Supplemental Material:

Article title: Regulation of Hepatic Drug-metabolizing Enzymes in Germ-free mice by Conventionalization and Probiotics

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Journal: Drug Metabolism and Disposition

Figure s1

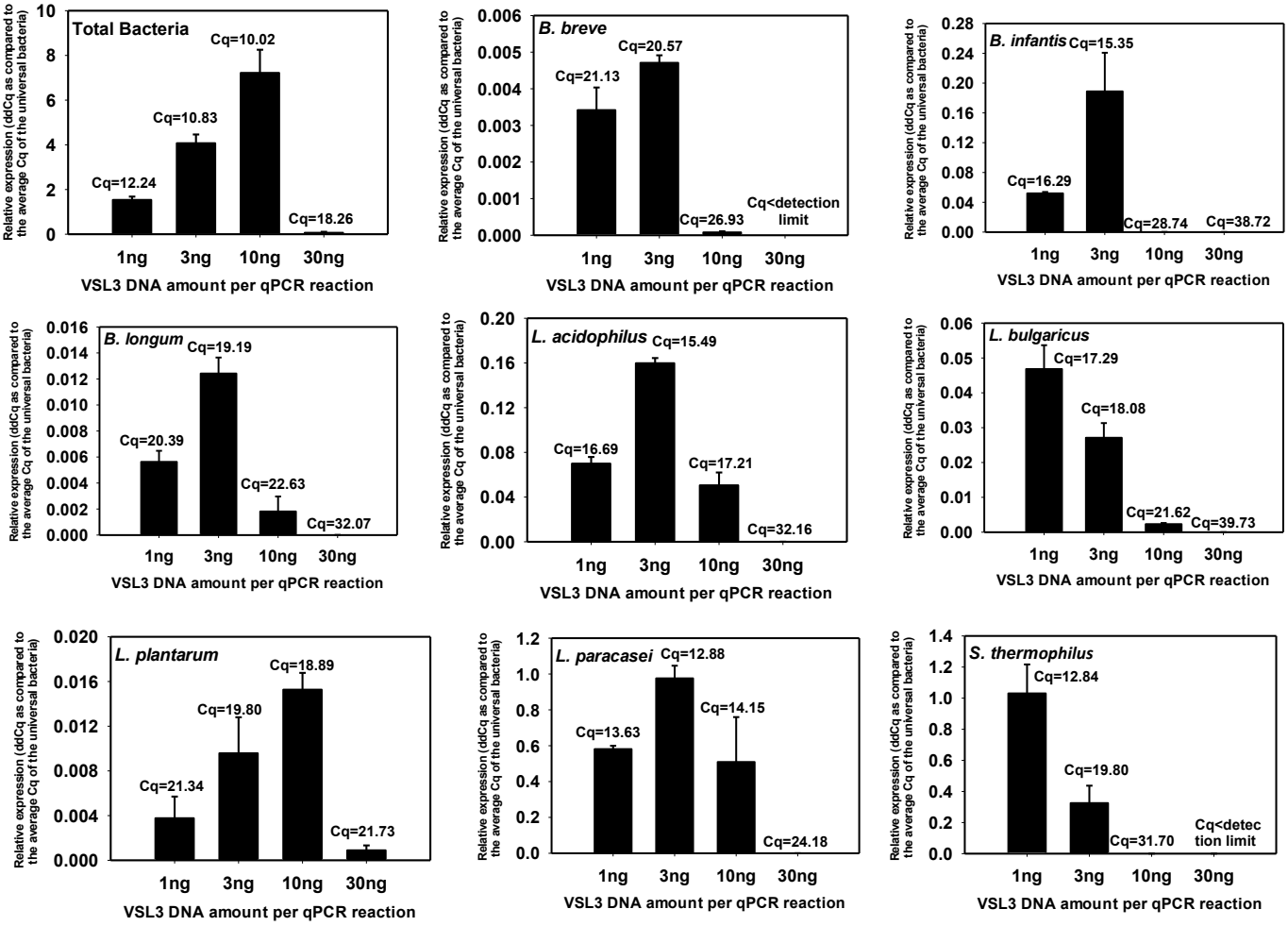
Total Bacteria
Cq=12.24
Cq=10.83
Cq=10.02
Cq=18.26
B. breve
Cq=21.13
Cq=20.57
Cq=26.93
Cq<detection limit
B. infantis
Cq=16.29
Cq=15.35
Cq=28.74
Cq=38.72
B. longum
Cq=20.39
Cq=19.19
Cq=22.63
Cq=32.07
L. acidophilus
Cq=16.69
Cq=15.49
Cq=17.21
Cq=32.16
L. bulgaricus
Cq=17.29
Cq=18.08
Cq=21.62
Cq=39.73
L. plantarum
Cq=21.34
Cq=19.80
Cq=18.89
Cq=21.73
L. paracasei
Cq=13.63
Cq=12.88
Cq=14.15
Cq=24.18
S. thermophilus
Cq=12.84
Cq=19.80
Cq=31.70
Cq<detection limit
1ng 3ng 10ng 30ng
VSL3 DNA amount per qPCR reaction
Relative expression (ddCq as compared to the average Cq of the universal bacteria)

Figure s2

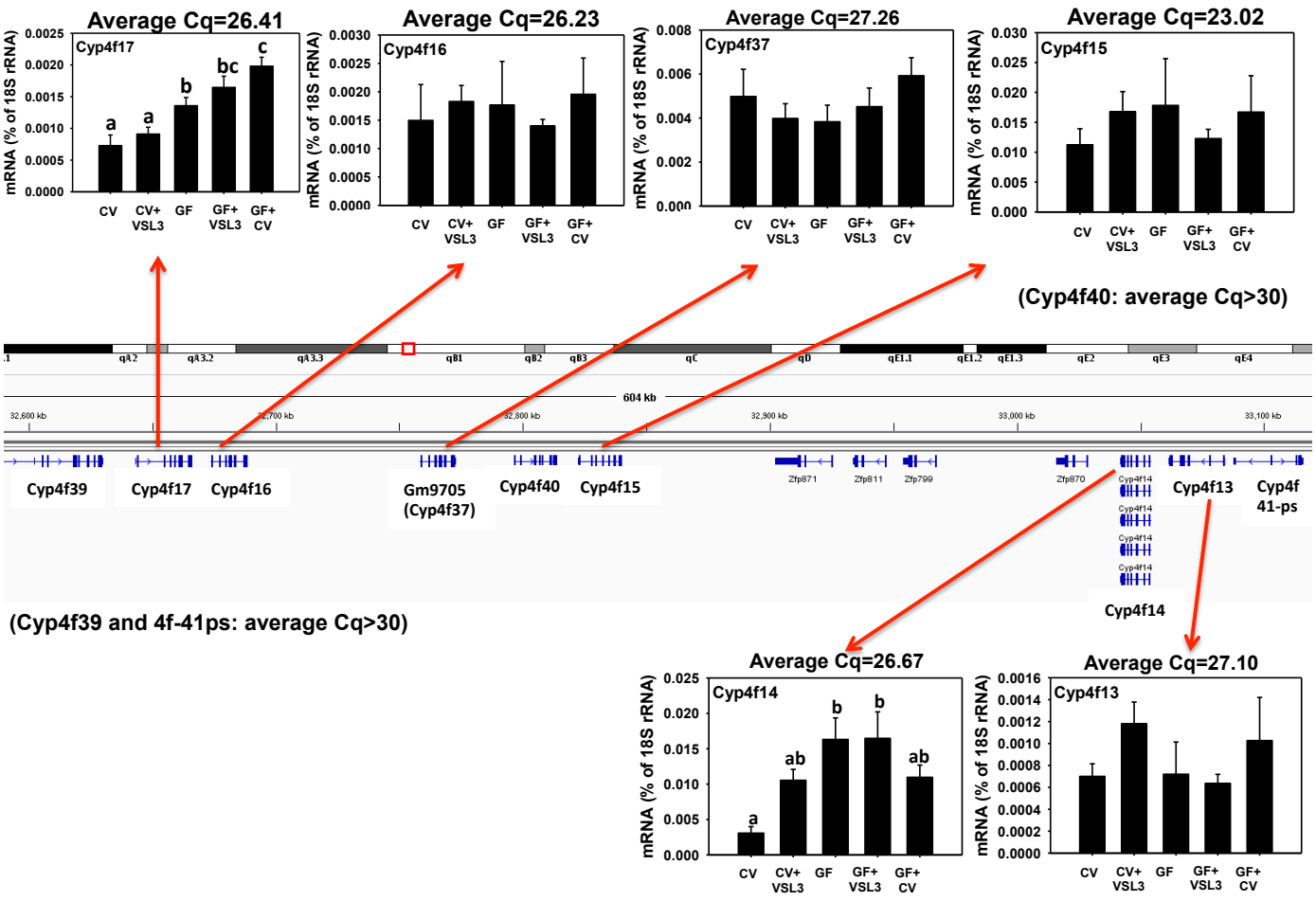
Cyp4f gene cluster
Average Cq=26.41
Cyp4f17
mRNA (% of 18S rRNA)
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=26.23
Cyp4f16
Average Cq=27.26
Cyp4f37
Average Cq=23.02
Cyp4f15
(Cyp4f40: average Cq>30)
604 kb
Cyp4f39
Cyp4f17
Cyp4f16
Gm9705 (Cyp4f37)
Cyp4f40
Cyp4f15
Cyp4f13
Cyp4f 41-ps
Cyp4f14
(Cyp4f39 and 4f-41ps: average Cq>30)
Average Cq=26.67
Average Cq=27.10

Figure s3

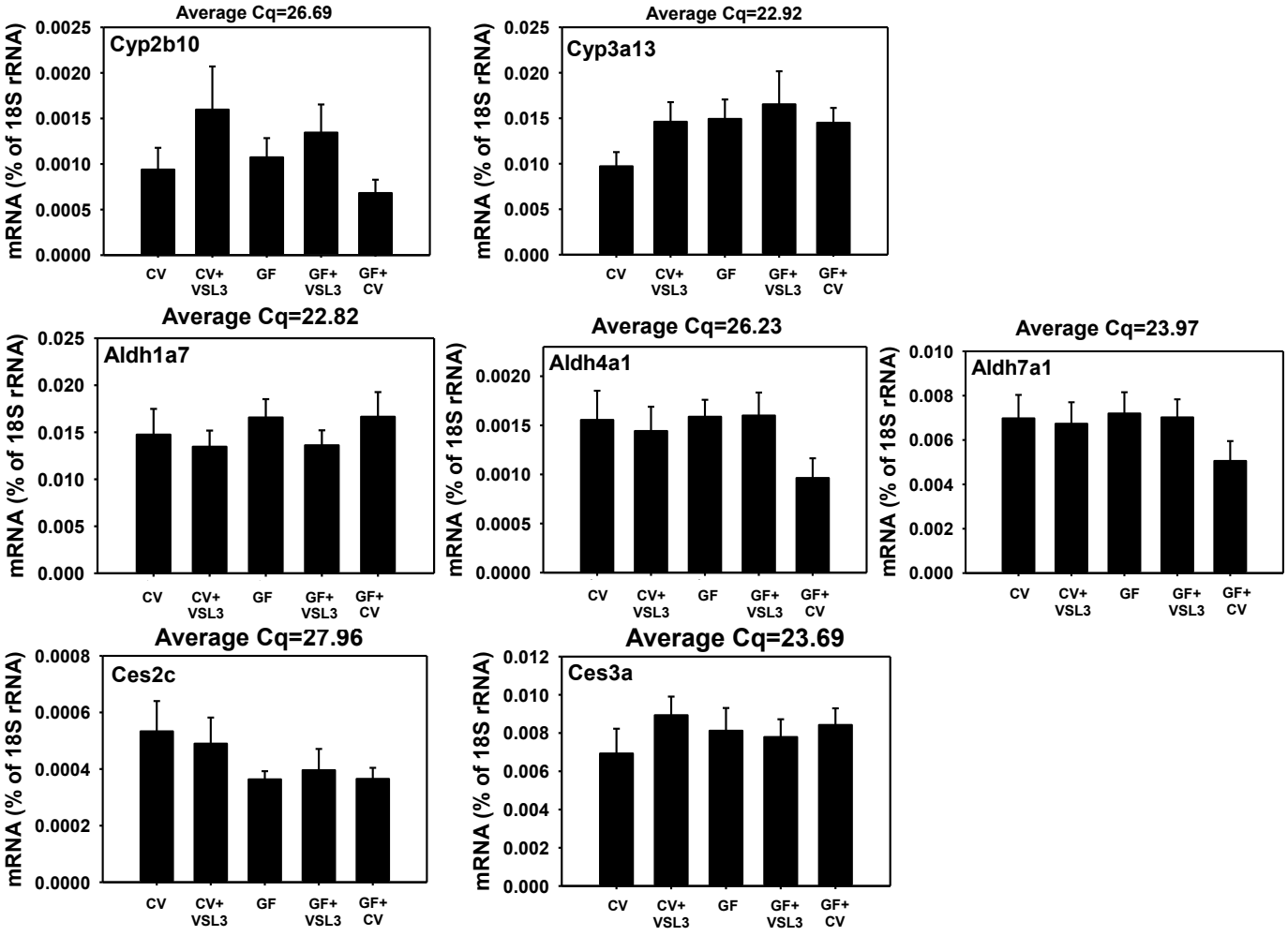
Average Cq=26.69
Cyp2b10
mRNA (% of 18S rRNA)
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=22.92
Cyp3a13
0.025
0.020
0.015
0.010
0.005
0.000
Average Cq=22.82
Aldh1a7
Average Cq=26.23
Aldh4a1
0.0020
0.0015
0.0010
0.0005
0.0000
Average Cq=23.97
Aldh7a1
0.010
0.008
0.006
0.004
0.002
0.000
Average Cq=27.96
Ces2c
0.0008
0.0006
0.0004
0.0002
0.0000
Average Cq=23.69
Ces3a
0.012
0.010
0.008
0.006
0.004
0.002
0.000

Figure s4

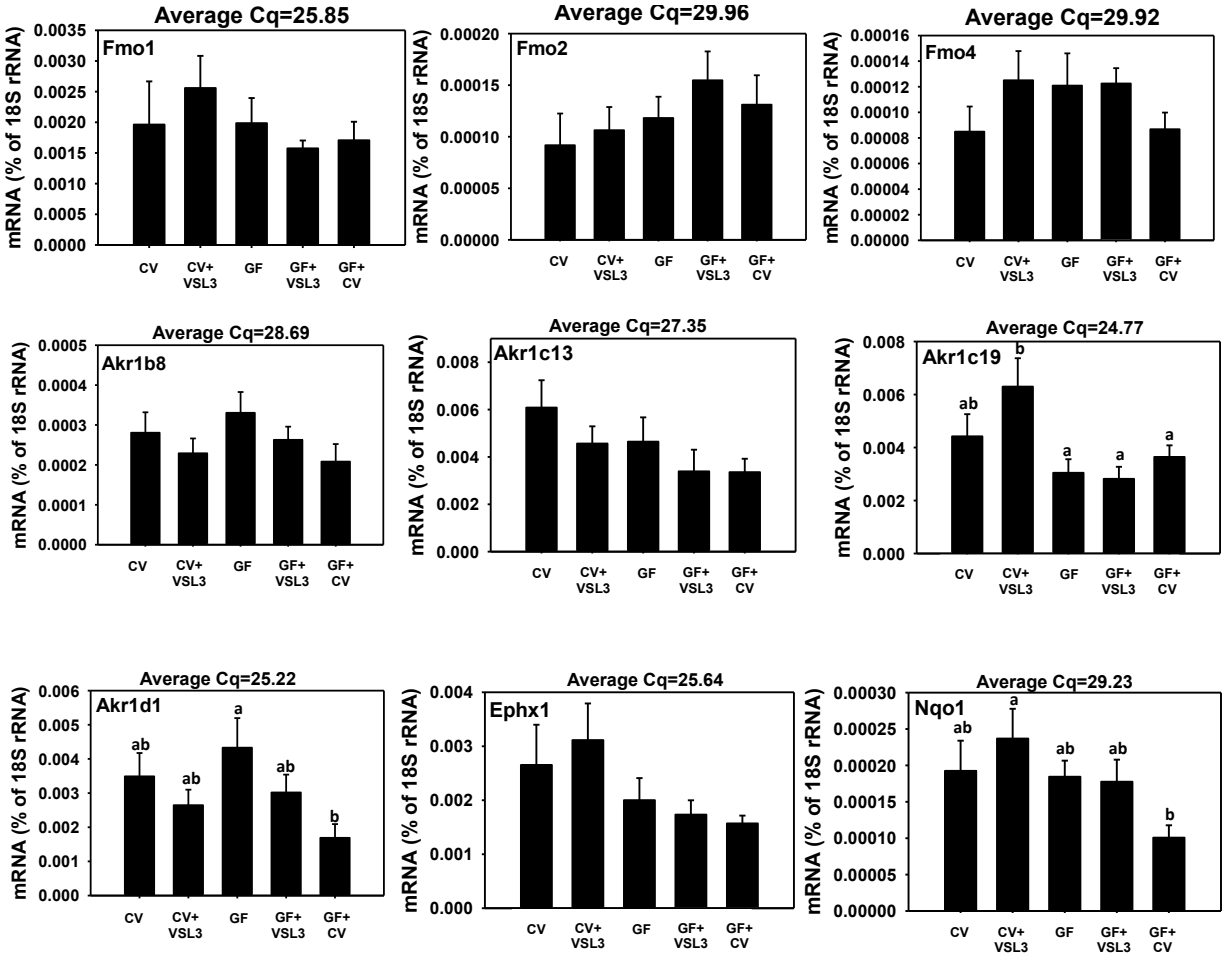
Average Cq=25.85
Fmo1
mRNA (% of 18S rRNA)
0.0035
0.0030
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=29.96
Fmo2
mRNA (% of 18S rRNA)
0.00020
0.00015
0.00010
0.00005
0.00000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=29.92
Fmo4
mRNA (% of 18S rRNA)
0.00016
0.00014
0.00012
0.00010
0.00008
0.00006
0.00004
0.00002
0.00000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=28.69
Akr1b8
mRNA (% of 18S rRNA)
0.0005
0.0004
0.0003
0.0002
0.0001
0.0000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=27.35
Akr1c13
mRNA (% of 18S rRNA)
0.008
0.006
0.004
0.002
0.000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=24.77
Akr1c19
mRNA (% of 18S rRNA)
0.008
0.006
0.004
0.002
0.000
ab
b
a
a
a
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=25.22
Akr1d1
mRNA (% of 18S rRNA)
0.006
0.005
0.004
0.003
0.002
0.001
0.000
ab
ab
a
ab
b
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=25.64
Ephx1
mRNA (% of 18S rRNA)
0.004
0.003
0.002
0.001
0.000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=29.23
Nqo1
mRNA (% of 18S rRNA)
0.00030
0.00025
0.00020
0.00015
0.00010
0.00005
0.00000
ab
a
ab
ab
b
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV

Figure s5

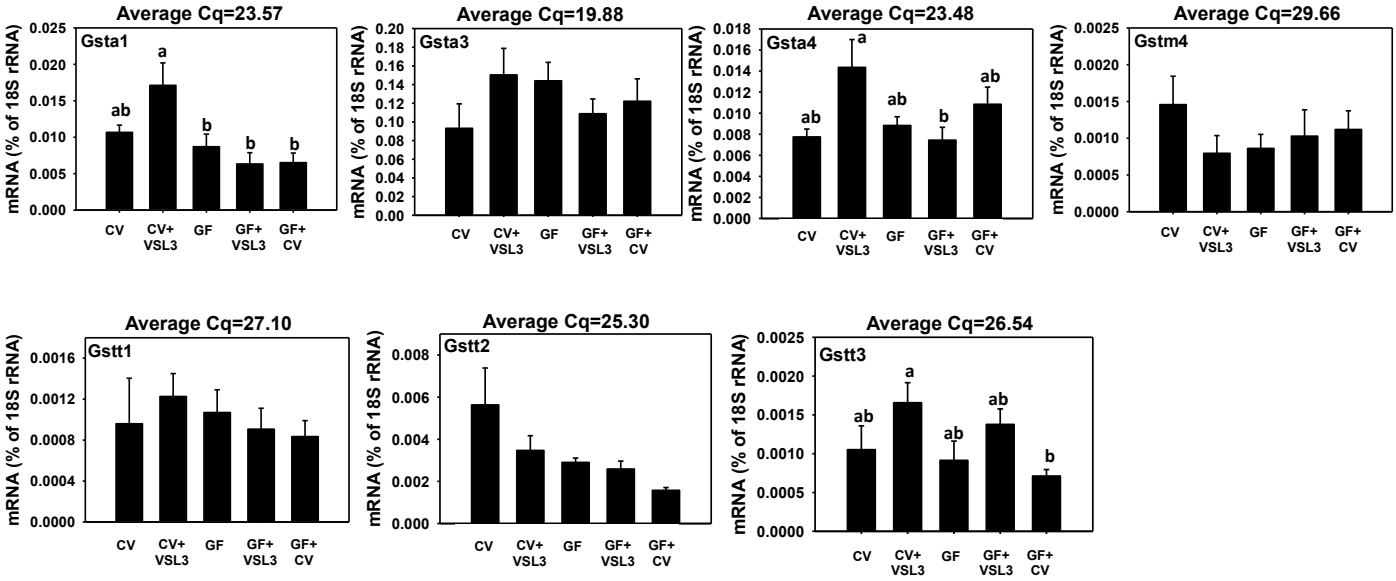
Average Cq=23.57
Gsta1
mRNA (% of 18S rRNA)
0.025
0.020
0.015
0.010
0.005
0.000
a
ab
b
b
b
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=19.88
Gsta3
mRNA (% of 18S rRNA)
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=23.48
Gsta4
mRNA (% of 18S rRNA)
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
a
ab
ab
b
ab
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=29.66
Gstm4
mRNA (% of 18S rRNA)
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=27.10
Gstt1
mRNA (% of 18S rRNA)
0.0016
0.0012
0.0008
0.0004
0.0000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=25.30
Gstt2
mRNA (% of 18S rRNA)
0.008
0.006
0.004
0.002
0.000
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV
Average Cq=26.54
Gstt3
mRNA (% of 18S rRNA)
0.0025
0.0020
0.0015
0.0010
0.0005
0.0000
ab
a
ab
ab
b
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV

Figure s6

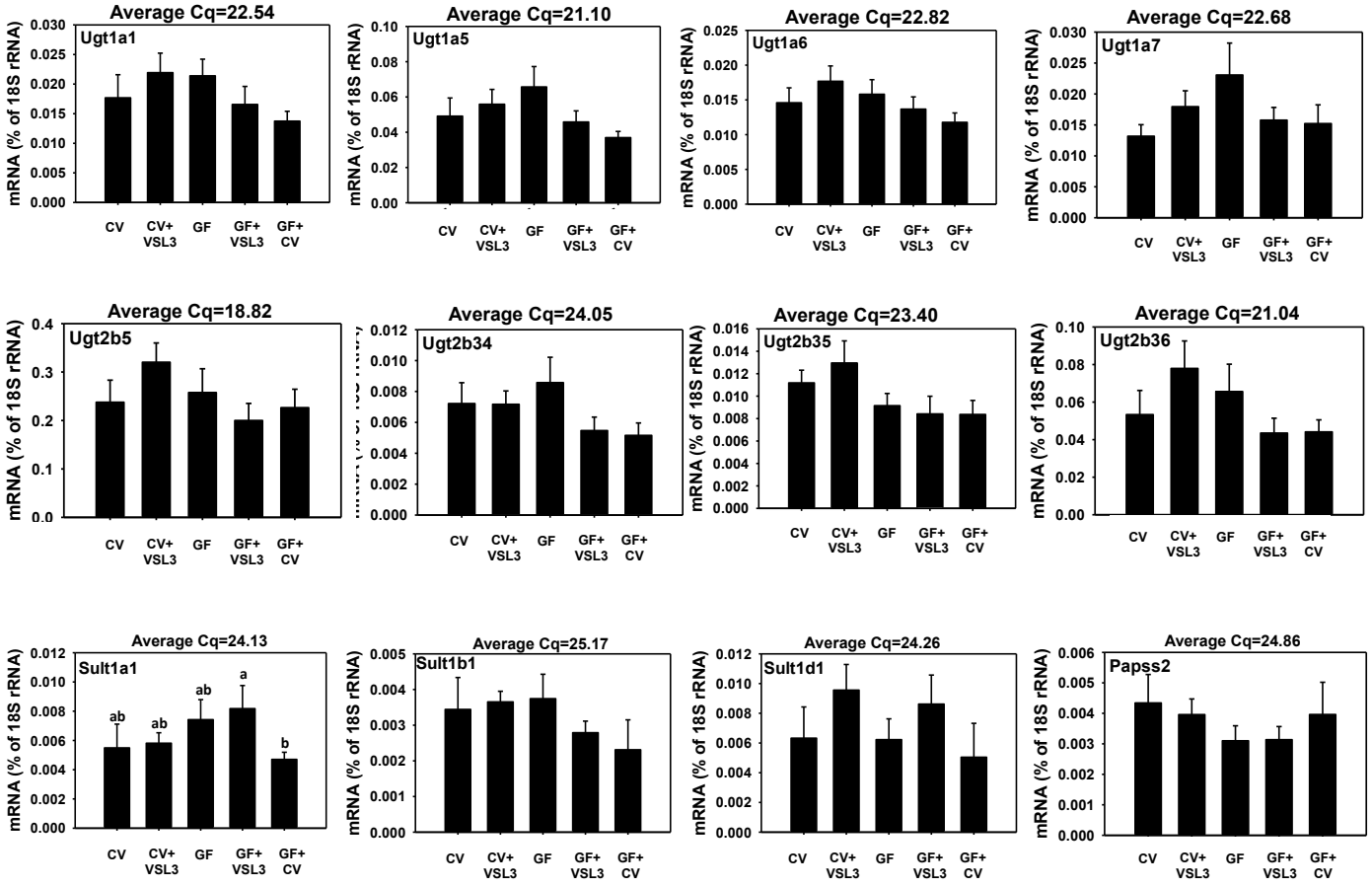
Average Cq=22.54
Ugt1a1
Average Cq=21.10
Ugt1a5
Average Cq=22.82
Ugt1a6
Average Cq=22.68
Ugt1a7
Average Cq=18.82
Ugt2b5
Average Cq=24.05
Ugt2b34
Average Cq=23.40
Ugt2b35
Average Cq=21.04
Ugt2b36
Average Cq=24.13
Sult1a1
ab
ab
ab
a
b
Average Cq=25.17
Sult1b1
Average Cq=24.26
Sult1d1
Average Cq=24.86
Papss2
mRNA (% of 18S rRNA)
CV
CV+ VSL3
GF
GF+ VSL3
GF+ CV

Figure s7

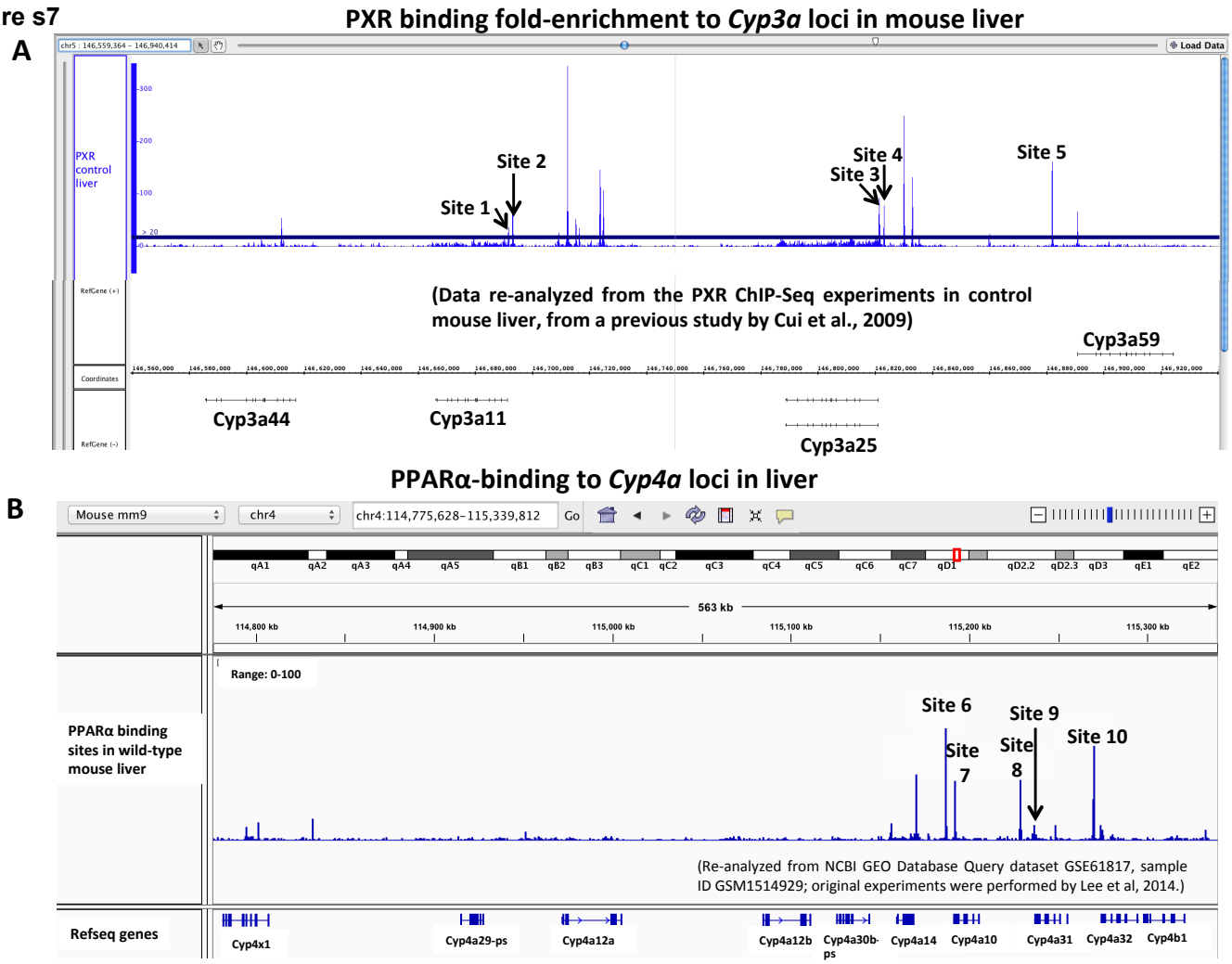
A
PXR binding fold-enrichment to *Cyp3a* loci in mouse liver
Load Data
PXR control liver
Site 1
Site 2
Site 3
Site 4
Site 5
(Data re-analyzed from the PXR ChIP-Seq experiments in control mouse liver, from a previous study by Cui et al., 2009)
Cyp3a59
Cyp3a44
Cyp3a11
Cyp3a25
B
PPARα-binding to *Cyp4a* loci in liver
Mouse mm9
chr4
chr4:114,775,628-115,339,812
Go
563 kb
Range: 0-100
PPARα binding sites in wild-type mouse liver
Site 6
Site 7
Site 8
Site 9
Site 10
(Re-analyzed from NCBI GEO Database Query dataset GSE61817, sample ID GSM1514929; original experiments were performed by Lee et al, 2014.)
Refseq genes
Cyp4x1
Cyp4a29-ps
Cyp4a12a
Cyp4a12b
Cyp4a30b-ps
Cyp4a14
Cyp4a10
Cyp4a31
Cyp4a32
Cyp4b1

Table s1. Primer Sequences and Specificity for the bacterial 16S rRNA quantification.

Bacterial 16S rRNA targeted	Primer sequences	Cross-reactivity
Universal bacteria	Forward: GTGSTGCAYGGYTGTCGTCA	Universal
	Reverse: ACGTCRTCCMCACCTTCCTC	
L. acidophilus	Forward: AGCGAGCTGAACCAACAGAT	***L. acidophilus*** NBRC13951, VPI6032, JCM1132, and BCRC10695 strains.
	Reverse: TGATCATGCGATCTGCTTTC	***L. acidophilus*** strains NCFM, NBRC 13951, VPI 6032, JCM 1132, and BCRC 10695; ***L. crispatus*** strains DSM 20584, ST1, NBRC 15019, ATCC 33820; ***L. helveticus*** strains DPC 4571, NBRC 15019, DSM 20075; ***L. gallinarum*** strainsATCC 33199, JCM 2011; ***L. ultunesis*** strains CCUG 48460, Kx146C1; ***L. kitasatonis*** strain JCM 1039.
L. plantanum	Forward: TTTGAGTGAGTGGCGAACTG	***L. plantarum*** strains CIP WCFS1, CIP 103151, NBRC 15891, JCM 1149, NRRL B-14768, subsp. argentoratensis strain DKO22, DSM 10667, JCM 1149; ***L. paraplantarum*** strain DSM 10667; ***L. mudanjiangensis*** strain 11050; ***L. fabifermentans*** strains DSM 21115, LMG 24284; ***L. xiangfangensis*** strain 3.1.1; ***L. pentosus*** strain 124-2.
	Reverse: CCAAAAGTGATAGCCGAAGC	***L. plantarum*** strains WCFS1, CIP 103151, NBRC 15891, JCM 1149, NRRL B-14768, subsp. argentoratensis strain DKO 22; ***L. paraplantarum*** strain DSM 10667; ***L. xiangfangensis*** strain 2.1.1; ***L. pentosus*** strain 124-2.
B. longum	Forward: TTTTGTGGAGGGTTCGATTC	***B. longum*** strains subsp. suis strain ATCC 227533, ATCC 15707; NCC2705 strain NCC2705; ***B. bifidum*** S17 strain S17; B. breve ACS-0710V Sch8b strain ACS-071-V-Sch8b; ***B. animalis*** subsp. Lactis AD011 strain AD011; ***B. adolescentis*** strain ATCC15703
	Reverse: GGAGCTATTCCGGTGTATGG	***B. longum*** strains subsp. Suis strain ATCC 27533, ATCC15070, NCC2705 strain NCC2705, KCTC3128, subsp. Infantis strain ATCC 15697; ***B. dentium*** strain B764, Bd1 strain Bd1, ***B. moukalabense*** strain GG01; ***B. stercoris*** strain Eg1; ***B. adolescentis*** strain ATCC15703; ***B. pseudocatenulatum*** strain B1279; ***B. catenulatum*** strain DSM 16992; ***B. ruminantium*** strain Ru 687; ***B. indicum*** strain JCM1302.
B. breve	Forward: CTGAGATACGGCCCAGACTC	Many including ***B. breve*** strains
	Reverse: ACAAAGTGCCTTGCTCCCTA	***B. breve*** strains DSM 20213 and ACS-071-V-Sch8b strain ACS-071-V-Sch8b
L. paracasei	Forward: CGAGATTCAACATGGAACGA	***L. paracasei*** strains ATCC334 strain ATCC 334, NBRC 15889, ATCC25302, subsp. Tolerans strain NBRC 15906, R094
	Reverse: AGCTTACGCCATCTTTCAGC	***L. paracasei*** strains NBRC 15889, ATCC 25302, subsp. Tolerans strain NBRC 15906, R094; ***L. rhamnosus*** GG strain GG (ATCC 53103), NBRC 3425, JCM 1136; ***L. casei*** ATCC 334 strain ATCC 334; ***L. saniviri*** strain YIT 12363; ***L. zeae*** strain RIA 482
L. bulgaricus	Forward: CAAGTTTGAAAGGCGGCGTA	***L. delbrueckii subsp. Bulgaricus*** strains ATCC 11842, NBRC 13953, ATCC 11842
	Reverse: TTGCTCCATCAGACTTGCGT	Many including ***L. delbruieckii subsp. Bulgaricus strains***

Table S2 RT-qPCR primer sequences

Gene Symbol	Forward	Reverse
18S	CGAACGTCTGCCCTATCAACTT	CCGGAATCGAACCCTGATT
Adh1	GTTGAGAGCGTTGGAGAAGG	TCGCTTCGGCTACAAAAGTT
Akr1b8	TCCTCTTTGCTGATGCACAC	GCAACAGTCTGTCCCTGGTT
Akr1c13	CCTTCCAGCAGAGTTCCTTG	ACTGTCCACACACAGGGACA
Akr1c19	TTGCCTACTGTGCTCTTGGA	CAATCTGAGCTGGACTTCGC
Akr1d1	GAGTGCCACCCGTATTTCAC	CAAGGGTGGAGAAGAGACGT
Aldh1a1	CTCTGTTCCCCAGGTGTTGT	CATGCAAGGGTGCCTTTATT
Aldh1a7	TGCTATTTGGCTGTCCCTGT	ACCATGTTCGCCCAGTTCTC
Aldh1b1	GAACGATCAGTGAAGGACGC	CAACTGTGTCCATTGCCCAA
Aldh3a1	CCCCTGGCACTCTATGTGTT	GTGGGCACAGTGATGTGAAC
Aldh3a2	CACCACCCAAAGTCTGTGTG	AAGATGCTCTGAGTGGCCTT
Aldh4a1	GGAAGGAGACAGCTCTGGTG	GGAGCTAGCACAGACCAAGG
Aldh7a1	TGAAGAAACCATCGGGAAAG	TTCCCCATCTCCAAAGACAC
Ces1e/1g	TTGCTGGCTGTAAAACCACC	CTTTGGCAGCAACACTCCAT
Ces2a	GTACTGGGCCAATTTCGCAA	GTCCTGAGAACCCTTGAGCT
Ces2c	AGGAATGGCTTCCATGTTTG	AGGTATCCCCAGTTGCCTCT (also recognizes Ces2a and Ces2h)
Ces3a	CACAGACCGCATGGTAATTG	TTGATGCTGGCATCTCTCAC
Cyp1a2	GACATGGCCTAACGTGCAG	GGTCAGAAAGCCGTGGTTG
Cyp2b10	AAGGAGAAGTCCAACCAGCA	CTCTGCAACATGGGGGTACT
Cyp3a11	ACAAACAAGCAGGGATGGAC	GGTAGAGGAGCACCAAGCTG
Cyp3a13	AAGTACTGGCCAGAGCCTGA	AATGCAGTTCCTTGGTCCAC
Cyp3a16	GTATGAAACCACCAGCAGCA	AGGTATTCCATCGCCATCAC
Cyp3a41a/b	AGCAGAAGCACCGAGTTGAT	GACTGGGCTGTGATCTCCAT
Cyp3a44	CTGAGCTTTCTCAGTGTCTGTGCA	CCCATGAGAAACGGTGAAGGCA
Cyp3a57	TCTATCCTCTTCATCGGGACCCCG	GGTTGCCTGCTGATCTTCACAGGG
Cyp3a59/25	AGTACTGGCCAGAGCCTCAA	TCGTTCTCCTTGCTGAACCT
Cyp4a10	CACACCCTGATCACCAACAG	TCCTTGATGCACATTGTGGT
Cyp4a12a/b	CTCATTCCTGCCCTTCTCAG	GGTATGGGGATTGGGACTCT
Cyp4a14	CTGGGTGATGGAACCTCTGT	CATCTGGGAAGGTGACAGGT
Cyp4a29	TGATGGGAGCAGCTTGTCTG	GGTCGGGATGTGTAGCCAAA
Cyp4a30b	GGTGATACTGGGGCGATCAG	GAGGGCAATCTTGGTCCACA
Cyp4a31	TGCAGGCAGCCTCTCTGGCT	GGGCGGTGATGGGAACTGCT
Cyp4a32	TCTGCTCTAAGCCCGACCCGA	GCAGCAGGAGCAGACCGAGC
Cyp4b1	CTGCATGGCCCTTTATCCTA	GAAGCACTCCTTCATGCACA
Cyp4f13	TATCTCACTGCTGATGGGCG	AGGAATTCAACACCCTGCGT
Cyp4f14	GTCACGTGGGCATGGTAACT	TCGGACGATGTCAGAATGGC
Cyp4f15	GACAGGGAACCAGCAGTTGT	ATCCTGCCTAGACACTTCCCT
Cyp4f16	GGCAGAGGCTGACACCTTTA	ATCTCCTCAGGCTCTCGGTC
Cyp4f17	TGATGACCTTGGACAGCTTG	AAGGTACAGGAAGGGCTGGT
Cyp4f18	GAGGAGATTGAATGGGACGA	GGGAGCACAATGTCCTGAGT
Cyp4f37	ACTGAAGCAGGCCAGACTTACCG	GGGGGCAACAAATGCAGGGTCA
Cyp4f39	GACTTCCGCATTACCTGTCG	AGAAAGGTCCAACCCATGCC
Cyp4f40	GGCTGTGAAGAGAAACGAGC	GGCATCGGTGAAGTCGTGTA
Cyp4v3	TCCGAGTTTTCCCATCTGTC	CGGTGTAGTGCGTAGGGAAT
Cyp4x1	TGGTCCAAGGAACTGCATCG	TGGTGAGGTCTGGAGCTACT
Cypy4f41-ps	AGAACTGAGTTATCAGGTTCAGC	GTCACCTGGAAGTCTGACCG
Ephx1	AGGCATCCAGCAAGAAAGGT	AGATGAGAGACCCCCAGTCG
Fmo1	AAACAAGCATAGCGGGTTTG	ATCCGGTTTTGCGTTGATAG
Fmo2	AATGGCAAAGAAGGTTGTGG	TCAGTCCTTTCGAAGCAGGT
Fmo3	GGGGGAAAAGTTCAAATGGT	CCTGGGATCCTTGAGAAACA
Fmo4	CGCCCAGACTTCTCTGAAAC	AAATGTGGGCTCAGGAATTG
Fmo5	ACAGGGCTCTGAGTCAGCAT	CCTGGAGCCATCCTCAAATA
Fmo6	ACTGAAAAGGAAGGCAAGCA	GTAGGCACTTGCCTCGAAAG
Fmo9	GAGGAGCGTGAGAAAACGTC	AAGGACTTGAGTGGCAGGTG
Gsta1	CGCCACCAAATATGACCTCT	TTGCCCAATCATTTCAGTCA
Gsta3	TACTTTGATGGCAGGGGAAG	GCACTTGCTGGAACATCAGA
Gsta4	TGATGATGATTGCCGTGGCT	ACGAGAAAAGCCTCTCCGTG
Gstm1	CTCCCGACTTTGACAGAAGC	TTGCTCTGGGTGATCTTGTG
Gstm2	ATGGTTTGCAGGGAACAAGGT	CTTCAGGCCCTCAAAGCGAC
Gstm3	AGAGGAGGAGAGGATCCGTG	GGGACTGCAGCAGACTATCAT
Gstm4	TATGACACTGGGTTACTGGGACATC	TCCACGCGAATCTTCTCTTCC
Gsto1	ATTGATGCCAAGACCTACCG	CAGTGAGGGGAAACAGCATT
Gstpi	TGGGCATCTGAAGCCTTTTG	GATCTGGTCACCCACGATGAA
Gstt1	CTTGCTCTACCTGGCACACA	CTTCTCCGAAGGCCCGTATG
Gstt2	GTACCAGGTGGCAGACCACT	GTTGCAGAACCAGGACCATT
Gstt3	TCCAGCTGCGTACCATAGAG	ACACTCTCTGCCAAGACGAA
Nqo1	TATCCTTCCGAGTCATCTCTAGCA	TCTGCAGCTTCCAGCTTCTTG
Papss2	ACCTTGGAGACCGAAGGTTT	TTCTTGGCAACAATGAACCA
Por	GGCAAGGAGCTGTACCTGAG	CGACGAGGCAATGGAATAGT
Sult1a1	GGATGTAGCTGAGGCAGAGG	CAGCTCCCAGTGGCATTTAT
Sult1b1	GGTGGGAAAAGAGGGAAGAG	AAGGCCTCTTCATCCAAGGT
Sult1d1	GCCGTCTCCTCGAATAGTGA	TTCCCACCAGCTCTTCACAT
Sult1e1	TCCGTATGGTTCCTGGTATGA	GTTGAACGATTCTGTCCACAAG
Sult2a1	ATTTGGAACCGCTCACCCTGGATA	GCCTGGGCCTTGGAACTGAAGAAA
Sult2b1	AAGGCATTCTTCAGCTCCAA	GAAGGAACTGGTCGGGTGTA
Sult3a1	GGACCTCAGAAGCTCAGTGC	TTTGCTCTTGGGTCAGCTTT
Sult5a1	CCAGTCCAAGATGGGTGACT	AGACCAGGGTTGTAGCATGG
Ugt1a1	CACCTGAAGCCTCAATACCAT	CAGTCCGTCCAAGTTCCACC
Ugt1a5	ACACCGGAACTAGACCATCG	ATACCATGGGAGCCAGAGTG
Ugt1a6	ATACCATGGGAGCCAGAGTG	ACCAGAACTGTGAGGGTTGG
Ugt1a7	TCTCAACCTGCCCTCTGTCT	GTGGGCTGAGAATTTGGTGT
Ugt1a9	CTGGTTCAGCCAGAGGTTTC	TTGGCGACAATTAATCCACA
Ugt2a3	CCCAGAAGGTTTTGTGGAGA	CCACCATGTGTGATGAAAGC
Ugt2b1	CTACAAGTGGATCCCCCAGA	AGGAATGCCATGGTAGATCG
Ugt2b34	AGCTGCCAAAGCAGTCATTT	GCCAGGATCACATCAAACCT
Ugt2b35	GCTCAACTGCTCCAGATTCC	GGCCACCTAATCCTGACAAA
Ugt2b36	TGTGGGAAGGTGTTGGTATGG	TCCACAGCCTTTGCAAAAATAA
Ugt2b36/37/38	GTGGGGCCAACAGTGTCTAT	GTAACAGCTGCTCCTTTGGC
Ugt2b5	ATGTTGGAGGACTCCATTGC	TTGCGTTGGCTTTTTCTTCT

Table s3. ChIP-qPCR primers, targeted genomic regions and motifs.

Targeted genomic regions	qPCR primer sequences	Antibody used	Motifs
Site 1. Cyp3a11, upstream	Forward: CCAGGGATCAAGCCAGTAGATG Reverse: CACAGAATGTTAGCTCAAAGTA	PXR	DR-3 DR-4
Site 2. Cyp3a11, upstream	Forward: CATCTACCCTGCAATGTTGTGAG Reverse: TAGAACAACATGGTCTCTTGGAT	PXR	DR-3
Site 3. Cyp3a25, upstream	Forward: GCCACTTGCACAATGCTCG Reverse: TAGTGCCAATAGATGGATTTGAGC	PXR	ER-6
Site 4. Cyp3a25, upstream	Forward: TGGCCCGGGTTAAACATCAA Reverse: TCAGACCACATGTCTACCCCT	PXR	DR-3
Site 5, Cyp3a59	Forward: AGCGTTGGTGTTGTCCCTAGTG Reverse: AACAGAGAACTGGACTGACCAC	PXR	DR-4 ER-6
Site 6. Cyp4a10, upstream	Forward: GGGTGACAAATGGGTTCTTGGATA Reverse: AGCAAAGGGCAATGGAATAACT	PPARα	DR-1
Site 7. Cyp4a10, in gene	Forward: TTCTTAGAAAGACATGGGTATGCCA Reverse: TCTGAGAGTCCTGTTGGATGG	PPARα	DR-2
Site 8. Cyp4a31	Forward: CCACGCACTTGCATGTATTCTGA Reverse: TCGAGGTGTGGAAAAGACACAC	PPARα	DR-2
Site 9. Cyp4a31, in gene	Forward: AGTCCACTACCTTATCTTTCCTTCA Reverse: TTATGCTCACCTGATCGCCC	PPARα	DR-1
Site 10. Cyp4a32, upstream	Forward: TGTTCCTTCATTTTAGGGGTGA Reverse: TGCACATTGTACTCTTCTCCTC	PPARα	DR-1
Cyp3a11 promoter	Forward: TCCTCCTCAATGCTTCCCTC Reverse: GGTCAAGTTGGGCTGTGGAT	RNA-Pol-II	TATA box
Cyp3a25 promoter	*Forward: GGGGATGAGCTCCATCTTAGC Reverse: ACACCAGACCTACAAGTTCGAG *Also recognizes Cyp3a57/59 genes	RNA-Pol-II	TATA box
Cyp3a59 promoter	Forward: ACAAATGCCAGGTGGAGAGG *Reverse: TTCAGGCCTCCAAGTTTCCC *Also recognizes *Cyp3a25/57* genes	RNA-Pol-II	TATA box
Cyp4a14 promoter	Forward: TCACTAAATGTTTAGAAACCCGC Reverse: CATTCCCCCTCCCACAAGTAG	RNA-Pol-II	TATA box
Cyp4a32 promoter	Forward: AGCTCTCACAAGTCCAAGACA Reverse: ATCTACTGTTAGTCTACCAAGGC	RNA-Pol-II	TATA box

Supplemental Figure and Table Legends:

Figure s1. The 16S rRNA abundance of universal bacteria, as well as the 8 bacterial components in VSL3, namely *B. breve, B. infantis, B. longum, L. acidophilus, L. bulgaricus, L. plantarum, L. paracasei*, and *S. thermophilus*, in the VSL3 DNA. DNA from VSL3 was extracted as described in MATERIALS AND METHODS, and was loaded in each well of the qPCR reactions at 1ng, 3ng, 10ng, and 30ng. Results are expressed as delta-delta cycle value (calculated as 2^[-(Cq - average reference Cq)] of the quantitative PCR (ddCq) as compared to the universal bacteria.

Figure s2. The mRNA expression of the Cyp4f gene cluster (namely Cyp4f17, 4f16, 4f37, 4f15, 4f14, 4f13, 4f39, and 4f41-ps) in liver samples from CV, CV+VSL3, GF, GF+VSL3, and GF+CV groups. The genomic locations of the Cyp4f genes are displayed using the Integrated Genome Viewer (IGV). RT-qPCR for each gene was performed as described in MATERIALS AND METHODS. Data are expressed as % of the housekeeping gene 18S rRNA. Statistical analysis was performed using ANOVA followed by Duncan's Post Hoc Test with $p<0.05$ considered statistically significant. Treatment-groups that are not statistically different are labeled with the same letter.

Figure s3. The mRNA expression of other phase-I enzymes, namely Cyp2b10, Cyp3a13, Aldh1a7, Aldh4a1, Aldh7a1, Ces2c, and Ces3a, in liver samples from CV, CV+VSL3, GF, GF+VSL3, and GF+CV groups. RT-qPCR for each gene was performed as described in MATERIALS AND METHODS. Data are expressed as % of the housekeeping gene 18S rRNA. Statistical analysis was performed using ANOVA followed by the Duncan's Post Hoc Test with $p<0.05$ considered statistically significant. Treatment-groups that are not statistically different are labeled with the same letter.

Figure s4. The mRNA expression of other phase-I enzymes, namely Fmo1, Fmo2, Fmo4, Akr1b8, Akr1c13, Akr1c19, Akr1d1, Ephx1, and Nqo1, in liver samples from CV, CV+VSL3, GF, GF+VSL3, and GF+CV groups. RT-qPCR for each gene was performed as described in MATERIALS AND METHODS. Data are expressed as % of the housekeeping gene 18S rRNA. Statistical analysis was performed using ANOVA followed by the Duncan's Post Hoc Test with $p<0.05$ considered statistically significant. Treatment-groups that are not statistically different are labeled with the same letter.

Figure s5. The mRNA expression of other phase-II Gst enzymes, namely Gsta1, Gsta3, Gsta4, Gstm4, Gstt1, Gstt2, and Gstt3, in liver samples from CV, CV+VSL3, GF, GF+VSL3, and GF+CV groups. RT-qPCR for each gene was performed as described in MATERIALS AND METHODS. Data are expressed as % of the housekeeping gene 18S rRNA. Statistical analysis was performed using ANOVA followed by the Duncan's Post Hoc Test with $p<0.05$ considered statistically significant. Treatment-groups that are not statistically different are labeled with the same letter.

Figure s6. The mRNA expression of other phase-II Ugt and Sult enzymes, namely Ugt1a1, Ugt1a5, Ugt1a6, Ugt1a7, Ugt2b5, Ugt2b34, Ugt2b35, Ugt2b36, Sult1a1, Sult1b1, Sult1d1, and Papss2 (enzyme that produces the co-substrate for sulfation reactions), in liver samples from CV, CV+VSL3, GF, GF+VSL3, and GF+CV groups. RT-qPCR for each gene was performed as described in MATERIALS AND METHODS. Data are expressed as % of the housekeeping gene 18S rRNA. Statistical analysis was performed using ANOVA followed by the Duncan's Post Hoc Test with $p<0.05$ considered statistically significant. Treatment-groups that are not statistically different are labeled with the same letter.

Figure s7. Genomic locations of positive PXR (A) and PPARα (B) DNA binding sites to the *Cyp3a* (A) and *Cyp4a* (B) gene clusters, respectively. These binding sites were re-analyzed based on previously published ChIP-Seq experiments (Cui et al., 2010; Lee et al., 2014).

Table s1. Primer Sequences and Specificity for the bacterial 16S rRNA quantification.

Table s2: RT-qPCR primer sequences.

Table s3. ChIP-qPCR primers, targeted genomic regions and motifs.