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Molecular Diagnostics in Histopathology

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About the Study

In most cases in the histopathology laboratory a diagnosis is made from examination of routine stains. Additionally dye-based stains can be used to identify, for example, microorganisms or minerals, or where the diagnosis is more difficult than immunocytochemistry can be used to identify different cell types. In the few cases that cannot be diagnosed using a combination of these methods, such as some cancers, then molecular biology techniques can provide the pathologist with essential information.

Many conditions have characteristic specific molecular changes which were detected are diagnostic of that particular disease. At present, most of these diseases are inherited genetic disorders and various types of cancer. However, this is a rapidly expanding field. In addition, certain molecular changes are increasingly recognized for their predictive information, as the activity of some genes affects the way a patient responds to drug therapies. The histopathology laboratory is increasingly being asked not only to provide a diagnosis but also information about the most suitable treatments for individual patients. Positive and negative controls are essential to demonstrate that the technique has worked properly. For ISH, a negative control may be obtained by omitting the probe. Alternatively, a non-sense probe can be used in place of the test probe. Another type of positive control is an internal control, which is a component of the test tissue or cell that always contains some target.

Molecular diagnostics is a rapidly expanding field with new equipment and more reliable techniques being developed in the research world that can be applied to the diagnostic setting. When RT-PCR was introduced, the quality of RNA required meant that it was not applicable to the NHS laboratory setting. Not only were diagnostic samples inappropriate, but the staff time required was also too great. Now many larger hospitals have facilities for the automation of RT-PCR, mostly in microbiology field for the detection and quantification of viruses. Another example of a technique introduced quite recently to the histopathology laboratory is FISH. When research demonstrated that Herceptin therapy improved survival in some breast cancer patients, the race was on to produce certified testing kits. Initially FISH was performed on metaphase spreads in the cytogenetics department; however advances in probe manufacture soon resulted in its application to paraffin sections. This approach has pawned several other initiatives looking at using molecular techniques to screen patients for targeted therapy regimes.

Bladder cancer is another field in which this approach seems likely to develop. Now that histopathology departments are familiar with FISH, the possibility to extend the molecular repertoire offers real prospects. The introduction of tests designed to screen for multiple cancer-related mutations are now available from a number of commercial sources. The number of histopathology departments with facilities to carry out molecular diagnostics testing is increasing slowly, as probes, primers and equipment become more easily available commercially. it is more common, however for larger hospital trusts to have a multidisciplinary molecular diagnostics department in which clinical chemistry, molecular genetics, hematology, histopathology and immunology testing is undertaken. It is a n expanding area but the future probably lies in a few large, centralized laboratories, rather than a situation in which each district general hospital offers a limited repertoire of routine molecular diagnostics tests.