

Murine Hematopoiesis Time Series: The Value of Experimental Design

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Abstract:

Gene expression profiles from Affymetrix GeneChip experiments were used to examine the role that retinoic acid (RA) and RA receptors play in murine hematopoiesis. Hematopoiesis was studied using an artificially immortalized multipotent cell line (MPRO). Terminal development of these MPRO cells was triggered by the introduction of RA. RNA was then harvested from these cell lines in 2 distinct time periods. One time course experiment was replicated 4 times over the first 8 hours. The second time course was replicated 4 times over the first 6 days. Analysis was performed using standard General Linear Model techniques, including corrective data transformation, weights, multiple comparison corrections, and residual analysis. The hourly time course identified a small class of early transcripts, of which several encode for DNA binding proteins (as defined by GO). The daily time course, by contrast, demonstrated substantial statistically significant changes in over 1300 transcripts. The analytical results demonstrate that diagnostics developed for least squares methods are useful for microarrays data. The results also demonstrate the value of biological understanding in experimental design. As these time series are relatively small, expert time point selection is a critical component of success.