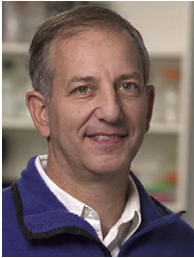


Preface



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Guest Editor

Brute force genetic linkage efforts, combined with scientific and technological advances in deciphering the human genome during the 1990s, are now beginning to bear fruit in the clinic. This is evident in the current decade as we appreciate the clinical translatability of discoveries relevant to identifying and managing subjects with hereditary colorectal cancer. This issue of *Surgical Oncology Clinics of North America* provides a practical update on this subject and a glimpse of further advances in the field.

The identification of mutations of the *APC* and mismatch repair genes as the causes of familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, respectively, has made a significant impact on genetic counseling, cancer surveillance, and tailored surgical approaches for gene carriers and their relatives. More recently, *MYH*-associated polyposis has also been characterized as a cause of high-penetrant colorectal neoplasia with a unique pattern of recessive inheritance.

The aforementioned genetic conditions and other rare syndromes described herein explain only 2% to 3% of all colorectal cancer and only a small fraction of hereditary cases. What syndrome or syndromes are associated with the remainder? Are there additional undiscovered high-penetrant genes? How do environmental factors interact with genetic variation? These questions remain for future generations of scientists to answer. In the meantime, the term *familial colorectal cancer type X* has been coined to describe a likely heterogeneous group of families with higher risk for colorectal cancer, but not associated with tumor microsatellite instability.

If we assume that almost all cases of cancer have a genetic component, then even sporadic cases of colorectal cancer should be explained by germline genomic variation. The era of genome-wide association studies is upon us and first-generation interrogation of the human genome has revealed curious findings that are enlightening our understanding of the contribution of common alleles to colorectal cancer risk. As more dense single nucleotide polymorphism chips and other tools for exploring epigenetic variation are developed and employed, it is certain that novel genetic models of risk

will be created for individualized assessment of colorectal cancer risk. Moreover, the role of genetic counselors will be expanded as the scientific and medical community translates these findings for the public.

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