FUTURE PROSPECTS
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Identification of the breast cancer predisposition genes, BRCA1 and BRCA2, has led to a better understanding of the molecular pathogenesis of a subgroup of hereditary breast cancers and to a new era in breast cancer research that promises ultimately to reduce morbidity and mortality from this disease. Although most commonly thought of with respect to breast cancer risk, it is important to note that these genes also predispose to a variety of other cancers. This area of research is in its infancy, and much remains to be learned. Moreover, a substantial percentage of breast cancer families do not carry mutations in BRCA1 or BRCA2, indicating that additional breast cancer susceptibility genes are also likely to exist (Antoniou et al., 2002; Wooster and Weber, 2003; Narod and Foulkes, 2004). Several candidate regions for a third high-penetrance breast cancer gene (BRCA3) have been proposed, including 2q, 8p12-p22 and 13q21, but these results have not been replicated in independent studies (Kainu et al., 2000; Thompson et al., 2002c). Despite rapid advances in new high-throughput techniques, the search for BRCA3 has been difficult. One of the reasons is that no distinctive phenotype for a third class of inherited breast cancer has emerged. It has been suggested that several common, low penetrance genes with multiplicative effects on risk may account for the residual non-BRCA1/2 familial aggregation of breast cancer (Antoniou et al., 2002). Therefore, the search must continue to find those additional breast cancer genes, using all the available traditional and new genomic techniques.

However, the major obstacle has been, and continues to be, the transition of these findings into clinical practice. As demonstrated by the success of Herceptin® in Her2/ErbB2-positive breast tumours (Gibbs, 2000) and ST1571 (Gleevec™), an inhibitor of Bcr- Abl tyrosine kinase for the treatment of CML (Druker, 2001), molecularly targeted treatments is much more effective, with fewer side effects than the other currently used anti-cancer therapies. Many new
putative breast cancer therapeutic and diagnostic targets are being investigated in the clinic and many more are likely to follow. The identification of additional breast cancer susceptibility genes and understanding of the different pathways of tumorigenesis of breast cancer is sure to aid the identification of individuals at risk and the design of targeted cancer preventive therapies. This will eventually help to develop better diagnostic strategies, more targeted chemopreventive agents, and targeted management of specific subgroups of breast cancer patients and families. Specific gene therapy may become available. More information about the magnitude of risk reduction, mortality reduction, and the proper timing of surveillance or prophylactic measures among BRCA2 carriers is urgently needed.