Preface

Until recently it was thought that variation in the human genome was, except for some large scale variants encountered in both tumor cells and normal cells, mostly restricted to so-called single nucleotide polymorphisms (SNPs). However, with the development of novel genome-wide technologies emanating from the human genome project such as microarray-based genomic profiling, it has become clear that large-scale DNA copy number variations (CNVs), ranging from single kilobases to several megabases, are much more common than expected before (current estimate $>3 \times 10^8$ bases of DNA in the human genome). This novel information, which may have a profound impact on a wide range of disciplines ranging from molecular genetics to clinical genetics, is currently being stored and catalogued in comprehensive data bases. Depending on the platform used, CNVs can be detected with varying degrees of accuracy and resolution, and additional information on loss of heterozygosity and/or uniparental disomy can be retrieved. It is widely assumed now that (cryptic) CNVs may be associated with disease, particularly when arising de novo. In case of congenital malformation, neurocognitive and/or mental retardation syndromes, several CNVs could be linked to specific subsets of these disorders and, in some cases, these links have indeed led to the identification of (candidate) disease genes. Additionally, in various malignant disorders (cancer), cryptic and/or large-scale genomic deletions and/or amplifications have pointed at the location and involvement of specific tumor suppressor genes and proto-oncogenes, respectively.

In this special issue of *Cytogenetic and Genome Research* several aspects of these newly identified large-scale genome variations are discussed, including their etiology and the putative role of flanking low copy repeats therein, questions on to what extent CNVs may act as harmless bystanders or not, and suggestions on how to employ this novel information for the delineation of genotype-phenotype associations, disease gene identification and, ultimately, clinical practice including diagnosis, prognosis and treatment.

With special thanks to all of those who contributed,

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