UNIVERSITÄT LEIPZIG

Medizinische Fakultät

Genome-wide mRNA Expression Profiles of in vitro Adipocyte Differentiation

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Motivation

Obesity already develops in the early years of childhood and can lead to metabolic and cardiovascular disease. Which genes are associated with obesity and corresponding parameters of adipose tissue dysfunction, and contribute to the development of clinical comorbidities? Differential gene expression time-course analysis of adipocyte differentiation and subsequent pathway analysis will be performed to answer this question.

Methods

Gene Expression Data

	SGBS	LONZA	SVF
Sample	4 replicates x 11 time points	5 replicates x 6 time points	8 replicates x 2 time points
Probe	48,107 = 47,231 expression + 876 controls		

Pre-processing

Sample filter
Transcript filter
Quantile normalization
log-2 transformation
Batch adjustment
Gene annotation

Sample	3 replicates x 11 time points	4 replicates x 6 time points	5 replicates x 2 time points
Probe	23,439	21,336	22,678

Gene Expression Time-course Analysis

Repeated Measures Analysis of Variance (RM ANOVA) has been applied to expression data of each cell line separately (SGBS, LONZA, SVF). Expression data were measured on *Illumina HumanHT-12 v4 Expression BeadChip* arrays. Outcome in each analysis was the logarithm to base 2 of fold change (log2FC) of subsequent measurement in contrast to the first measurement. Groups were defined by the time points of subsequent measurements. Intersection of the three top lists yielded the candidate list for post hoc-analysis.

Pathway Analysis

Results based on this statistical inference method were further analyzed considering their biological function. Therefore, *Ingenuity Pathway Analysis* (IPA) was used.

Contact

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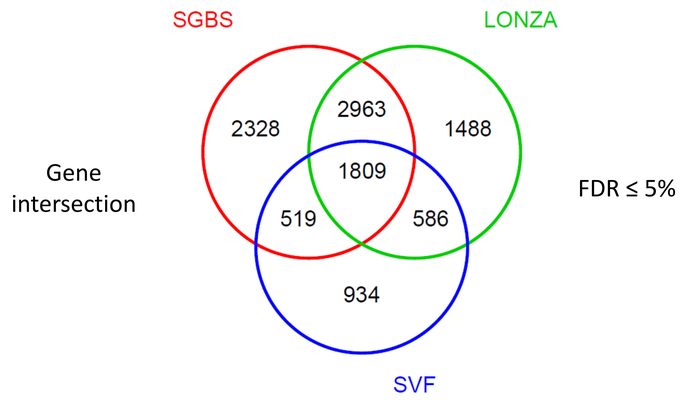
Results

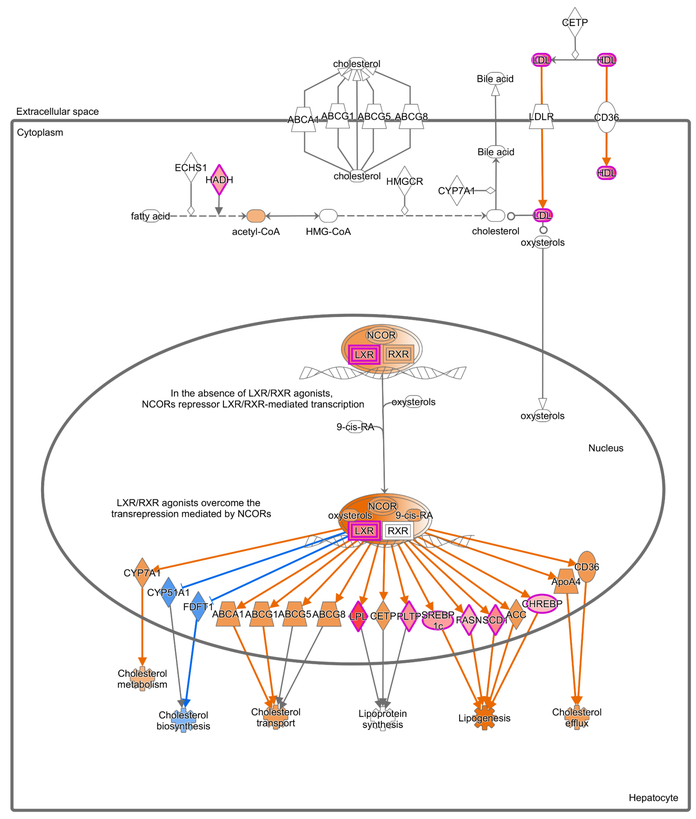
Repeated Measures ANOVA

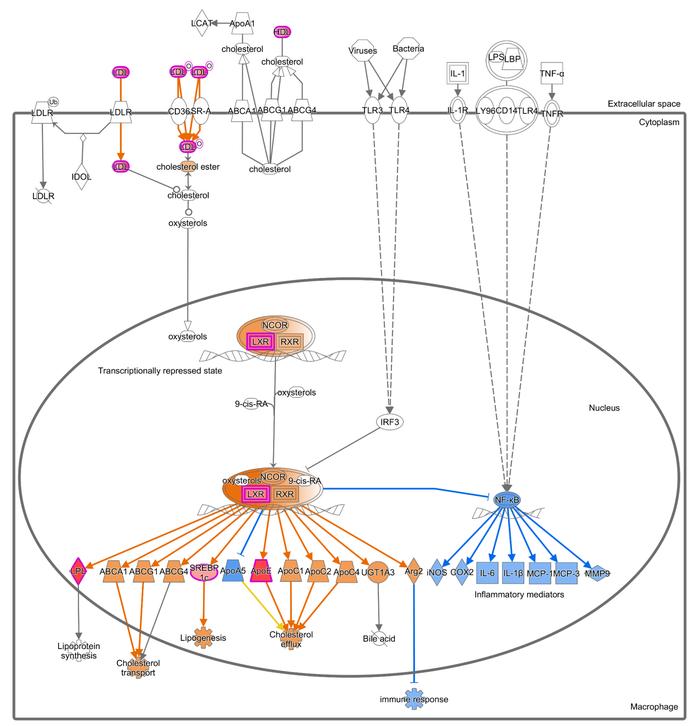


Subset of Top Genes	FDR (SGBS)	FDR (LONZA)	FDR (SVF)
APOE	4.59×10^{-11}	1.61×10^{-8}	0.0226
SCD	2.12×10^{-12}	6.99×10^{-12}	0.0002
MLXIPL	6.99×10^{-12}	1.88×10^{-10}	0.0102
SERPINF1	1.47×10^{-9}	5.45×10^{-12}	0.0014
NR1H3	4.32×10^{-11}	4.37×10^{-9}	0.0009
SREBF1	1.98×10^{-10}	1.37×10^{-9}	0.0077
FASN	1.09×10^{-11}	5.57×10^{-12}	0.0003
LPL	1.88×10^{-12}	2.39×10^{-10}	6.33×10^{-5}
PLTP	2.83×10^{-9}	4.12×10^{-5}	0.0082
HADH	2.31×10^{-11}	5.84×10^{-13}	0.0117
APOD	1.07×10^{-9}	0.0127	0.0002
AGT	1.49×10^{-10}	7.41×10^{-5}	0.0143
RBP4	4.97×10^{-13}	3.89×10^{-12}	0.0026

Ingenuity Pathway Analysis

Intersection of RM ANOVA results of SGBS, LONZA, and SVF (each FDR ≤ 5%) yielded 1,809 candidate genes. A subset of 250 of these candidate genes were subject to functional analysis with *IPA*. log2FC between -1 and 1 were excluded from pathway analysis.





Conclusion

Candidate genes were extracted by intersection of RM ANOVA results of gene expression data of three cell lines. Most important detected canonical pathway was LXR/RXR Activation. Liver X receptors (LXR) play a key role in lipid metabolism and inhibit inflammation which is of high interest for drug discovery.

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