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Cancer Genomics: Chapter 11. Genetic Basis of Hereditary Cancer Syndromes

David Malkin

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Cancer is the most common cause of disease-related death in children beyond the newborn period. Most cancers are thought to arise sporadically; however, classical studies of well-defined familial cancer associations, known as cancer predisposition syndromes (CPS), together with emerging work arising from new high-resolution genomic platforms have confirmed that at least 25% of childhood cancers result from hereditary factors. The spectrum of cancers found in the diverse array of known hereditary cancer syndromes is vast. Similarly, the number of genes linked to these syndromes continues to expand. This chapter explores the genotype:phenotype correlations in several defined cancer predisposition syndromes that primarily affect children. In particular, a selection of syndromes that are caused by germline mutations in classical tumor suppressor genes (RB1, TP53, WT1) and oncogenes (RET), syndromes associated with congenital developmental anomalies (Beckwith–Wiedemann syndrome, Gorlin syndrome) and an emerging syndrome associated with microRNA processing (DICER1) provide examples of the heterogeneity that these syndromes exhibit. The chapter concludes with a discussion of the clinical impact of genetic testing and clinical surveillance for early cancer detection.

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