

COSA Cancer Biology and Biobanking Workshop Report

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Melbourne Convention and Exhibition Centre



Background

Pathology is a fundamental part of cancer care and all diagnoses rely on careful examination of the anatomy and histology of the tumour itself. We understand cancer to be a genetic disease, that is, cancers arise due to aberrations in the control of cellular proliferation and progress due to their ability to metastasise to other sites in the body. Understanding how cancers are caused and how they behave in response to treatment requires careful study of tumours themselves, underpinned by access to tumour specimens linked to clinical information.

The COSA Cancer Biology group has been working to find ways to enhance access to human biospecimens and data for researchers. However, funding cuts in all states but NSW has meant there is limited opportunity to make biobanking initiatives core infrastructure for cancer research. This workshop held at the 2014 COSA ASM sought to identify novel approaches to solve this problem without recourse to large new injections of funding.

Session 1

Setting the Scene: Biobanking as part of routine pathology practice

In session one, chaired by Professor Nick Hawkins (University of NSW), presenters examined how pathology practices, and in particular anatomical pathology, has been a core part of biobanking for many years and that recently there has been a move to bring the biobanks back under pathology services (WA and NSW). Renewed interest in using human biospecimens has been prompted by molecular companion diagnostics that are mandated by the PBS listing for several targeted cancer therapeutics.

Discussion centred on how pathology could absorb the marginal costs of biobanking, including managing access to material and linked clinical data. Dr Nik Zeps (St John of God) outlined how this was working well at St John of God Subiaco Hospital, where it is integrated into pathology and managed under multi-disciplinary teams. Similarly, Prof Rodney Scott (The University of Newcastle) reported that there was still some way to go with bringing research and clinical care toward common understanding.

An initiative in NSW is bringing together NSW health pathology (integrated, manager appointed), the NSW ministry of health (support), CINSW (infrastructure) and CCNSW (additional funding support) and is working toward a stable and functioning network of biobanks that are part of healthcare delivery. While significant progress has been made, access to clinical data remains a challenge that requires a more integrated approach to information technology. While NSW is leading the way, this is a national issue and there is no clear pathway or funding for a national approach.

Important to any cancer research activity is support by patients themselves and Heidi Turon (The University of Newcastle) presented data in which oncology patients supported biobanking of their biospecimens surplus to diagnostic need. The overwhelming majority believed that consent could be generic, that is, delegated to an ethics committee to decide which projects could use the

specimens. Experience in WA and Canada indicates that opt-out consent posed some practical difficulties and probably did not meet the expectations of respect that is at the core of consent.

Australia is not alone in working through these issues and Professor Peter Watson (British Columbia Cancer Agency) reviewed the Canadian experience and illustrated how his own research is supported by access to biospecimens. His analysis indicates that approximately 40% of 3000 cancer papers relied on a biospecimen to draw their conclusions. There are a wide range of biobanks in Canada and a survey revealed that they have as many as 10,000 specimens that are captured under a standard definition. Work is underway to rationalise this and to standardise process to ensure high quality and efficiency.

Dr Roger Bjugn (Oslo University Hospital) challenged attendees to look at where the risks to a project may lie, in particular, failure to identify key stakeholders who have the power to halt a program. He illustrated this with an example from their national diabetes study where a GP was uncomfortable with patient questions regarding the use of the tests. An investigation subsequently ruled that the test was not legally sound. The failure of the study hinged on failure to identify the key stakeholders (here a GP) and Dr Bjugn emphasised the need to perform proper stakeholder analysis, including a power versus interest matrix to establish where risk lies. He proposed a five step process; identification, attributing values, priority, engagement, monitor. Dr Bjugn also highlighted the need to distinguish the difference between the intention to support and the capacity or will to do so when called upon.

Session 2

Clinical research enabled by pathology: Tales from the field

Chaired by Professor Peter Gibbs (University of Melbourne) this session heard presentations from pathologists engaged in programs aimed at bringing molecular diagnostics into clinical practice.

Professor Stephen Fox (Peter MacCallum Cancer Centre) presented an update on the Cancer 2015 program, which involves molecular screening as an adjunct to standard pathology and examines both the practicality and utility of this information in managing the care of cancer patients. The project aims to screen 10,000 patients at five pilot sites in Victoria. The development of the *mytumour* app has demonstrated that patients want data and that there is a need to integrate molecular diagnostics into routine care as currently there is no Australian model to achieve this. Significant barriers include cost, accreditation, human resources and adequate for bioinformatics.

The advantage of the model adopted by Cancer 2015 is that standard diagnostic material is used, therefore recruitment has included regional patients in both public and private hospitals. To date 1,750 patients have been recruited with about 15% of samples of inadequate quality (degraded or insufficient material). The mutation frequency is as expected and 63% of patients have at least one clinically relevant mutation.

An additional aim of Cancer 2015 is to facilitate the development and implementation of clinical trials that will recruit patients screened by this program. The group are looking at other technologies and approaches including liquid biopsy (blood samples screened for circulating tumour DNA). An economic assessment is ongoing to determine if this is cost effective or sustainable.

Professor Lindeman (South Eastern Area Laboratory Services) presented the challenges and triumphs the South Eastern Area Laboratory Services (SEALS) have experienced when integrating molecular information into routine pathology reporting. SEALS is a network that includes the Lowy Cancer Centre, the Prince of Wales Hospital and area health services south east to Wollongong.

This work is aligned with their biobank and their experience has been that managing samples is relatively simple compared to data linkage.

NSW Health has conducted an assessment of biobanking and has published a position paper highlighting the difficulties with integrating their Laboratory Information Management Systems (LIMS) with biobanks. They are presently undertaking a process of integrating biobanking into routine pathology services. However, data linkage between clinical service information management tools, biospecimen LIMS and molecular outputs is undeveloped and not as functional as it needs to be.

Professor Lindeman identified the need for high-level commitment to the program and a need to allocate sufficient resources to deliver it, especially where there are competing interests. The SEALS experience (led by Professor Hawkins) has demonstrated that efficient and integrated consent for universal access, as part of patient management was ideal. In conclusion, pathology services were willing and able to take on biobank and data management responsibilities but this needs proper resourcing and commitment from all those involved at every level (see Dr Bjugn's presentation).

Professor Paul Waring (The University of Melbourne) provided an overview of biomarker enabled clinical trials, illustrating the need for targeted therapeutic trials to have accurate and useful companion diagnostics to ensure adequate patient enrichment and proper evaluation of efficacy. He discussed the experiences of EGFR as a useful warning to the potential pitfalls of this type of research if not adequately controlled for.

Professor Waring also outlined how biomarkers could be used to design clinical trials and gave EVICT and ICECREAM as examples of Australian clinical trials in which this had been done. He suggested that one opportunity is to utilise the increased NextGen sequencing of tumours to provide a means to screen for patients who, while perhaps ineligible for the study they were screened for, might be eligible for others, including those not yet developed. That is, if there were a means to collate molecular testing data it would not only enable patients to be identified for current studies but might also enable new trials to be designed based upon the prevalence of potentially targetable mutations.

Further opportunities lie in identifying mutations that arise during treatment, which may allow a better understanding of resistance mechanisms and the development of robust biomarkers of drug resistance and even potential new targets. Professor Waring challenged the attendees to think about how we would solve this and suggested that we may need to alter our current biobank paradigm to one in which pathology is central and molecular data is as useful as the specimen itself.

Finally, Dr Brett Kennedy (Illumina) gave an overview of advances in clinical genomic cancer analysis led by the Actionable Genome Consortium (AGC) in the USA, UK and Canada. The intentions of this project is to demonstrate the clinical utility and standardisation of processes with the higher goal of democratising genomic testing. A publication scheduled for early 2015 will set out the minimum standards for panels that are in use for next generation sequencing in clinical decision making in oncology. The AGC hope to identify what they call class 1 and 2 actionable gene targets (currently over 100 in adult solid tumours) which should form the basis for a universal oncology test. Dr Kennedy highlighted the inclusive nature of this project and welcomed the involvement of Australian programs.

Conclusions

The presentations and discussion at this workshop highlighted the central issue of cancer biobanking: how do we achieve a sustainable model with a high probability of generating translational data? Discussion identified disengaged state, territory and federal governments in wishing to facilitate solutions, demonstrable through a lack of adequate funding. However, there were examples in NSW and Victoria of important initiatives (outlined in the presentations) that gave cause for optimism. All workshop attendees identified the need to work more cooperatively and several examples of how this had already worked well were provided, including joint submissions to government and MSAC (although the success rate of some was identified as a clear sign that we have not yet found the right way to sell our message).

The challenge we face is something I believe COSA is well placed to address as a joint work program led by the Cancer Biology Group together with the cooperative trials groups, the Royal College of Pathologists of Australasia and any interested COSA group.

Nik Zeps

Chair, COSA Cancer Biology Group

Thank you to the workshop sponsors

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