## ECMC Annual Network Meeting

**Thursday 21 May 2015**

The King’s Fund, No. 11 Cavendish Square, London, W1G 0AN

**DRAFT AGENDA**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>0930 - 1000</td>
<td>Registration and Refreshments</td>
</tr>
<tr>
<td>1000 - 1010</td>
<td>Morning Plenary Session - Successful collaborations and patient experience</td>
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<tr>
<td>1010 - 1055</td>
<td>Welcome and introductions</td>
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<tr>
<td>1055 - 1125</td>
<td>ECMC Trial Harmonisation Programme (ETHP) Update; Single Technical Pharmacy Review - by a pharmacist</td>
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<td>1125 - 1145</td>
<td>Collaborating with industry: the Good, the Bad and the Ugly</td>
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<td>1145 - 1200</td>
<td>UK Therapeutic Cancer Prevention Network (UKTCPN) Update</td>
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<tr>
<td>1200 - 1225</td>
<td>CRUK Accelerator Award in Molecular Pathology</td>
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<td>1225 - 1255</td>
<td>ECMC Patient Experience Survey</td>
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<td>1230 - 1400</td>
<td>Concluding Remarks</td>
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**THE NORTHERN IRELAND MOLECULAR PATHOLOGY LABORATORY AND THE NORTHERN IRELAND BIOBANK**

**CRUK Accelerator Award in Molecular Pathology**
2015 will be a good year for Molecular Pathology in the UK

### 2015 – Molecular Pathology

#### INITIATIVES
- ECMC – CMPath Proposal (Elli & Bridget)
- MRC Molecular Pathology Document
- RCPath - FRCPath for Clinical Scientists

#### FUNDING OPPORTUNITIES
- MRC Molecular Pathology Nodes
- Precision Medicine Catapult
- CRUK – Accelerator Award
Centres Network Accelerator Awards

Our research strategy is built on the understanding that effective partnerships are crucial for delivering the greatest impact. We want to support a united Cancer Research UK community in which our Centres work as a network, not just as individual locations.

To support this aim, we have launched a new funding scheme, the Cancer Research UK Centres Network Accelerator Awards. These awards provide additional infrastructure support that aim to enable Centres to increase collaboration, promote translational research and build capacity in areas of strategic priority for the Centres and Cancer Research UK. The basic remit and eligibility requirements are:

Maximum of £1m per annum for up to five years

Cancer Research UK Centre directors may lead one application

Centres, Major Centres and other non-centre locations may collaborate on any applications
Scientific Need – the genotyping of tissue-based cellular compartments in cancer

Technical Need – the development of digital molecular pathology as an available commodity in cancer research

Strategic Need – the training of future molecular pathologists

BELFAST CR-UK ACCELERATOR PROPOSAL

Research Resource – A national digital molecular pathology platform to genotype the epithelial-immune compartments in solid tumours, complemented by a comprehensive Clinical Fellowship programme in Molecular Pathology.
**Lead Institution - Belfast**

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>David Waugh</td>
<td>Centre Director</td>
</tr>
<tr>
<td>Manuel Salto-Tellez</td>
<td>Deputy Centre Director and Molecular Pathology Director</td>
</tr>
<tr>
<td>Peter Hamilton</td>
<td>Digital Pathology Lead</td>
</tr>
<tr>
<td>Jackie James</td>
<td>Molecular Pathologist and Training Lead</td>
</tr>
<tr>
<td>Richard Kennedy</td>
<td>Biomarker Discovery Lead</td>
</tr>
<tr>
<td>Mark Lawler</td>
<td>Associate Director of Postgraduate Studies</td>
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**Co-leading Institution - Southampton**

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Peter Johnson</td>
<td>Centre Director</td>
</tr>
<tr>
<td>Gareth Thomas</td>
<td>Lead Molecular Pathology Immune Response</td>
</tr>
<tr>
<td>Christian Ottensmeier</td>
<td>Immunotherapeutics</td>
</tr>
<tr>
<td>Pandurangam Vijayanand</td>
<td>Micro-transcriptomic &amp; epi immune cell analysis</td>
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**Network Members**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tbody>
<tr>
<td>Sebastian Brandner</td>
<td>UCL Neuropathology</td>
</tr>
<tr>
<td>Andy Hall</td>
<td>Newcastle</td>
</tr>
<tr>
<td>David Gonzalez de Castro</td>
<td>London</td>
</tr>
<tr>
<td>John Le Quesne</td>
<td>Leicester</td>
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<tr>
<td>Caroline Dive</td>
<td>Manchester</td>
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</table>
Our mission is to improve patient care through the development of:

1. Biomarkers for prognosis, prediction and markers of response
2. Biologically determined targeted therapies.
### Test with a Predominant Diagnostic Value

- Sarcoma Translocation Detection
- Lymphoma Translocation Detection
- Clonality Testing

### Test with a Predominant Genetic Value

- Microsatellite Instability Testing
- Mismatch Repair Protein Expression

### Tests with a Predominant Therapeutic Value

- KRAS/NRAS Mutation Testing
- BRAF Mutation Testing
- EGFR Mutation Testing
- ALK Protein Expression
- EML4-ALK Translocation Detection
- Multiple Central Nervous System Molecular Testing
- ER, PR and Her2 Protein Expression
- Her2 Amplification
- c-KIT Mutation Analysis
- PDGFRA Mutation Analysis

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**Integrating molecular diagnostics into histopathology training: the Belfast model**

C Flynn, J James, P Maxwell, S McQuaid, A Ervine, M Catherwood, M B Loughrey, D McGibbon, J Somerville, D T McManus, M Gray, B Herron, M Salto-Tellez.
## AN INTEGRATED MOL PATH MODEL

<table>
<thead>
<tr>
<th>Table 1 — Pathology-centred activities in the research endeavour.</th>
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<tbody>
<tr>
<td>Molecular diagnostics in the context of clinical trials</td>
</tr>
<tr>
<td>Analysis of tissues ahead of molecular analyses</td>
</tr>
<tr>
<td>Tissue biobanking</td>
</tr>
<tr>
<td>Digital pathology</td>
</tr>
<tr>
<td>Pathology informatics</td>
</tr>
<tr>
<td>Data manager</td>
</tr>
<tr>
<td>Biomarker validation</td>
</tr>
<tr>
<td>Integration of validated biomarkers into routine diagnostics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2 — Digital pathology.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automated digitalization of images for storage and multi-site</td>
</tr>
<tr>
<td>discussion</td>
</tr>
<tr>
<td>Automated scoring of IHC</td>
</tr>
<tr>
<td>Automated counting of hybridization signals</td>
</tr>
<tr>
<td>Automated identification of tumour in sections for subsequent</td>
</tr>
<tr>
<td>microdissection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3 — Pathology bioinformatics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital imaging</td>
</tr>
<tr>
<td>Pathology integration of pathological data, clinical data</td>
</tr>
<tr>
<td>and biomarker analytical results</td>
</tr>
<tr>
<td>Translation of high-throughput analysis to biomarkers with</td>
</tr>
<tr>
<td>meaningful diagnostic/clinical relevance</td>
</tr>
<tr>
<td>Translation of high-throughput analysis to pathology reports</td>
</tr>
</tbody>
</table>

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**Review**

**Molecular pathology — The value of an integrative approach**

*Manuel Salto-Téllez*<sup>a,b</sup>, *Jacqueline A. James*<sup>a,b</sup>, *Peter W. Hamilton*<sup>a</sup>

<sup>a</sup> Northern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queen’s University, Belfast, Northern Ireland, UK

<sup>b</sup>Tissue Pathology, Belfast Health and Social Care Trust, Belfast, Northern Ireland, UK
Review

Molecular pathology — The value of an integrative approach

Manuel Salto-Tellez\textsuperscript{a,b,*}, Jacqueline A. James\textsuperscript{a,b}, Peter W. Hamilton\textsuperscript{a}

\textsuperscript{a}Northern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queen’s University, Belfast, Northern Ireland, UK
\textsuperscript{b}Tissue Pathology, Belfast Health and Social Care Trust, Belfast, Northern Ireland, UK
Northern Ireland Molecular Pathology Laboratory (NI-MPL)
End to End Diagnostic and Research Service
Cutting Across Technologies and Infrastructures

BACKGROUND 1
AN INTEGRATED MOL PATH MODEL

Salto-Tellez et al. Molecular Oncology, 2014
**Clinical Information**

**FFPE Material**

**PICan**

**Clinical Information**

**Discovery HT Technologies**

**Fresh sample collection**

**PDX**

**In-vitro confirmation of the relevance of the discoveries**

**New Biology**

**New Taxonomy**

**New Treatments**

**New Clinical Trial**

**Single biomarker validations**

**Bioinformatics Analysis**

**New Clinical Trials**
Fig. 9. The role of digital pathology in drug development and companion biomarker discovery and validation.
HOW TO ADDRESS HETEROGENEITY:

**TOPOGRAPHIC** HETEROGENEITY: Analyzing as many different parts of the tumor as possible

**HISTOGENETIC** HETEROGENEITY: Analyzing many cell types as available

**TEMPORAL** HETEROGENEITY: Analyzing as many samples from the same tumor in the course of time

**COMPARTMENTAL** HETEROGENEITY: Analyzing as many body compartments as possible, such as primary tumor, circulating tumor cells, and exosomes or plasma.

Salto-Tellez M. In: *Tan & Lynch’s Principles of Molecular Diagnostics and Personalized Cancer Therapy*, Lippincott Williams & Wilkins, 2012
Therapeutic Targeting of Integrin $\alpha v \beta 6$ in Breast Cancer

Keywords: human papillomavirus; tumour-infiltrating lymphocytes; oropharyngeal cancer; survival; prognosis

Tumour-infiltrating lymphocytes predict for outcome in HPV-positive oropharyngeal cancer

Co-leading Institution - Southampton

Peter Johnson (Centre Director)

Gareth Thomas (Lead Molecular Pathology Immune Response)

Christian Ottensmeier (Immunotherapeutics)

Pandurangam Vijayanand (Micro-transcriptomic & epi immune cell analysis)
Identification and Validation of an Anthracycline/Cyclophosphamide-Based Chemotherapy Response Assay in Breast Cancer


Table 4. Association of the DNA damage response deficiency (DDRD) assay with estrogen receptor (ER) status, HER2 status, and lymphocytic infiltration within validation datasets

<table>
<thead>
<tr>
<th>Adjuvant dataset</th>
<th>Total No.</th>
<th>DDRD-positive, %</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER-positive</td>
<td>112</td>
<td>25.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ER-negative</td>
<td>77</td>
<td>52.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HER2-positive</td>
<td>46</td>
<td>41.3</td>
<td>.26</td>
</tr>
<tr>
<td>HER2-negative</td>
<td>128</td>
<td>32.0</td>
<td></td>
</tr>
<tr>
<td>Triple negative</td>
<td>44</td>
<td>54.6</td>
<td>.001</td>
</tr>
<tr>
<td>Non–triple negative</td>
<td>135</td>
<td>28.2</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic infiltrate</td>
<td>35</td>
<td>74.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytic infiltrate</td>
<td>155</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER-positive</td>
<td>70</td>
<td>24.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ER-negative</td>
<td>134</td>
<td>67.9</td>
<td></td>
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Platinum Priority – Prostate Cancer
Editorial by Zoran Cigan on pp. 189–190 of this issue

Potentiation of Inflammatory CXCL8 Signalling Sustains Cell Survival in PTEN-deficient Prostate Carcinoma

Figure 1

Targets of antibody immune modulators. (a) Targetable members of the CD28/CTLA-4 immunoglobulin superfamily include cytotoxic T lymphocyte antigen 4 (CTLA-4) (1), programmed cell death protein 1 (PD-1) (5, 7), B and T cell attenuator (BTLA) (84), lymphocyte activation gene 3 (LAG3) (85), and inducible T cell costimulator (ICOS) (86). (b) Targetable members of the tumor necrosis factor (TNF) superfamily include CD40 (87, 88), OX40 (89), CD137/4-1BB (90), glucocorticoid-induced TNFR-related protein (GITR) (91), and CD27. (c) Programmed cell death 1 ligand 1 (PD-L1). Mel: melanoma. (d) Killer inhibitory receptor (KIR). (e) T cell Ig and mucin-containing domain 3 (TIM3).
Hamilton P (Salto-Tellez M). Oncotarget 2015 (accepted)
Comparative Expression Analysis Reveals Lineage Relationships between Human and Murine Gliomas and a Dominance of Glial Signatures during Tumor Propagation In Vitro

Nico V. Henriquez¹, Tim Forsheow², Ruth Tatevossian², Matthew Ellis¹, Angela Richard-Loendt¹, Hazel Rogers⁵, Thomas S. Jacques³, Pablo Garcia Reitboeck¹, Kerra Pearce⁴, Denise Sheer², Richard G. Grundy⁵, and Sebastian Brandner¹
Integrating molecular diagnostics into histopathology training: the Belfast model

C Flynn, 1 J James, 1, 2 P Maxwell, 1, 2 S McQuaid, 1, 2 A Envine, 1 M Cathrinwood, 1, 2 M B Loughrey, 1 D McGibbon, 1 J Somerville, 1 D T McManus, 1 M Gray, 1 B Herron, 1, 2 M Salto-Tellez 1, 2

Outline of topic | Description
---|---
DNA | Overview, structure, replication
RNA | Transcription, typesstructures, RNA polymerases, regulation of transcription, microRNAAses
Proteins | Amino acids, genes and genetic code, translation
NA extraction methods | Isolation of DNA and RNA, assessment of quality and quantity of nucleic acids
PCR | History of PCR, advanced PCR and PCR optimisation, PCR detection and evaluation techniques, limitations of PCR and troubleshooting
Analysis and characterisation of NA | Hybridisation technologies, detection systems, results interpretation
Nucleic acid amplification | Target, probe and signal amplification
Gene mutations | Types, detection and nomenclature of gene mutations
DNA sequencing | Direct sequencing, bioinformatics
Molecular oncology | Analytic targets of molecular testing, gene rearrangements
High-throughput technologies | DNA/RNA microarrays, NGS and TGS, whole genome sequencing
Validation and optimisation procedures | R&D within molecular diagnostics present and future
Quality control and quality assurance | Discussion of QA and QC in molecular diagnostics
Regulation in the use of human tissues for research | Introduction to biobanking, research ethics and research governance within academia and the healthcare setting
Core skills in slide annotation | Taught how to perform tissue macrodissection procedures
Core skills in macrodissection | Taught how to perform DNA extraction procedures
Core skills in DNA extraction | QA, quality assurance; QC, quality control; NA, nucleic acid; NGS, Next Generation Sequencing; TGS, Third Generation Sequencing.

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
Integrating molecular diagnostics into histopathology training: the Belfast model

C Flynn, J James, P Maxwell, S McQuaid, A Ervine, M Catherwood, M B Loughrey, D McGibbon, J Somerville, D T McManus, M Gray, B Herron, M Salto-Tellez

**Stage A** (0-12 months)
- Introductory lectures on molecular diagnostics

**Stage B** (12-18 months)
- Compulsory 2-3 month attachment in molecular diagnostics (See Table 1)

**Stage C** (24-36 months)
- Option 1: 1 year full-time tissue molecular diagnostics (see Table 2)
- Option 2: 1 year "superspecialty" attachment with part time practice in a subspeciality and part time reporting the related molecular tests
- Option 3: Mixture of diagnostics and research

**Stage D** (13 months)
- End of Training
THE CLINICAL FELLOWSHIP PROGRAMME
MSc in Molecular Pathology

THE CLINICAL FELLOWSHIP PROGRAMME
MSc in Molecular Pathology

CRUK DIGITAL MOLECULAR PATHOLOGY & TRAINING NETWORK

- **Leicester**
  - Lung Ca Training

- **Newcastle**
  - Clin Trials Training

- **Manchester**
  - Liq Bx Training

- **BELFAST**
  - Manpower, IT, Instrumentation
  - EPITHELIAL INTERROGATION Training

- **UCL Neuro**
  - Manpower Training

- **SOUTHAMPTON**
  - Manpower, IT Instrumentation
  - CANCER IMMUNE INTERROGATION Training

- **MARSDEN**
  - Manpower
  - WGS QA/QC Training
1. To create a “common digital pathology language” across the members of the proposal

2. To use digital pathology to describe tumour heterogeneity and cancer immunology

3. To improve the efficiency of NGS through digital pathology pre-analytical interventions

4. To develop “digital neuropathology” in CNS oncology

5. To create a structure of Clinical Fellowships /MSc in different aspects of Molecular Pathology (Including liquid biopsy pathology, lung digital pathology and the pathology of early-phase clinical trials)
True partnership to develop and consolidate molecular pathology in the UK

Focusing on an area of significant need (digital molecular pathology) and with a strong training programme

Attending to a very specific scientific purpose (tissue genotyping of specific cellular compartments)

Partnership (Belfast-Southampton) and a true network

Proposal that has the potential of transforming the molecular pathology scene in the UK