10e Genome-Wide Analysis of the Transcriptional Response of Murine Hybridomas to Osmotic Shock

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Hyperosmotic stress has been shown to increase specific antibody productivity in murine hybridoma systems; however, the mechanisms underlying this phenomenon are still poorly understood. To elucidate the mechanisms for this phenomenon as well as other physiological changes that occur in response to hyperosmotic stress, we performed a genome-wide analysis of the transcriptional response of murine hybridoma OKT3 toward hyperosmotic stress using DNA microarrays. GeneChip® MOE430A from Affymetrix was used to determine the differences in transcription patterns between OKT3 in hyperosmotic culture (~100 mOsm above control) and control culture. 2,793 probe sets on the chip were differentially expressed with a $p < 0.05$. Among them, 349 probe sets exhibited a two-fold or greater change (with 202 up-regulated and 147 down-regulated) at one or more time points. Within the 215 characterized, differentially expressed genes, many are involved in metabolism/catabolism (18 induced, 13 repressed), cell-cycle regulation (10 induced, 5 repressed) and apoptosis (8 induced, 2 repressed), regulation of transcription (18 induced, 13 repressed) and translation (3 induced, 2 repressed), transport and signaling pathways (23 induced, 12 repressed). Surprisingly, there were very few changes within the stress-response genes. Interestingly, the transcription levels of both the immunoglobulin kappa and lambda light chains showed a significant change in response to hyperosmotic stress, although there is no detectable lambda chain in the immunoglobulin produced in this cell line. Quantitative PCR assays with TaqMan® probes were applied to selected genes to validate the results obtained from microarray analysis.

Current research is focused on pathway analysis to identify targets likely to play a role in increased antibody secretion in response to hyperosmotic stress and validation of these targets using siRNA.