with an intimate mixture of morphologically similar cell types. Immunohistochemical staining of tissue sections could help to identify and isolate specific cell populations, even of identical morphology, according to their antigen expression. Fend et al. (1999) developed a rapid immunostaining procedure for frozen sections followed by laser microdissection and RNA extraction. They reported that the RNA recovered from immunostained tissue was of high quality.

## Molecular Analysis of Cancer Progression

Tumour development and progression are dynamic processes accompanied by accumulation of molecular genetic alterations. Genetic changes may involve amplification or gain of functional mutations in dominant oncogenes, or may involve loss of function by deletion, mutation or methylation in recessive tumour suppressor genes (Walch et al., 2000). To complicate the picture, accumulations of mutant genes in neoplasms tend to be accompanied by other genetic and epigenetic changes, including loss of heterozygosity or loss of imprinting genes and/or gene amplifications, all of which can alter gene expression profiles. Genome-wide monitoring of gene expression is therefore of great importance to disclose the numerous and diverse events associated with carcinogenesis (Kitahara et al., 2001). Before microdissection techniques, tumours were screened for purity of cancer cells, and valuable samples had to be discarded because the proportion of tumour cells was overwhelmed by lymphocytes or stromal cells. It is obviously an advantage to use microdissected cell samples in molecular analysis, because the confounding effect of contaminating cells is eliminated. In cancer, laser-assisted microdissection provides the capacity for isolating specific cells, including normal, precancerous, malignant and metastatic cells. Applied to cancer research, microdissection in conjunction with a variety of highly sensitive molecular techniques has the potential to assess genetic changes associated with each of the various morphological stages of tumour progression (Fig. 3). Sgroi et al. (1999) described that using carefully controlled conditions, *in vivo* subpopulations of malignant cells from multiple stages of cancer progression can be simultaneously screened for thousands of genes.

Traditionally, tumours have been categorized on the basis of histology. However, the staining pattern of cancer cells viewed under the microscope is insufficient to reflect the complicated underlying molecular events that drive the neoplastic process. Biomedical researchers are demanding more sophisticated platforms for studying the activity of many genes or proteins in parallel - an approach known as molecular profiling (Liotta and Petricion, 2000). Currently, some sophisticated and powerful technologies for molecular analysis include the use of microarrays. Within the last year, several publications have described the use of microarrays to profile differences in expression patterns between cancers and normal cells (Alon et al., 1999; Alizadeh et al., 2000; Luzzi et al., 2001). A distinctive feature discovered in all of these studies was that the same types of cancer from different individuals differed extensively in their gene expression patterns. In the case of B-cell lymphoma, the results were particularly dramatic in that the disease previously recognizable as a single entity by conventional pathology could be divided into two separate categories with different survival by molecular pathology (Alizadeh et al., 2000).

Using RNA and DNA arrays with appropriate experimental models, the ultimate goal is to move beyond correlation and classification to achieve new insights into tumour mechanisms and treatment targets. Gene profiling, in addition to contributing to the basic understanding of cancer cell biology, may also play a role in strategies for drug development. In the future it would appear that knowledge of the molecular profile of a tumour will be required prior to therapeutic intervention, so that more aggressive therapies can be tailored to the more aggressive tumours (Bertram, 2000). However, one of the conditions for this is the analysis of a homogeneous tumour cell population. Laser-assisted microdissection is therefore potentially one of the most useful techniques in molecular cancer research.

## Conclusion

The new technologies becoming available for studying DNA, RNA and proteins will have an enormous impact in cancer research, and the ability to isolate homogeneous populations of cells with laser-assisted microdissection will add real value to these approaches.

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