

Abstract

Distinct profiles of gene expression mirror the complex molecular mechanisms that regulate development during cellular differentiation and throughout life. To study the key events and processes in adipogenesis the gene expression of 3T3-L1 cell line during differentiation from fibroblast like preadipocytes to mature adipocytes with a 27.648 element focused murine cDNA microarray, comprising adipose specific genes and ESTs from early embryonic stages (NIA 15k clone set) was analyzed. Three independent time series experiments of 3T3-L1 adipocyte differentiation were performed in reference design. RNA from 8 time points (0d, 6h, 12h, 24h, 2d, 3d, 7d, 14d) was hybridized against RNA from the preconfluent stage in duplicate with reversed dye assignment to study the gene expression profile over the whole differentiation process. 780 genes found to be more than twofold up- or downregulated in at least 4 timepoints in comparison to the preconfluent stage were selected for further analysis.

A number of automated methods were proposed to extract biological meaning in the wealth of data. Clustering algorithms were performed (k-means, principal component analysis) to categorize these genes by their expression course. Additionally, an iterative reverse engineering approach based on mutual information and correlation were applied to elucidate gene-gene relations. To study the gene expression profiles in the context of relevant pathways, a database and web portal for genomics of lipid-associated disorders (GOLD.db) was initiated.

Many known and unknown differentially expressed genes in the mitotic clonal expansion phase and the late terminal adipocyte differentiation as well as transcriptional regulators could be identified and confirmed by Real Time PCR. Due to the focused approach and a novel thorough functional annotation process new promising targets were revealed.

Supplementary information is available at <http://genome.tugraz.at/adipocyte>

Keywords: Adipogenesis, Microarray, Transcriptional Profiling, Functional Annotation