Pathology Facilities and Potential for Collaboration
UWA Pathology and Laboratory Medicine

Pathology Research Themes

- Experimental pathology
- Infection and Immunity
- Translational pathology

Cores

- Core Pathology
- Comparative Pathology
- Genomics
1. Core Pathology

- Centralised facility for the analysis of human, animal and microbiological research specimens.
- Conceptual project design
- State-of-the art pathology services for:
  - Processing and staining
  - Phenotypic and *in situ* genomic analysis of tissue, cells and fluid samples
  - Pathologist interpretation.
- Activities essential to many research groups within WA, are currently performed ad hoc
2. Comparative Pathology Core

- Animal models to enhance our understanding of the pathophysiology of human disease and for the discovery of novel therapeutic agents.

- Experimental studies with animals are a key foundation for scientific and translational research.

- UWA: 40,000 animals are studied annually
  - Diverse range of animal research programmes
  - No systematic pathology provided

- Comparative pathology “core” to provide pathology expertise to animal models of disease.
Comparative Pathology (continued)
Of Mouse and Man

- Genetically engineered mouse mutants: increasing in number and complexity
- Knockout, transgenic, transposon-driven etc
- The effect of specific changes in the genome on disease processes
- Genetic manipulation results in very specific and unexpected tumour phenotypes
- Comparative mouse pathology requires unique skills aided by a knowledge of human pathology
- Comparative pathologists - the gatekeepers of translational research
3. Genomics Core

- UWA has the largest sequencing facility in WA

- Facilities:
  - Multiple technology platforms
  - Genomic databases
  - Extensive bioinformatics tools; metagenomics

- To provide access to efficient, accurate, high-throughput technology (e.g. genomic sequencing, transcriptomics, miRNA detection, genotyping)

- To translate experimental findings to understand the genomic basis of disease.
UWA Core Pathology Facility: proposal

- Further develop and integrate of research in the pathological basis of human disease
- Co-localise research laboratories and core equipment which will be a hub for pathology research in WA
- Promote interaction and collaboration in pathology research within UWA and extramurally
- Ensure rational use of equipment, resources, skills, expertise and infrastructure
- Facilitate translation of discoveries in experimental and applied pathology to patient care
UWA Core Pathology Facility

- A proposal: opportunities and potential outcomes
- Why?
- What is it?
- Expertise and resources available
- How would it work?
- Who would use it?
- Costs and charges
- Advantages
UWA Core Pathology Facility: Why?

- Many disparate groups undertaking a variety of biomedical research projects in WA
  - Sophisticated scientific specialties
  - Many lack the critical support of diagnostic pathology necessary for the analysis of their experimental material, both human and animal
  - Unreasonable to build this expertise into each individual group or research centre.

- “Pre-analytical” processes prior to CMCA
- CMCA: emphasis on instrumentation and analysis
UWA Core Pathology Facility: What?

- Comprehensive pathology services for research projects, including:
  - Sample processing (frozen, FFPE, TMA)
  - Staining of tissue, cells and fluid samples
  - *in situ* phenotyping
  - *in situ* genomic analysis
  - Pathology interpretation of biopsy / cellular samples
- State-of-the-art equipment and pathologist expertise
- Support basic and applied research
- In School of Pathology and Laboratory Medicine
Tissue Processing, Embedding, Microtomy, Staining and Cover-Slapping

- Human or animal specimens
- Tissues, cells
- Standard pathology tissue processing
- Sections: stained or unstained
- Routine stains
- Cytochemical stains
- In situ mRNA and mutations
- Automated cover-slipper
- Other
Tissue Microarrayer (automated)

- 0.6, 1.0, 1.5 or 2mm cores
- Up to 50 cores per block
- Enables high throughput analysis
- For large scale screening

Automated
OpTMA software
CMCA digitisation
Enumeration software
Automated Immunocytochemistry

- **Automated immunophenotyping**
  - Multiple protocols
  - Fluorescent and chromogenic
  - Multiple species

- **Antibody characterisation:**
  - New antibody work-up & optimisation
  - Characterisation on normal tissue

- **Specimen / cell analysis:**
  - Tumour characterisation
  - Cell phenotyping
  - Antibody – Antigen
  - Probe - mRNA
New antibody workup and characterisation
Specimen Analysis
Human (mRNA) and Mouse

Fig 1: MPN bone marrow stains for UbC RNA detection in BM (Fast red) (a.), BCL-XL protein in MK (b.) and pAkt (c.) (DAB).
Imaging Flow Cytometry

AML: *NPM1* mutations, cNPM and Survival

NPM (green) and nuclear stain (pink). Figs E, F show NPM to be in cell nuclei. Figs G, H and J-N show cytoplasmic NPM, features of *NPM1* mutation in AML and good prognosis subtype.

Group A: *NPM1* mutation (cNPM)
Pathologist - Morphologic Interpretation
Comparative Pathology: Transposon driven mutagenesis

Collaborator: The Wellcome Trust Sanger Institute
The Pathologist - Morphologic Interpretation

Cells: Yield, morphology, lineage, purity, quality

Collaborator: BLUEPRINT (EU Epigenetic Programme)
UWA Core Pathology Facility

Customers / Users
- UWA
- PaLM
- PathWest
- WAIMR
- LEI
- ANRI
- Universities
- Hospitals
- Industry
- Other

Consultation with PaLM

Specimens (Animal / Human)

Processing
- Cells & tissue
- Fixation
- Decalcification
- Embedding
- Cytocentrifuge
- Microtomy
- Tissue arrays

Sections & Staining
- H & E
- Giemsa
- Romanowsky
- Cytochemistry

Phenotyping
- Immunocytochemistry
- Imaging flow cytometry

Genetics
- In situ hybridisation
- In situ PCR
- In situ mRNA Sequencing

Pathology
- Haematology
- Cytology
- Anatomical pathology
- Diagnosis

Special Microscopy
- Multi-header teaching microscopes
- Projection microscope
- Scanning electron microscope

Centre for Microscopy, Characterisation and Analysis
- Laser micro-dissection
- Flow cytometry
- Image analysis
- Cell sorting
- Digital images

Outputs
- Translational Pathology
- Personalised Pathology
- Research
- Cell Biology
- CMCA
The Scientist and Pathologist

- Key personnel
- Range of scientific and pathology expertise
- “Up-front” consultation to assist with project design and research question being asked
- Advice re specimen types, processing, staining protocols
- Animal (comparative), human; tissues and cells
- Trouble-shooting
- Interpretation
Advantages of a Core Pathology Facility

- Such comprehensive range of pathology services does not currently exist in UWA or other WA university
- Complement and enhance biomedical research
- Improve quality of pathology and research generated
- Improve data generated with CMCA:
  - The “pre-analytical phase”
  - Standardisation of sample preparation
  - Geographical proximity with QEII node of CMCA
- PaLM already taking advantage of pathology / CMCA relationship
Who Would Use a Core Pathology Facility?

- Research groups:
  - Models of pathological disease processes
  - Genetically engineered mutant animals
  - Pharmacological effects
  - Translational and applied human pathology

- Promote interaction and collaboration in pathology research within UWA and extramurally

- Facilitate translation of discoveries in experimental and applied pathology to patient care
The “Business End”

➔ Department of Commerce
   “Research Centre Program”

➔ “Fee-for-service”

➔ Collaboration:
   • Genuine collaboration on a project
   • Current collaborators:
     – WAIMR
     – The Sanger Institute
     – BLUEPRINT (Uni Cambridge)
Funding Model

- Department of Commerce “Research Centre Program”

- “Fee-for-Service”:
  - Staff costs
  - Consumables
  - 35% infrastructure levy
  - No detail …..

- Costs to be included in research grants

| Consultation with PaLM re project design |
| Tissue processing and embedding (paraffin) |
| Tissue microarray: planning and preparation |
| Tissue microarray: block creation |
| Tissue sections (routine block) |
| Tissue sections (TMA block) |
| H&E stain (single section) |
| H&E stain (TMA) |
| Other stains (e.g. Romanowsky) |
| Immunohistochemistry: antibody provided |
| Immunohistochemistry: antibody work up |
| Immunohistochemistry: rodent antibodies |
| Cytocentrifugation |
| Technical / Scientific time |
| Pathologist interpretation |
| Photomicrography (digital) |
Concluding Remarks

- Centralised core pathology facility to advise, support or carry out work for research groups
- Discuss project with pathology prior to commencing
- Equipped with state-of-the art facilities
- Expertise: technical, scientific and pathology
- Aim to provide investigators with the highest quality pathology with rapid turn-around to help meet individual research needs
- Complements services in CMCA