modifying enzyme towards its natural substrate bound to an array could be characterized.

So, such arrays fulfil the key requirements for the development of a carbohydrate chip, and importantly, are compatible with recently reported methods for automatic synthesis of complex carbohydrates, suggesting that chips constructed by this chemical approach could find broad application in glycobiology, from research to drug discovery and diagnostics. Moreover, the surface chemistry involved could also prove valuable in the preparation of peptide and protein chips.

Peter Kirkpatrick

References and links

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FURTHER READING

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MICROARRAYS

Validation on target

Microarray analysis of human multiple sclerosis (MS) lesions has revealed pronounced differences in gene expression in autopsy tissue from MS patients compared with similar tissue from individuals without MS. In a study published in *Nature Medicine*, Lock and colleagues establish the power of the microarray approach by validating two genes as potential therapeutic targets in a mouse model of MS.

MS is an autoimmune disease of the central nervous system (CNS) that is caused by immune-cell infiltration of the CNS white matter. Inflammation and subsequent destruction of myelin cause progressive paralysis. Environmental factors and a genetically determined susceptibility are both implicated in the aberrant immune response to myelin. Patients can have chronic symptoms or suffer acute attacks. Histologically, two types of lesion are seen: acute lesions, which are characterized by inflammation, and chronic regions that show scarring and demyelination.

Comparing transcripts from different lesions uncovered several genes that were previously unassociated with MS, and which showed differential gene expression in the two lesion types. Genes with at least a twofold change in expression were visualized using cluster analysis, which determines the correlation coefficients between pairs of genes and organizes them according to similarities in expression patterns. In each of the MS samples, the expression of 39 genes was increased, whereas the expression of 49 was decreased.

Genes with increased expression included those encoding immune-response proteins, adhesion molecules, complement molecules, B-cell and macrophage-specific proteins and a number of pro-inflammatory cytokines. By contrast, the expression of neuron-associated genes and those associated with myelin production decreased. The reduced expression of myelin-associated enzymes suggests that there is a reduced capacity for repair. For the first time, comparing these two types of lesion supports a molecular difference between the acute and chronic lesions, with selective upregulation of 22 and 32 genes, respectively.

The authors tested the value of the microarray approach using the experimental autoimmune encephalomyelitis (EAE) mouse model of MS. The immunoglobulin G (IgG) Fc receptor was upregulated in chronic lesions. EAE mice that were deficient for the IgG Fc receptor had less severe acute disease and no chronic disease compared with wild-type mice. Granulocyte colony-stimulating factor (G-CSF) was upregulated in acute lesions. The capacity of G-CSF to alter the course of EAE was tested by treating the mice with G-CSF before and during onset of the disease. Early treatment decreased the severity of the disease but had no effect later, which indicates that G-CSF might be a regulatory molecule that naturally suppresses acute attacks.

Although EAE is a useful model for MS, clinical trials have shown that many efficacious therapies in the mouse have not translated into humans. So, caution must be exercised in spite of animal validation of two MS targets. However, this study provides proof of principle for the power of microarray technology to identify new therapeutic targets. An enormous amount of data are produced in these types of microarray experiment. Databanks that contain such raw gene-array data should allow more meaningful comparisons across datasets, enabling the increasing numbers of these analyses to be exploited to their full advantage.

Melanie Brazil

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