SNP array data and quantitative determination of cell fraction bearing Copy Neutral-LOH regions in tumoral samples

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Motivation

Molecular cytogenetic technology by last generation single nucleotide polymorphism (SNP) array provides a high resolution mapping of two different tumor-associated genetic alterations undetectable by conventional metaphase cytogenetics: submicroscopic copy number abnormalities (CNAs) and copy neutral loss of heterozygosity (CN-LOH), also known as acquired uniparental disomy. Recent advances in analysis of SNP-array data allow a quantification of tumoral cell fraction bearing specific CNAs or CN-LOH regions. In the present work we set up a a method to exploit a novel parameter for representation of SNP array data, the so called “allele difference”, in order to provide a quantitative estimation of the fraction of cells bearing specific CN-LOH regions and report some applications in clinical oncological cases.

Methods

High-resolution genome-wide DNA copy number and SNP genotyping analysis was performed by Affymetrix SNP 6.0 arrays that interrogate 906,600 SNPs and 945,826 copy number probes (SNP/CNV array). The “allele difference value” is the difference of allele A signal and allele B signal each standardized with respect to their median values in the reference HapMap population. Mathematical simulation of the results obtained with different mixture of CN-LOH bearing and not bearing cells were used to derive a calibration curve useful to determine the cell fraction bearing the CN-LOH in the unknown sample.

Results

By the implemented script we analysed SNP array data related to hematological malignancies (acute myeloid leukemias, myelodysplastic syndromes) and colorectal cancer containing different amounts of normal and pathological cells. A good correlation with independent methods able to evaluate the cell fraction bearing a specific chromosomal abnormality was found

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