Supplementary Table 6: List of selected downregulated genes involved in different metabolic pathway of SIV infected enteroids compared to uninfected enteroids Pathway Gene Protein Log2 fold change Biological function PDHA1 Pyruvate Dehydrogenase E1 Subunit Alpha 1 1.5 Converts pyruvate to acetyl-coA PDHB Pyruvate Dehydrogenase E1 Subunit Beta 2.6 Converts pyruvate to acetyl-coA PGAM1 Phosphoglycerate Mutase 1 2 Conversion of 3-phosphoglycerate to 2-phosphoglycerate ENO2 Enolase 2 3.3 Dehydratation of 2-phosphoglycerate to phosphoenolpyruvate 2.1 HK1 Hexokinase 1 Catalyzes the phosphorylation of various hexoses PFKL Phosphofructokinase, Liver Type 2.3 Conversion of fructose-6-phosphate to fructose-1,6-bisphosphate PGK1 Phosphoglycerate Kinase 1 3.8 Transfer of a phosphate group from 1,3-bisphosphoglycerate (1,3-BPG) to ADP Glycolysis Aldolase A Conversion of fructose 1-6-diphosphate to alveeraldehyde 3-phosphate and dihydroxy-ALDO A 1.6 acetone phosphate Aldolase B Conversion of fructose 1-6-diphosphate to glyceraldehyde 3-phosphate and dihydroxy-ALDO B 3.3 acetone phosphate Aldolase C Conversion of fructose 1-6-diphosphate to glyceraldehyde 3-phosphate and dihydroxy-ALDO C 3.2 acetone phosphate PGM1 1.5 Phosphoglucomutase 1 Transfer of phosphate from position 1 to 6 on glucose ACSS 1 Acyl-CoA Synthetase Short Chain Family Member 1 1.9 Synthesis of acetyl-CoA ACSS 2 Acyl-CoA Synthetase Short Chain Family Member 2 2.4 Synthesis of acetyl-CoA PDHA1 Pyruvate Dehydrogenase E1 Subunit Alpha 1 1.5 Conversion of pyruvate to acetyl-CoA PDHB Pyruvate Dehydrogenase E1 Subunit Beta 2.6 Conversion of pyruvate to acetyl-CoA Pyruvate metabolism 2.6 LDH A Lactate Dehydrogenase A Synthesizes (S)-lactate from pyruvate I DH D Lactate Dehydrogenase D 1.9 Synthesizes (S)-lactate from pyruvate DLAT Dihydrolipoamide S-Acetyltransferase 1.5 Conversion of pyruvate to acetyl-CoA PCK2 Phosphoenolpyruvate Carboxykinase 2.3 Converts oxaloacetate into phosphoenolpyruvate and carbon dioxide PECR Peroxisomal trans-2-enoyl-CoA reductase 2.1 Chain elongation of fatty acids ACAA2 3-ketoacyl-CoA thiolase, mitocondrial 1.4 Production of energy from fats OXSM 3-oxoacyl-[acyl-carrier-protein] synthase, mitocondrial 4.2 Biosynthesis of lipoic acid as well as longer chain fatty acids ACSL4 Long-chain-fatty-acid--CoA ligase 4 1.9 Conversion of long-chain fatty acids to their active form acyl-CoA 2.3 MCAT Malonyl-CoA-acyl carrier protein transacylase, Transfer of a malonyl moiety from malonyl-CoA Short/branched chain specific acyl-CoA dehydrogenase, Formation of trans-2-enoyl-CoA ACADSB 3 1 mitochondrial Fatty acid metabolism HADH A Trifunctional enzyme subunit alpha, mitochondrial Mitochondrial beta-oxidation pathway 3.3 HADH B Trifunctional enzyme subunit alpha, mitochondrial Mitochondrial beta-oxidation pathway ACOX3 Peroxisomal acvl-coenzyme A oxidase 3 2.6 Oxidizes the CoA-esters of 2-methyl-branched fatty acids Medium-chain specific acyl-CoA Mitochondrial fatty acid beta-oxidation ACADM dehydrogenase, mitocondrial 4.3 HADH Hydroxyacyl-CoA Dehydrogenase 2.6 Beta-oxidation cycle for medium and short-chain 3-hydroxy fatty acyl-CoAs ACADS 2.2 Short-chain specific acyl-Mitochondrial fatty acid beta-oxidation BDH1 D-beta-hydroxybutyrate dehydrogenase Conversion of 3-hydroxybutanoate to acetoacetate and NADH

3.5

3.4

3.9

Conversion of 3-hydroxybutanoate to acetoacetate and NADH Condensation of acetyl-CoA with acetoacetyl-CoA to form HMG-CoA

Key enzyme for ketone body catabolism

BDH2

HMGCS1

OXCT1

etone bodies metabolis

3-hydroxybutyrate dehydrogenase type 2

cytoplasmic Succinvl-CoA:3-ketoacid coenzyme A

Hydroxymethylglutaryl-CoA synthase,

3-Oxoacid CoA-Transferase 1

transferase 1