Anatomical Pathology

BIOMARKERS IN CUTANEOUS MELANOMA: CASTLES IN THE SKY AND USEFUL DEVELOPMENTS

Peter Ferguson^{1,2}

¹Department of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, New South Wales Health Pathology, Sydney, NSW, Australia; and ²Melanoma Institute Australia, The University of Sydney, North Sydney, NSW, Australia

Recent advances in systemic therapy have improved outcomes for patients with advanced stage cutaneous melanoma. This has led to an increased clinical need for biomarkers to identify patients with early stage disease who are likely to benefit from adjuvant treatment. Prognostic calculators can refine prediction of the risk of recurrence by incorporating additional clinicopathological parameters that are not included in melanoma staging by the 8th edition of the AJCC Cancer Staging Manual. Novel prognostic biomarkers are being developed through a range of molecular methods, including gene expression profiling, targeted sequencing and proteomics. There is also a need for improved predictive biomarkers, to identify patients whose melanomas will respond to immunotherapy and distinguish those who are at risk of toxicity without therapeutic benefit. This presentation provides a snapshot of recent developments and future challenges in the development and application of biomarkers in the management of primary cutaneous melanoma.

PREDICTING ENDOCRINE SENSITIVITY IN BREAST CANCER

Cameron E. Snell^{1,2}, Deborah Smith^{1,2}, Madeline Gough^{1,2}, Cheng Liu², Kathryn Middleton^{3,5}, Christopher Pyke^{4,5}, Catherine Shannon^{3,5}, Natasha Woodward^{3,5}

¹Cancer Pathology Research Group, Mater Research Institute – The University of Queensland, Translational Research Institute, Qld, Australia; ²Department of Anatomical Pathology, Mater Pathology, Mater Hospital Brisbane, Qld, Australia; ³Department of Medical Oncology, Mater Hospital Brisbane, Qld, Australia; ⁴Department of Breast and Endocrine Surgery, Mater Hospital Brisbane, Qld, Australia; and ⁵Mater Research Institute – The University of Queensland, Translational Research Institute, Qld, Australia

Approximately 75% of breast cancers express oestrogen receptors (ER), progesterone receptors (PR) or both. Endocrine therapy is a cornerstone of systemic therapy for ER+ breast cancer in both the adjuvant and metastatic setting. Despite adjuvant endocrine therapy, over 20% of women with early-stage disease suffer a relapse which can occur years or decades after diagnosis. ER expression only poorly predicts outcome and better predictive markers of response or resistance are required. Molecular signature assays such as Oncotype Dx, Prosigna, Mammprint and Endopredict have produced information on prognosis and aid in the decision as to whether

patients should have adjuvant chemotherapy in addition to surgery and endocrine therapy.

We have recently shown that a physical interaction between ER and PR exists and is potentiated by the presence of oestrogen and progesterone.¹ PR alters the interaction between ER and chromatin to change the transcriptional output of the ER complex. We have quantified interactions between ER and PR in breast cancer to demonstrate that low ER/PR interactions are associated with relapse on adjuvant aromatase inhibitors. We are currently utilising a novel patient-derived explant (PDE) culture model to measure the sensitivity of tumours to oestrogen, progesterone, tamoxifen and targeted treatments including CDK4/6 inhibitors.

Reference

1. Snell CE, Gough M, Liu C, *et al.* Improved relapse-free survival on aromatase inhibitors in breast cancer is associated with interaction between oestrogen receptor-alpha and progesterone receptor-b. *Br J Cancer* 2018; 119: 1316–25.

BACKGROUND, TESTING METHODS, AND LABORATORY APPROACHES TO SARS CORONAVIRUS-2 (SARS-COV-2) AND COVID19

William D. Rawlinson^{1,2}, Sebastiaan van Hal³, Malinna Yeang¹, Anna Condylis¹, Zin Naing¹, Jane-Phan Au^{1,2}, Mariana Ruiz da Silva^{1,2}, Charles Foster^{1,2}

¹Serology and Virology Division, NSW Health Pathology Microbiology, SEALS Prince of Wales Hospital, NSW, Australia; ²Schools of Women's and Children's Health, Medicine and Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, NSW, Australia; and ³Department of Microbiology and Infectious Diseases, NSW Health Pathology, Royal Prince Alfred Hospital, NSW, Australia

Introduction: A pandemic is an epidemic occurring worldwide, crossing international boundaries and affecting many people. The spread of SARS-CoV-2 from Hubei province in China globally has led to rapid changes in our approaches to diagnosis, with rapid use of molecular methods such as whole genome sequencing (WGS) to characterise mutations, and deployment of novel therapeutics including mRNA vaccines and monoclonal antibodies.

Methods: New methods for diagnosis, including WGS, and different approaches to emerging mutations in virus variants of concern (VOC) will be discussed.

Results and conclusions: Diagnosis now uses standard molecular methods including commercial and inhouse techniques, more recently rapid antigen detection, and research into rapid smartphone based nanoparticle assays. Laboratory practices of sample pooling, reflex testing using WGS, and workflow changes are now routine.

The use of rapid WGS techniques,¹ and available Australian data,^{2,3} have informed assessment of the accuracy and utility of these methods in the diagnostic laboratory. Assessment of changes in PCR primer binding sites, and of the influence of how sequence

data are assessed (Foster *et al.*, in press) means accreditation and QA programs need to be continuously updated.

References

1. Bull RA, Adikari TN, Ferguson JM, *et al.* Analytical validity of nanopore sequencing for rapid SARS-CoV-2 genome analysis. *Nat Commun* 2020; 11: 6272.
2. Rockett RJ, Arnott A, Lam C, *et al.* Revealing COVID-19 transmission in Australia by SARS-CoV-2 genome sequencing and agent-based modeling. *Nat Med* 2020; 26: 1398–404.
3. Seemann T, Lane CR, Sherry NL, *et al.* Tracking the COVID-19 pandemic in Australia using genomics. *Nat Commun* 2020; 11: 4376.

CORONIAL CASES: SARS-COV-2 INFECTION AND COVID-19

Linda Iles

Victorian Institute of Forensic Medicine, Melbourne, Vic, Australia

Victoria's second wave of SARS-CoV-2 infections saw a number of reports of deaths of SARS-CoV-2 positive persons made to the coroner. Whilst COVID-19 deaths are natural and do not routinely fall under the coroner's jurisdiction, these cases were brought to the coroner's attention due to deaths being unexpected and unexplained and subsequently being diagnosed as COVID-19 post-mortem, concerns around care in those dying with a known diagnosis of COVID-19, or co-incidental SARS-CoV-2 infection with a cause of death unrelated to viral infection. This had a significant impact on workloads at VIFM, ranging from changes in admission procedures, extensive viral testing, and contributions to contact tracing. Aspects of the management of these cases will be discussed, along with the pathological aspects of some of these presentations.

A REVIEW OF EXTERNAL QUALITY ASSURANCE PROGRAM PERFORMANCE PD-L1 FOR NSCLC

Julia Pagliuso

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), Anatomical Pathology, St Leonards, NSW, Australia

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) are accredited against International Standard (ISO/IEC) 17043 Conformity assessment – General

requirements for proficiency testing. In 2017, the RCPAQAP began collaborating with the United Kingdom National External Quality Assessment Services for Immunocytochemistry and In-Situ Hybridisation (UK NEQAS ICC and ISH) for technical proficiency testing in PD-L1 for non-small cell lung cancer (NSCLC). RCPAQAP laboratories participating in the program has increased steadily over the last few years to 43 in 2021; 2018–2020 results will show that RCPAQAP participant results are comparable with results from the total number of 153 UK NEQAS participants.

The RCPAQAP also collaborates with the International Quality Network for Pathology (IQNPath) for PD-L1 for NSCLC interpretation proficiency testing. RCPAQAP participants are invited to participate in this and other IQNPath programs free of charge. Outcomes from this collaboration will be presented.

The Merck Sharpe Dohme (MSD) BioPlaza platform is a tool that will enable RCPAQAP participants to load de-identified patient tumour proportion scores (TPS) to allow dynamic laboratory average comparison against the Australian average in a 'real time' external quality assurance paradigm.

WILL THE BOT TAKE THE LOT? LOOKING RATIONALLY AT THE PROMISES AND THREATS OF ARTIFICIAL INTELLIGENCE IN PATHOLOGY

Jeremy Parry^{1,2}

¹*Western Diagnostic Pathology, WA, Australia; and* ²*Murdoch University, WA, Australia*

While one casual observer might regard artificial intelligence (AI) as the golden future of the planet, the next may see it as a menacing threat to human sovereignty, or simply over-rated hype. As pathology tentatively enters the digital age, we can justifiably ask the questions – is AI going to make us better pathologists? Have minimal impact? Or make the *discipline* of pathology better, with or without *us*? In either case, pathologists must engage with the debate and take an active role in shaping how clever machines are rolled out into our vocation.

This talk takes a birds-eye view of the topic of AI in pathology, examining what we do, how we (currently) do it and how the clever deployment of machine learning and other AI technologies can possibly help us do it better, without displacing the human element from the process. Topics covered include the potential role of robotics in the cut-up room; the role of machines in things we already do superbly well (such as image analysis); the things we do less well (like counting and scoring!); and some possible future exciting directions for our profession.