Microarray cross-platforms differential expression validation

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Motivation

The microarray technology it is now a consolidated instrument for genome-wide analyses. Microarray exists in two different configurations: two channels microarray, i.e. two different species of RNA are investigated at the same time on the same array, and single channel microarrays, i.e. a single RNA specie is hybridized on each microarray. Many commercial platforms are now available as single channel arrays and cross-platform validation studies indicate that homogeneous results can be obtained independently by the platform used. Multiple microarray platforms analysis of the same expression data could be a powerful approach to large scale differential expression validation. Statistical tools used for differential expression validation, although optimized for microarray analysis, suffer of the limitations induced by the limited number of replicates. Especially type I error correction approaches, which is a critical step in the computational pipe-line for microarray analysis, is an important source of false negatives due to the limited efficacy of false-discovery estimation (Choe et al. Genome Biol. 2005, 6,R16). Furthermore, massive differential expression validation can not be afforded by quantitative RT real time PCR (qPCR), due to the high cost of experiments.

Methods

Three prototypic situations, derived by a time-course experiment designed to study the synergic effects of HGF and cis-platin on ovarian cancer, were used (Olivero et al. submitted): SK-OV-3 cells untreated cells (ctrl), SK-OV-3 cells treated with HGF for 48 hours (hgf) and SK-OV-3 cells treated for 24 hours with cis-platin (hgf/cddp) after 48 hours HGF pretreatment. Ctrl and hgf are available as biological triplicate as instead the hgf/cddp as duplicate. The three conditions were investigated using three different single channel platforms: Affymetrix hgu133av2, Illumina 24K arrays and Applera AB1700 Human arrays. Data where acquired with platform specific instruments and raw numerical data were normalized using the cyclic-loess approach.

Results

The availability of technical replicates on three different platforms, each characterized by some peculiarity (i.e. Affymetrix gene expression is derived by multiple different 25mer probes integration, Illumina gene expression is derived by the average of multiple replicates of the same 50mer probe, Applera gene expression is investigated using 60mers and a chemoluminescence detection system, as instead Affymetrix and Illumina use fluorescence detection) offers the opportunity to investigate the possibility to identify differential expression limiting the loss of information associated to type I error correction (Choe et al. 2005). On the basis of our observations we will discuss the possibility to design differential expression analysis pipe-lines based on data derived by at least two different single channel platforms.

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