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Predicting genes associated with prostate cancer

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Abstract

A sensitive coexpression algorithm detects new genes associated with markers of prostate cancer.

Significance and context

Genomic screens for proteins associated with a disease typically attempt to identify genes that show different expression patterns between diseased and healthy tissues. Walker *et al*. turn this approach around to find new factors that might be involved in prostate cancer, searching instead for genes that are expressed in the same places as others known to be associated with the disease. The authors employ an unusual approach to assess similarity in gene expression patterns. Such similarity is often defined using measures of correlation or covariance - that is, genes are considered to have related expression patterns if plotting the level of their transcripts across a variety of conditions or tissue types yields plots of similar shape. Genes that are rare, or that show complex relationships with each other for biological or experimental reasons, may be hard to detect using these methods, and so the development of other methods should still be important. Walker *et al.* simply look at whether or not each given gene is expressed at detectable levels in each sample, which results in a binary pattern for each sample. They then use a combinatorial argument to determine whether two such patterns of 'positives' and 'negatives' should be considered related. One could think of this approach as maximally increasing the brightness and contrast of the 'shape' of the expression pattern; subtle patterns will disappear, but gross similarities that might otherwise be obscured will become clearer.

Key results

The authors use their 'guilt-by-association' strategy to screen 522 human cDNA libraries for genes related in expression pattern to a set of five proteins previously linked to prostate cancer. They obtain four known genes - MAT8, neuropeptide Y, sorbitol dehydrogenase and ZN-β-2 glycoprotein - each previously reported to be associated with cancer or toxin damage, and eight previously unreported genes, seven of which have no known homologs. The eighth novel gene is a prostate-specific serine protease. To control for the possibility that the screen might be identifying tissue-specific expression rather than disease-related patterns, the authors screen a set of 52 libraries derived from male reproductive tissues and obtain similar results. Given that the genes show similar patterns of association

across samples all from the same type of tissue, the apparent link to prostate cancer is likely to be related to the disease state, not the tissue of origin.

Links

Other approaches to the analysis of large databases of expression data can be found at the Stanford genomic resources site. The cDNA libraries screened in this paper are commercially available from Incyte Genomics and can be ordered via the Incyte products pages.

Reporter's comments

It is not entirely clear whether the binary approach used in this paper yields significantly more useful results than those obtained from other techniques of coexpression analysis, and the authors do not make a rigorous comparison to support this claim. On the other hand, the seven new genes detected are certainly likely to be interesting both as subjects for biological investigation and as potential drug targets. This paper also publicizes the wide range of tissues and disease states for which Incyte has cDNA libraries.

Table of links

Genome Research

Stanford genomic resources

Incyte Genomics

Incyte products

References

1. Walker MG, Volkmuth W, Sprinzak E, Hodgson D, Klingler T: Prediction of gene function by genome-scale expression analysis: Prostate cancer-associated genes. Genome Res. 1999, 9: 1198-1203. 1088-9051