Recent Progress in Bioinformatics for Microarray Analysis

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Following the completion of the Human Genome Project in 2003, we now could clarify the comprehensive profile of all human genes expressed in specific subsets of the cell by using DNA microarray. The global analysis of transcriptome, along with proteome, has greatly facilitated the genome-based drug discovery research aimed at mining the best molecular target for the rational drug design from huge numbers of disease-related and drug-responsive genes. Multiple sclerosis (MS) is an inflammatory demyelinating disease of unknown etiology that affects exclusively the human central nervous system white matter. By using DNA microarray, we have recently studied gene expression profile of T lymphocytes of MS patients and healthy controls, and from MS patients in relapse and during remission. We found a set of differentially expressed genes between MS and healthy subjects, and between acute relapse and complete remission. Hierarchical clustering analysis of the discriminator genes established classification of MS subgroups exhibiting distinct gene expression profiles and relapse-specific molecular signatures. By using KeyMolnet, a novel data-mining tool of bioinformatics, we identified the principal molecular network involved in development of MS and induction of acute relapse. Prion diseases are an intractable neurodegenerative disease of animals and humans mediated by an abnormal prion protein (PrPSc). The protein conformational conversion from PrPC to PrPSc requires an as yet unidentified species-specific auxiliary factor named “Protein X”. By using protein microarray, we identified a set of novel PrPC interactors as the candidate for Protein X. Because the network of PrPC and interactors involves signaling pathways essential for regulation of cell survival, differentiation, proliferation and apoptosis, our observations proposed a logical hypothesis that dysregulation of the PrPC interactome could induce extensive neurodegeneration in prion diseases. Thus, molecular network analysis is a valuable approach to extract biological implications from massive array data.