Cytogenetic alterations in prostate carcinomas

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Introduction Alterations in the genome that lead to changes in DNA sequence copy number are a characteristic of solid tumors. Within the past 15 years, tremendous technical progress has been achieved to detect and map chromosomal anomalies in tumor cells.
Material and Methods Comparative genomic hybridization (CGH) was first described for whole-genome analysis in 1992 [1]. Since then, it has become to an important technique for the detection of amplified and deleted regions in tumor DNA, although its sensitivity and resolution is limited. The most recent development of microarray-based CGH [2] which replaces the target metaphase chromosome of conventional CGH with arrays of genomic or cDNA clones or oligonucleotides on a microscope slide, delivers an enhanced mapping resolution of DNA copy number variations compared to conventional CGH.
Results Conventional CGH on prostate cancer revealed genomic alterations in 90% of the tumors analyzed. Two observations are most outstanding: (i) There is a high tumor-to-tumor variability of the complexity of detected chromosomal alterations; (ii) Besides common chromosomal changes reported in the literature, we have evidence for novel loci, which may harbor relevant genes for prostate cancer development. Using array CGH with microarrays containing 35 k longmer oligonucleotides, a more detailed mapping of the extent of regions with gains and losses compared to conventional CGH was achieved. Furthermore, very distinct regions of amplification and deletion were disclosed, which remained undetected by conventional CGH.
Discussion Whole-genome analysis is a highly suitable approach for delivering insight into the mechanisms of prostate cancer development. Conventional as well as arrayCGH in prostate cancer reveals that tumors differ not only in the regions that are aberrant, but also in the types of copy number aberrations that are present. Thus, it appears that tumor specific types of copy number profiles can be distinguished representing the basis for the identification of potential new biomarkers.

Literature

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