

FUTURE TECHNOLOGY ADVANCEMENT IN HEALTHCARE – Perspectives from Pathological Diagnosis

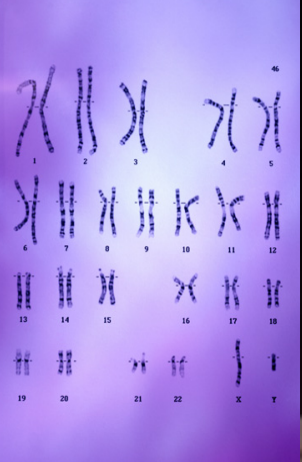
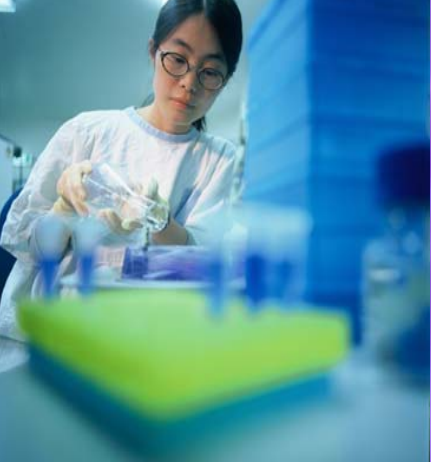
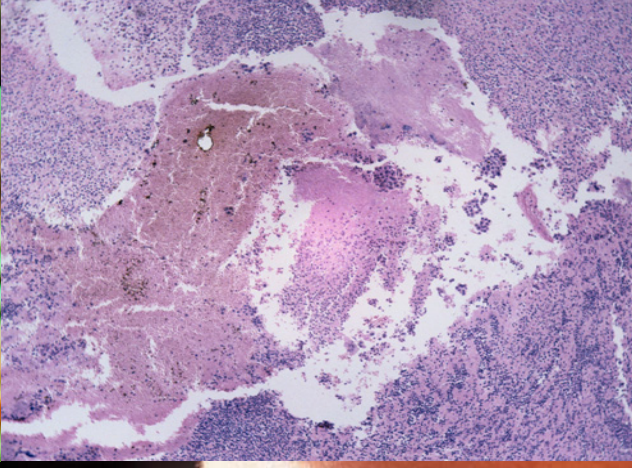
Dr Debra Graves
Chief Executive Officer
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of Pathologists of Australasia



"MEDICINE IS PATHOLOGY"



- Currently 70% of all diagnoses involve pathology testing
- Many chronic conditions require ongoing monitoring using pathology



WHAT IS PATHOLOGY?

- Pathologists are medical practitioners who undertake a minimum of 5 years additional training to become a pathologist
- Also Scientists and Medical Technicians as part of team





A Case for the Coroner



Role of the RCPA

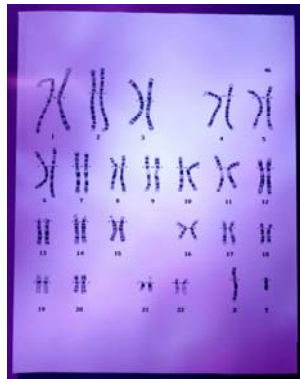
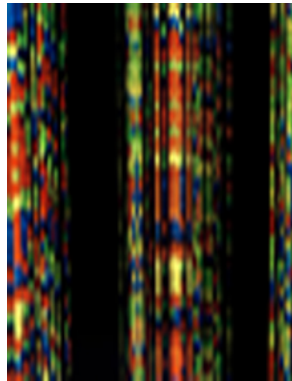
- The College trains in the following 9 sub-disciplines of Pathology:
 - Anatomical Pathology – Cytopathology, Neuropathology
 - Chemical Pathology
 - Clinical Pathology
 - Forensic Pathology
 - General Pathology.
 - Genetic Pathology
 - Haematology
 - Immunopathology
 - Microbiology



OVERVIEW OF PRESENTATION

- The Genetics/Genomics revolution
 - The Need for a National Framework for Genetics
- Advances in diagnostics in each discipline
- Other Issues
 - Point of Care Testing
 - Nanotechnology
 - Informatics

Genetic Pathology



- The College trains in Genetics in three areas
 - Molecular (*the study of the flow and regulation of genetic information between DNA, RNA and proteins*).
 - Biochemical (*study of genetics in terms of chemical events involved*)
 - Cytogenetics (*study and structure of chromosomes*)
- All disciplines have some component of genetics in them

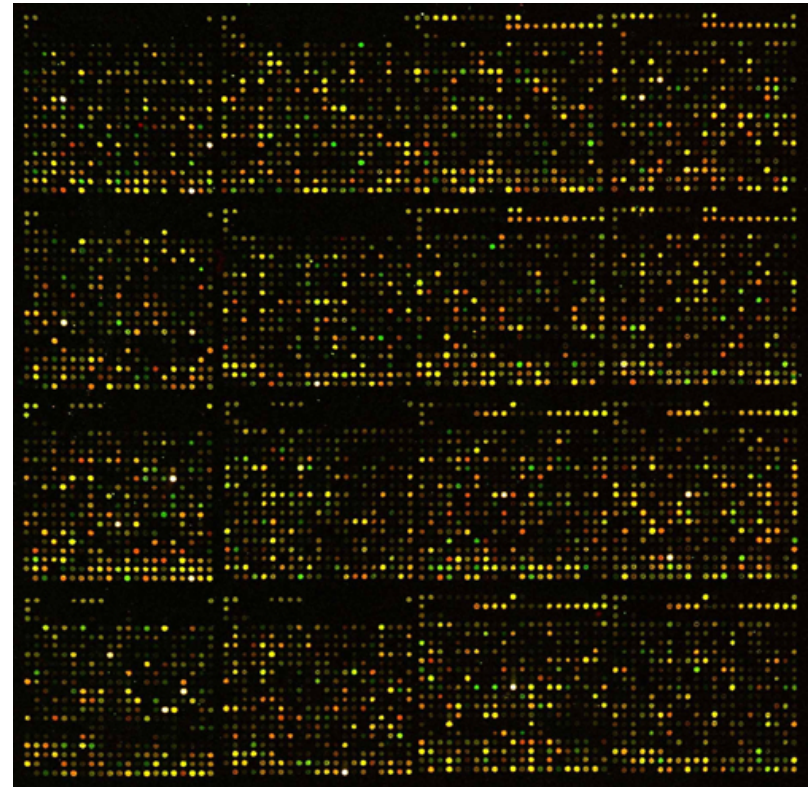
GENETICS and GENOMICS

- Watson and Crick discover DNA 1953
- Polymerase Chain Reaction (PCR) discovery 1983
- PCR allowed application of genes in vitro
- Miniaturisation of Test Platforms e.g. Microarray Technology



Miniaturisation/Microarray

- Miniaturisation has and will have a huge impact on the future of diagnostics
- One blood or tissue sample can be tested for 500,000 genetic variants
- DNA is spotted onto glass, silicon or plastic substrates
- DNA is probed using oligonucleotides, amplicons, (PCR products) or mRNA
- Probes are labeled usually with fluorescent dye and applied to chip where they bind and hybridise to the target DNA and give off fluorescent signal
- This explosion on information is driving the development of very sophisticated pathology informatics to cope with the massive volume of data



Applications for Genetics

- Currently for 4 Major Applications

1. Prenatal Testing

- Examples of current tests: Down's Syndrome, Cystic Fibrosis, Duchene Muscular Dystrophy
- Available to variable extent
- Many more tests possible
- Some ethical issues for this testing

Foetal Cell Isolation from PAP smears rather than Chorionic Villous Sampling

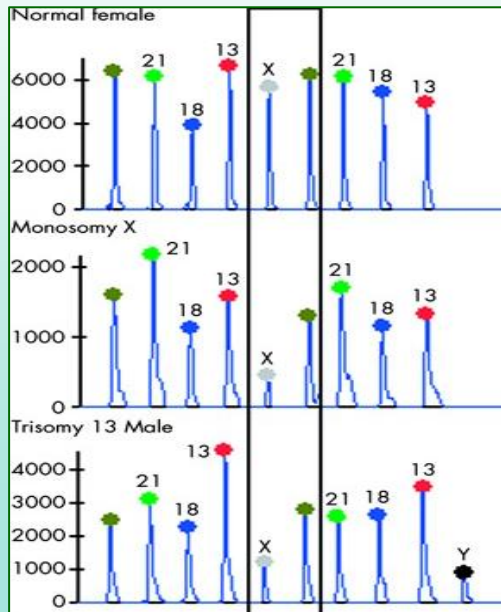
Cell free Foetal DNA in Maternal Plasma-RhD phenotyping

Examples of Prenatal Genetic Tests

PCR-based quantification of gene number

eg rapid screening of amniotic fluid samples for specific trisomies

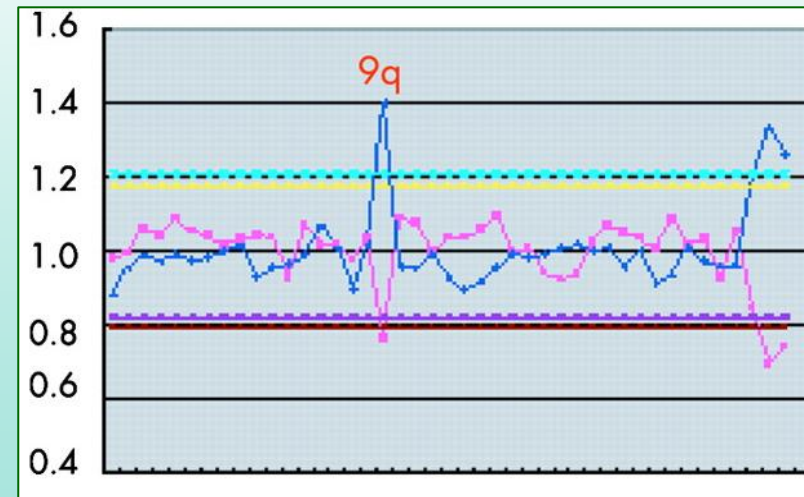
J Med Genet 40:907 (2003)



Microarray detects deletions & duplications

eg screening children with idiopathic intellectual disability

J Med Genet 41:130 (2004)

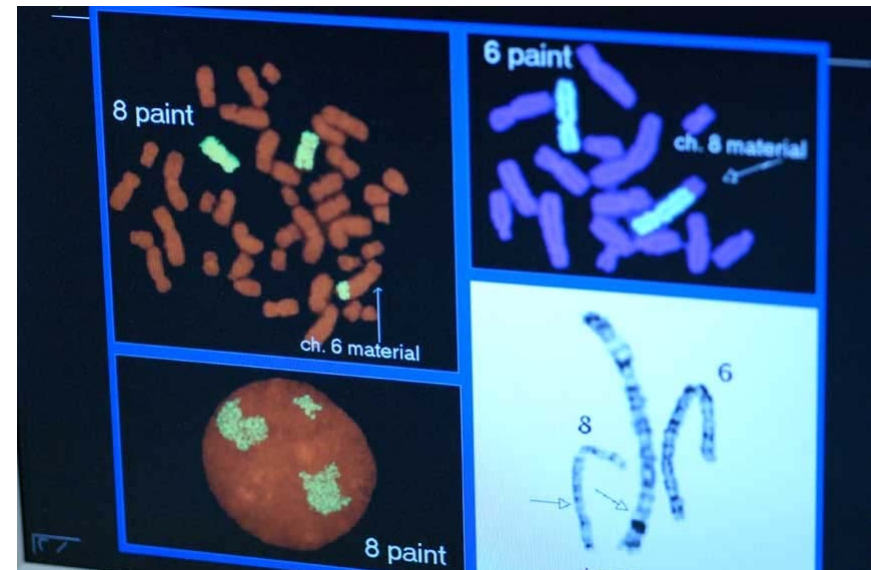


Subtelomeric deletion of 9q not visible on high resolution karyotype

Applications for Genetics

2. Predictive Testing

- Genetic Tests that predict a predisposition to certain conditions and diseases
- Some conditions associated with one gene but many will be caused by multiple genes
- BRAC1 and 2, Familial Polyposis Coli Gene
- Familial Hypercholesterolaemia
- Haemochromatosis
- Long QT Syndrome causing Sudden Death



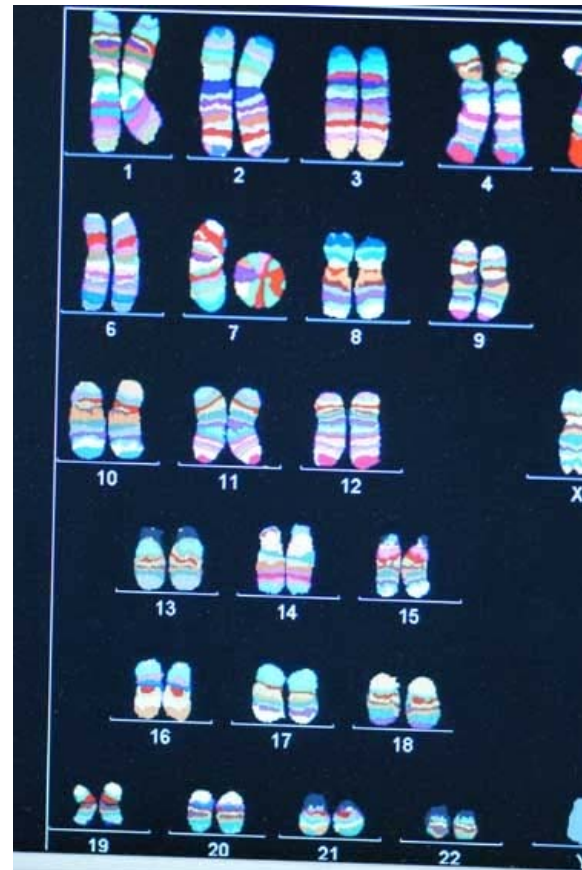
Applications for Genetics

2. Predictive Testing (Continued)

- Fragile X
- Huntingtons' Chorea
- Pharmacogenetics-predisposition to toxicity or lack of benefit from certain drugs eg azathioprine, mercatopurine. In the future warfarin and codeine

*Many more being discovered using
Microarrays*

*This type of testing has major ethical
issues*

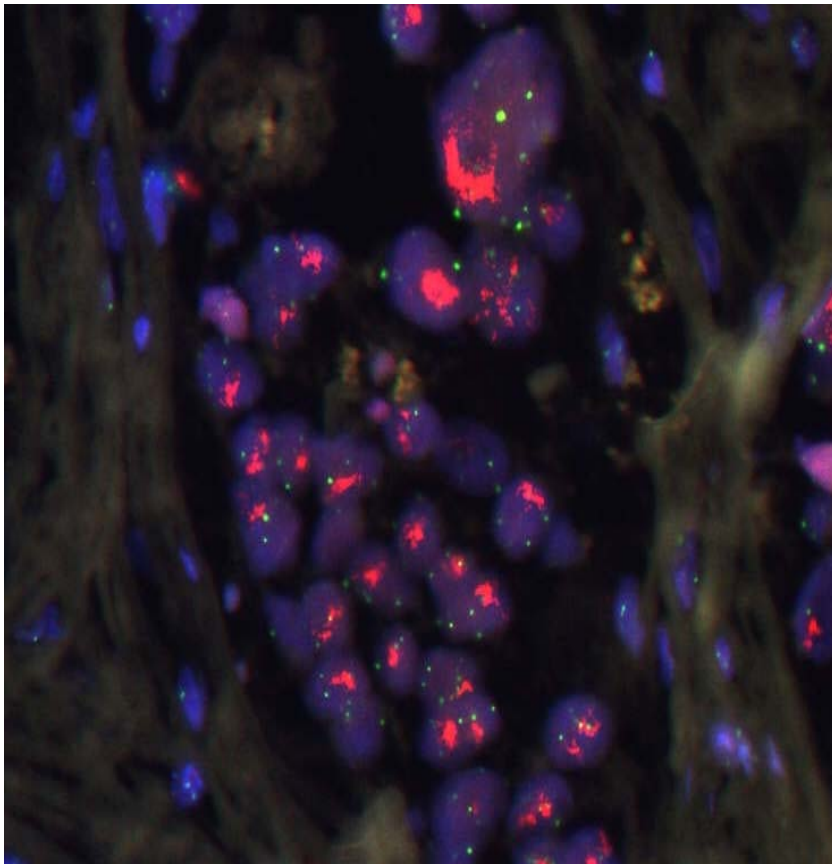


Applications for Genetics

3. **Cancer Diagnosis and Management**

- Rapid genotyping of haematological and solid tissue cancers
- More individual diagnoses for patients
- Development of more targeted therapies eg HER 2 Receptors and Herceptin
- Free EBV DNA sensitive marker for Nasopharyngeal Cancer
- Able to better monitor disease progression
- Potential to detect cancer markers earlier with miniaturisation platforms

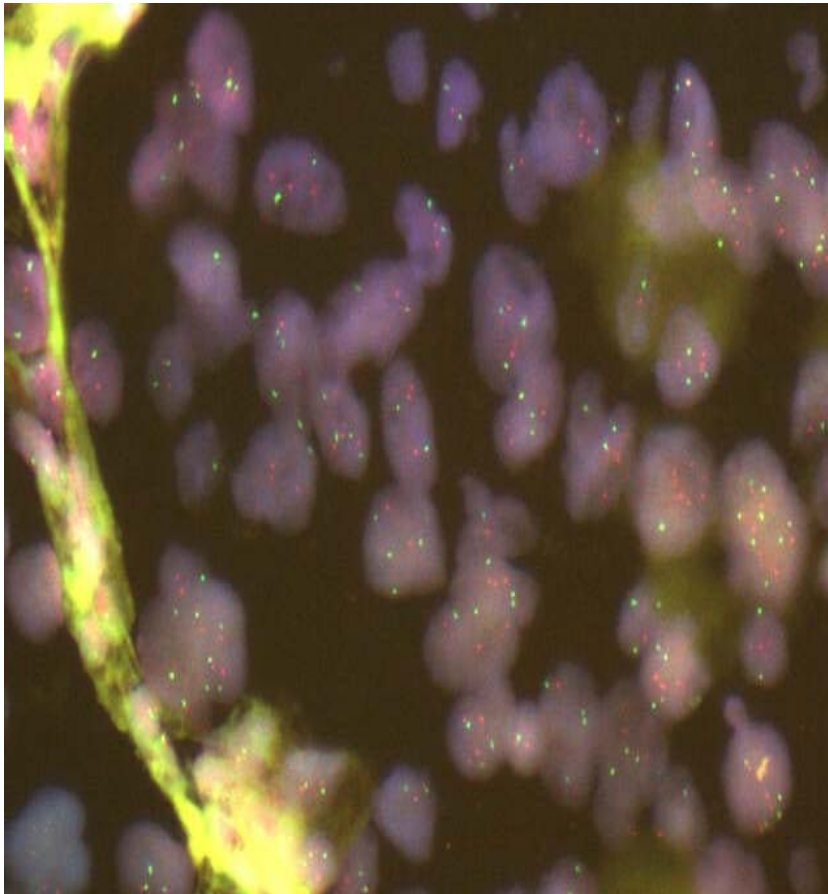
FISH Testing



- FISH testing for HER2 (fluorescent in situ hybridization for HER2 oncogene amplification in breast cancer).

a positive (amplified) case

FISH Testing



- FISH testing for HER2
- a negative (non-amplified) case

Applications for Genetics

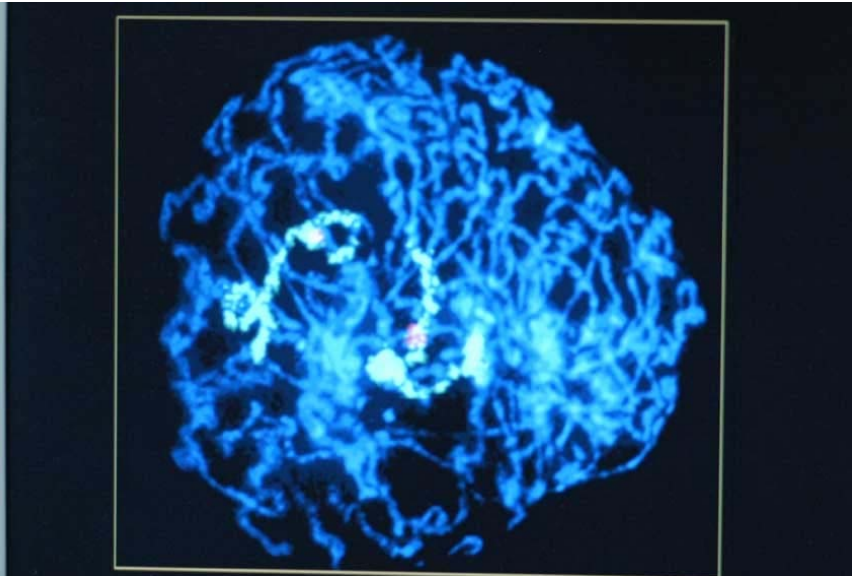
4. Microorganism Detection

- Many microorganisms are now able to be genotyped, rather than performing cultures, serology etc
- Detection of specific bacterial, viral, fungal, protozoal, parasitic or plasmid DNA, viral or ribosomal DNA or viral RNA, using nucleic acid probes with or without preceding PCR amplification.

Diagnosis of donovanosis using PCR of *phoE* gene followed by restriction enzyme digestion



Applications for Genetics

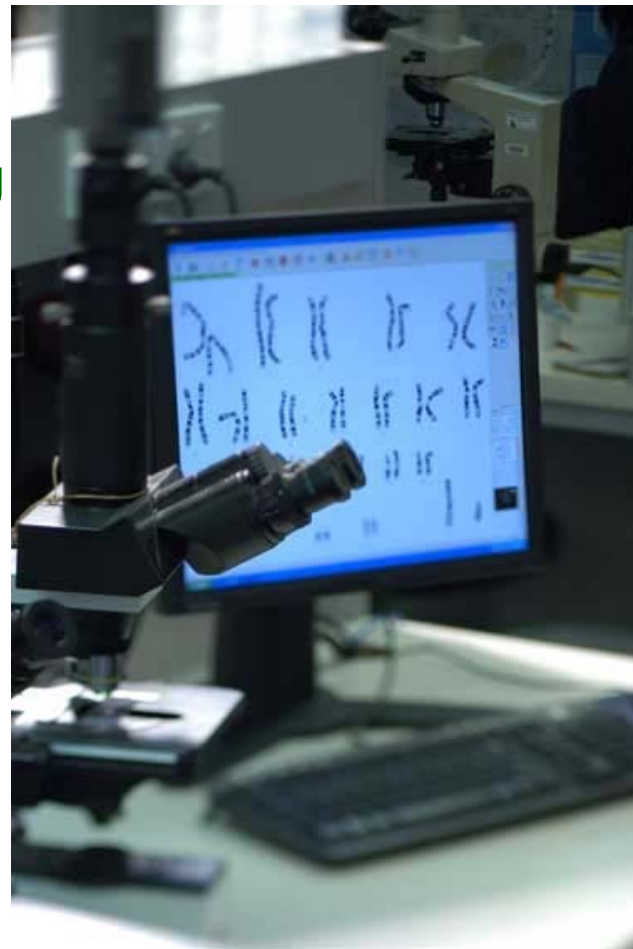


4. Microorganism Detection (Continued)

- Hepatitis C, HIV, Chlamydia
- Important in SARS identification, Influenza
- Human Papilloma Virus Genetic Testing currently available on MBS for Test of Cure
- Should it be used as a general screening tool or for triage after abnormal PAP Smear?

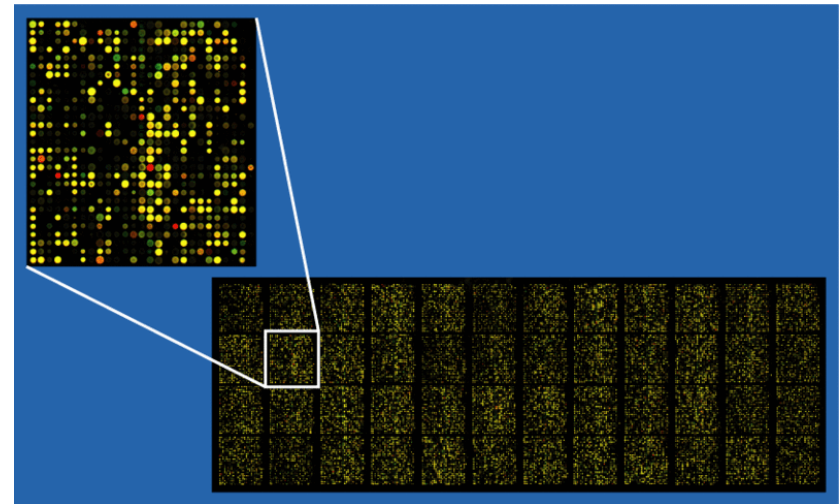
Issues in the Management of Genetics for the Healthcare System

- Australia and NZ and South East Asia are lagging behind places like the UK in planning to deal with this revolution
- Six areas to be considered
 - Regulatory
 - Technology
 - Ethics
 - Funding
 - Workforce
 - Conceptual



Regulatory Issues for Genetics

- Pathology as a discipline has well developed accreditation and quality systems in the traditional areas of pathology
- Need to ensure appropriate accreditation and extend external quality assurance programs to Genetic Testing



Technological Issues for Genetics

- Molecular Genetics is an incredibly powerful diagnostic tool
- Many forget it is just like any other diagnostic tool ie results are not black and white
- Validation of data is needed
- Need very high powered informatics to crunch data
- However what is vital is the further interpretation of what the data means in a clinical setting and this is not straight forward.

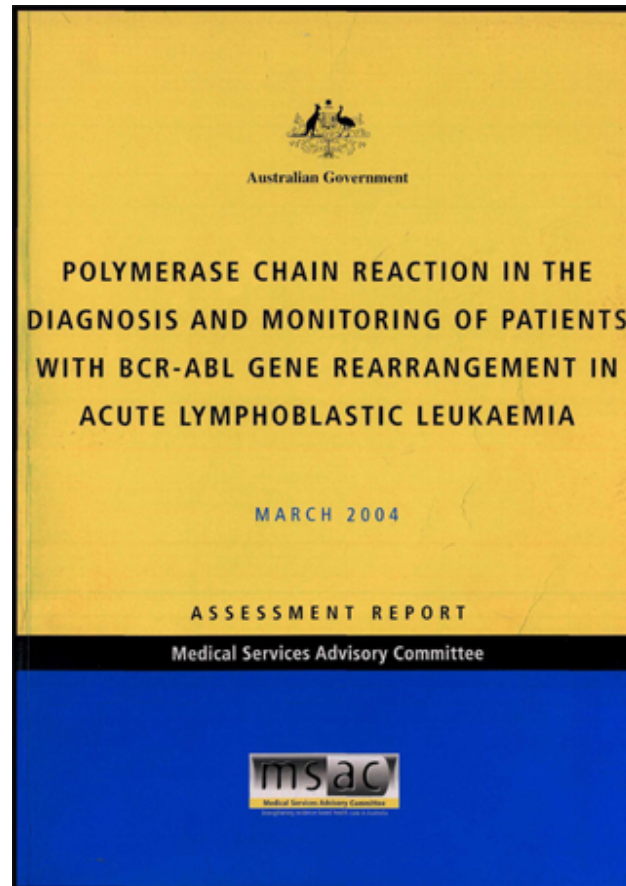
Ethical Issues for Genetics

- The potential impact of genetic testing from an ethical perspective
 - You do not choose your relatives but share genetic information with them
 - Is the concept of personal ownership of genetic data meaningful?
- College considers concern over how to deal with the ethics of genetic testing is a major issues preventing appropriate planning for Genetic Testing in Australia
- Genetic Testing is occurring regardless, without an appropriate framework
- These issues need addressing now in a systematic manner

Funding Issues for Genetic Tests

- Australia, NZ and South East Asia lagging behind places like UK
- In Hong Kong no formal mechanism for funding or identifying which tests are necessary
- Over 300 tested funded by NHS
- NHS also has a National Framework for Genetics

Funding for Genetic Tests



Workforce Issues for Genetics

- A new specialty but no planning for how to grow and manage it
- There are 8 qualified Genetic Pathologists in Australia, there is one Pathologist in Hong Kong with Genetics as their Scope of Practice
- Very few training positions in Australia, none in Hong Kong
- Hard to get Genetic Scientists
- Insufficient Clinical Geneticists and Genetic Counsellors

Conceptual Issues for Genetics

- Potential in the future for genetics to challenge how we look at healthcare
- It is possible, albeit experimental, to test DNA for the degree of genetic fragility or degradation using internationally accepted benchmark assays.
- Cells can be assessed in vitro to determine which nutrients (folate, B6 etc) will reduce the degree of degradation and at what dose the damage will be reduced.
- This is known as Nutrigenomics
- Giving such supplements may reduce the risk of cancer and dementia
- Should it be available to all, only to the rich or mandatory to reduce the burden of degenerative diseases in the community?

National Genetics Framework

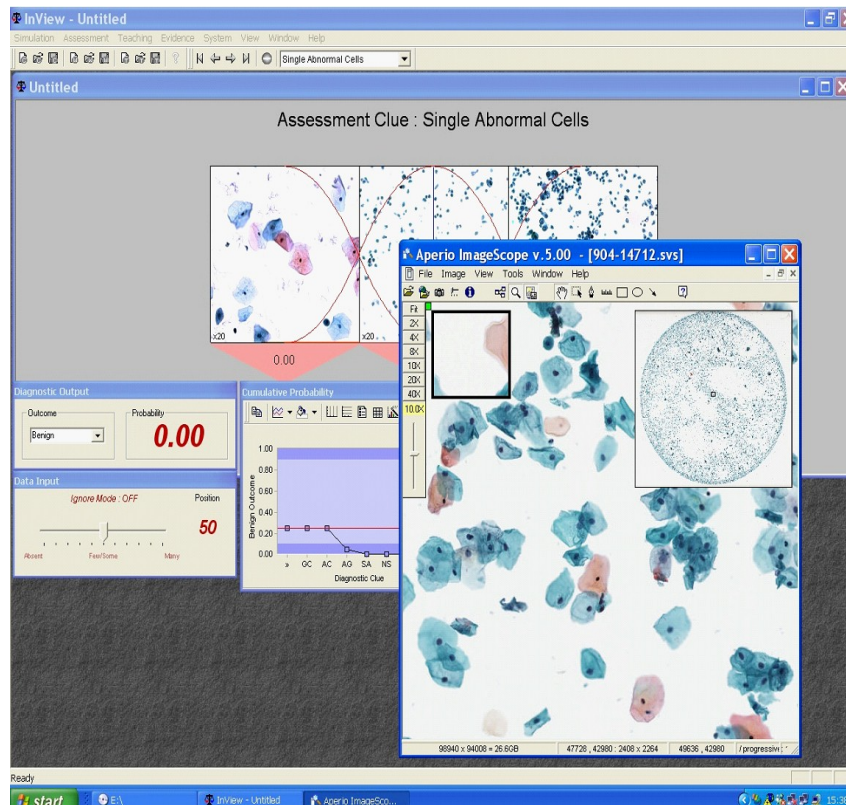
- College calling on Governments to develop National Genetics Framework
- College happy to work with Governments to do this

Other Advances in Diagnostics- Anatomical Pathology

- Virtual Microscopy
- Use in Education and QA
- In the future will be used for diagnostics
- Automated readers

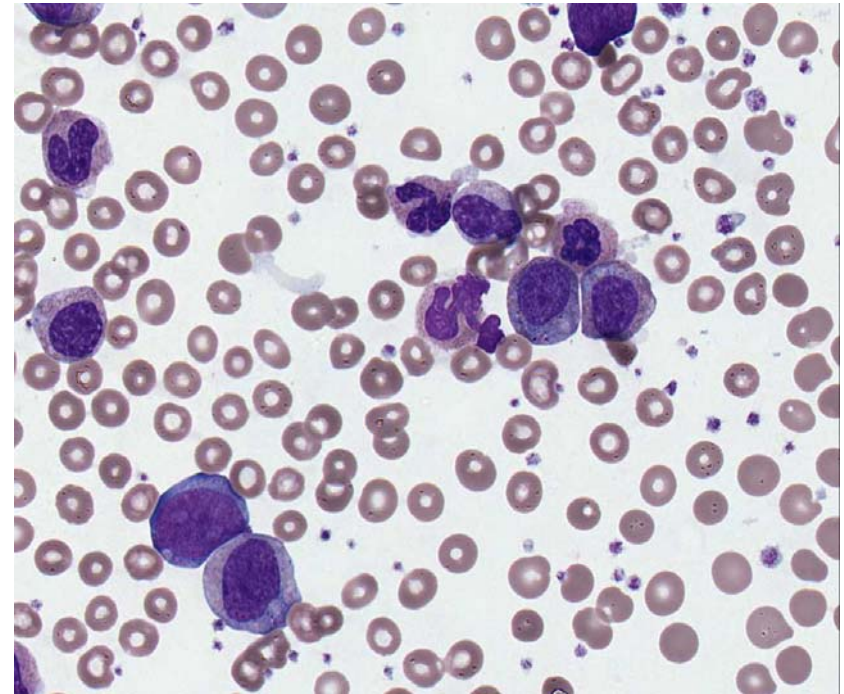
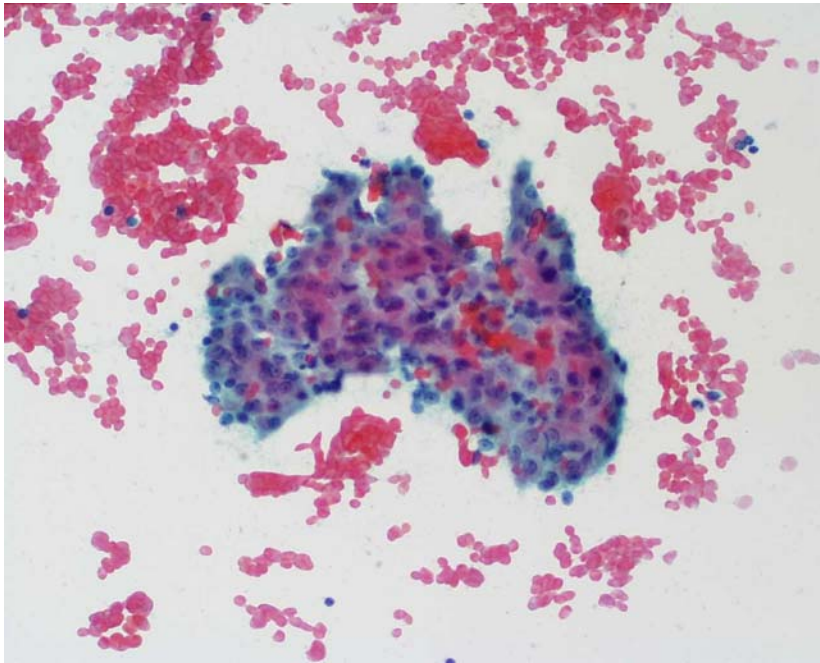


InView



InView is a software platform that provides a completely novel approach to training and education in pathology. The system is designed to teach diagnostic skills using digital slides, virtual microscopy and diagnostic simulation, guiding the user through the diagnosis of each case and comparing a users performance against an experienced pathologist.

Examples of VM in Cytopathology and Haematology



Chemical Pathology

- Use of Pathology Testing in Clinical Algorithms
 - B-Natriuretic Peptide (BNP) to help decrease admission rate, admission to ICU and LOS
- Use of inflammatory markers ie high sensitivity C-Reactive Protein for CVD
 - Highly sensitive therefore useful in ruling out CVD



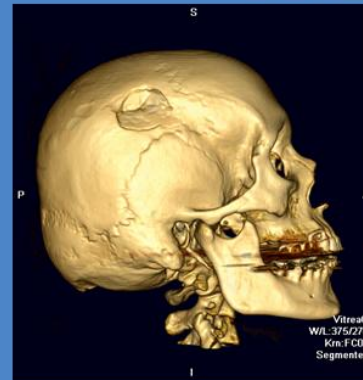
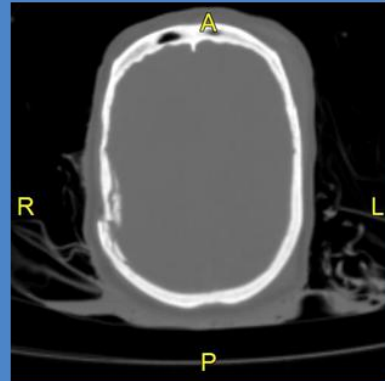
Forensic Pathology

- Molecular Diagnosis had huge impact on Forensics
- CT/MRI Autopsy as an adjuvant not replacement for Autopsy



CT Autopsy

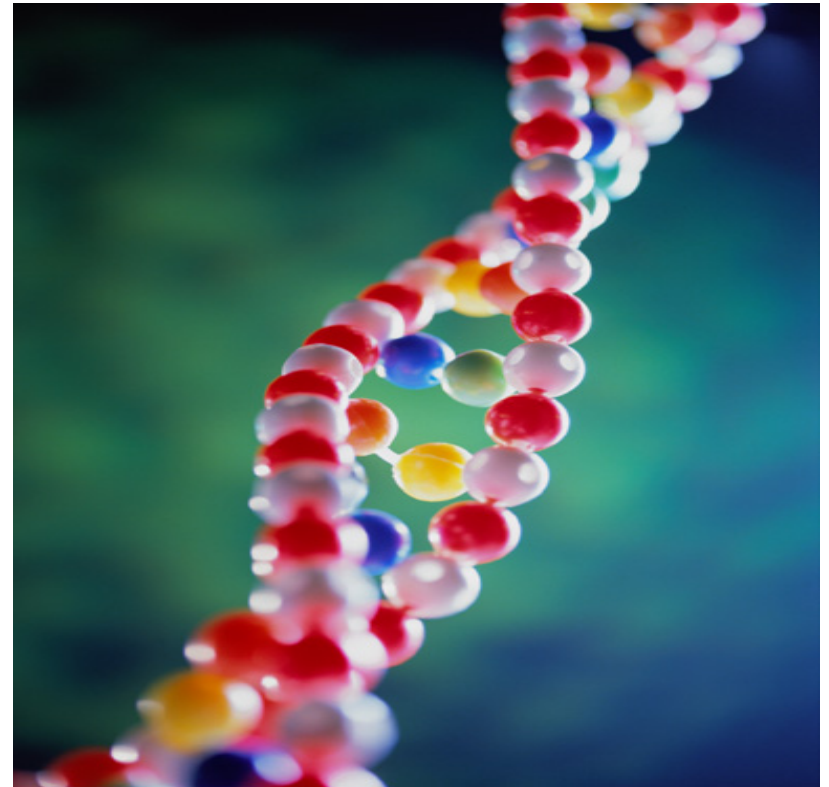
Hammer



VICTORIAN INSTITUTE OF FORENSIC MEDICINE
David Ranson - Deputy Director

Genetic Pathology

- Recent discovery of the importance of micro RNA
- Initially only thought to be important in plants to protect against plant viruses
- Junk DNA codes for them
- They do not produce proteins
- Rather influence protein and gene expression
- Drugs already being made using micro RNA that block proteins that cancers need to grow
- Micro chips have been developed that can detect cancer cells in patients blood



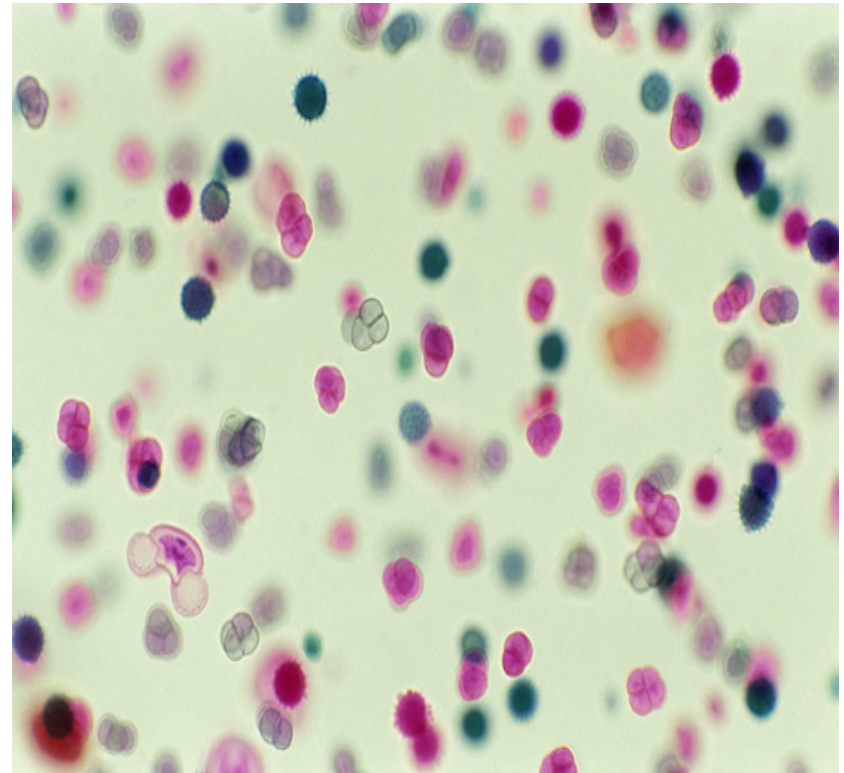
HAEMATOLOGY

- Molecular Genetics has had a huge effect
- Simplification of Blood Cross Match procedure using Computer Cross Matching for straight forward cases



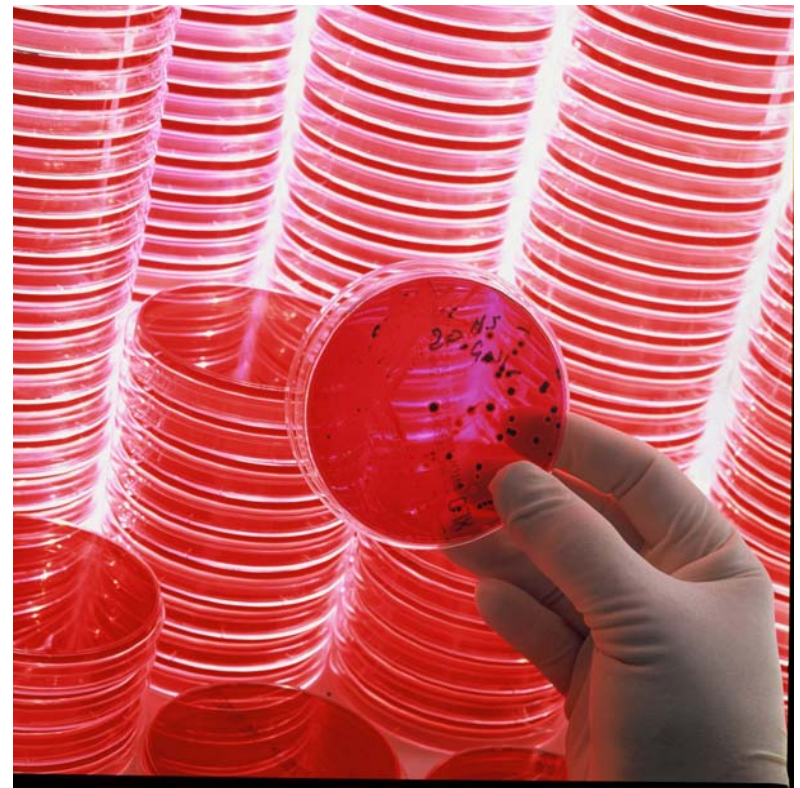
Immunopathology

- The Monoclonal Antibody revolution has already changed how laboratories do tests
 - Have been high molecular weight analytes eg pregnancy testing
- New advances in UK for low molecular weight analytes
 - Very important break through for therapeutic and illicit drug testing at the point of need site eg digoxin, cocaine
- Cancer Vaccine Developments, trials for Melanoma, Prostate



MICROBIOLOGY

- POCTs are a valuable tool for surveillance, for rapid investigation of outbreaks of community acquired pneumonia, and for use in laboratories with limited diagnostic facilities.
- Testing available for Influenza A and B, Pneumococcal disease, Legionella, RSV



POINT OF CARE

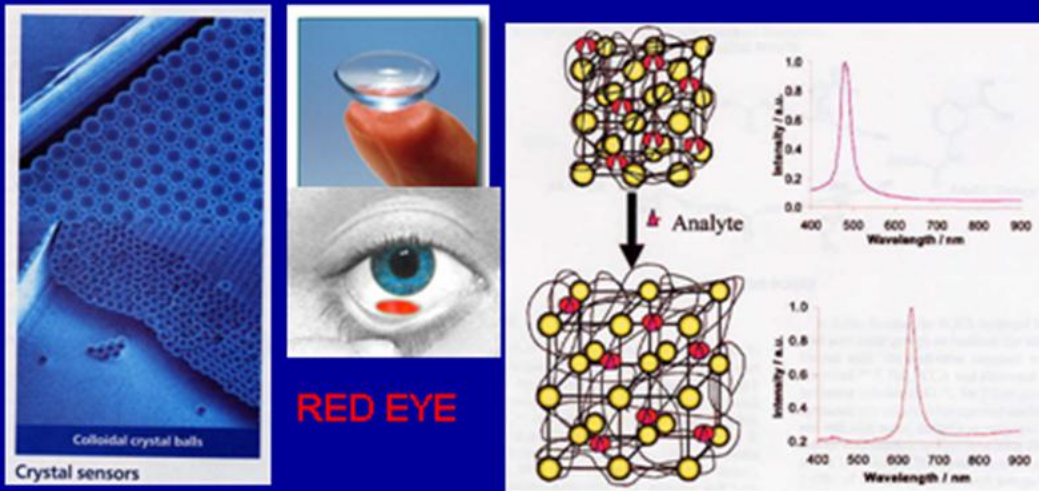
- Miniaturisation of technologies using monoclonal antibodies, microarrays, nanotechnology has and continues to, allow the development of Point of Care/Need Devices
- Any such device still needs to operate in an environment of Accreditation and QA
- Some are better than others
- Best integrated with other testing modalities
- Requiring changes to definition of laboratories for regulatory purposes
- Results must be integrated into patient records

NANOTECHNOLOGY

- DNA Microarrays are starting to evolve into DNA Nanoarrays
- Essentially this will mean that there will again be an increased diagnostic capacity with huge amounts of data
- Research is underway for diagnosis of various cancers using Nanoarrays
- Nanotechnology platform for HbA1c testing trial RNS
- Some interesting examples of Nanotechnology in medicine: wearable and implantable glucose sensors, colour change contact lens with high glucose

Example of Nanotechnology from Professor Larry Kricka USA

3-D NANOARRAY: Photonic hydrogel sensor



Functionalized
polyacrylamide hydrogel

Diffraction of light

INFORMATICS

- Genetics driving need to develop improved systems- huge volumes of data
- Digitisation eg Virtual Microscopy
- Nanotechnology
- Clinical Decision Support Systems
- Laboratory Information systems at higher level of technical development than Hospital Information Systems
- Some thoughts that informatics will drive pathology and radiology practices closer together eg Siemens

QUESTIONS?

