

## Supplemental Table 1: Gene Set Enrichment Analysis

### Pathways upregulated in LFH, HFL and HFH compared to LFL

	LFH vs LFL		HFL vs LFL		HFH vs LFL	
	NES	FDR q	NES	FDR q	NES	FDR q
VALINE_LEUCINE_AND_ISOLEUCINE_DEGRADATION	2.3	0	2.4	0	2.6	0
MITOCHONDRIAL_FATTY_ACID_OXIDATION	2.2	0	2.6	0	2.5	0
MISCELLANEOUS_LIPID_METABOLISM	2.1	0.01	1.9	0.01	2.4	0
BENZOATE_DEGRADATION_VIA_COA_LIGATION	2.0	0.02	1.6	0.09	1.9	0.01
PROPANOATE_METABOLISM	1.9	0.03	2.3	0	2.5	0
PEROXISOMAL_FATTY_ACID_OXIDATION	1.9	0.03	2.3	0	2.2	0
LIPOGENESIS	1.9	0.03	1.5	0.13	2.0	3.56E-03
MM_NUCLEAR_RECEPTORS_IN_LIPID_METABOLISM_AND_TOXICITY	1.9	0.03	1.8	0.02	1.8	0.02
NUCLEAR_RECEPTORS_IN_LIPID_METABOLISM_AND_TOXICITY	1.8	0.04	1.8	0.02	1.8	0.02
MM_AMINO_ACID_METABOLISM	1.8	0.04	1.9	0.01	1.8	0.01
MM_KREBS-TCA_CYCLE	1.8	0.05	1.8	0.01	2.0	3.18E-03
NICOTINATE_AND_NICOTINAMIDE_METABOLISM	1.8	0.05	1.6	0.05	2.0	3.71E-03
PANTOTHENATE_AND_COA_BIOSYNTHESIS	1.8	0.05	1.8	0.02	1.5	0.14
CITRATE_CYCLE_(TCA_CYCLE)	1.7	0.06	2.0	2.08E-03	2.3	0
GLYCAN_STRUCTURES_-_DEGRADATION	1.7	0.07	1.4	0.22	2.1	8.00E-04
MM_FATTY_ACID_BETA_OXIDATION_META_BIGCAT	1.7	0.08	2.0	3.05E-03	2.2	0
PPAR_SIGNALING_PATHWAY	1.7	0.10	1.9	0.01	1.8	0.02
FATTY_ACID_METABOLISM	1.6	0.11	2.3	0	2.2	2.46E-04
ALANINE_AND_ASPARTATE_METABOLISM	1.6	0.12	1.8	0.02	1.7	0.05
MM_MITOCHONDRIAL_FATTY_ACID_BETAOXIDATION	1.6	0.12	2.2	7.21E-04	2.2	5.22E-04
LIMONENE_AND_PINENE_DEGRADATION	1.6	0.14	1.5	0.15	1.9	0.01
MM_FATTY_ACID_BETA_OXIDATION_1_BIGCAT	1.5	0.14	1.8	0.01	2.0	3.73E-03

### Pathways upregulated exclusively in HFH compared to LFL

	LFH vs LFL		HFL vs LFL		HFH vs LFL	
	NES	FDR q	NES	FDR q	NES	FDR q
CHOLESTEROL_SYNTHESIS_ESTERIFICATION	0.8	1	1.3	0.26	2.1	5.80E-04
NRF2-REGULATED_GENES_COMBINED	0.8	1	-0.9	0.89	2.0	3.98E-03
CELL_CYCLE	-0.7	1	0.7	1	1.9	0.01
ATM_SIGNALING_PATHWAY	1.2	0.50	-0.8	0.98	1.9	0.01
CELL_COMMUNICATION	0.8	1	-1.3	0.49	1.8	0.01
CYCLINS_AND_CELL_CYCLE_REGULATION	-0.5	1.00	-0.8	0.97	1.8	0.02
PYRIMIDINE_METABOLISM	0.8	1	1.1	0.58	1.8	0.02
MM_2-TISSUES-BLOOD_AND_LYMPH	0.9	0.97	-0.9	0.89	1.8	0.02
HOW_PROGESTERONE_INITIATES_THE_OOCYTE_MATURATION	1.2	0.59	1.0	0.79	1.7	0.03
PURINE_METABOLISM	1.2	0.60	1.2	0.54	1.7	0.03
P53_SIGNALING_PATHWAY	-0.6	1	-1.2	0.59	1.7	0.04
MM_2-TISSUES-MUSCLE_FAT_BONE_AND_CONNECTIVE	1.3	0.49	1.3	0.26	1.6	0.08
MM_MATRIX_METALLOPROTEINASES	-0.8	1	-1.4	0.42	1.6	0.08
SEL_EXPR_OF_CHEMOKINE_RECEPTORS_DURING_T-CELL_POLAR.	0.8	1	-0.9	0.93	1.6	0.08
TNFR1_SIGNALING_PATHWAY	-1.0	1	0.7	1.00	1.6	0.08
MM_CELL_CYCLE-G1_TO_S_CONTROL_REACTOME	-0.9	1	0.8	1	1.6	0.08
MM_PROSTAGLANDIN_SYNTHESIS_REGULATION	0.9	0.91	-1.0	0.75	1.5	0.09
MM_CELL_CYCLE_KEGG	-0.9	1	0.8	1	1.5	0.10
MM_OXIDATIVE_STRESS	0.5	1	-1.0	0.78	1.5	0.11
OXIDATIVE_STRESS_INDUCED_GENE_EXPRESSION_VIA_NRF2	1.1	0.74	0.7	1	1.5	0.13
ST_TUMOR_NECROSIS_FACTOR_PATHWAY	0.7	1	-0.8	0.97	1.5	0.13
AMINOSUGARS_METABOLISM	0.7	1	-0.7	1	1.5	0.14
CELL_CYCLE_G2_M_CHECKPOINT	-0.5	1	0.9	0.89	1.4	0.14
OXIDATIVE_PHOSPHORYLATION	0.9	0.91	1.0	0.84	1.4	0.15
ASCORBATE_AND_ALDARATE_METABOLISM	0.7	1	1.2	0.48	1.4	0.15
MM_1-TISSUE-INTERNAL_ORGANS	1.4	0.37	1.0	0.79	1.4	0.22
FAS_SIGNALING_PATHWAY_(CD95_)	-0.9	1	1.0	0.85	1.4	0.21
MM_HYPERTROPHY_MODEL	1.0	0.86	1.0	0.89	1.4	0.21
MM_WNT_SIGNALING	1.0	0.87	1.0	0.87	1.4	0.23
ECM-RECEPTOR_INTERACTION	-1.0	1	-1.4	0.43	1.4	0.23
NUCLEOTIDE_SUGARS_METABOLISM	0.9	0.99	-0.5	1	1.3	0.24

**Supplemental Table 2:** *Regression coefficients of the association between plasma levels of selected proteins and final liver triglyceride content.* Regression coefficients were generated using multivariate analysis. Statistically significant associations (inverse RSD>2) are shown in red. All other proteins analyzed did not show any significance.

	Week						
	0	2	4	8	12	16	20
CRP	0.39	0.45	0.72	1.17	1.91	2.05	1.90
Haptoglobin	0.35	0.46	0.56	1.13	1.67	2.09	1.93
Leptin	0.38	0.53	0.57	1.27	1.80	2.39	2.21
MIP-1 $\alpha$	0.20	0.29	0.27	0.68	0.91	1.30	1.20
Eotaxin	-0.29	-0.31	-0.60	-0.83	-1.48	-1.39	-1.29
IL-18	0.26	0.36	0.39	0.86	1.22	1.61	1.49
IL-1 $\beta$	0.29	0.42	0.40	0.98	1.34	1.88	1.74
MIP-1 $\gamma$	0.21	0.27	0.35	0.67	1.01	1.22	1.12
MIP-1	0.15	0.21	0.23	0.50	0.71	0.95	0.88
MDC	-0.22	-0.22	-0.46	-0.60	-1.11	-0.99	-0.92
TIMP-1	0.16	0.23	0.22	0.53	0.72	1.02	0.94
Insulin	0.12	0.24	0.03	0.50	0.45	1.09	1.01
MPO	0.28	0.36	0.44	0.89	1.32	1.63	1.51
GCP-2	-0.19	-0.19	-0.41	-0.52	-0.98	-0.85	-0.79