

Anatomical pathology

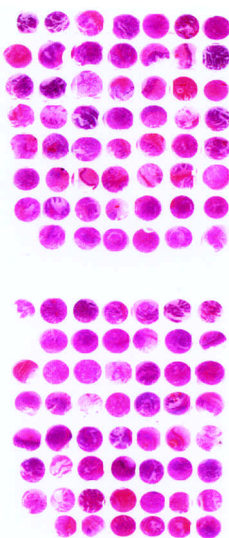
AN AUSTRALIAN STUDY, published in 1998, described histological features of breast cancers occurring in young women with germline mutations in two specific genes.¹ In 2000, a multicentre US group conducting molecular analysis of a series of diffuse large B-cell lymphomas reported that, within this group of morphologically indistinguishable tumours, two distinct types of lymphoma could be identified by gene-expression profiles, and that these two types had significantly different prognoses.²

These two studies have important implications for the future of diagnostic medicine and anatomical pathology, although the message is different in each case. In the first study,¹ Armes and colleagues identified morphological features associated with specific genetic alterations in a group of cancers, combining morphological interpretation and pattern recognition with knowledge of mutations at specific points of the chromosomes in the cancer cells. By examining thin tissue sections stained with vegetable dyes, a pathologist can not only name these cancers, grade them and provide staging information, but can now also suggest likely molecular and genetic events occurring in the tumour cells and assess the likelihood that cancer risk was inherited from the patient's parents and will be passed on to her children.

In the second study,² Alizadeh and colleagues used molecular techniques to identify biological differences between tumours that histopathologists were unable to distinguish microscopically. These techniques allowed a deeper understanding of the biology of the cancer than was possible by morphological examination alone, with significant prognostic implications for patients.

So, what will be the impact of molecular biology on diagnostic tissue pathology? Skill in identifying the gross and microscopic features of diseases will remain important in the next few decades. The management of cancer demands more than simply a diagnosis, and much of the information provided by traditional histopathology (eg, margins of surgical excision and data for staging) will still be required. Moreover, much routine diagnostic histopathology and cytopathology involves diagnosis of non-neoplastic conditions — in the foreseeable future, this is likely to be performed most efficiently by individuals trained to recognise these conditions by microscopy.

Nevertheless, there is no argument about whether molecular techniques will become important in diagnostic medicine — they already have. Array technology already allows profiles of gene expression to be developed for any specific tumour (see Figure),³ with the prospect in the next few years of therapy directed at specific molecular targets in an individual's tumour. Expertise in morphological interpretation will remain necessary for the utilisation of such techniques (eg, in both the studies described,^{1,2} morphological recognition of the cancers was vital before molecular analysis could be undertaken).



Some histo- and cytopathologists are likely to incorporate molecular techniques into their repertoire, while others will focus on their expertise in morphology and leave molecular technology to non-pathologists, being content to provide diagnoses and tissue for other studies. The findings of Armes and colleagues were the result of merging the skills of morphological diagnosis and molecular biology within a small group; the analysis by Alizadeh and colleagues involved two distinct steps — morphological diagnosis then molecular analysis — that could have been carried out by different people at different times and places.

Molecular biology will continue to alter our concepts of disease, and pathologists will have to adapt to providing new information required by clinicians for prognosis and therapy. In large centres, both public and private, pathologists will be expected to contribute tissue and information for clinical trials, which may require a willingness to be flexible in styles and protocols for handling and reporting specimens. At the same time, pathologists will retain their custodial responsibilities for tissue, and will be required to decide on the appropriate allocation of tissue for immediate diagnostic purposes, for clinical trials, and for other research projects.

Many of the most obvious changes to histopathology and cytopathology relate to molecular biology, but debates and decisions in tissue pathology will not only be about advances in biotechnology. Although the attention of government and the media has moved on from the autopsy, the future of hospital autopsies is by no means clear, and pathologists will need to clarify their own commitment to the autopsy, possibly in the face of diminishing support from clinicians and hospital administrators. Medical teaching in Australia is undergoing a revolution, and the allocation of time and resources to pathology teaching has suffered considerably in many of the new integrated curricula. The consequences of this remain to be seen.

The spectacular advances in molecular technology are costly, requiring sophisticated laboratories and highly trained people. One of the many challenges in healthcare in the future will be to minimise inequities in access to diagnostic information necessary for appropriate management, not just between richer and poorer nations but within each nation, including Australia.

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Figure: A tissue array containing 109 samples of a specific cancer type, courtesy of Associate Professor Deon Venter, University of Melbourne.

- Armes JE, Egan AJ, Southey MC, et al. The histological phenotypes of breast carcinoma occurring before age 40 years in women with and without BRCA1 or BRCA2 germline mutations. *Cancer* 1998; 83: 2335-2345.
- Alizadeh AA, Eisen MB, Davis RE, et al. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. *Nature* 2000; 403(6769): 503-511.