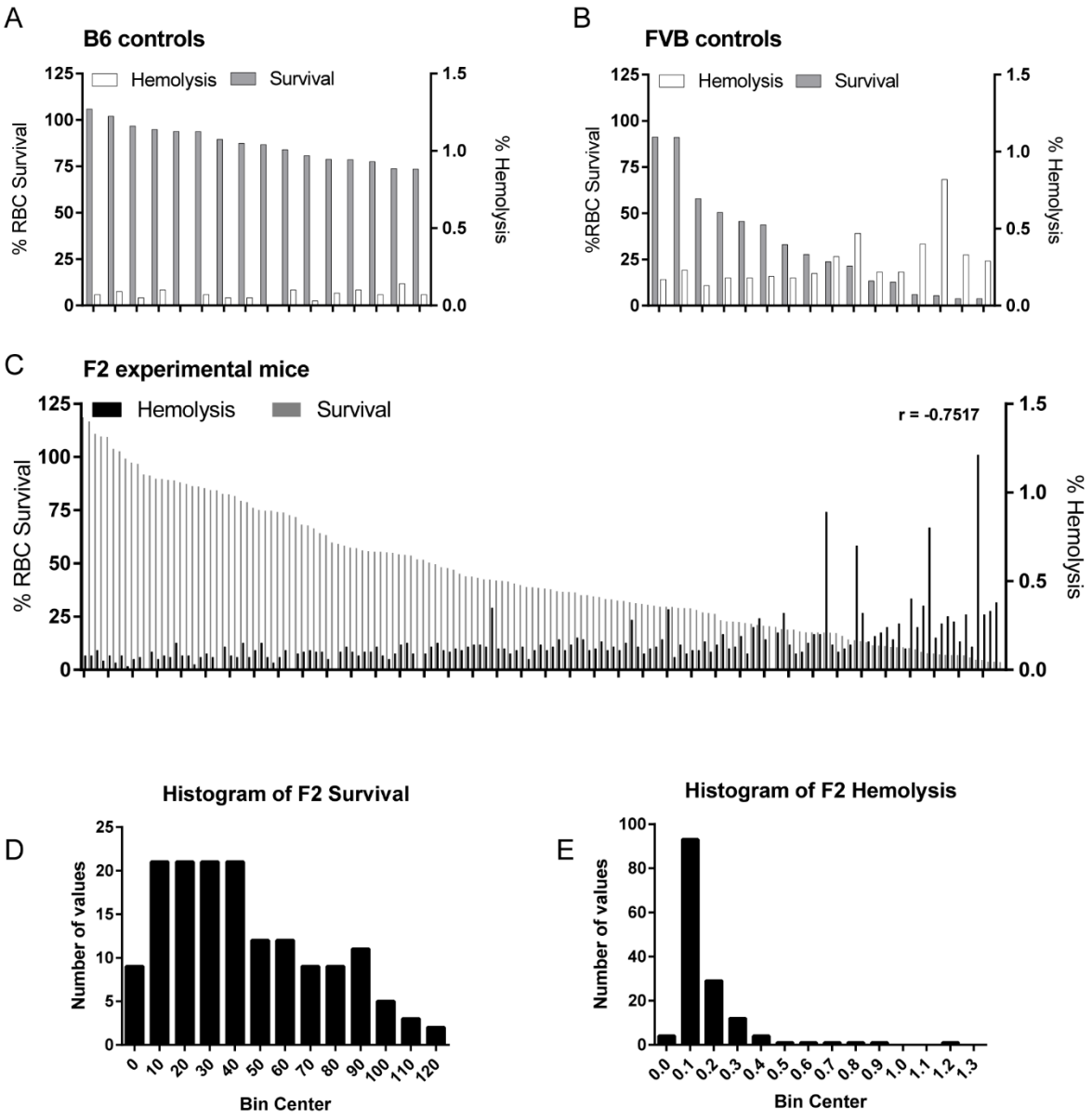
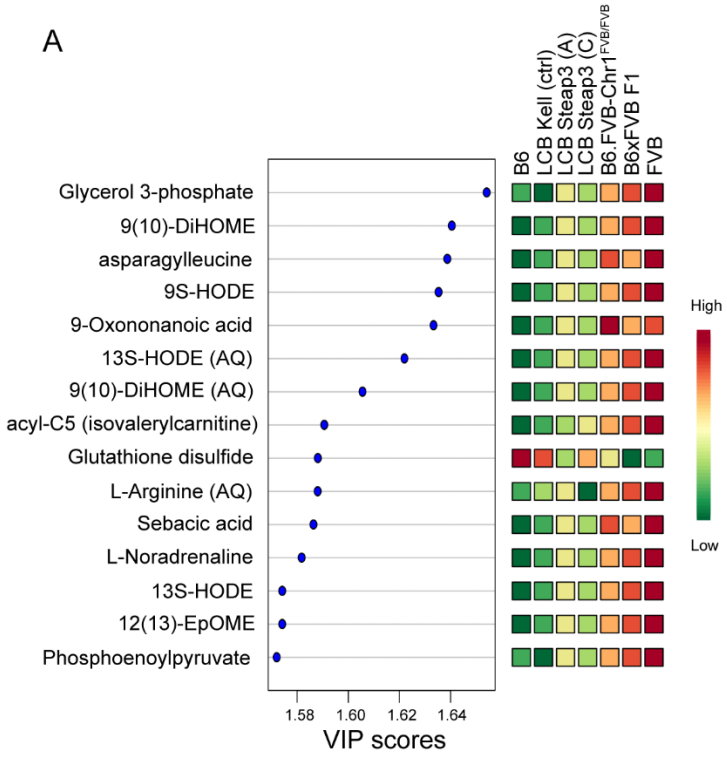
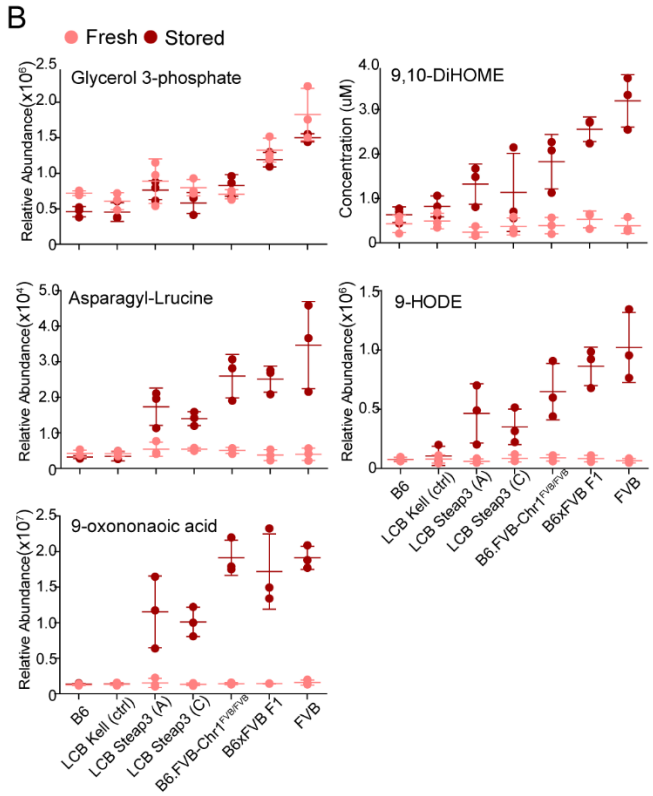
Supplemental Figure 1: *Distribution of 24hr post-transfusion recoveries and spontaneous hemolysis from controls and the 156 F2 mice.* 24hr recoveries (left axis; grey bars) and spontaneous hemolysis (right axis; white bars) of RBCs from 16 individual B6 mice (A), 16 individual FVB mice (B), and each of the 156 F2 experimental mice (C). (D) Frequency distributions of the 24hr survival data from the 156 experimental F2 mice. (E) Frequency distributions of the spontaneous hemolysis from the 156 experimental F2 mice.

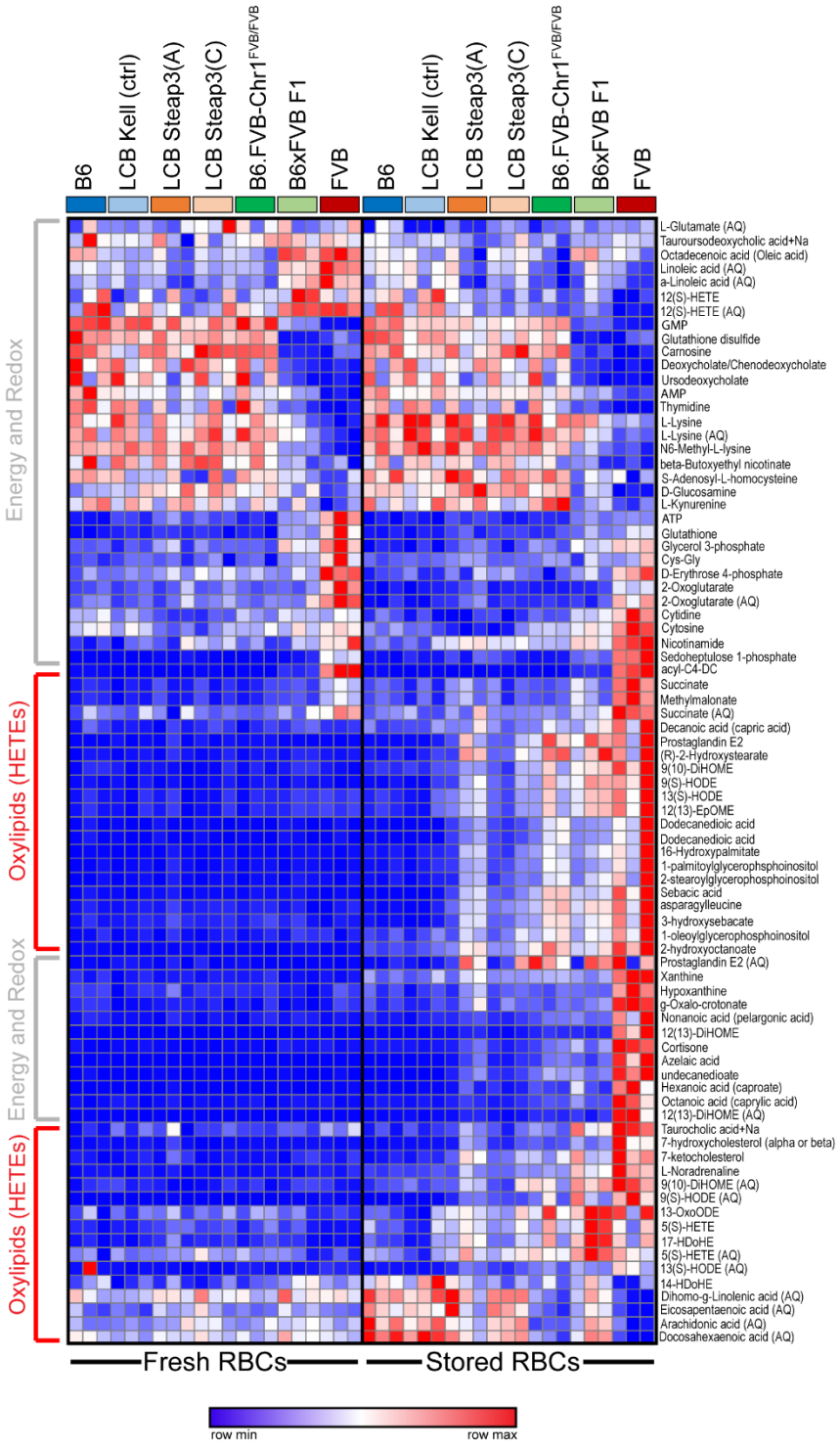


Supplemental Figure 2: *VIP and top 5 metabolites:* (A) Variable importance in projection analysis (VIP) was applied to the data set with a focus on which analytes carried over from FVB mice into congenic and transgenic systems. (B) The top 5 VIP identified metabolites are shown.

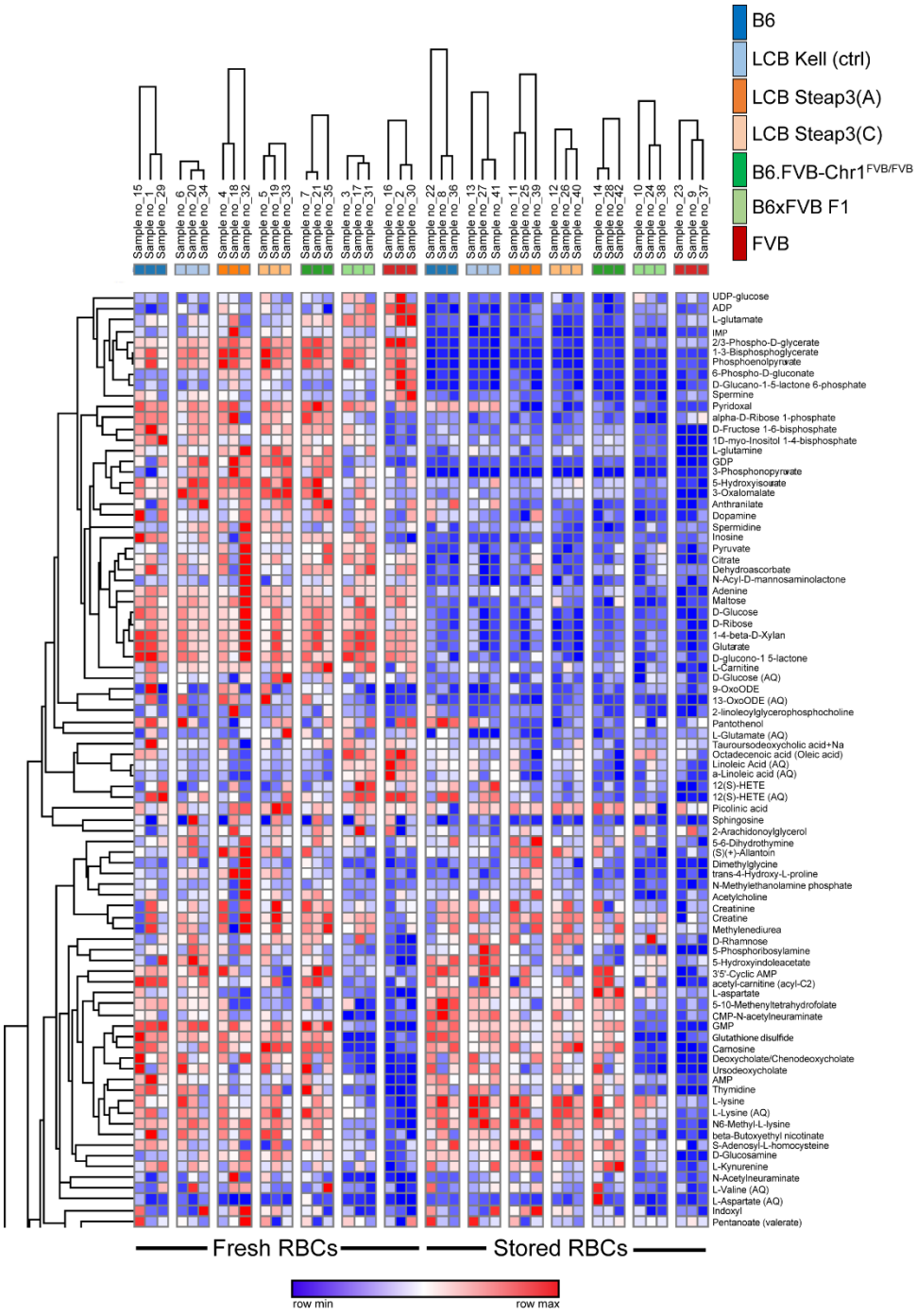


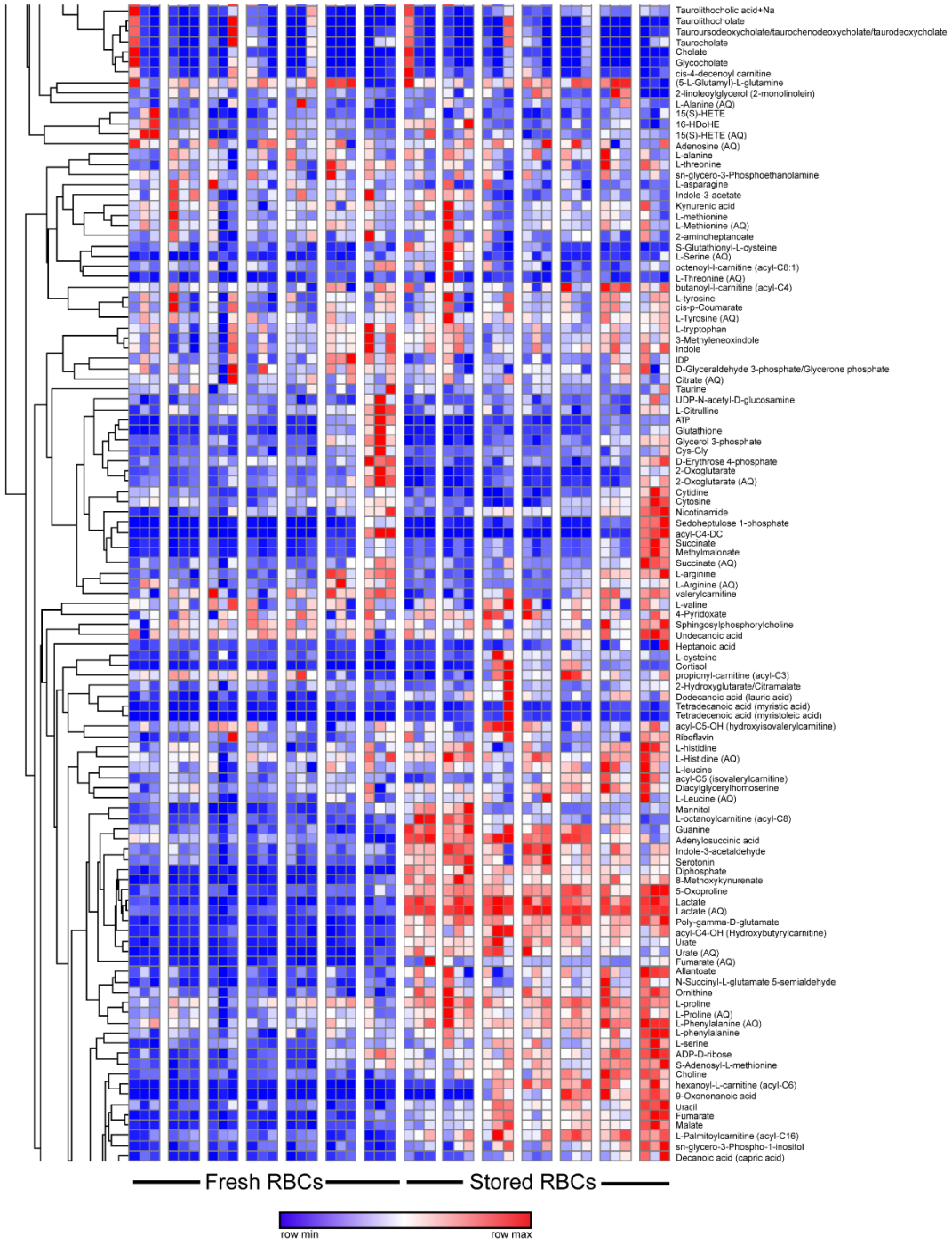


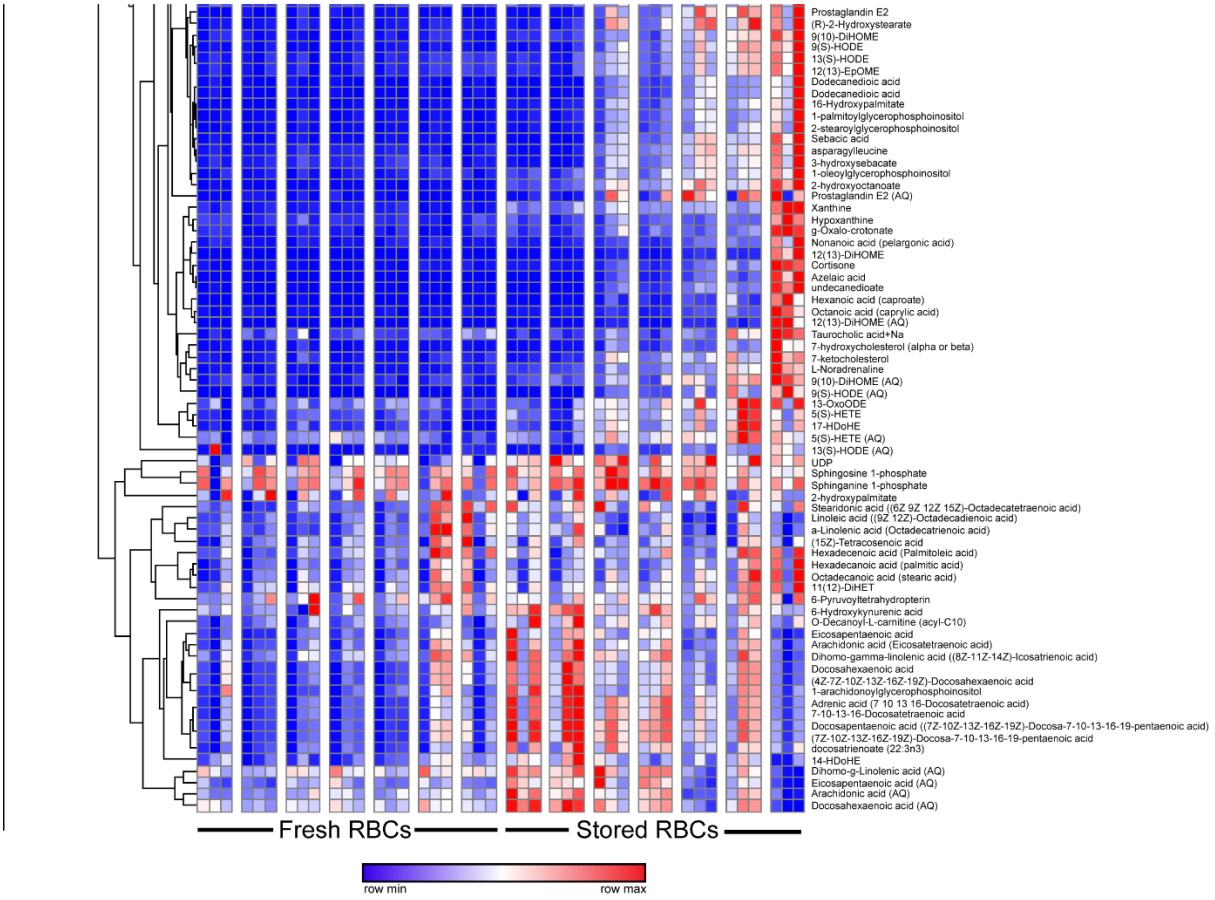
Supplemental Figure 3: *Select Classes of Metabolites Carry Forward into Congenic Mice and Steap3 Transgenic Mice.* A heat map depicts the relative quantitations of the indicated analytes for RBCs from each strain from each of 3 experiments. Left: fresh RBCs. Right: stored RBCs. Analytes are broken down by chemical class. Classes of compounds that generally carry forward are indicated by a red label (left), whereas those that do not carry forward are indicated by a gray label.



Supplemental Figure 4 (3 parts): An expanded list of compounds is presented that is too large to be included in the main text.




Taurolithocholic acid+Na
Taurolithocholate
Tauroursodeoxycholate/taurochenodeoxycholate/taurodeoxycholate
Taurocholate
Cholate
Glycocholate
cis-4-decenoyl carnitine
(5-L-Glutamyl)-L-glutamine
2-linoleoylglycerol (2-monolinolein)
L-Alanine (AQ)
15(S)-HETE
16-HDoHE
15(S)-HETE (AQ)
Adenosine (AQ)
L-alanine
L-threonine
sn-glycero-3-Phosphoethanolamine
L-asparagine
Indole-3-acetate
Kynurenic acid
L-methionine
L-Methionine (AQ)
2-aminoheptanoate
S-Glutathionyl-L-cysteine
L-Serine (AQ)
octenoyl-l-carnitine (acyl-C8:1)
L-Threonine (AQ)
butanoyl-l-carnitine (acyl-C4)
L-tyrosine
cis-p-Coumarate
L-Tyrosine (AQ)
L-tryptophan
3-Methyleneoxindole
Indole
IDP
D-Glyceraldehyde 3-phosphate/Glycerone phosphate
Citrate (AQ)
Taurine
UDP-N-acetyl-D-glucosamine
L-Citrulline
ATP
Glutathione
Glycerol 3-phosphate
Cys-Gly
D-Erythrose 4-phosphate
2-Oxoglutarate
2-Oxoglutarate (AQ)
Cytidine
Cytosine
Nicotinamide
Sedoheptulose 1-phosphate
acyl-C4-DC
Succinate
Methylmalonate
Succinate (AQ)
L-arginine
L-Arginine (AQ)
valerylcarnitine
L-valine
4-Pyridoxate
Sphingosylphosphorylcholine
Undecanoic acid
Heptanoic acid
L-cysteine
Cortisol
propionyl-carnitine (acyl-C3)
2-Hydroxyglutarate/Citramalate
Dodecanoic acid (lauric acid)
Tetradecanoic acid (myristic acid)
Tetradecenoic acid (myristoleic acid)
acyl-C5-OH (hydroxyisovalerylcarnitine)
Riboflavin
L-histidine
L-Histidine (AQ)
L-leucine
acyl-C5 (isovalerylcarnitine)
Diacylglycerylhomoserine
L-Leucine (AQ)
Mannitol
L-octanoylcarnitine (acyl-C8)
Guanine
Adenylosuccinic acid
Indole-3-acetaldehyde
Serotonin
Diphosphate
8-Methoxykynurenate
5-Oxoproline
Lactate
Lactate (AQ)
Poly-gamma-D-glutamate
acyl-C4-OH (Hydroxybutyrylcarnitine)
Urate
Urate (AQ)
Fumarate (AQ)
Allantoate
N-Succinyl-L-glutamate 5-semialdehyde
Ornithine
L-proline
L-Proline (AQ)
L-Phenylalanine (AQ)
L-phenylalanine
L-serine
ADP-D-ribose
S-Adenosyl-L-methionine
Choline
hexanoyl-L-carnitine (acyl-C6)
9-Oxononanoic acid
Uracil
Fumarate
Malate
L-Palmitoylcarnitine (acyl-C16)
sn-glycero-3-Phospho-1-inositol
Decanoic acid (capric acid)
Fresh RBCs
Stored RBCs
row min
row max


Prostaglandin E2
(R)-2-Hydroxystearate
9(10)-DiHOME
9(S)-HODE
13(S)-HODE
12(13)-EpOME
Dodecanedioic acid
Dodecanedioic acid
16-Hydroxypalmitate
1-palmitoylglycerophosphoinositol
2-stearoylglycerophosphoinositol
Sebacic acid
asparagylleucine
3-hydroxysebacate
1-oleoylglycerophosphoinositol
2-hydroxyoctanoate
Prostaglandin E2 (AQ)
Xanthine
Hypoxanthine
g-Oxalo-crotonate
Nonanoic acid (pelargonic acid)
12(13)-DiHOME
Cortisone
Azelaic acid
undecanedioate
Hexanoic acid (caproate)
Octanoic acid (caprylic acid)
12(13)-DiHOME (AQ)
Taurocholic acid+Na
7-hydroxycholesterol (alpha or beta)
7-ketocholesterol
L-Noradrenaline
9(10)-DiHOME (AQ)
9(S)-HODE (AQ)
13-OxoODE
5(S)-HETE
17-HDoHE
5(S)-HETE (AQ)
13(S)-HODE (AQ)
UDP
Sphingosine 1-phosphate
Sphinganine 1-phosphate
2-hydroxypalmitate
Stearidonic acid ((6Z 9Z 12Z 15Z)-Octadecatetraenoic acid)
Linoleic acid ((9Z 12Z)-Octadecadienoic acid)
a-Linolenic acid (Octadecatrienoic acid)
(15Z)-Tetracosenoic acid
Hexadecenoic acid (Palmitoleic acid)
Hexadecanoic acid (palmitic acid)
Octadecanoic acid (stearic acid)
11(12)-DiHET
6-Pyruvoyltetrahydropterin
6-Hydroxykynurenic acid
O-Decanoyl-L-carnitine (acyl-C10)
Eicosapentaenoic acid
Arachidonic acid (Eicosatetraenoic acid)
Dihomo-gamma-linolenic acid ((8Z-11Z-14Z)-Icosatrienoic acid)
Docosahexaenoic acid
(4Z-7Z-10Z-13Z-16Z-19Z)-Docosahexaenoic acid
1-arachidonoylglycerophosphoinositol
Adrenic acid (7 10 13 16-Docosatetraenoic acid)
7-10-13-16-Docosatetraenoic acid
Docosapentaenoic acid ((7Z-10Z-13Z-16Z-19Z)-Docosa-7-10-13-16-19-pentaenoic acid)
(7Z-10Z-13Z-16Z-19Z)-Docosa-7-10-13-16-19-pentaenoic acid
docosatrienoate (22:3n3)
14-HDoHE
Dihomo-g-Linolenic acid (AQ)
Eicosapentaenoic acid (AQ)
Arachidonic acid (AQ)
Docosahexaenoic acid (AQ)
Fresh RBCs
Stored RBCs
row min
row max

Supplemental Table 1: *SNP assays used for genotyping crossover mice.* SNP ID #s are shown along with the location of each SNP on Chromosome 1 and the predicted nucleotide at that position for both the B6 and FVB genome. Assay IDs indicate the catalog # of the Taqman SNP genotyping assay used.

Supplemental Table 2*: Genes and Genetic Elements in the 3Mb Chromosome 1 region.* The 20 open reading frames (ORFs) contained within the B6.FVB-Chr1 region, along with their respective MGI database numbers, position within the chromosome 1 region and the Taqman gene expression assay used for expression determination (Top panel). 42 additional genetic elements have been identified in the B6.FVB-Chr1 region, including rRNAs, snRNAs, miRNAs, lincRNAs and a few unclassified predicted genes (Bottom panel). Taqman gene expression assays were available for 4 of these genetic elements (in bold) however no amplification was seen for any of them (data not shown).

Supplemental Table 3: *Genes with Non-Synonymous SNPs in the 3Mb Chromosome 1 region.* The presence of non-synonymous SNPs within coding regions of genes in the B6.FVB-Chr1 region was assessed by searching the MGI database (Jackson Labs) using the coordinates delineated by the B6.FVB-Chr1 SNP genotyping. 7 non-synonymous SNPs located within 4 different ORFs were identified.

SNP ID (dbSNP Build 142)	Map Position (GRCm38)	Gene	Category	B6	FVB
rs30812533	Chr1:118,868,087	Gli2	Coding-NonSynonymous	C	T
rs30698944	Chr1:119,002044	Gli2	Coding-NonSynonymous	G	T
rs31178208	Chr1:120,063,246	Sctr	Coding-NonSynonymous; mRNA-UTR	G	T
rs31842162	Chr1:120,063,257	Sctr	Coding-NonSynonymous; mRNA-UTR	G	A
rs32405796	Chr1:120,176,728	3110009E18Rik	Coding-NonSynonymous; intron	G	A
rs30773456	Chr1:120,227,750	Steap3	Coding-NonSynonymous	T	C
rs30771292	Chr1:120,234,4378	Steap3	Coding-NonSynonymous	G	A