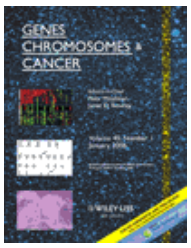

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Research Article

Comprehensive analysis of loss of heterozygosity events in glioblastoma using the 100K SNP mapping arrays and comparison with copy number abnormalities defined by BAC array comparative genomic hybridization

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ABSTRACT

We have undertaken an extensive high-resolution analysis of loss of heterozygosity (LOH) in 30 high grade gliomas using the Affymetrix 100K SNP mapping array. Only 70% of LOH events were accompanied by a copy number loss (CNA_{loss}), and of the other 30%, the distal region of 17p preferentially showed copy number neutral (CNN)-associated LOH. Combined analysis of CNA_{loss} and LOH using MergeLevels analysis software predicts whether the observed losses occurred on a diploid or tetraploid background. In a side-by-side comparison between SNP and bacterial artificial chromosome (BAC) arrays, the overall identification of CNAs was similar on both platforms. The resolution provided by the SNP arrays, however, allowed a considerably more accurate definition of breakpoints as well as defining small events within the cancer genomes, which could not be detected on BAC arrays. CNN LOH was only detected by the SNP arrays, as was ploidy prediction. From our analysis, therefore, it is clear that simultaneously defining CNAs and CNN-LOH using the SNP platform provides a higher resolution and more complete analysis of the genetic events that have occurred within tumor cells. Our extensive analysis of SNP array data has also allowed an objective assessment of threshold LOH scores that can accurately predict LOH. This capability has important implications for interpretation of LOH events since they have consistently been used to localize potential tumor suppressor genes within the cancer genome. © 2007 Wiley-Liss, Inc.

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ADDITIONAL MATERIAL

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