

# **Reference Alignment of SNP Microarray Signals for Copy Number Analysis of Tumors**

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A new procedure to align single-nucleotide polymorphism (SNP) microarray signals for copy number analysis is proposed. For each individual array, this reference alignment procedure (RAP) uses a set of selected markers as internal references to direct the signal alignment. RAP aligns the signals so that each array has a similar signal distribution among its reference markers. An accompanying reference selection algorithm (RSA) uses genotype calls and initial signal intensities to choose two-copy markers as the internal references for each array. After RSA and RAP are applied, each array has a similar distribution of signals of two-copy markers so that across-array signal comparisons are biologically meaningful. An upper bound for a statistical metric of signal misalignment is derived and provides a theoretical basis to choose RSA-RAP over other alignment procedures for copy number analysis of cancers. In our study of acute lymphoblastic leukemia, RSA-RAP gives copy number analysis results that show substantially better concordance with cytogenetics than do two other alignment procedures.