A NOVEL METHOD FOR IDENTIFICATION OF DEREGULATED GENES USING DIFFERENTIAL COEXPRESSION ANALYSIS: A PROSTATE CANCER CASE STUDY

Obi L. Griffith and Steven J.M. Jones
Canada's Michael Smith Genome Sciences Centre, British Columbia Cancer Agency, Vancouver, Canada

Numerous studies have used the correlation of gene expression (coexpression) to identify potentially coregulated genes. However, few have attempted to use loss of coexpression (differential coexpression) to identify potentially deregulated genes. We present an approach that calculates the change in coexpression for individual genes and ranks them according to which is most likely to be deregulated. This approach was tested on a published prostate cancer dataset consisting of 52 tumour and 50 normal samples analyzed on the Affymetrix HG-U95Av2 chip (Singh *et al*. 2002). A Pearson correlation coefficient (PCC) was calculated between every possible gene pair. Generally, all genes had at least some highly coexpressed gene pairs. For each gene in the normal dataset, the *n* closest gene neighbours (most coexpressed) were identified and the mean PCC calculated. Next, the mean PCC for these same gene neighbours was determined for the tumour dataset. A differentially coexpressed gene was defined as a gene with a large change in coexpression (difference in mean PCC for *n* nearest neighbours) between normal and cancer datasets. A random permutation test was performed to assess the significance of the differentially coexpressed genes observed. Of the top 25 most differentially coexpressed microarray probes, 2 could not be mapped unambiguously, 5 map to genes of unknown function (LOC153561, MGC5576, DNAJA2, C7orf24, SNX4), 6 to genes previously implicated in cancer (SLC26A3, G1P2, RAD23B, TFDP2, ABL1, GSPT1), 5 to genes implicated specifically in prostate cancer (AMACR, SOX9, DLGAP2, RAD51C, HGF) and 2 to genes that interact with PSA and play a role in sexual reproduction (SEMG1, SEMG2). In most of these cases, the implicated gene would not have been identified by standard differential expression methods. Differential coexpression analysis thus represents a useful and complementary method to traditional differential expression methods for identifying potentially relevant cancer genes.

Contact Information:
Obi L. Griffith
Genome Sciences Centre, BC Cancer Agency
Suite 100 - 570 West 7th Ave, Vancouver, BC, V5Z 4S6
Phone: 604-707-5900 x.5401, Fax: 604-876-3561
Email: obig@bcgsc.ca

Dr. Steven J.M. Jones
Genome Sciences Centre, BC Cancer Agency
Suite 100 - 570 West 7th Ave, Vancouver, BC, V5Z 4S6
Phone: 604-877-6083, Fax: 604-876-3561
Email: sjones@bcgsc.ca