

aCGH Explorer: A Tool for High-Resolution Analysis of Chromosomal Imbalances Using cDNA and Oligo DNA Arrays

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Comparative genomic hybridization (CGH) identifies DNA copy number variation in a whole genome format. In this technique, total genomic DNA from a reference sample and a test sample are labeled with different fluorescent dyes and hybridized to metaphase chromosome spreads obtained from a normal cell. One shortcoming of CGH is its low-resolution (5-10 Mbp), which decreases the mapping accuracy and prevents precise localization of genomic imbalances. Array-based comparative genomic hybridization (aCGH) is an emerging technique that addresses some of the limitations of conventional CGH. Moreover, the use of cDNA or oligo DNA arrays allows direct transcriptional and gene dosage comparison on the same high-resolution platform. However, when a sample as complex as human or mouse genome is hybridized to this small size-low complexity spotted DNA, the signal to noise ratio of individual probes is poor. To cope with this compression of the dynamic range for DNA copy number measurements, we have developed an interactive data analysis tool that: 1) removes inconsistent outliers in replicated array and averages the remaining individual clone values, 2) subtracts a replicated reference-to-reference experiment from the test sample experiment, and 3) calculates moving averages to smooth and further remove noise from the data. Results are then visualized and compared using a suite of graphic display functions including direct comparison of array CGH and mRNA expression results. As an application example, we used this program to delineate chromosomal imbalances in spontaneously transformed mouse ovarian cell lines and correlate it with gene expression patterns. The potential and usefulness of this tool to monitor cancer progression and class discovery is discussed.

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