
Preface

The completion of a consensus draft sequence for the human genome approximately 10 years ago was the starting point for more thorough investigations of individual genome variation. Initially, the focus of variation discovery was targeted toward microsatellites and single nucleotide polymorphisms (SNPs) for use as markers in linkage and association analysis. The development of array-based strategies made it possible to look at our genome in new ways and for new types of variation to be discovered and characterized. Application of comparative genomic hybridization (CGH) arrays used for detection of unbalanced rearrangements led to the discovery that copy number variation (CNV) is abundant in the human genome. Characterization of CNV and other forms of structural genetic variation has highlighted the complexity of human genetic variation, and also provided significant insight into the evolution and dynamic nature of the genome. Another important technical advance is the development of high-density SNP genotyping arrays. The SNP arrays have enabled the discovery of hundreds of genes associated with complex disease through whole genome association studies. The SNP arrays are also used for the identification of CNVs, and many studies are now designed to take both SNPs and CNVs into consideration when analyzing variation in patient and control cohorts.

Over the past decade, the introduction of array-based technologies has revolutionized genomics and genetic diagnostics. Array-based screening has replaced karyotyping as the primary analysis of patient samples in cytogenetic diagnostics, and this has led to a significant increase in the number of patients for whom a clinically relevant aberration can be detected. The number of patients referred for genetic screening is increasing rapidly, and diagnoses for referral have expanded from developmental delay and intellectual disability to a wider range of developmental disorders. Other diagnoses, such as epilepsy and congenital heart disease, may be added in the near future.

Now, we are on the brink of a new paradigm shift in genetics with the advent of massively parallel sequencing in research and diagnostics. In the next few years, we will witness the identification of causative genes for most of the monogenic disorders and achieve better insight into the true spectrum of variation contributing to complex disease.

This book provides an in-depth description of the developments in our understanding of structural genetic variation and its implications for human disease, from the introduction of microarrays up to current state-of-the-art sequencing strategies. The book covers the major technologies used for research and diagnostics, Web-based resources for variation data, and goes into depth regarding specific regions of the genome that differ in variation content. Specific patient groups where CNV has been shown to be of great importance are highlighted, and implications for both prenatal and standard diagnostics are described.

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