

Fun&Co: identification of key functional differences in transcriptomes

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Motivation

The massive production of biological data by means of highly parallel devices like microarrays for gene expression has paved the way to new possible approaches in molecular genetics. This approach yields a global view of gene expression that can be used in several ways. Functional insight into expression profiles is routinely obtained by using Gene Ontology terms associated to the cellular genes. For a thorough understanding of genome wide experiments, it is essential to extract in the most efficient and straightforward way information from microarray datasets.

Methods

In this work we present Fun&Co, a novel method, based on the study of the correlations between probes and their relations to Gene Ontology (GO), capable to highlight differentiations in biological samples, such as tissues or cell lines. More specifically, this method identifies differences in gene correlations found in normal and cancer tissues capable to reveal interesting functional differences between them. The final goal is to understand which key functional modules are peculiar to a very important human organ: the heart. In order to identify these heart specific functional modules, we used as a reference, the most similar tissue to heart, that is skeletal muscle. Fun&Co starts the analysis considering a general term of the GO tree. As a first step, it selects the probes related to this term or more specific ones. Considering the selected genes, it computes the correlation and p-value between each probe pair expression and identifies the pairs with a correlation level higher than a threshold.

Correlation p-values can be adjusted by means of False Discovery Rate (FDR). Finally, it compares two dataset groups (e.g. a group of heart datasets and a group of skeletal muscle datasets), searching for the GO terms which show a different behavior among samples. For testing the system, we used datasets produced on Affymetrix U133 platforms, downloaded from GEO public data repository.

Results

Some GO terms related to important functions or processes were chosen, in particular we investigated response to stimuli and extracellular environment. Fun&Co is a novel and very efficient way of mining functional differences between normal and cancer tissues. The application extracts the most significant functional differences from the molecular expression data on skeletal muscle and heart. The results are highly informative and synthetic.

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