

Differential Immune Response Gene Expression in a Mouse Model of AIDS

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Murine acquired immunodeficiency syndrome (MAIDS) is a retrovirus-induced disease caused by the specific mixture of the murine leukemia virus (MuLV) called LP-BM5 (Mosier, 1996). Two strains of mice are used in MAIDS investigations: (1) the disease resistant strain, BALB/c and (2) the susceptible strain, C57BL/6 (BL/6). In the susceptible strain, the virus induces immunologic symptoms similar to those of human-AIDS: lymphoproliferation, depletion of T-cell progenitors, and progressive destruction of the host's immune system (Mosier, 1996). The objective of this research project is to identify the immune genes that are important in establishing the strain-specific disease induced by MuLV during the first week post-infection using a DNA microarray approach. This approach allows analysis of the entire transcriptome induced by MuLV in the two strains of mice to be observed simultaneously.

RNA was isolated from spleens and lymph nodes of individual mice three days and seven days post viral- or mock-infection. These RNAs were used as templates for cDNA synthesis. Using dendrimer-based technology, the Cy3/Cy5 primed cDNA was used as a target to hybridize to mouse 70-mer oligonucleotide DNA microarrays. After hybridization, the microarrays were washed and then scanned in two channels using a confocal laser scanner (Axon Instrument). The intensity of the fluorescence was measured using microarray image processing software (Axon GenePix). To determine differential gene expression between the two strains of mice, the image data files were converted to .tav format, normalized and analysed for statistical significance using The Institute for Genomic Research's (TIGR) TM4 software package. Preliminary results show a BL/6 gene expression profile with up-regulated genes associated with increased B-cell activation, B-cell proliferation, and some T_H2-like responses. The same profile suggested down-regulation of some T-cell costimulation markers and signal transduction genes, and decreased expression of some MHC Class II genes. In contrast, the BALB/c profile showed signs of increased macrophage activation, anti-viral cytokines, and some T_H1-like responses. Decreased expression of binding protein associated with T-cell growth, B-cell Ig synthesis, and T_H2 inhibitors also characterized this profile. These data suggest a trend toward T-cell mediated responses in the MuLV-exposed disease resistant animals (BALB/c) but a more B-cell oriented response in the susceptible mice (BL/6).