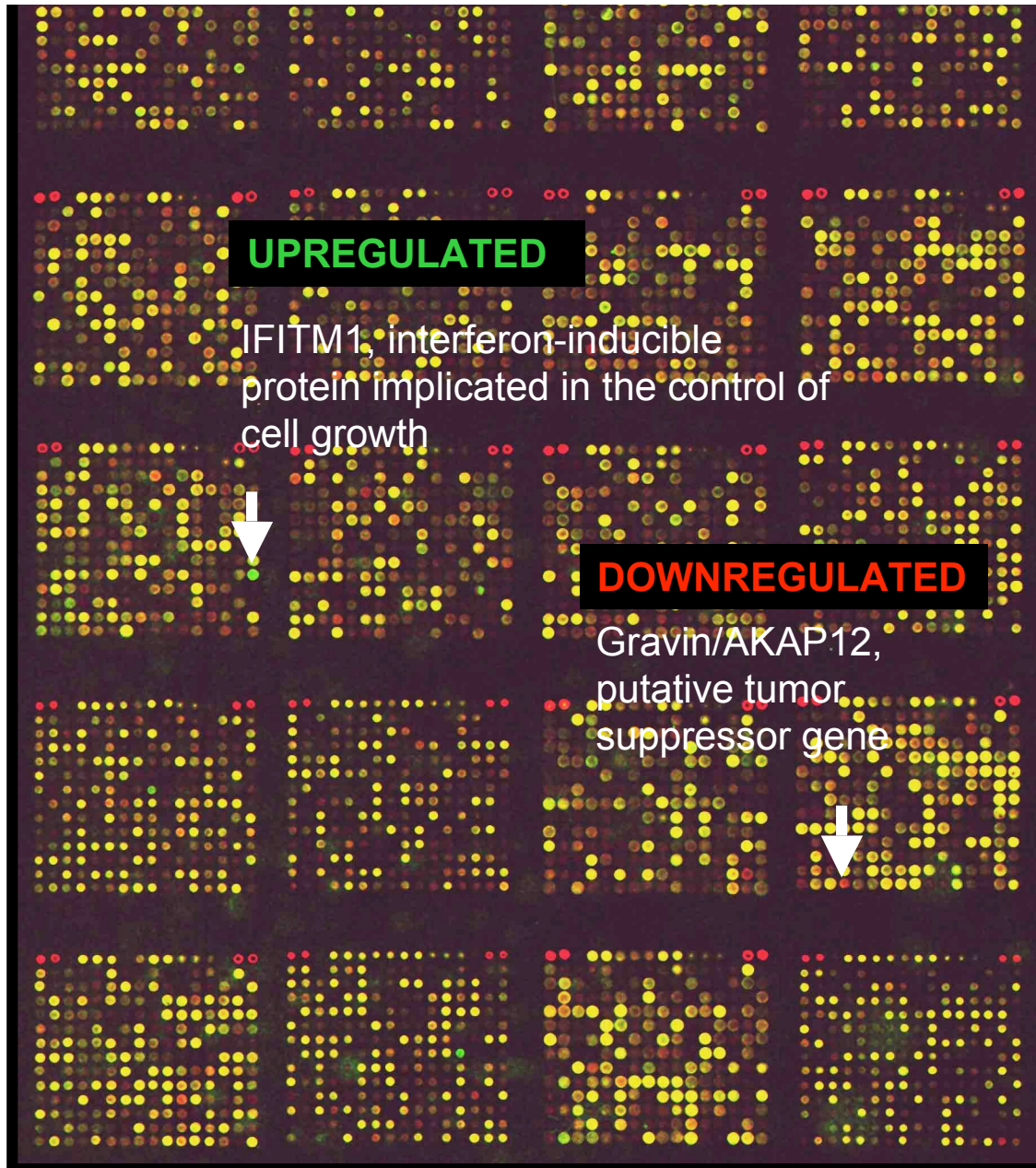


Laser Scanning

- 2-laser system
- Confocal microscope
- Grey-scale TIFF images
- Spot-finding performed using software
- Export raw data in excel or CSV



Immune cells analysed in MDS patients



Leukaemia Classification

Distinguish:

acute lymphoblastic leukemia (ALL)

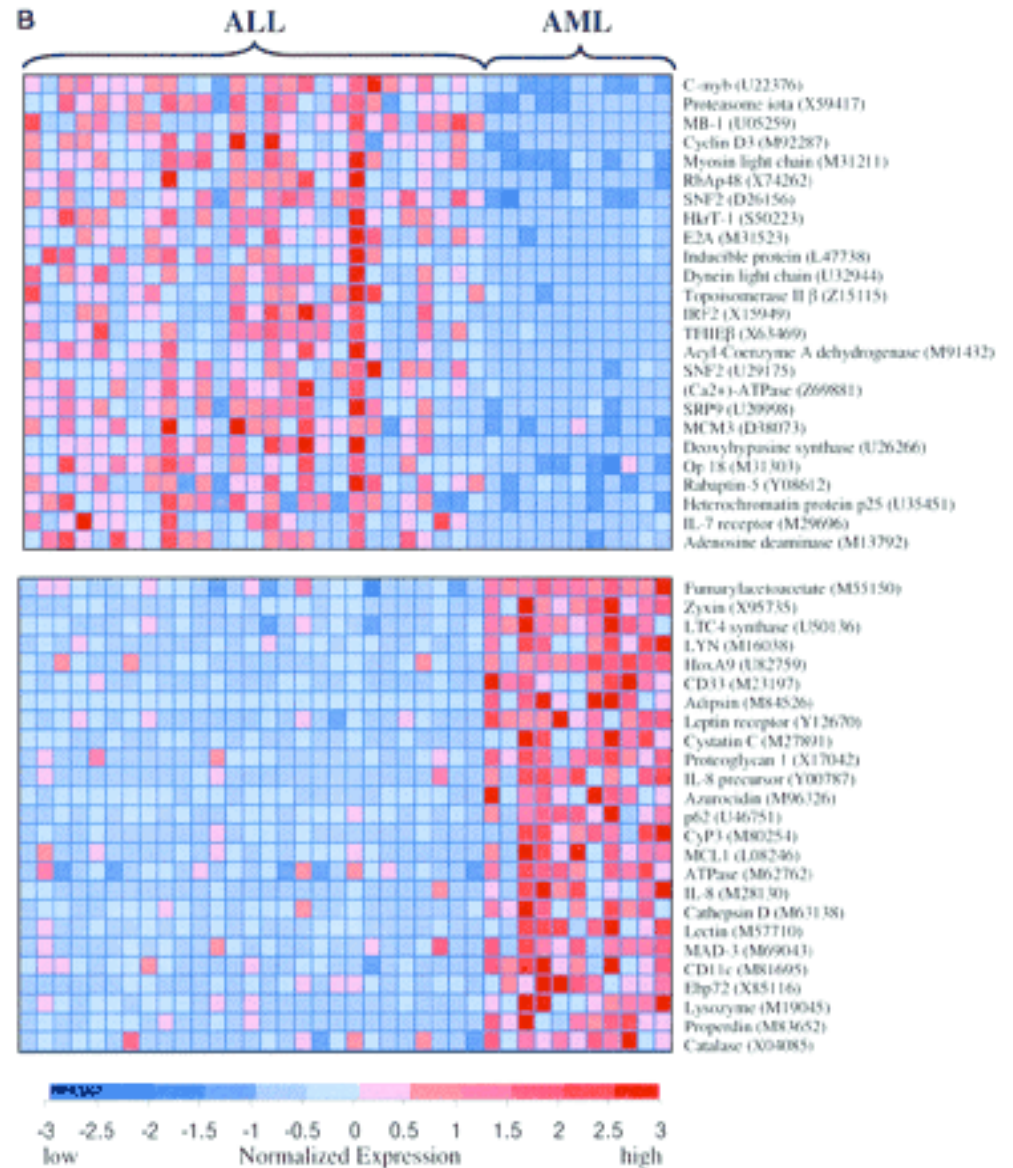
acute myeloid leukemia (AML)

Critical for successful treatment

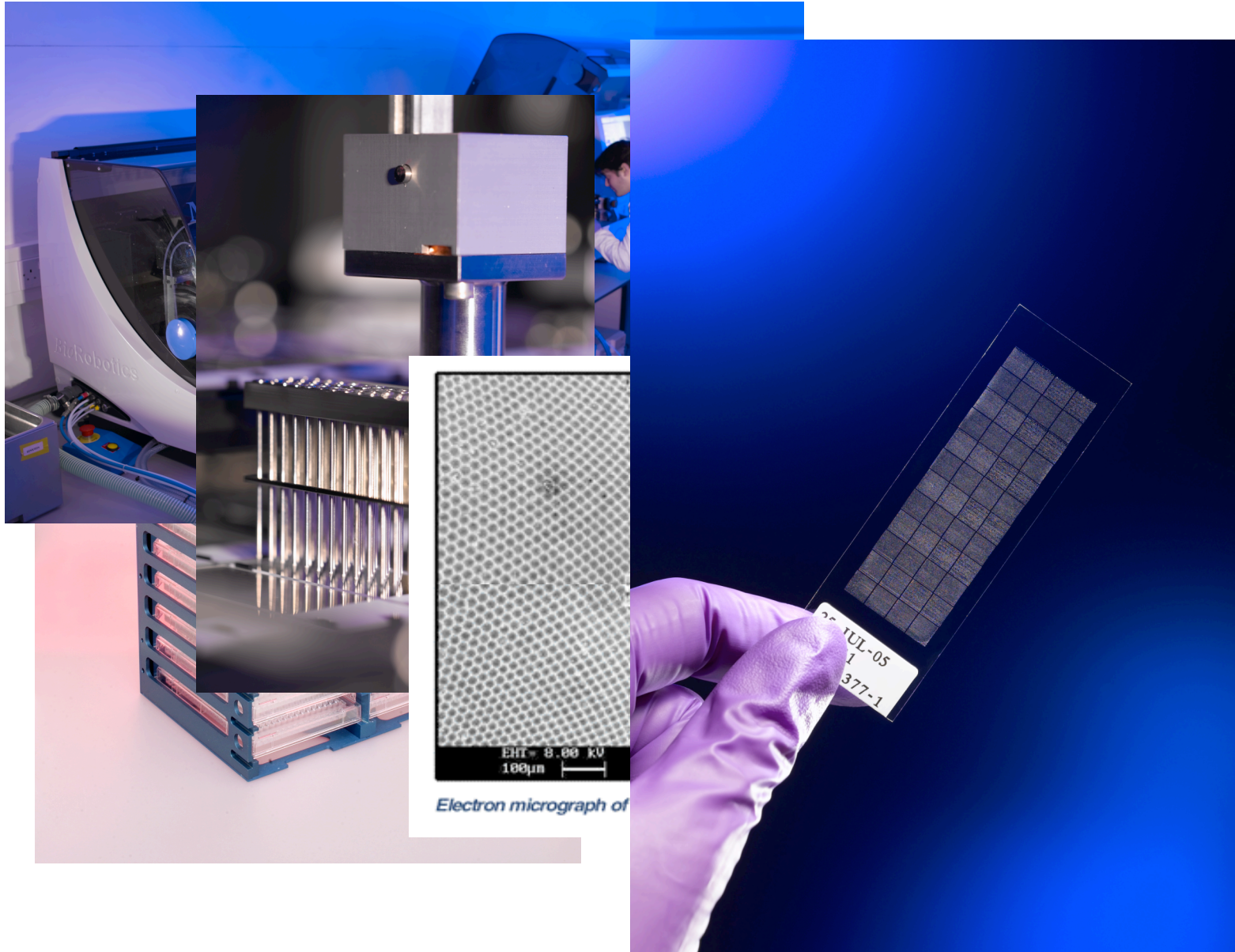
Previously no single test sufficient to establish diagnosis



Golub *et al.* Science (1999) 286:531-7



Spotted Arrays



Next-Generation Array Platforms- State of the Art

- Illumina



- Massive improvement in scale, accuracy and reproducibility

Ethical Considerations

- Microarray experiments generate unprecedented amounts of data
- Information about structure and function of an individual's genome
- Data release policy means data is freely available to all researchers (managed access)
- Anonymised ~ What should it be used for?

In summary

- Millions of DNA probes in a microscopic grid
- Genome variation and influence on gene function
- High-throughput systematic studies
- Gene function and environmental interactions
- Technology continues to evolve
- Ethics
- yourgenome.org

yourgenome.org

Animations
 Video interviews
 Downloadable activities
 Contemporary topics & issues

Wellcome Trust Sanger Institute's
yourgenome.org
 Stimulating interest in and discussion of genetic research

About Us | DNA, Genes & Genomes | Human Genome | Genomes, Health & Society | For Teachers

HUMAN GENOME PROJECT

Discover how the human genome was sequenced, and the data provided free to the world, in this unprecedented international project.

Human Genome Project
 DNA, genes and genomes
 For Teachers
 Sequencing pipeline
 Pharmacogenomics
 Direct - to - consumer

YOUR INTRODUCTION TO DNA, GENES AND GENOMES

A guide to DNA, genes and genomes - and how the instructions they contain are used to build cells and bodies.

- Genomes: The Basics
- Genomes: In Detail

YOUR HUMAN GENOME

Find out about the Human Genome Project, see how DNA is sequenced and explore key genes and locations in our genome.

- The Human Genome Project
- Genome Sequencing Centre
- Genome Explorer

GENOMES, HEALTH AND SOCIETY

Glimpse how new genome research and technologies could affect our health and lives in these topics focusing on contemporary science and issues.

- Genomic disorders
- Pharmacogenomics
- Direct-to-consumer testing
- Personal genome sequencing
- UK National DNA Database

FOR TEACHERS
 Teaching resources including animations, activities and worksheets that support UK curriculum and science specifications for 14-19 year olds.

RESOURCES

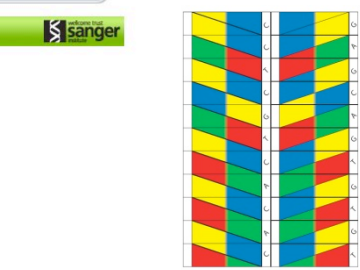
- Animations
- Activities
- Researchers
- Glossary
- Links

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Meet some of the people who have made contributions to genome sequencing and research. Click on a person to access information about them.

 INES BARROSO Metabolic Disease	 JOHN BURTON Sequencing	 PHIL BUTCHER Information Technology	 CAROL CHURCHER Sequencing operations	 CHRIS CLEE Sequencing	 ALISON COFFEY Human genetics
 FRANCIS COLLINS Second Director HGP	 TONY COX Sequencing informatics	 RICHARD DURBIN Informatics	 DARREN GRAFHAM Finishing	 NANCY HOLROYD Sequencing	 TIM HUBBARD Informatics
 SEAN HUMPHRAY Mapping	 MATT JONES Subcloning	Wellcome Trust Sanger Institute's yourgenome.org			
 FRED SANGER Sanger sequencing method	 MIKE STRATTON Cancer Genome Project	<p>The Human Genome Project was an international effort to decode all the DNA letters in our genome.</p> <p>Roll over the pie chart below to see the countries that were the largest contributors.</p> <p>Wellcome Trust Sanger Institute, UK</p>			

Introductions to:
 DNA, genes and genomes
 Human Genome Project



Chimpanzee (*Pan troglodytes*)
 G T A T T T G G G T A A A C C C A G T G

Wellcome Trust Sanger Institute's
yourgenome.org

DNA libraries - making a BAC (Bacterial Artificial Chromosome) library

Sections: 1 2 3 4