A National Co-ordinating Cellular and Molecular Pathology Programme (CM-Path) to reinvigorate UK academic cellular pathology

Dr Bridget S Wilkins, NCRI Pathology Engagement Lead

Background

Cellular and molecular pathology is vital for patients

Almost all cancer patients, plus many patients with non-malignant diseases, require a histological or cytological test for initial diagnosis. Increasing stratified treatment options and prolonged survival with disease, including cancer relapses, are creating new requirements for further cellular pathology input. There is a rapidly escalating need for innovative testing to assess prognosis and to support stratified medicine approaches. The challenges of integrating new technologies (e.g., molecular and proteomic analyses, digital infrastructure) must be addressed by cellular pathology in the next 5-10 years to meet the needs of patients. This requires a culture of innovation and up-skilling of the cellular pathology workforce that has been substantially eroded (against national trends in academic medicine), over the past 15 years:

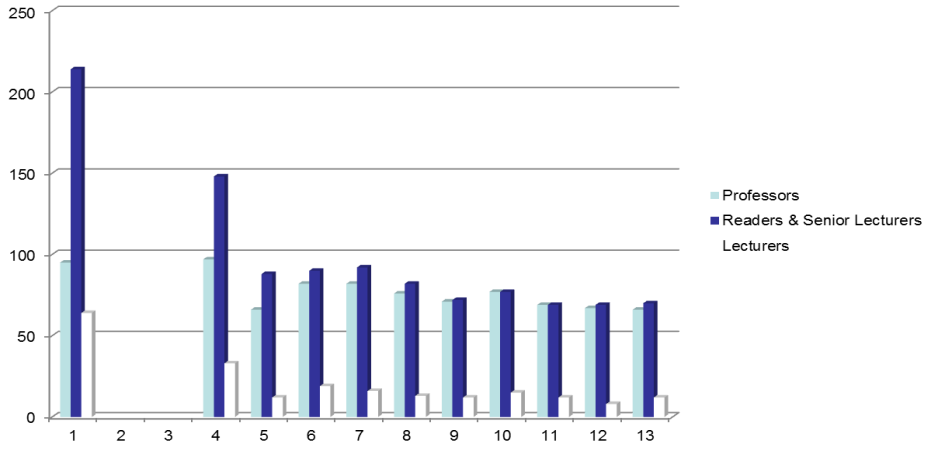


Fig. 1. Decline in academic pathology posts 2000 (yr 1) to 2012 (yr 13)

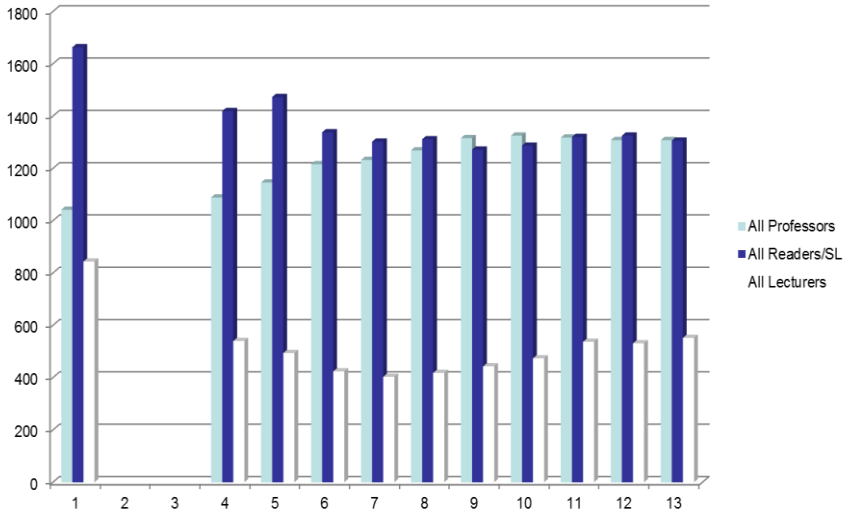


Fig. 2. For comparison, change in all clinical academic posts 2000-12

(Data from the annual Clinical Academic Staff Survey conducted by all medical schools in England, Wales, Scotland and Northern Ireland)

Cellular Pathology as an academic discipline has declined steeply:

- For academic medicine overall (2013 survey): ~3,100fte (+5% since 2000)
- NHS consultant workforce is ~46,400 (+64% since 2000)
- In pathology: NHS consultants 2286 in 2000, 2876 in 2013 (+25%)
- Academics 308 (2000) to 127(2013) (-60%)
- Decline in academic pathology is greatest of all clinical specialities

- **Academic Pathology community in 2000:**
  - 373 full time equivalents (fte)
  - 95 Professors
  - 214 Readers/Senior Lecturers
  - 64 Lecturers

- **Academic Pathology community in 2008/9** (at the time of the NCRI 'Fostering the Role of Pathology in Research' report**):**
  - 155 fte
  - 71 Professors
  - 72 Readers/Senior Lecturers
  - 12 Lecturers

- **Academic Pathology community in 2012/3** (latest UK medical school survey):
  - 148 fte
  - 66 Professors
  - 70 Readers/Senior Lecturers
  - 12 Lecturers

The decline has affected all grades from Lecturer to Professor and is continuing. The Medical Schools' annual survey does not provide any data regarding numbers of academic training posts funded within the specialist training post allocations in cellular pathology – these are very few; the entire pipeline for academic pathology has been greatly reduced, with few suitable candidates currently recruited into cellular pathology training. In parallel, ready access to research laboratory facilities has also declined severely. All of these features were described in detail in the 2009 NCRI 'Fostering Research in Pathology' report, which was issued as the recent economic crisis hit; none of its recommendations have been implemented to any substantial effect to date. The charts above confirm absence of significant change resulting post-2008 from any actions arising from this report.

Cellular Pathology is a broad discipline - why is this a cancer problem?

More than 80% of all cellular pathology tests are for the confirmation or exclusion of cancer, including screening for major cancer types. Professional practice and innovation in cellular pathology are therefore driven primarily by cancer medicine. The current requirement for rapid development of diagnostic tools to support stratified and personalised therapies is overwhelmingly cancer-related. It is this drive currently that provides the greatest need for cellular pathology to re-engage academically and to innovate fast. Delivery of the Genomics England '100,000 genomes' project is also critically dependent on pathology capacity to deliver suitable material from accurately and fully characterised tumours.

Why now?

After a 15-year period of academic attrition, posts at professorial, reader, senior lecturer and lecturer level are at a historic low. It has yet to be seen whether long-term appointments at these grades will be sustained when the current appointees retire. Senior posts have a long tenure and do not reflect recent fluxes; impact of the results of REF 2014 are awaited. Few cellular pathologists appointed to NHS consultant posts after 2000 have undertaken research; almost none have supervised others doing research. Meanwhile, a large cohort of cellular pathologists, trained in academic posts and many initially employed as lecturers/senior lecturers, are in mid- and late careers in NHS service posts. They have no current academic remit, time allocation or supporting infrastructure. A substantial cohort of keen potential research mentors exists among these mid/late career cellular pathologists whose posts were transferred to the NHS between 2000 and 2009 but many of these individuals have 5 years or fewer before they are eligible to retire. For each year that passes, the pipeline for support of new academic entrants into cellular pathology therefore becomes more challenging outwith a tiny elite cohort in surviving academic centres of excellence. Without critical mass, even elite departments and individuals are threatened, since new recruits into cellular pathology are progressively less motivated for/engaged with academic endeavour.

Options

1. Do nothing**.** 'Academic Pathology' as such may not justify specific additional resourcing. Academics in clinical disciplines, such as oncology, and in genetics could incorporate pathological assessment in their portfolios of skills.

At best, the current levels of academic output in pathology will be maintained, with likelihood of ongoing attrition as current post-holders are not or unable to be replaced when they leave/retire. Non-replacement will occur even if posts technically remain available, with a lack of suitable candidates to appoint.

2. Invest further in the few centres of active academic pathology that remain, preserving a small number of hubs of academic activity and training.

Doing this alone identifies academic endeavour in pathology as an elite activity for the few, separates it from 'mainstream' pathology and offers at best a fragile pipeline for a very limited number of new entrants. Capacity will remain severely restricted for support of innovation for stratified medicine, slowing development and limiting roll-out. Lack of direct involvement of the wider pathology community will also limit the uptake and implementation of novel technologies.

3. Select a limited, but larger, number of centres with potential for academic pathology revival, initially as spokes networked to established hubs and invest in these. Potential based on technological platforms, subject focus, key individuals.

This is well aligned with other initiatives such as the ECMC network, DECs, TSB Precision Medicine Catapult centre and recently announced proposals from MRC for molecular pathology hubs. It probably offers the best scope, of all the individual proposed options, for collaborations with industrial partners of all sizes. It could align with the future distribution of major centres at which pathology trainees are

based. Research and molecular training in these centres would align with the RCPath intention to include these fields in revised training curricula; trainees would spend a high proportion of their training time in their 'hub' centres. Potential for mentoring of research training still exists in these centres through consultants trained pre-2000, plus a few additional exceptional younger individuals.

4. Incentivise NHS pathologists to participate in research within their NHS job plans; requires protection of time, payment, academic recognition, infrastructure.

This is not a viable or cost-effective solution alone; pathologists equipment, space, scientific/technical support and collaboration to pursue a modern research agenda . Infrastructure could be provided by resourced hubs and spokes or develop in networks confederated to hub-and-spoke arrangements. Risk would be return to 'productivity' equating with stand-alone, observational studies of limited value beyond refining conventional diagnostic precision. Could add value if aligned to support strategic agenda to validate new technologies and methods. There are substantial numbers of willing current consultants, especially those trained pre-2000 who represent a largely unused potential resource for research and mentoring for research training.

5. Combination of 2, 3 and 4

This is, in effect, what the CM-Path Executive Group would help make possible.

Where are the resources that might contribute to increasing academic endeavour in Cellular Pathology?

- Academia – HEFC, Research Councils, Research Charities
- NHS (including NIHR)
- Industry
- Philanthropy
- Government – Technology Strategy Board etc.
- Royal College of Pathologists
- Research-orientated professional societies such as the Pathological Society of GB and Ireland.

What do we need for the future?

A. Profession-wide Research Activity:

- Pathology support for clinical trials (e.g., provision of material for central review, modification of pre-analytical protocols to suit study needs, selection and supply of material for translational studies, review of outputs such as TMA)
- All trainees completing curriculum including molecular genetics and introductory research
- Molecular pathology education for cellular pathology consultants and clinical/biomedical scientists.

(Interest for investment: NHS > Academia > Industry)?

B. Middle-ground Research Activity:

- Biological validation (e.g., biomarker validation at scale, including stromal reactions, immune responses and other 'host factor' correlations)
- Technological validation (e.g., early adopters for roll-out of digital pathology, new genetic analytical platforms, optimisation of pre-analytical tissue processing)

(Interest for investment: Industry > Academia > NHS)?

C. Critical Mass in Centres of Excellence:

- Biological innovation (e.g., biomarker discovery, including stromal reactions, immune reactions and other 'host factor' correlations)
- Technological innovation (e.g., national strategy to set standards for digital pathology, new genetic analytical platforms, optimisation of pre-analytical tissue processing)
- Central and outreach education for clinical trainees, consultants and biomedical scientific staff in middle-ground centres and networked peripheral hospitals.

(Interest for investment: Academia > Industry > NHS)?

How would CM-Path, as a national strategic initiative, support these?

Providing oversight for strategic development:

Monitoring changes to the current situation (staffing, income, outputs)
Publicising advances, opportunities, setbacks
Influencing all stakeholders
Supporting hub, spoke and networked centres, and individuals
Coordinating activities between organisations and workstreams

Developing high quality research:

- Translational research to feed clinical trials pipeline
- Development of pathology components in clinical trial protocols
- Delivering pathology in clinical trials
- Quality assurance of pathology research
- Assuring patient and public engagement
- Ensuring realisation of patient and economic benefit through industrial translation of valuable tests

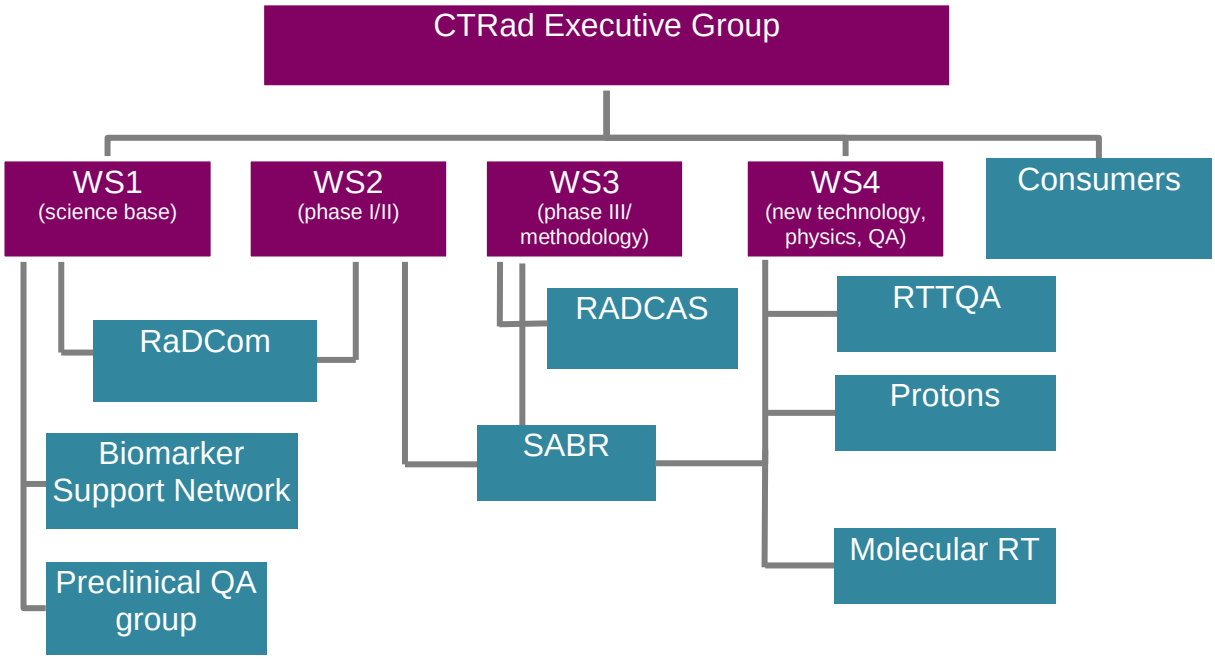
Developing infrastructure:

- Developing centres of excellence
- Supporting the research workforce
- Promoting networking and collaboration

Exploiting opportunities:

- Engaging with industry
- Engaging with research funders
- Driving the research agenda for innovative technologies

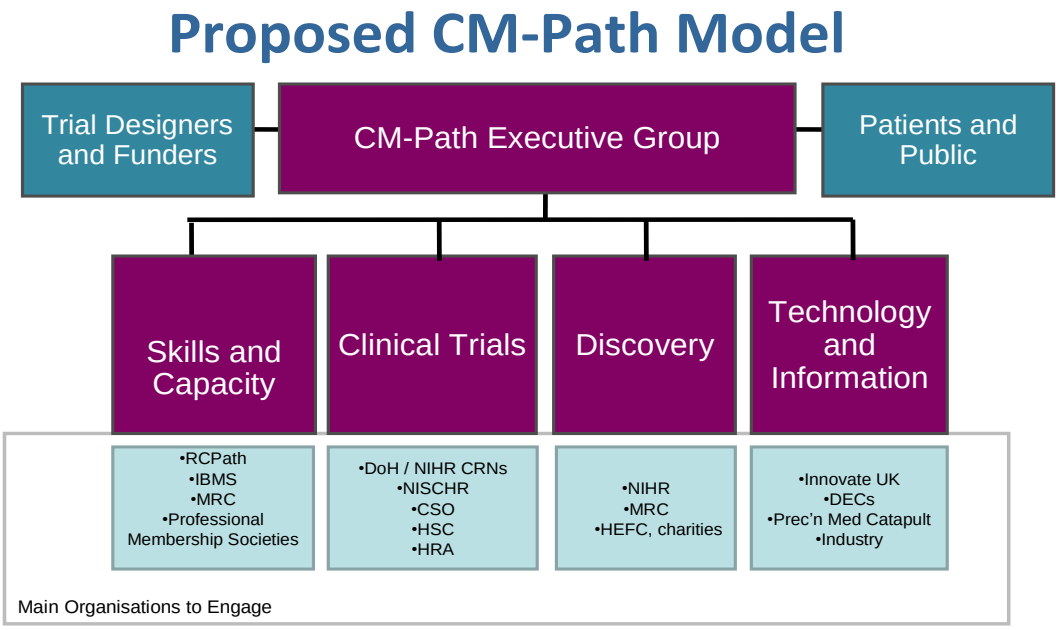
Existing NCRI CT-Rad structure suggests model for organisation:



Within this structure, NCRI funds:

- Sessional time for Chair and Deputy Chair of Executive Group
- 1.0 WTE Programme Manager
- 0.5 WTE Administrative support
- Running costs (mainly teleconferencing)
- Meetings and workshops

Proposed CM-Path structure:



(Workstreams are not intended as spatially or thematically independent activities but to network and cross-fertilise under strategic oversight of the Executive)

Workstream themes:

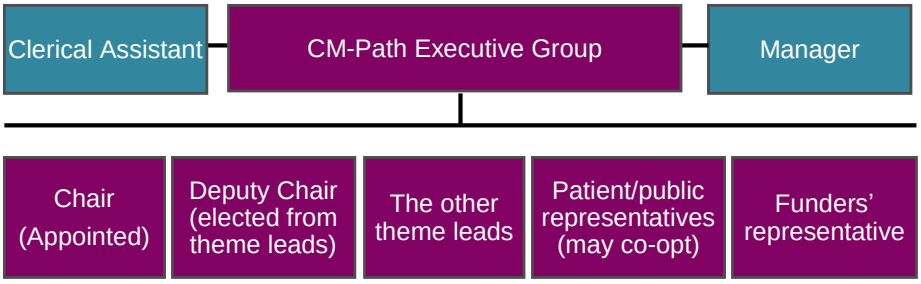
Workstream 1 Skills and Capacity: has its focus on education and continuous updating of the cellular pathology workforce

Workstream 2 Clinical Trials: represents profession-wide engagement with clinical trials and other research needing relatively straightforward cellular pathology support. Also the adoption and dissemination of validated new technologies.

Workstream 3 Discovery: reflects activities predominantly located in 'hub' centres of excellence.

Workstream 4 Technology and Information: is the 'middle ground' of R&D weighted towards 'D' for continuous innovation in cellular pathology and dissemination of uptake of new technologies/tests.

Proposed CM-Path Executive Structure



The executive group will:

- Support funding initiatives to build capacity within each workstream
- Ensure information-sharing and promote collaboration between workstreams
- Coordinate and, when beneficial, integrate activities of different workstreams
- Seek opportunities to promote pathology elements, where appropriate, as key components of oncology research
- Facilitate introduction and adoption of new technologies
- Facilitate public/patient engagement with tissue-based research

Benefits of an Executive Group to drive a National Strategy for Cellular Pathology Research

The major benefit will be coordination of effort to maximise effectiveness in seeking core funds to build and maintain cellular pathology research capacity. Strategic direction will ensure a consistent drive for equipping the cellular pathology workforce to become the 'morpho-molecular' pathologists and biomedical scientists required to deliver continuously innovating diagnostic services for stratified/personalised medicine. The strategy will be robust for support of anticipated development beyond the current genomic focus into a 'polyomic future'. Patients will benefit significantly from faster development, adoption and roll-out of appropriate and improved diagnostic methods. Translation of basic scientific insights gained into pathological processes into procedures and products of clinical utility will be achieved more quickly and effectively. Industrial stakeholders will have a clear framework within which to work.

Threats/Risks

Funding may be allocated and academic capacity may still not be increased to critical mass, particularly if the initiative has a short life. Existing academically active centres may be degrade or lost as a result of REF 2014. Centres of excellence may resist initiatives requiring contribution to collaborative efforts with other workstream partners if no benefits are seen. NHS culture may resist roll-out of innovations.

Next Steps

The proposal at this stage has deliberately been formulated at high level and is not prescriptive with regard to specific research content. We are seeking views widely to establish its final shape, to decide what components should potentially be NCRI-funded, what other funding for specific components might be pursued, and how the proposed structure aligns with the activities, plans and visions of a wide range of potential stakeholders. The proposal will be finalised during April and May for presentation to the NCRI Board in June.