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RCPA
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Position Statement

Subject:	**Best Practice Position Statement on the Role of Pathologists in the Supervision and Performance of Genetics and Genomic Testing in Laboratories**
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It is the RCPA's position that to minimise risk to patients and ensure laboratories are operating at the highest level of clinical and scientific governance, all laboratories conducting Genetic and Genomic Testing should have both a pathologist and clinical scientist with a scope of practice in their particular disciplines of pathology.

Introduction

The RCPA has developed this position statement to provide information to pathologists, clinical scientists, clinicians, other health care providers, regulatory and administrative bodies, governments, and the broader community about the skills required to oversee the performance and supervision of genetic and genomic tests.

Pathologists are specialist medical practitioners who study the cause of disease and the ways in which diseases affect our bodies. Genetic Pathology is a separate specialty of pathology in Australasia, reflecting the specialisation available in genetic testing, especially in germline testing. Genetic and genomic testing is increasingly an integral part of the routine practice of all branches of pathology. Genetic testing is the basis of personalised medicine and is increasingly a contributor to improved patient outcomes. Genetic Pathologists and other cross-disciplinary pathologists who specialise in genetic testing, complement the existing pathologist workforce, to diagnose and monitor complex disease using molecular testing methods.

Clinical Scientists (including Molecular Scientists) play a key role in regulatory compliance and quality management. They are responsible for instrument and method selection, validation and ongoing monitoring. They can offer advice on testing and result interpretation to clinical colleagues and play a key role in the training of laboratory staff including pathologists. In specialist fields they are involved in research and development of new assays and in bringing new developments into clinical use.

It is essential that the pathologist and clinical scientist overseeing this testing have the appropriate level of training and expertise, participate in the applicable documented continuous professional development programme (CPDP) and have recency of practice in an appropriate laboratory.

The expanding range of Genetic and Genomic testing

The range of tests covered by genetic and genomic testing is extensive andcontinuing to expand at a rapid pace. This includes looking for an increasingly broad range of genetic abnormalities in both constitutional and somatic genetic settings, and using a wide variety of technologies. Examples of genetic testing are:

- targeted analysis for presence or absence of predefined mosaic or clonal genomic variation
- screening for undefined variants in a single gene
- screening for undefined variants in a limited number of specified genes
- screening for undefined variants in a large number of specified genes.

Testing at the genomic level can include:

- untargeted screening of all chromosomes (karyotyping)
- higher resolution screening of all chromosomes (also known as molecular karyotyping, or chromosomal microarray)
- whole-exome and whole-genome screening.

Other specialised tests are also emerging that include:

- targeted testing for uniparental disomy, chimerism, methylation anomalies
- targeted testing for microsatellite instability
- circulating tumour DNA (ctDNA) analysis including minimum residual disease and tumour mutational burden analysis
- oncogenic HPV nucleic acid testing, chimerism, other epimutations
- gene expression profiling.

The Goals of Genetic and Genomic testing

The primary goal of genetic and genomic investigations is to identify genetic variants that are of direct relevance to the clinical phenotype (the observable characteristics or traits in an individual) in question. These variants can be used to:

- confirm or exclude a diagnosis
- provide information on disease course and prognosis
- select targeted therapies
- monitor response to treatment
- detect recurrence of disease.
- predict risk of future disease in asymptomatic individuals and their family members
- identify individuals or couples at risk of having children with disorders to inform reproductive planning and decisions.

Similarly, the absence of genetic and genomic variants can often be equally informative. Some tests may simultaneously detect additional disease-causing variants that are not directly relevant to the clinical indication for the specified test or identify variants of uncertain clinical significance. Questions arise as to whether these additional/incidental finding should be reported or not, particularly where there is no known treatment.

Clinical utility of Genetic and Genomic testing

The clinical utility of genetic and genomic testing relies on supervising pathologists working with appropriately trained clinical scientists in attaining the theoretical, practical and clinical standards required to ensure that:

- the appropriate test is selected to detect the genetic/genomic variant relevant to the clinical question.
- the appropriate sample is submitted for testing. This includes selection of the sample type to enable the correct genetic/genomic target to be tested, accounting for sample characteristics such as formalin fixation, neoplastic content, macro/micro dissection, and meeting sample collection requirements to achieve necessary quality parameters for testing.
- the clinical and technical limitations of the test are understood
- unusual or atypical results are investigated appropriately (including technical trouble-shooting).
- the result is interpreted correctly and in the appropriate clinical context, and is communicated clearly.

- unanticipated and uncertain findings are managed appropriately and according to current guidelines for the health service for that individual.

Roles and responsibilities

Genetic Pathology is a broad discipline which provides information underpinning much of healthcare delivery. An understanding of the genetic basis of disease is now a component of every discipline of health care with errors and inefficiencies at any point in the testing process having compounding consequences across many health disciplines.

Genetic Pathologists supervise and undertake testing and diagnosis across all disciplines of pathology. Cross-disciplinary pathologists who specialise in genetic testing, undertake testing for diagnosis and monitoring of diseases within their discipline/s of expertise. To achieve this in a safe and effective manner, Genetic Pathologists and other pathologists have three overlapping areas of responsibility:

As a specialist medical consultant

- Pathologists are accountable both professionally and legally for expert judgements made regarding the medical significance of clinical laboratory data. This accountability is reflected in the requirement for enrolment in CPDP, membership of a national medical specialty body and annual medical registration.
- Pathologists work at the interface of genetic science and medical practice. Knowledge of both these domains means they can apply this knowledge in clinical reasoning for patient benefit.
- Pathologists are communicators who understand the needs of the requester and the patient. They can provide clear interpretations of genetic test results either across all areas of pathology or in their specific discipline to inform and guide decision-making by the requester and patient, including by participating in multidisciplinary teams and discussions
- The consultative role of a pathologist is particularly important with the implementation of genomic testing, involving analysis of potentially thousands of genes simultaneously. Such testing should only be undertaken in the context of an explicit medical consultation involving the requesting clinician, the patient, and the pathologist at a testing laboratory. This consultation:
    - must include issues of consent and the reporting of incidental findings
    - may include technical aspects of test performance, recognising that the same test may have high validity in one clinical context, but diminished validity in another.

  With the rapid developments in genomic testing currently being implemented, the ability to relate ‘state of the art’ contemporary genetic testing to specific clinical settings is an essential role as many clinicians will not be familiar with the strengths and weaknesses of the new developments in testing.
- Pathologists advise requesting clinicians of the comparative attributes and performance of genetic tests in a specific clinical setting. This may involve determining whether the requested test is fit for purpose for a particular patient and the limits that may be placed on the interpretation of the test result for a particular patient and setting.
- Pathologists use their understanding of genetic science, technical aspects of genetic testing, and the clinical implications of genetic knowledge to guide the development and maintenance of accurate genetic tests. This requires consultation with other laboratory personnel, other pathologists, clinicians, and stakeholders to ensure that an efficient test is provided in an appropriate fashion.

As educators and researchers all Pathologists:

- must ensure that there are sufficient personnel with adequate documented training and experience to meet the current needs of the laboratory. This is particularly

pertinent at a time of rapid change in our understanding and the technical capabilities in delivering genetic testing. Pathologists communicate with other staff in the genetic laboratory and work with clinical scientists to facilitate the development and maintenance of accurate useful pathology tests.

- contribute to formal and informal activities such as multidisciplinary meetings, peer review sessions, and educational activities to enhance the understanding of colleagues about genetic/genomic data and test capabilities to inform individual patient diagnosis, treatment and prognosis.
- are responsible for establishing and maintaining communication with the broader healthcare community of funders, providers, and regulators to guide policy and resourcing of genetic/genomic testing with regard to diagnostics, treatment and prognosis.
- are responsible for developing communication with the broader community to foster understanding of the strengths and limitations of this type of testing. This is of particular importance with the rise of both “point of care” and “direct to consumer” genetic testing that is provided without the involvement of a healthcare practitioner.
- are responsible for training the next generation of medical and science students, trainee pathologists and scientists and other medical specialists and health professionals in the rapidly advancing field of genetics and genomics.
- are also involved in conducting and managing genetic research. The rapidly expanding knowledge in genetics and genomics is effectively and efficiently translated into meaningful outcomes for patients.

As an Administrator

- As head of a genetic laboratory or another discipline of pathology undertaking genetic or genomic testing, the pathologist is legally, morally, and ethically responsible for the overall supervision, operation and administration of the laboratory, particularly concerning safety and the quality of the genetic testing providedas these relate to individual test results.

Conclusion

- Genetic and genomic testing is a rapidly growing field of science, medicine including laboratory medicine with huge benefits (and risks) for patients and the public.
- Pathologists are the medical specialists who specialise in laboratory testing. They have the skills to supervise genetic and genomic testing in with responsibility for individual test results and bridge the gap between science and patients via assisting requesting clinicians.
- Genetic and genomic testing exists on various scales, from the complex entire genome testing to being another tool in the diagnostic tool-box of the Microbiologist, Haematologist, Chemical Pathologist, Immunopathologist and Anatomical Pathologist. As such, each craft group has the training and capacity to supervise and advise on their discipline specific range of testing.