“Models of molecular pathology training”

Manuel Salto-Tellez, MD (LMS), FRCPath, FRCPI
Professor and Chair of Molecular Pathology
Clinical Consultant Pathologist
Lead, Precision Medicine Centre of Excellence
DISCLOSURES

Senior Scientific Advisor & Consultant, Philips
Scientific Advisory Board, Visiopharm
Scientific Advisory Board, Targos

Last 5 years:
Almac Diagnostics
Visiting Pathologist, Targos

Advisory boards and honoraria from:
Roche, MSD, Pfizer, Astra Zeneca, BMS
<table>
<thead>
<tr>
<th>Speaker</th>
<th>Location</th>
<th>Time</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fred Bosman, Switzerland</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philip Quirke, United Kingdom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katrien Grünberg, The Netherlands</td>
<td></td>
<td>14:00 - 14:10</td>
<td><em>Postgraduate pathology training should be general; subspecialty comes later</em></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicki Cohen, United Kingdom</td>
<td></td>
<td>14:10 - 14:40</td>
<td><em>Postgraduate training in pathology includes a phase of sub-specialisation</em></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manuel Salto-Tellez, United Kingdom</td>
<td></td>
<td>14:40 - 15:15</td>
<td><em>Models of molecular pathology training</em></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peter Schirmacher, Germany</td>
<td></td>
<td>15:15 - 15:25</td>
<td><em>Training of academic pathologists: the German way</em></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philip Quirke, United Kingdom</td>
<td></td>
<td>15:25 - 15:35</td>
<td><em>Training of academic pathologists: the British way</em></td>
</tr>
<tr>
<td>Speaker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folkert van Kemenade, The Netherlands</td>
<td></td>
<td>15:35 - 16:00</td>
<td><em>Training of academic pathologists: the Dutch way</em></td>
</tr>
</tbody>
</table>
References


THE 3 REVOLUTIONS IN PATHOLOGY (*)

EARLY To MID XX Century

PATHOLOGY AS A CLINICAL DISCIPLINE

( * ) Salto-Tellez, Maxwell and Hamilton. Artificial Intelligence - The Third Revolution in Pathology Histopathology, 2018, accepted for publication
Early 1980s, peroxidases begin to be favoured and IHC begins to be a general technique.
Tissue Specificity
(lineage specific)
Content In this article, we would like to analyse the three distinct roles of IHC and review their individual impacts on modern diagnostic pathology: (1) diagnostic IHC; (2) genetic IHC and (3) therapeutic IHC.

Background Immunohistochemistry (IHC) plays a central role in the histopathological classification of diseases, including cancer. More recently, the importance of immunohistochemical staining is increasing. IHC usage in diagnostics is invaluable; however, the genetic and therapeutic significance of biomarker immunostaining has become equally relevant.

Summary Thus, we will characterise the different analytical processes that are required in the three approaches to IHC usage stated above, as well as the clinical significance and overall importance in patient management. This will allow us to hypothesise on the most appropriate laboratory environment and detection methods for the future.
EARLY To MID XX Century

1953

Watson, Crick and Franklin discover the DNA double-helix

EARLY 1980s

Early 1980s, peroxidases begin to be favoured and IHC begins to be a general technique

2018

PATHOLOGY AS A CLINICAL DISCIPLINE

THE 3 REVOLUTIONS IN PATHOLOGY

1st Revolution in Pathology

Precision Medicine Centre of Excellence

Queens's University Belfast
THE 3 REVOLUTIONS IN PATHOLOGY

1953
Watson, Crick and Franklin discover the DNA double-helix

EARLY To MID XX Century
PATHOLOGY AS A CLINICAL DISCIPLINE

1st Revolution in Pathology
EARLY 1980s
Early 1980s, peroxidases begin to be favoured and IHC begins to be a general technique

2nd Revolution in Pathology
2004-8
Main solid tumour tests are available

2018

?
Early 1980s, peroxidases begin to be favoured and IHC begins to be a general technique.
THE 3 REVOLUTIONS IN PATHOLOGY

1953

Watson, Crick and Franklin discover the DNA double-helix

EARLY To MID XX Century

PATHOLOGY AS A CLINICAL DISCIPLINE

1st Revolution in Pathology

EARLY 1980s

Early 1980s, peroxidases begin to be favoured and IHC begins to be a general technique

2nd Revolution in Pathology

2004-8

Main solid tumour tests are available

3rd Revolution in Pathology

2018

Artificial Intelligence Digital Pathology

2010

NGS begins to be widely available

?
“The 14 Steps of Routine Tissue Diagnostics”. In Salto-Tellez, Maxwell & Hamilton; *Histopathology* 2018, accepted for publication.
THE FUTURE OF PATHOLOGY IN THE NEXT 10 YEARS... HOW AMBITIOUS DO YOU WANT TO BE?
THE FUTURE OF PATHOLOGY IN THE NEXT 10 YEARS... HOW AMBITIOUS DO YOU WANT TO BE?

THE FUTURE OF PATHOLOGY IN THE NEXT 10 YEARS... HOW AMBITIOUS DO YOU WANT TO BE?

The Value of traditional Pathology has not diminished. It is simply no longer sufficient.

Jared Schwartz, CAP President, 2007

Under this new model DNA sequence data produced centrally would be distributed via a central database to local NHS Genomic Medicine Centres, where NHS staff, often supported by their colleagues in academia, will be responsible for the interpretation of the DNA sequencing results. The longer this system is in place the better it should become for patients; the consistent reporting will be increasingly supported by knowledge about the DNA sequence, which flows from regularly updating and analysing the central DNA database.
The future of medicine will be dictated by MDT-like decision making diagnostics and therapeutics.

More Than a Decade of Molecular Diagnostic Cytopathology Leading Diagnostic and Therapeutic Decision-Making

Editorial

Manual Salto-Tellez, IMS/MD, FRCPath, FRCP
HOW DO WE TRAIN
THE MODERN PATHOLOGIST?
The CM-Path initiative is a National Cancer Research Institute programme, which aims to achieve the change needed to support academic cellular molecular pathology in the UK and make the resulting benefits available to the wider diagnostic and research community, in the UK and globally.

CM-Path WS1
Genomic Impact in Tissue-Cellular Pathology
Towards a new Training in Molecular Pathology

Co-Leads:
Professor Manuel Salto-Tellez (until 2017)
Professor Louise Jones

#CMPath
CM-Path Workstream 1

Skills and Capacity Workstream

- Molecular Pathology Training
- Developing academic pathology
- Training pathologists in clinical trials
- Pathology in the undergraduate curriculum

Input from trial designers and funders

Input from patients and public

Dr Tomoko Iwata, University of Glasgow
Dr David Moore, University of Leicester
Dr Jackie James, Queen’s University Belfast
Professor Kikkeri Naresh, Imperial College London
Dr Caroline Young, University of Leeds
Dr Hayley Morris, University of Glasgow
Dr Emily Shaw, University of Southampton
Dr Nick West, University of Leeds
Dr Maria Calaminici, Barts Cancer Institute
Professor Richard Byers, University of Manchester
Professor Mohammad Illyas, University of Nottingham
Dr Shirley Henderson, University of Oxford
Dr Nicki Cohen, King’s College London
Dr Aislinn Stevens, Queen’s University Belfast
Dr Kathryn Griffin, University of Leeds

Professor Louise Jones
Morphomolecular pathology: setting the framework for a new generation of pathologists

J Louise Jones,1,2 Karin A Olen,3 Jessica L Lee1 and Manuel Salto-Tellez4

Time for change: a new training programme for morpho-molecular pathologists?

David A Moore,1 Caroline A Young,1 Hayley T Morris,2 Karin A Olen,3 Jessica L Lee4 J Louise Jones,1 Manuel Salto-Tellez4


Copyright Article author (or their employer) 2017. Produced by BMJ Publishing Group Ltd under licence.

Most Read Articles

Time for change: a new training programme for morpho-molecular pathologists?
7 November, 2017

Future-proofing pathology: the case for clinical adoption of digital pathology
5 August, 2017
Training Models in Pathology

- 2 weeks to 3 months of attachment to a Mol Path Lab + Self-study
- 0.7 – 5% in a 5 year training
# Training Models in Pathology

<table>
<thead>
<tr>
<th>TRADITIONAL</th>
<th>CURRENT</th>
<th>C FYNN et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>YEAR 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YEAR 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YEAR 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YEAR 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YEAR 5</td>
<td></td>
<td>Optional</td>
</tr>
</tbody>
</table>

Optional
The Belfast Model...

<table>
<thead>
<tr>
<th>Stages</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage A</td>
<td>Introductory lectures on molecular diagnostics</td>
</tr>
<tr>
<td>Stage B</td>
<td>Compulsory 2-3 month attachment in molecular diagnostics (See Table 1)</td>
</tr>
<tr>
<td>Stage C</td>
<td>Option 1: 1 year full-time trainee molecular diagnostics (See Table 2)</td>
</tr>
<tr>
<td></td>
<td>Option 2: 1 year “superspeciality” attachment with part-time practice in a subspecialty and part-time reporting the related molecular tests</td>
</tr>
<tr>
<td></td>
<td>Option 3: Mixture of diagnostics and research</td>
</tr>
</tbody>
</table>

**Molecular Pathology**

**General Training Framework**

- Year 1: Assessment at end of year to exit stage
- Exit stage with FRPCPath part 1 examination
- Exit stage with FRPCPath part 2 examination with/without extra modules in autopsy and Cytopathology cytology (additional 3 months each)
- End of Training

### The Belfast Model...

#### Table 1 Topics to be covered during the 2–3-month attachment

<table>
<thead>
<tr>
<th>Outline of topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA</td>
<td>Overview, structure, replication</td>
</tr>
<tr>
<td>RNA</td>
<td>Transcription, types/structures, RNA polymerases, regulation of transcription, microRNAases</td>
</tr>
<tr>
<td>Proteins</td>
<td>Amino acids, genes and genetic code, translation</td>
</tr>
<tr>
<td>NA extraction methods</td>
<td>Isolation of DNA and RNA, assessment of quality and quantity of nucleic acids</td>
</tr>
<tr>
<td>PCR</td>
<td>History of PCR, advanced PCR and PCR optimisation, PCR detection and evaluation techniques, limitations of PCR and troubleshooting</td>
</tr>
<tr>
<td>Analysis and characterisation of NA</td>
<td>Hybridisation technologies, detection systems, results interpretation</td>
</tr>
<tr>
<td>Nucleic acid amplification</td>
<td>Target, probe and signal amplification</td>
</tr>
<tr>
<td>Gene mutations</td>
<td>Types, detection and nomenclature of gene mutations</td>
</tr>
<tr>
<td>DNA sequencing</td>
<td>Direct sequencing, bioinformatics</td>
</tr>
<tr>
<td>Molecular oncology</td>
<td>Analytic targets of molecular testing, gene rearrangements</td>
</tr>
<tr>
<td>High-throughput technologies</td>
<td>DNA/RNA microarrays, NGS and TGS, whole genome sequencing</td>
</tr>
<tr>
<td>Validation and optimisation procedures</td>
<td>R&amp;D within molecular diagnostics present and future</td>
</tr>
<tr>
<td>Quality control and quality assurance</td>
<td>Discussion of QA and QC in molecular diagnostics</td>
</tr>
<tr>
<td>Regulation in the use of human tissues for research</td>
<td>Introduction to biobanking, research ethics and research governance within academia and the healthcare setting</td>
</tr>
<tr>
<td>Core skills in slide annotation</td>
<td>Be able to identify and annotate areas for macrodissection relevant to downstream testing. Be able to assign percentage tumour content</td>
</tr>
<tr>
<td>Core skills in macrodissection</td>
<td>Taught how to perform tissue macrodissection procedures</td>
</tr>
<tr>
<td>Core skills in DNA extraction</td>
<td>Taught how to perform DNA extraction procedures</td>
</tr>
</tbody>
</table>
The Belfast Model...

Box 2  Content of training for molecular diagnostics
1-year fellowship (Option 1, Stage C)

**Principles**

Knowledge and skills in core molecular technologies and techniques
Expertise in the molecular pathology of breast cancer
Expertise in the molecular pathology of colorectal cancer
Expertise in the molecular pathology of lung cancer
Expertise in the molecular pathology of malignant melanoma
Expertise in the molecular pathology of gastrointestinal stromal tumours (GISTs)
Expertise in the molecular pathology of sarcomas
Expertise in the molecular pathology of paediatric cancers, thyroid cancer, central nervous system neoplasias and others
Research, development and innovation in molecular pathology
Leadership and management of a molecular diagnostic laboratory
Training and education

Training Models in Pathology

<table>
<thead>
<tr>
<th>TRADITIONAL</th>
<th>CURRENT</th>
<th>C FYNN et al</th>
<th>MSc Fellowship Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>YEAR 1</td>
<td><img src="Optional" alt="Optional" /></td>
<td><img src="Optional" alt="Optional" /></td>
<td></td>
</tr>
<tr>
<td>YEAR 2</td>
<td><img src="Optional" alt="Optional" /></td>
<td><img src="Optional" alt="Optional" /></td>
<td></td>
</tr>
<tr>
<td>YEAR 3</td>
<td><img src="Optional" alt="Optional" /></td>
<td><img src="Optional" alt="Optional" /></td>
<td></td>
</tr>
<tr>
<td>YEAR 4</td>
<td><img src="Optional" alt="Optional" /></td>
<td><img src="Optional" alt="Optional" /></td>
<td></td>
</tr>
<tr>
<td>YEAR 5</td>
<td><img src="Optional" alt="Optional" /></td>
<td><img src="Optional" alt="Optional" /></td>
<td></td>
</tr>
</tbody>
</table>

Optional
MSc Molecular Pathology with Cancer

- Queens University Belfast has an international reputation for the application of Molecular Pathology in high quality translational research.
- Students will engage with leading Academics through the Cancer Research UK (CRUK) Accelerator network and with global biotechnology companies who have international reputations.
- Integrates traditional pathology, genomics, digital pathology and bioinformatics, in a clinical framework
- Students can progress in careers in academic, health care delivery or bioindustry sectors.

Table 1. Course outline for CRUK Accelerator funded MSc in Molecular & Digital Pathology

1. Introduction

2. Part 1
2.1 Cancer Biology, Immunology and Genomics
2.2 Molecular Pathology – Diagnostics and Technologies
2.3 Translational Research

3. Part 2
3.1 Digital Pathology
3.2 Biostatistical Informatics
3.3 The Academic-Industry Intersect

4. Part 3
Molecular Pathology of Cancer Research Project
## Training Models in Pathology

<table>
<thead>
<tr>
<th>Year</th>
<th>Traditional</th>
<th>Current</th>
<th>MSc Fellowship Model</th>
<th>TRADITIONAL PATHOLOGISTS</th>
<th>MORPHO-MOLECULAR PATHOLOGISTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Year 2</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Year 3</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Year 4</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Year 5</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

*Optional*
<table>
<thead>
<tr>
<th>Period</th>
<th>Program Description</th>
<th>Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months 1-12</td>
<td>General Histopathology &amp; Cytopathology</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exam 1</strong></td>
<td></td>
</tr>
<tr>
<td>Months 13-30</td>
<td>Subspecialty Training in GI, Breast and Lung Pathology</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exam 2</strong></td>
<td></td>
</tr>
<tr>
<td>Months 31-36</td>
<td>Good Scientific Practice Curriculum</td>
<td></td>
</tr>
<tr>
<td>Months 37-60</td>
<td>Specialty-specific Molecular Pathology Science Curriculum</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exam 3</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Molecular Pathology of Acquired Disease**

2015–2016
# "NEW PROGRAMME" – Main Characteristics

FRCPath (HSST) Molecular Pathology of Acquired Disease

**Index**

**GOOD SCIENTIFIC PRACTICE CURRICULUM**
- Domain 1: Professional Practice
- Domain 2: Scientific Practice
- Domain 3: Clinical Practice
- Domain 4: Research, Development and Innovation
- Domain 5: Clinical Leadership

<table>
<thead>
<tr>
<th>Main Characteristics</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td></td>
</tr>
</tbody>
</table>

**SPECIALTY-SPECIFIC MOLECULAR PATHOLOGY SCIENCE CURRICULUM**

<table>
<thead>
<tr>
<th>STAGE 1: Core Molecular Techniques and Technologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 Module 1: Core Molecular Techniques &amp; Technologies</td>
</tr>
<tr>
<td>Stage 1 Module 2: Health and Safety in Laboratory Practice</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STAGE 2: Specialty Options: Neoplastic Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2: Option 1A Molecular Pathology of Haematopoietic Neoplasms and related diseases</td>
</tr>
<tr>
<td>Stage 2: Option 1A (i) Basic Principles of Laboratory Haematology</td>
</tr>
<tr>
<td>Stage 2: Option 1A (ii) Genetic Basis of Haematopoietic Neoplasms</td>
</tr>
<tr>
<td>Stage 2: Option 1A (iii) Molecular Pathology of Myeloid Neoplasms</td>
</tr>
<tr>
<td>Stage 2: Option 1A (iv) Molecular Pathology of Lymphomas</td>
</tr>
<tr>
<td>Stage 2: Option 1A (v) Myeloma, Paraproteinaemias and Related Disorders</td>
</tr>
<tr>
<td>Stage 2: Option 1B Molecular Pathology of Solid Neoplasms and related diseases</td>
</tr>
<tr>
<td>Stage 2: Option 1B (i) General Principles</td>
</tr>
<tr>
<td>Stage 2: Option 1B (ii) Breast Cancer</td>
</tr>
<tr>
<td>Stage 2: Option 1B (iii) Colorectal Cancer</td>
</tr>
<tr>
<td>Stage 2: Option 1B (iv) Lung Cancer</td>
</tr>
<tr>
<td>Stage 2: Option 1B (v) Malignant Melanoma</td>
</tr>
<tr>
<td>Stage 2: Option 1B (vi) Gastrointestinal Stromal Tumours (GISTs)</td>
</tr>
<tr>
<td>Stage 2: Option 1B (vii) Sarcomas</td>
</tr>
<tr>
<td>Stage 2: Option 1B (viii) Paediatric Cancers, Thyroid Cancer, CNS Neoplasias, and Others</td>
</tr>
</tbody>
</table>
# “NEW PROGRAMME” – Main Characteristics

*e.g. Techniques & technologies*

---

**FRCPath (HSST) Molecular Pathology of Acquired Disease**

## Specialty-specific Molecular Pathology of Acquired Disease curriculum

### STAGE 1: Core Molecular Techniques and Technologies (12 months)

### Stage 1 Module 1: Core Molecular Techniques & Technologies

<table>
<thead>
<tr>
<th>Topic</th>
<th>Stage 1 Module 1</th>
<th>Core Molecular Techniques &amp; Technologies</th>
<th>Assessment Methods</th>
<th>GSP Reference</th>
</tr>
</thead>
</table>
| **Learning Objective**    |                  | By the end of the training period trainees will, in respect to core molecular techniques and technologies relevant to Molecular Pathology of Acquired Disease be able to:  
  - analyse, synthesise, evaluate and apply knowledge  
  - perform a range of technical and clinical skills and procedures and  
  - demonstrate the attitudes and behaviours necessary for professional practise as a Consultant Clinical Scientist dealing with the complexities, uncertainties and tensions of professional practise at this level. |                | |
| **Knowledge Competence**  |                  | By the end of the training period the trainee will be able to demonstrate the ability to analyse, evaluate and synthesise relevant knowledge and its application to their professional practice in relation to:  
  - basic principles of Molecular Biology  
  - human genetic variation  
  - genetic basis, clonal evolution and molecular heterogeneity of cancer  
  - germline vs somatic genetics  
  - DNA, RNA and protein extraction (microbes, blood, fresh and formalin-fixed tissue samples)  
  - Polymerase Chain Reaction (PCR), Reverse-Transcriptase PCR (RT-PCR) and quantitative PCR (qPCR)  
  - primer design  
  - nucleotide and protein gel electrophoresis  
  - restriction endonucleases  
  - DNA hybridisation techniques: Southern Blotting, Fluorescence-in-situ Hybridisation (FISH) and Array Comparative Genomic Hybridisation (aCGH)  
  - gene expression profiling  
  - Capillary (Sanger) sequencing of DNA: principles and applications  
  - Next Generation Sequencing (NGS) technologies: principles and applications (including NGS library) | FRCPath Part 1, WPBA | 1.2 |

---
"NEW PROGRAMME" – Main Characteristics
e.g. Lymphomas

Stage 2
Option 1(A,v): Molecular Pathology of Lymphomas

Learning Objectives
By the end of the training period the trainees will be able to:
- analyse, synthesise, evaluate and apply knowledge;
- perform, adapt and master a range of technical and clinical skills and procedures and demonstrate the attitudes and behaviours necessary for professional practice as a Consultant Clinicalopathologist, uncertainty and limits of professional practice at all levels.

Knowledge
By the end of the training period the trainees will be able to:
- apply and extend "ignore" based principles of classification of lymphoid malignancies including recognition of clinical, morphological, immunophenotypic and genetic features required for accurate characterization of individual entities;
- Entities recognised in the current WHO classification of lymphoid neoplasms (2008 revision) including:
  - Most common lymphomas: Chronic lymphocytic leukemia/small lymphocytic lymphoma; B-cell chronic lymphocytic leukemia;
  - Indolent lymphomas: Mycosis fungoides and Sezary syndrome; Mantle cell lymphoma; MALT lymphoma; Plasma cell myeloma; Multiple myeloma; Diffuse large B-cell lymphoma not otherwise specified and specific variants of large B-cell lymphomas; Burkitt lymphoma; B-cell lymphomas, unclassifiable with features intermediate between large B-cell lymphoma and follicular lymphoma; B-cell lymphoma, unclassifiable with features intermediate between diffuse large B-cell lymphomas and classical Hodgkin lymphomas;
  - Aggressive lymphomas: Diffuse large B-cell lymphoma; Burkitt lymphoma; Anaplastic large cell lymphoma; T-cell large granular lymphocytic leukemia; Chronic lymphocytic leukaemia (BCL2, BCL6, and CD10 positive T-cell lymphoproliferative disorder of cd8 T cell); Lymphoma; Angioimmunoblastic T-cell lymphoma; Anaplastic large cell lymphoma (ALK positive and ALK negative);
  - Neurolymphomatosis: Classical Hodgkin lymphoma;
  - Immunoproliferative small round cell tumour:
  - Langerhans cell histiocytosis;
  - AIDS-related lymphomas: Primary cutaneous gamma-delta T-cell lymphoma; Primary T-cell lymphoma not otherwise specified; Angioimmunoblastic T-cell lymphoma; Anaplastic large cell lymphoma (ALK positive and ALK negative);
  - Hodgkin, classical: Lymphocyte rich type; Lymphocyte depleted type; Lymphocyte predominance:
  - Epidemiology and pathobiology of lymphoid neoplasms;
  - Clinical, morphological, immunophenotypic, cytogenetic & molecular genetic characteristics of individual lymphoid malignancies;
  - Targeting and progenticosis;
  - Pathobiological role and practical diagnostic utility of chromosomal gene mutations, rearrangements and numerical abnormalities in lymphoid malignancies involving:
    - Immunoglobulin and other gene rearrangements: p53; CDKN1A: BCL2, BCL6, MUM1; RASSF1A; BRAF; IL6; TCF3; MYC; ALK;
    - Activity of specific molecular pathways as basis for specific and targeted therapies (different mechanisms of action of tyrosine kinase inhibitors and microtubulin inhibitors in NHL and BCL2, BCL6, and CD10 positive T-cell lymphoma); activity of the insulin/insulin-like growth factor I receptor signaling pathway in certain lymphoid malignancies involving phosphorylation and activation of IRF1 and PI3K/AKT, leading to increased proliferation and survival;
    - Role of B and T cell identity in diagnosis;
    - Design and technical aspects of donor assessment utilising the BIOMED-2 primer sets;
    - Most common reactive conditions in the differential diagnosis of lymphomas with emphasis on pitfalls in diagnosis.
  - Non-specific follicular and polymorphous hyperplasia: Viral lymphoid infiltrates including infectious mononucleosis, infectious mononucleosis-like post-viral syndromes and sarcoidosis; Autoimmune disease associated lymphoid hyperplasia; Kikuchi lymphadenitis; Light chain restricted reactive B-cell lymphoid proliferations;
  - Mycosis nodular disease.

Technical Skills and Procedures
By the end of the training period the trainees will be able to demonstrate a critical understanding of current relevant research, theory and knowledge and its application to the performance, adaptation and mastery of the following skills to:
- Have a knowledge of practical laboratory aspects of lymphoma diagnosis including conventional techniques, immunohistochemistry, in situ hybridisation, flow cytometry, conventional and karyotype preparation, and molecular genetic analysis;
- Have a multidisciplinary laboratory approach to lymphoma diagnosis incorporating pathology, haematology, immunology, flow cytometry, conventional and karyotype preparation, and molecular genetic analysis;
- Produce a fully interpretative clinical diagnostic laboratory report and incorporate diagnostic data into integrated pathology reports.

Clinical Skills
By the end of the training period the trainees will be able to apply knowledge of the molecular pathology of lymphoma to perform:
- Clinical presentation, staging, prognosis and basic principles of lymphoma management including "targeted" therapies;
- Impact of genetical/molecular features and other biomarkers on clinical management and the design of targeted therapies of lymphoma;
- Mechanisms of drug resistance maintaining resistance mutations;
- Role of MRD monitoring in the clinical management of lymphoid neoplasms.

FRCP (Medicine) Molecular Pathology of Acquired Disease

Molecular Pathology of Acquired Disease

Queens University Belfast
“NEW PROGRAMME” – Main Characteristics  
e.g. Lung Cancer

FRCPath (HSST) Molecular Pathology of Acquired Disease

Stage 2  
Option 1B(iv) : Lung Cancer

<table>
<thead>
<tr>
<th>Topic</th>
<th>Stage 2: Option 1B(iv)</th>
<th>Assessment Methods</th>
<th>GSP Reference</th>
</tr>
</thead>
</table>
| Learning Objectives           | By the end of the training period trainees will, in respect to a thorough understanding, theoretical and practical, of the knowledge, theoretical skills and clinical skills necessary to be proficient in lung cancer molecular testing, be able to:  
- analyse, synthesise, evaluate and apply knowledge  
- perform, adapt and master a range of technical and clinical skills and procedures and  
- demonstrate the attitudes and behaviours necessary for professional practise as a Consultant Clinical Scientist dealing with the complexities, uncertainties and tensions of professional practise at this level. | FRCPath Part 2, WPBA | 1, 2, 3 |
| Knowledge                     | By the end of the training period the trainee will be able to demonstrate the ability to analyse, evaluate and synthesise relevant knowledge and its application to their professional practice in relation to:  
- Epidemiology and pathophysiology of disease  
- Laboratory and clinical phenotypic diagnosis and classification  
- Molecular classification of lung cancer at a mutation, gene amplification and protein expression levels  
- Clinical aspects: therapeutically principles and measures | WPBA | 1, 2, 3 |
| Technical Skills and Procedures | By the end of the training period the trainee will be able to demonstrate a critical understanding of current relevant research, theory and knowledge and its application to the performance, adaptation and mastery of the following skills:  
- Competency in the laboratory investigation, diagnosis and follow-up of patients with lung cancer  
- Knowledge to validate, carry out and trouble-shoot tests for EGFR mutations, KRAS mutations and ALK translocations  
- Readiness to validate, whenever needed, single tests around biomarkers such as: Her-2 insertions, BRAF mutations, PIK3CA mutations, RET and ROS1 rearrangements, FGFR1 amplification and DDR2 mutations  
- Knowledge to validate, carry out and trouble-shoot multiple biomarker testing, at a DNA or RNA level, whenever relevant | WPBA, MSF | 1, 2, 3 |
| Clinical skills               | By the end of the training period the trainee will be able to apply knowledge of the general principles of lung cancer to perform, adapt and master the clinical skills necessary to manage and to understand the:  
- production a fully interpretable clinical diagnostic laboratory report  
- clinical management of lung cancer | WPBA, MSF | 1, 2, 3 |
Training Models in Pathology

<table>
<thead>
<tr>
<th>YEAR 1</th>
<th>YEAR 2</th>
<th>YEAR 3</th>
<th>YEAR 4</th>
<th>YEAR 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRADITIONAL</td>
<td>CURRENT</td>
<td>C FYNN et al</td>
<td>MSc Fellowship Model</td>
<td></td>
</tr>
<tr>
<td>TRADITIONAL PATHOLOGISTS</td>
<td>PATHOLOGISTS</td>
<td>MORPHO-MOLECULAR PATHOLOGISTS</td>
<td>CLINICAL SCIENTISTS</td>
<td></td>
</tr>
</tbody>
</table>

Optional
After 4-5 years of training, young pathologists should be competent in all areas of morphological pathology...

... but we encourage them to subspecialise as soon as possible...

... with the adequate knowledge in molecular diagnostics...

... able to report in digital formats and in an “algorithm-assisted scenario”

**MODULAR TRAINING – TAKE SPECIALIZATION DECISIONS EARLY IN TRAINING**

**THE “HOLISTIC” DEPARTMENT**
TISSUE PATHOLOGY – THE BROADER PICTURE

Diagnostic Histopathologists and Cytopathologists
Academic Histopathologists and Cytopathologists
Molecular Tissue Pathologists
“Immunopathologist”
Superspecialist in Morpho-molecular Pathology
Superspecialist in Digital/Computational Pathologist
Information Pathologist (“Computational Pathology”) – DP, Bioinfomr., LIMS
Biobanker
Clinical Trial Pathologist
Biomarker discovery & Validation Pathologist
Comparative Pathologist (different from vet Pathologist)

None of this will happen without having a fair knowledge of Molecular & Digital Pathology in the future.
<table>
<thead>
<tr>
<th>IDEAL PATHOLOGIST</th>
<th>PATHOLOGIST TYPE 1</th>
<th>PATHOLOGIST TYPE 2</th>
<th>PATHOLOGIST TYPE 3</th>
<th>PATHOLOGIST TYPE 4</th>
<th>PATHOLOGIST TYPE 5</th>
<th>PATHOLOGIST TYPE 6</th>
<th>PATHOLOGIST TYPE 7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molec Diagnostics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dig Path</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acad Path</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

THE PATHOLOGY DEPARTMENT OF THE FUTURE
From:

Jared N Schwartz, MD, PhD, FCAP
Director, Pathology & Lab Medicine
Presbyterian Healthcare Charlotte,
Past President, College of American Pathologists