In the past decade, advances in next-generation sequencing technologies have enabled us to define a new molecular taxonomy of human cancer based on the genetic and epigenetic basis of cancer. These efforts are based on the fundamental belief that a comprehensive knowledge of the genes that cause human cancer is a critical foundation for cancer diagnostics, therapeutics and clinical trial design. In particular, the International Cancer Genome Consortium and The Cancer Genome Atlas have collectively sequenced tens of thousands of cancers across a number of tumour types.

Colorectal cancer is a major cause of cancer mortality. The heterogeneity of response to therapy in this disease has led to speculation that as yet undiscovered molecular subtypes (each with differing clinical behaviour and outcomes) may be responsible. Thus, the detection of such subtypes could fundamentally alter the treatment paradigm for colorectal cancer. That such subtypes may regulate treatment response and outcome has been suggested by the discovery that approximately 15% of colorectal cancers are characterized by deficient DNA mismatch repair, leading to microsatellite instability (MSI) and mutations in critical genes involved in carcinogenesis, such as transforming growth factor-β type II receptor and BAX. Such tumours tend to be right-sided, BRAF mutant, have a better prognosis yet derive less benefit from standard 5FU chemotherapy. We now have a complete repertoire of the mutational, copy number, methylation and gene expression features that are dysregulated in colorectal cancer, and molecular subtypes that predict for clinical outcome are presenting themselves. Most recently, a combined analysis of gene expression data from 4,000 colorectal tumour samples has defined 4 consensus clusters, each with different patterns of mutations, dysregulated pathways and MSI status. The challenge for the clinical research community will be to determine whether a new molecular taxonomy for colorectal cancer based on such subtypes has therapeutic implications and will play a role in our management of patients.

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