CM-Path Annual Report

June 2018

1. CM-Path Summary

Pathologists are essential for cancer research, from understanding tissues and diagnosing disease, to supporting precision medicine approaches; without pathologists, we would be unable to identify and provide the high-quality tissue samples which are essential for histological, molecular and other analyses, or to integrate and interpret those results for patient care and cancer research.

In 2015, when the NCRI partners kindly approved the proposal for CM-Path and our funding, pathology was facing major challenges. The number of clinical academic pathologists had declined steeply compared with other specialties since the 1990's. At the same time there was an increasing need for NHS pathology services and perceived to be a disconnect between pathology research, clinical practice and industry.

Thus, our vision in CM-Path is to re-energize academic cellular and molecular pathology across the UK. We are working to build capacity and expertise in research and clinical trials pathology, from students and trainees through to consultants. To deliver this ambitious plan we work in close partnership with key stakeholders in pathology (especially the Royal College of Pathologists and Pathological Society), healthcare, academia, regulatory organisations, industry and our funders. Closer working "on the ground" of pathologists with the wider cancer research community is also key, and CM-Path has already helped to increase pathology representation on NCRI clinical study groups (CSGs) which in turn will benefit clinical trial design, development, resourcing and delivery.

The next pages demonstrate the highlights of Year Two of the CM-Path Programme. We have already delivered a great deal but much remains to be done and there is still an urgent need for the CM-Path initiative, at full strength.

2. Highlights from Year Two of CM-Path

Workstream 1 (Skills & Capacity)	• A two-week molecular pathology module was adopted by the Royal College of Pathologists (RCPath) for the five-year pathology training programme, which currently contains no **molecular pathology**. • CM-Path was awarded a grant of £3,500 from the Pathological Society to conduct a **Delphi analysis of molecular pathology** in the undergraduate curriculum. • A training workshop in molecular pathology was delivered in July 2017 and attended by over 90 postgraduate pathology students. The workshop was delivered by a US-based thought leader in molecular pathology training, Dr Richard Haspel, using the Training Residents in Genomics (TRIG)[1] curriculum. • A round table meeting was organised in July 2017 to influence UK leadership in molecular pathology training, where it was agreed that CM-Path would revise the **three-month optional module** in 'research methodology' and create a new three-month optional module on 'molecular diagnostic pathology'. • CM-Path's **vision for molecular pathology** training has been published in peer-reviewed journals[2, 3]. This led to a blog being published in BMJ Opinion[4], raising awareness of the need for change.
Workstream 2 (Clinical Trials)	• The second 'Pathologists Guide to Research and Clinical Trials' meeting was delivered in February 2018 in partnership with the RCPath, with 50 attendees sharing knowledge and experience. Talks highlighted the NCRI CSGs, CT-PAG, opportunities for training offered by the NIHR, costing for trials, trial design and statistics for beginners. A consultant pathologist also gave an inspiring talk on how to get into clinical trials as a trainee. • A survey was completed on UK pathologists' attitudes and practices relating to the **release of human tissues** from diagnostic archives to identify barriers to, and good practice in tissue access, which is key to translational research. • A suite of five papers was developed on **quality assurance in clinical trial** pathology to share outcomes and best practice identified in a CM-Path workshop undertaken in 2017.
CT-PAG (Clinical Trial Pathology Advisory Group) (WS2 & WS3)	• CT-PAG was set up and provides constructive feedback on **tissue-based biomarker studies** through a panel of 35 members with expertise in several different specialities. • CT-PAG has supported funders, including CRUK, and researchers with the first call-for-proposals opening in May 2018, to help development of pathology-related research proposals.

[1] http://www.pathologylearning.org/trig/about

[2] Moore, D., Young, C., Morris, H., Oien, K., Lee, J., Jones, J. and Salto-Tellez, M. (2017). Time for change: a new training programme for morpho-molecular pathologists?. Journal of Clinical Pathology, 71(4), pp.285-290. http://jcp.bmj.com/content/71/4/285

[3] Jones, J., Oien, K., Lee, J. and Salto-Tellez, M. (2017). Morphomolecular pathology: setting the framework for a new generation of pathologists. British Journal of Cancer, 117(11), pp.1581-1582. https://www.nature.com/articles/bjc2017340

[4] http://blogs.bmj.com/bmj/2017/12/20/pathology-risks-being-left-behind-as-conceptual-and-technological-advances-accelerate/

Workstream 3 (Discovery)	• A biobank quality improvement tool was developed, piloted and launched in May 2018, aiming to support high quality sample curation and facilitate researcher access. • 'The **Liquid Biopsy**: ctDNA, Circulating Tumour Cells and Blood-borne Biomarkers' symposium[5] was delivered in March 2018. 110 delegates attended the workshop and heard the latest developments in liquid biopsy, its potential applications, and work towards its adoption into clinical practice. • Plenary oral presentations were delivered by CM-Path trainees at the Pathological Society Meeting (June 2017, Belfast) on a survey of UK pathologists' attitudes towards **academic and molecular pathology**, identifying drivers, challenges and solutions, to support strategy.
Workstream 4 (Technology & Informatics)	• A survey on the **digital pathology access and usage in the UK** was published in a peer-reviewed journal[6]. • CM-Path colleagues led on recent **RCPath guidelines**: Best practice recommendations for implementing digital pathology[7]. • A second industry forum meeting brought pathologists, regulators, industry and other expert colleagues together in January 2018, to consider challenges and solutions for **uptake of molecular diagnostic tests**, especially in commissioning.
Crosscutting Themes	• **Patient and public involvement** – CM-Path currently works with two consumers who provide invaluable guidance to our Executive group and Workstream 2. CM-Path sessions have been held at the NCRI Consumer Forum in 2017 and 2018. • **Supporting trainees** – Over 30 pathologists have joined the CM-Path trainee scheme, see case study 8.1 below. • **Biosample consent** – CM-Path is working to streamline consent for the use of tissue for research. A workshop was held in February 2018, bringing together researchers and regulators. • **Engaging with wider initiatives** – CM-Path is engaging directly and via CM-Path colleagues with roles also in Pathological Society, RCPath, MRC Molecular Pathology Nodes, CRUK Accelerators and wider initiatives. • **Engaging with wider specialities** – This is taking place throughout CM-Path activities, including having: multi-disciplinary speakers at CM-Path events; joint BASO/CM-Path breast cancer workshop at NCRI Conference 2017; contribution to ECMC Junior Investigator Network Group meetings 2017 and 2018.

[5] http://cmpath.ncri.org.uk/wp-content/uploads/2018/03/The-Liquid-Biopsy-CMPath-Symposium-Report.pdf – Report of a recent CM-Path event, The Liquid Biopsy Symposium. A shortened version of this report by CM-Path WS3 member, Susan Richman, to be published in July 2018 RCPath College bulletin.

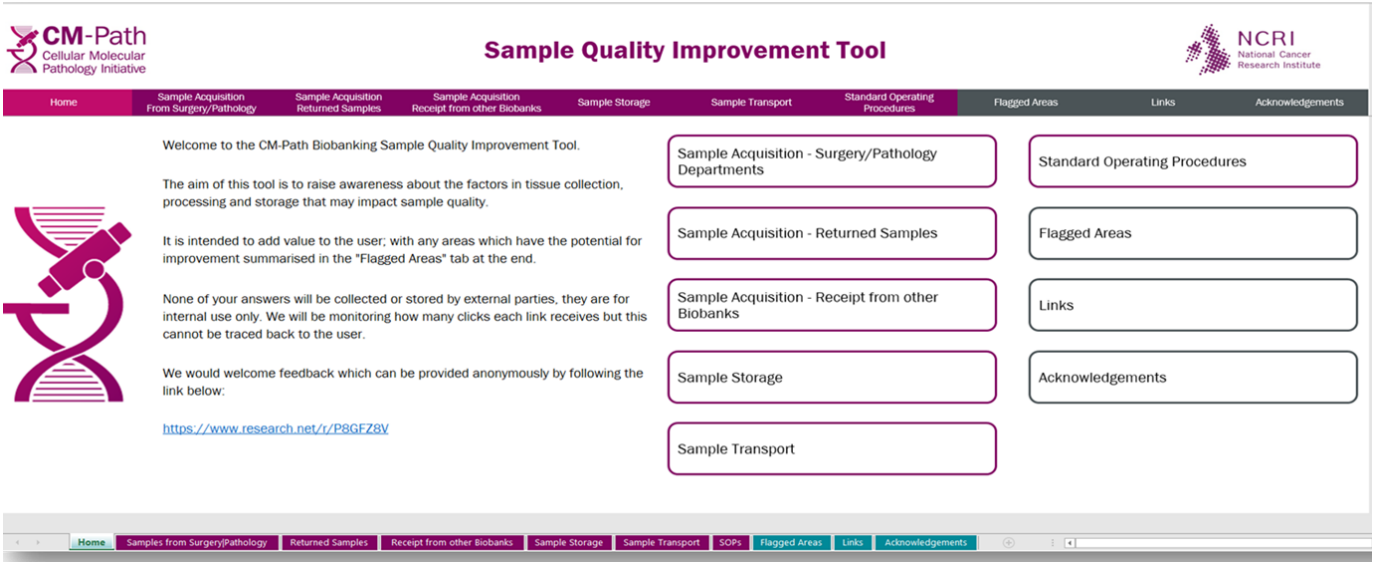
[6] Williams, B., Lee, J., Oien, K. and Treanor, D. (2018). Digital pathology access and usage in the UK: results from a national survey on behalf of the National Cancer Research Institute's CM-Path initiative. Journal of Clinical Pathology, 71(5), pp.463-466. http://jcp.bmj.com/content/71/5/463.info

[7] https://www.rcpath.org/resourceLibrary/best-practice-recommendations-for-implementing-digital-pathology-pdf.html

3. Case Studies: How CM-Path is making a difference in the research and pathology community

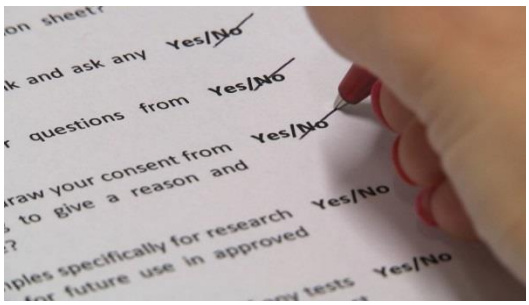
3.1 Emphasising the importance of sample quality in pathology research

Sample quality is very important in enabling the production of accurate and reliable research results. In order to help biobanks and others to focus on improving tissue sample quality, CM-Path has developed and piloted a simple quality improvement tool, which we launched at a workshop in May 2018 attended by nearly 100 delegates, including biobank managers, pathologists and representatives from the pharmaceutical industry. The aim is to support the curation and provision of high-quality tissue samples (and data) which are key to successful research and development in healthcare, academia and industry.

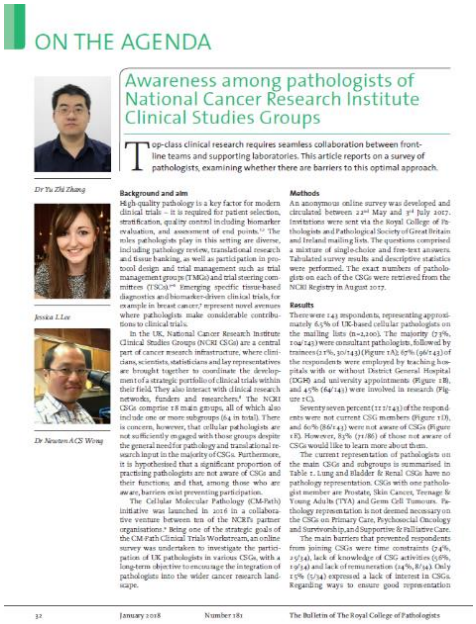


3.4 Streamlining consent for the donation of tissues for research

Obtaining appropriately informed consent underpins ethically sound research and is a key requirement for approval by NHS Research Ethics Committees. The preparation of good quality information which is readily understood by donors is a time-consuming and difficult task. To discuss the development of a template which would be acceptable to the HRA and other relevant regulatory authorities, a workshop was held in February 2018 bringing together representatives from the HRA (Health Research Authority), HTA (Human Tissue Authority), Genomics England, patient representatives and data governance experts. A draft template has been produced and is under revision. The aim is to submit the final version for adoption by the HRA. This will be used initially to support the use of samples which are held by pathology departments and surplus to diagnostic requirements.



3.3 The CM-Path Trainee Scheme and promoting the role of pathology within clinical trials and the NCRI



ON THE AGENDA

Awareness among pathologists of National Cancer Research Institute Clinical Studies Groups

Top-class clinical research requires seamless collaboration between front-line teams and supporting laboratories. This article reports on a survey of pathologists, examining whether there are barriers to this optimal approach.

Dr Yu Zhi Zhang

Jessica Lee

Dr Newton ACS Wong

Background and aim

High-quality pathology is a key factor for modern clinical trials – it is required for patient selection, stratification, quality control including biomarker evaluation, and assessment of end points.[1,2] The roles pathologists play in this setting are diverse, including pathology review, translational research and tissue banking, as well as participation in protocol design and trial management such as trial management groups (TMGs) and trial steering committees (TSCs).[3,4] Emerging specific tissue-based diagnostics and biomarker-driven clinical trials, for example in breast cancer,[5] represent novel avenues where pathologists make considerable contributions to clinical trials.

In the UK, National Cancer Research Institute Clinical Studies Groups (NCRI CSGs) are a central part of cancer research infrastructure, where clinicians, scientists, statisticians and lay representatives are brought together to coordinate the development of a strategic portfolio of clinical trials within their field. They also interact with clinical research networks, funders and researchers.[6] The NCRI CSGs comprise 18 main groups, all of which also include one or more subgroups (64 in total). There is concern, however, that cellular pathologists are not sufficiently engaged with those groups despite the general need for pathology and translational research input in the majority of CSGs. Furthermore, it is hypothesised that a significant proportion of practising pathologists are not aware of CSGs and their functions, and that, among those who are aware, barriers exist preventing participation.

The Cellular Molecular Pathology (CM-Path) initiative was launched in 2016 in a collaborative venture between ten of the NCRI's partner organisations.[7] Being one of the strategic goals of the CM-Path Clinical Trials Workstream, an online survey was undertaken to investigate the participation of UK pathologists in various CSGs, with a long-term objective to encourage the integration of pathologists into the wider cancer research landscape.

Methods

An anonymous online survey was developed and circulated between 22nd May and 3rd July 2017. Institutions were sent via the Royal College of Pathologists and Pathological Society of Great Britain and Ireland mailing lists. The questions comprised a mixture of single-choice and free-text answers. Tabulated survey results and descriptive statistics were performed. The exact numbers of pathologists on each of the CSGs were retrieved from the NCRI Registry in August 2017.

Results

There were 143 respondents, representing approximately 6.5% of UK-based cellular pathologists on the mailing lists (N=2,200). The majority (71%, 102/143) were consultant pathologists, followed by trainees (21%, 30/143) (Figure 1A). 67% (96/143) of the respondents were employed by teaching hospitals with or without District General Hospital (DGH) and university appointments (Figure 1B), and 47% (68/143) were involved in research (Figure 1C).

Seventy-seven percent (111/143) of the respondents were not current CSG members (Figure 1D), and 60% (86/143) were not aware of CSGs (Figure 1E). However, 83% (71/86) of those not aware of CSGs would like to learn more about them.

The current representation of pathologists on the main CSGs and subgroups is summarised in Table 1. Lung and Bladder & Renal CSGs have no pathology representation. CSGs with one pathologist member are Prostate, Skin Cancer, Teenage & Young Adults (TYA) and Germ Cell Tumours. Pathology representation is not deemed necessary on the CSGs on Primary Care, Psychosocial Oncology and Survivorship, and Supportive & Palliative Care.

The main barriers that prevented respondents from joining CSGs were time constraints (74%, 25/34), lack of knowledge of CSG activities (56%, 19/34) and lack of remuneration (24%, 8/34). Only 15% (5/34) expressed a lack of interest in CSGs. Regarding ways to ensure good representation

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The CM-Path Trainee scheme is regarded as useful for both CM-Path members and the trainee themselves. A Trainee from our 17/18 cohort recently gave us a testimonial;

'I felt that as a trainee, it is important to embrace academic pathology and the emerging technologies that will become mainstream in diagnostic specialties during my future career. CM-Path is leading the way with regards to shaping the future of academic/molecular pathology in the UK and it has been extremely helpful to be able to work alongside several senior academic pathologists as part of this initiative.'

Over 20 trainees have been involved with CM-Path over the last two years and a further 11 will be taken on as in our new 18/19 cohort. Trainees have been involved in several major projects. For example, Dennis Zhang on behalf of WS2 led an audit of pathologists' involvement in, and attitudes towards, NCRI CSGs[8].
This was written up and published in the RCPath Bulletin, to disseminate information about opportunities for pathologists to contribute to clinical trials, and the role of the NCRI. This project has helped to enhance recruitment of pathologists to NCRI CSGs, where Calls now include advertising for specific specialities need, and pathologists are now represented on 13 out of 15 CSGs where pathology may be relevant. We have also introduced CM-Path itself at the CSG Chairs' forum and are planning to present about CM-Path at each relevant CSG (with four achieved so far). Increased pathology representation should enhance clinical trials through optimal pathology involvement upfront in trial development and discussion.

[8] https://cmpath.ncri.org.uk/whats-new/cm-path-publishes-report-awareness-amongst-pathologists-of-ncri-csgs/ - 'Awareness among Pathologists of National Cancer Research Institutes Clinical Study Groups' published in the January 2018 RCPath College Bulletin

3.5 Publications - and Promoting Molecular and Research Pathology within Training

CM-Path has made reaching as wide an audience as possible, across both pathology and cancer research more widely, a key objective and one route is publication. To date five[1-5] papers are in print in high quality journals including the BMJ, BJC and Journal of Clinical Pathology and over ten more are in preparation. One example is "Time for change: a new training programme for morpho-molecular pathologists?[1]' which was published online in November 2017, during the NCRI conference. We were delighted when it was highlighted in April 2018 as the Journal of Clinical Pathology's article of the month.

CM-Path recognises there is a knowledge and skills gap in genomics within cellular pathology that needs to be bridged through an upskilling of the current workforce and evolution of training. This paper puts forward a range of suggestions which have generated significant international interest. The proposals had previously been presented at a July 2017 workshop attended by representatives from CM-Path, the Pathological Society, the Royal College of Pathologists, industry partners, Cancer Research UK and pathology trainees, and we look forward to continuing to work together to enhance molecular and research pathology training across the UK.

[9] Moore, D., Young, C., Morris, H., Oien, K., Lee, J., Jones, J. and Salto-Tellez, M. (2017). Time for change: a new training programme for morpho-molecular pathologists?. Journal of Clinical Pathology, 71(4), pp.285-290. http://jcp.bmj.com/content/71/4/285

[10] http://blogs.bmj.com/bmj/2017/12/20/pathology-risks-being-left-behind-as-conceptual-and-technological-advances-accelerate/

4. Next steps for CM-Path

Workstream 1 (Skills & Capacity)	• The pathology community will be consulted to determine the success of the two-week molecular pathology module, to inform future curriculum recommendations to be made by CM-Path. • Full proposals will be drafted for the revised three-month optional module in 'research methodology' and the new three-month optional module on 'molecular diagnostic pathology', for consideration by RCPath. • An **information guide** to summarise the available training opportunities in molecular pathology in the UK will be created, to ensure the community is aware of possible training opportunities. • A **Delphi analysis** of molecular pathology in the undergraduate curriculum will be undertaken.
Workstream 2 (Clinical Trials)	• Workstream 2 will continue to deliver the 'Pathologists Guide to Research and Clinical Trials' workshops and consider further training opportunities to support academic contribution from pathology. • A suite of papers on **quality assurance of pathology in clinical trials** will be published in a peer-reviewed journal. • Options for sessional NHS funding and other resourcing of pathologists for academic activity will be appraised, working with stakeholders including CRUK based on the "Testing Times to Come" report on workload and workforce challenges facing pathology.
CT-PAG (Clinical Trial Pathology Advisory Group) (WS2 & WS3)	• CT-PAG will link with funders and wider research networks to promote CT-PAG, and the potential for **pathology contribution** overall, and to support funding calls. • The first CT-PAG **call-for-proposals** will be completed, including holding a virtual workshop for applicant advice and feedback. • CT-PAG impact to funding schemes of NCRI Partner organisations will be monitored.
Workstream 3 (Discovery)	• The **CM-Path network** of pathology centres across the UK will be developed and launched, for sharing and harmonisation of best practice supporting research. • Workstream 3 will report on changes in academic pathology by submitting for publication a survey of **UK pathologists' attitudes** towards academic and molecular pathology, and a second survey providing updated figures on the numbers of academic pathologists across the UK. • Uptake of the new biobank **sample quality improvement tool** will be promoted, encouraging high quality sample curation and ease of access, and follow up on its impact. • Further tailored pathology research workshops on 'hot topics' will be developed, which aim to promote and support **pathology-led, tissue–based biomarker research.**
Workstream 4	• Close working with **stakeholders** including funders, NHS and industry will be continued. • A workshop on integrating results of **molecular tumour boards** will be developed and delivered, to align, support and create recommendations for the NHS genomic reconfiguration.

(Technology & Informatics)	• A **digital pathology** workshop will be undertaken in June 2018, which aligns with challenges from the **life science industrial strategy.**
Crosscutting Themes	• **Patient and public involvement** – Working with NCRI Consumer Lead to update strategy and identify projects for consumer involvement, which could include consent for and use of tissue in clinical trials. • **Supporting trainees** – A third cohort of trainees has been recruited and will be mentored by the original cohort (most of whom will continue for a further year). • **Biosample consent –** As a result of the workshop held in February 2018, CM-Path is working with Genomics England, HTA, MHRA and other key stakeholders to develop a simplified generic consent template. • **Engaging with wider initiatives** – CM-Path is developing a joint workshop in 2018 with the MRC Molecular Pathology Nodes. • **Engaging with wider specialities** – CM-Path is working with BASO to provide multidisciplinary events for trainee members.

Any questions please contact the CM-Path Programme Manager, Helen.Pitman@ncri.org.uk