

Supplementary Table 1. Primer and probe sequences used for determination of targeted mRNA levels

Species	Target mRNA	Forward Primer	Reverse Primer	Probe	Product size
Rat	CYP2B1/2	GCTCAAGTACCCCCATGTGCG	ATCAGTGTATGGCATTTACTGCGG	Not used	109bp
	CYP3A1	AGTCGTCCCTGGTGCCTCTAC	CCCAGGAATCCCTGTTCT	ATTGGGACCCGCACACATGGACT	73bp
	Ki-67	GCAGACAAGCCTTCAGCAGTAA	TGGTACCATTGTCATCAATTCTAGT	CCAACATCAAGGCAAAGTGTGCGATC	94bp
	PCNA	ACGTCTCCTTAGTGCAGCTTACTCT	CGCCCATGGCCAGGTT	AAGGCTTCGACACATACCGCTGCG	78bp
	GADD45β	CGGCCAAACTGATGAATGTG	CATCCTCCTCTTCTCGTCTATGG	CCCCGACAGCGTGGTCTTGTGC	75bp
	MDM2	TCCGACCACCGTGTCTCT	TCGGTAGACACAGACATGTTGGTA	CGCGCCTCCAGGCCAATGTG	69bp
	GAPDH	GCTGCCTCTTGACAAAGT	CTCAGCCTGACTGTGCCATT	TGTTCCAGTATGATTCTACCCACGGCAAG	129bp
Mouse	Cyp2b10	CAGGTGATCGGCTCACACC	TGACTGCATCTGAGTATGGCATT	Not used	70bp
	Cyp3a11	CCACCAGTAGCACACTTTCC	TTCCATCTCCATCACAGTATCA	CTCTGCCAACAAAGGCACCTCC	137bp
	Ki-67	GTGACAGTGGACAATCTGCAAA	CGTGAGGTTACTGAAGTGTCTGTTG	CTGCCCAGCTCGTCTCCACCACTAGA	77bp
	Pcna	CACGTCTCCTGGTACAGCTTACTC	CACGCCATGGCTAGGTT	AAGGCTTCGACACATACCGCTGCG	81bp
	Gadd45β	TCGCTCTGAGATTCACTTC	CCGGACGATGTCATGTCTT	CCTGATCCAGTCGTTCTGCTGCGA	68bp
	Mdm2	CGGATCACCCGCTTCT	AGCACCCCTGGTAGACACAGA	CTCCAGGCCAATGTGCAATACCAACA	75bp
	Gapdh	TGTGTCGTCGTGGATCTGA	CCTGCTTACCCACCTCTTGA	CCGCCTGGAGAACCTGCCAAGTATG	77bp
Human	CYP2B6	TTTTCTACCAAGACTTTCACTCATC	GGAAAGTATTCAAGAACGCCAGAGA	TCTGTATTGGCCAGCTGTTGAGCTC	83bp
	CYP3A4	TGCAGGAGGAAATTGATGCA	GTCAGAGATACTCCATCTGAGCACAGT	TTTACCCAATAAGGCACCACCCACCTATG	80bp
	Ki-67	CTCCCTTAAGACGGCAGTGTATTAG	GAAGGCTCTGTCAGTATCTGAAGTT	AGCAAAACGCCAGGAACACCTACAA	115bp
	PCNA	AAGCCGAAACCCAGCTAGACTTC	TGGCGGAGTGGCAACAA	CCCGCCTGCCTGTAGCGGC	66bp
	GADD45β	ACATGCCCTGCAAATCC	GCACGATGTTGATGTCGTTGT	CTTCACGCTCATCCAGTCCTCTGCTG	69bp
	MDM2	TCCCTCTCAAGCTCCGTGTTG	TCATGATGTTGTCAGGGTAGATG	TCAGTGGAGGCCATCGAGCTC	99bp
	GAPDH	GACACCCACTCCACCTT	CATACCAGGAAATGAGCTTGACAA	CTGGCATTGCCCTCAACGACCA	79bp
Rat, mouse and human	CAR	CTGACTTGTGAGGGCTGCAA	TGTCTTCCTCATGCCARCA	Not used	163bp
	18s	Unknown ^a	Unknown ^a	Unknown ^a	Unknown ^a

^a: Eukaryotic 18S rRNA Endogenous Control (VIC®/TAMRA™ probe, primer limited) (Applied Biosystems®) was used.

Supplementary Table 2. Mortality, body weight, total bodyweight gain, and food consumption in animals treated with NaPB for 7 days

	Wistar Hannover rats (n)	CD-1 mice (n)	Chimeric mice (n)	SCID mice (n)
<i>Mortality (number of death)</i>				
NaPB 0 ppm	0 (8)	0 (8)	1 (10)	0 (5)
NaPB 500ppm	0 (8)	0 (8)	0 (5)	ND
NaPB 1000ppm	0 (8)	0 (8)	0 (5)	ND
NaPB 1500ppm	0 (8)	0 (8)	3 (5)	0 (5)
NaPB 2500ppm	0 (8)	1 (8)	#	ND
<i>Body weight at commencement of treatment (g)</i>				
NaPB 0 ppm	296 ± 8.0 (8)	39.4 ± 1.7 (8)	22.5 ± 1.2 (9)	26.3 ± 0.5 (5)
NaPB 500ppm	298 ± 7.9 (8)	39.9 ± 1.4 (8)	23.7 ± 1.6 (5)	ND
NaPB 1000ppm	297 ± 6.7 (8)	39.2 ± 1.1 (8)	23.8 ± 1.5 (5)	ND
NaPB 1500ppm	297 ± 8.2 (8)	39.7 ± 1.6 (8)	22.8 (22.2, 23.3) (2)	26.5 ± 0.9 (5)
NaPB 2500ppm	298 ± 7.5 (8)	40.4 ± 1.6 (8)	#	ND
<i>Body weight at termination of treatment (g)</i>				
NaPB 0 ppm	331 ± 9.7 (8)	42.3 ± 1.1 (8)	21.5 ± 1.8 (9)	28.2 ± 0.4 (5)
NaPB 500ppm	336 ± 11.4 (8)	43.7 ± 2.1 (8)	24.2 ± 2.7 (5)	ND
NaPB 1000ppm	335 ± 11.2 (8)	44.6 ± 1.7 * (8)	24.4 ± 2.0 (5)	ND
NaPB 1500ppm	328 ± 11.4 (8)	43.2 ± 1.8 (8)	22.5 (20.2, 24.8) (2)	27.2 ± 1.3 (5)
NaPB 2500ppm	311 ± 10.3 ** (8)	39.9 ± 4.5 (7)	#	ND
<i>Total body weight gain (g)</i>				
NaPB 0 ppm	33 ± 4.9 (8)	3.0 ± 1.6 (8)	-1.0 ± 1.3 (9)	1.9 ± 0.4 (5)
NaPB 500ppm	31 ± 3.5 (8)	3.8 ± 1.2 (8)	0.5 ± 1.3 (5)	ND
NaPB 1000ppm	30 ± 5.9 (8)	5.4 ± 1.1 * (8)	0.6 ± 0.7 (5)	ND
NaPB 1500ppm	29 ± 6.4 (8)	3.5 ± 1.0 (8)	-0.3 (-2.0, 1.5) (2)	0.8 ± 0.7 * (5)
NaPB 2500ppm	12 ± 8.6 ** (8)	-0.3 ± 4.3 (7)	#	ND
<i>Food consumption at termination of treatment (g/animal/day, "n" means number of cages examined)</i>				
NaPB 0 ppm	19 ± 1.3 (4)	5.4 ± 0.4 (8)	3.5 ± 0.9 (9)	4.2 ± 0.7 (5)
NaPB 500ppm	19 ± 1.5 (4)	5.2 ± 0.5 (8)	3.0 ± 2.1 (5)	ND
NaPB 1000ppm	19 ± 1.0 (4)	5.3 ± 0.5 (8)	4.6 ± 0.7 (5)	ND
NaPB 1500ppm	18 ± 0.8 (4)	5.0 ± 0.5 (8)	4.1 (2.9, 5.2) (2)	4.4 ± 0.3 (5)
NaPB 2500ppm	15 ± 1.0 ** (4)	4.7 ± 1.0 (6)	#	ND

Results are presented as mean±SD.

means "not determined" due to high mortality in dose setting study.

ND means "not determined" due to focusing on the highest dose level in chimeric mouse study.

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 3. Overall NaPB intake during 7-day treatment and plasma NaPB concentration in animals treated with NaPB for 7 days

	Wistar Hannover (n)	CD-1 mice (n)	Chimeric mice (n)		SCID mouse (n)
<i>Overall NaPB intake (mg/kgBW/day, "n" means number of cages examined)</i>					
NaPB 500ppm	30.3 (4)	58.5 (8)	68.5 (5)	ND	
NaPB 1000ppm	59.1 (4)	121.2 (8)	154.1 (5)	ND	
NaPB 1500ppm	85.1 (4)	175.5 (8)	229.1 (203, 255) (2)	219.1 (5)	
NaPB 2500ppm	120.0 (4)	252.7 (6)	#	ND	
<i>Plasma NaPB concentration (μg/mL, "n" means number of animals examined)</i>					
NaPB 500ppm	8.0 ± 1.7 (8)	12.2 ± 4.1 (8)	27.3 ± 7.3 (5)	ND	
NaPB 1000ppm	19.6 ± 2.9 (8)	29.6 ± 9.0 (8)	75.2 ± 46.9 (5)	ND	
NaPB 1500ppm	35.1 ± 9.3 (7)	43.0 ± 12.4 (8)	116.2 (86, 146) (2)	42.7 ± 10.2 (5)	
NaPB 2500ppm	61.1 ± 14.4 (8)	70.2 ± 48.7 (7)	#	ND	
<i>Serum concentration per chemical intake</i>					
NaPB 500ppm	0.26	0.21	0.40	ND	
NaPB 1000ppm	0.33	0.24	0.49	ND	
NaPB 1500ppm	0.41	0.25	0.51	0.19	
NaPB 2500ppm	0.51	0.28	#	ND	

Overall NaPB intake are presented as cage mean value throughout treatment, and serum concentrations of NaPB are presented as mean±SD.

means "not determined" due to high mortality in dose setting study.

ND means "not determined" due to focusing on the highest dose level in chimeric mouse study.

Supplementary Table 4. Liver weight and CYP2B/3A induction in animals treated with NaPB for 7 days

	Wistar Hannover rats		CD-1 mice		Chimeric mice		SCID mice		
	(n)	Fold	(n)	Fold	(n)	Fold	(n)	Fold	
<i>Absolute liver weight (g)</i>									
NaPB 0 ppm	11.5 ± 0.8	(8)	1.0	2.3 ± 0.2	(8)	1.0	3.2 ± 0.4	(9)	1.0
NaPB 500ppm	13.2 ± 0.7	** (8)	1.1	2.8 ± 0.2	** (8)	1.2	3.8 ± 0.5	*	(5) 1.2
NaPB 1000ppm	13.9 ± 1.0	** (8)	1.2	3.3 ± 0.3	** (8)	1.5	3.9 ± 0.4	*	(5) 1.2
NaPB 1500ppm	13.9 ± 1.0	** (8)	1.2	3.4 ± 0.4	** (8)	1.5	3.8 (3.5, 4.1)	(2)	1.2
NaPB 2500ppm	14.1 ± 1.1	** (8)	1.2	3.6 ± 1.0	*	(7) 1.6	#		ND
<i>Relative liver weight (g/BW x 100)</i>									
NaPB 0 ppm	3.5 ± 0.2	(8)	1.0	5.3 ± 0.4	(8)	1.0	15.0 ± 1.3	(9)	1.0
NaPB 500ppm	3.9 ± 0.1	** (8)	1.1	6.4 ± 0.2	** (8)	1.2	15.9 ± 2.1	(5)	1.1
NaPB 1000ppm	4.1 ± 0.2	** (8)	1.2	7.4 ± 0.5	** (8)	1.4	16.0 ± 1.2	(5)	1.1
NaPB 1500ppm	4.2 ± 0.2	** (8)	1.2	7.8 ± 0.7	** (8)	1.5	17.0 (17.4, 16.7)	(2)	1.1
NaPB 2500ppm	4.5 ± 0.2	** (8)	1.3	8.9 ± 1.7	** (7)	1.7	#		ND
<i>Activity of 7-pentoxyresorufin O-deethylase (pmol/min/mg S9 protein)</i>									
NaPB 0 ppm	4 ± 0.6	(6)	1.0	9 ± 1.1	(6)	1.0	9 ± 4.2	(9)	1.0
NaPB 500ppm	87 ± 10.2	** (6)	21.8	40 ± 2.7	** (6)	4.4	61 ± 36.0	** (5)	6.8
NaPB 1000ppm	108 ± 16.5	** (6)	27.0	49 ± 5.1	** (6)	5.4	123 ± 69.7	** (5)	13.7
NaPB 1500ppm	94 ± 29.7	** (6)	23.5	58 ± 3.8	** (6)	6.4	128 (50, 206)	(2)	14.2
NaPB 2500ppm	79 ± 8.6	** (6)	19.8	58 ± 7.3	** (6)	6.4	#		ND
<i>CYP2B mRNA expression level (relative expression of GAPDH mRNA)</i>									
CYP2B1/2		Cyp2b10		CYP2B6		Cyp2b10			
NaPB 0 ppm	100 ± 20	(6)	1.0	100 ± 113	(6)	1.0	100 ± 32	(9)	1.0
NaPB 500ppm	17158 ± 4532	*	(6) 172	4336 ± 734	*	(6) 43	685 ± 197	** (5)	6.9
NaPB 1000ppm	21769 ± 3947	*	(6) 218	5874 ± 780	*	(6) 59	744 ± 193	** (5)	7.4
NaPB 1500ppm	22474 ± 5092	*	(6) 225	6071 ± 652	*	(6) 61	1134 (770, 1498)	(2)	11.3
NaPB 2500ppm	25055 ± 4422	*	(6) 251	6220 ± 3121	*	(6) 62	#		ND
<i>CYP3A mRNA expression level (relative expression of GAPDH mRNA)</i>									
CYP3A1		Cyp3a11		CYP3A4		Cyp3a11			
NaPB 0 ppm	100 ± 19	(6)	1.0	100 ± 20	(6)	1.0	100 ± 34	(9)	1.0
NaPB 500ppm	385 ± 117	*	(6) 3.9	156 ± 26	*	(6) 1.6	281 ± 57	** (5)	2.8
NaPB 1000ppm	728 ± 273	*	(6) 7.3	198 ± 15	*	(6) 2.0	356 ± 68	** (5)	3.6
NaPB 1500ppm	782 ± 139	*	(6) 7.8	214 ± 36	*	(6) 2.1	518 (360, 677)	(2)	5.2
NaPB 2500ppm	1368 ± 325	*	(6) 13.7	229 ± 66	*	(6) 2.3	#		ND

Results are presented as mean \pm SD.

means "not determined" due to high mortality in dose setting study.

ND means "not determined" due to focusing on the highest dose level in chimeric mouse study.

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 5. Summary of microscopic findings of liver in animals treated with NaPB for 7 days.

Wistar Hannover rats

Organs, Tissues Findings	Grade	NaPB				
		Control (8)	500ppm (8)	1000ppm (8)	1500ppm (8)	2500ppm (8)
Liver		(8)	(8)	(8)	(8)	(8)
Within normal limits		[4]	[0]	[0]	[0]	[0]
Cell infiltration, mononuclear cell		[4]	[8]*	[7]	[6]	[8]*
	+-	4	8	7	6	8
Hypertrophy, hepatocyte, centrilobular		[0]	[8]**	[6]**	[8]**	[8]**
	+-	0	1	4	5	4
	+	0	7	2	3	4
Necrosis, focal		[0]	[0]	[0]	[0]	[6]**
	+-	0	0	0	0	4
	+	0	0	0	0	2
Yellowish-brown pigment, hepatocyte, perilobular		[0]	[0]	[1]	[1]	[0]
	+-	0	0	1	1	0

+-:Slight, +:Mild, 2+:Moderate, 3+:Severe

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 5. Summary of microscopic findings of liver in animals treated with NaPB for 7 days.**CD-1 mice**

Organs, Tissues Findings	Grade	NaPB				
		Control (7)	500ppm (8)	1000ppm (8)	1500ppm (7)	2500ppm (7)
Liver		(7)	(8)	(8)	(7)	(7)
Within normal limits		[3]	[0]	[0]	[0]	[0]
Cell infiltration, mononuclear cell		[4]	[5]	[5]	[7]	[5]
	+-	4	5	5	7	5
Hypertrophy, hepatocyte, centrilobular		[0]	[8]**	[8]**	[7]**	[7]**
	+	0	2	1	0	1
	2+	0	5	4	2	3
	3+	0	1	3	5	3
Increased, mitosis		[0]	[4]*	[8]**	[7]**	[5]**
	+-	0	4	8	7	5
Necrosis, focal		[0]	[2]	[1]	[2]	[2]
	+-	0	2	1	0	0
	+	0	0	0	2	2
Necrosis, single cell		[1]	[4]	[6]*	[6]*	[5]*
	+-	1	4	6	6	5

+-:Slight, +:Mild, 2+:Moderate, 3+:Severe

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 5. Summary of microscopic findings of liver in animals treated with NaPB for 7 days.**Chimeric mice with human hepatocytes**

Organs, Tissues Findings	Grade	NaPB			
		Control (9)	500ppm (5)	1000ppm (5)	1500ppm (2)
Liver		(9)	(5)	(5)	(2)
Within normal limits		[3]	[0]	[2]	[0]
Cell infiltration, mononuclear cell		[1]	[0]	[0]	[0]
	+-	1	0	0	0
Glicogen, Decreased		[0]	[3]*	[3]*	[0]
	+-	0	2	3	0
	+	0	1	0	0
Hypertrophy, hepatocyte		[0]	[1]	[1]	[2]
	+-	0	1	1	2
Steatosis		[5]	[3]	[0]	[0]
	+-	3	1	0	0
	+	1	1	0	0
	2+	1	1	0	0

+-:Slight, +:Mild, 2+:Moderate, 3+:Severe

NaPB 2500 ppm in chimeric mice was not determined due to high mortality in dose setting study.

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 5. Summary of microscopic findings of liver in animals treated with NaPB for 7 days.

SCID mice

Organs, Tissues Findings	Grade	Control	1500ppm
		(5)	(5)
Liver		(5)	(5)
Within normal limits		[3]	[0]
Cell infiltration, mononuclear cell		[1]	[2]
	+-	1	2
Hypertrophy, hepatocyte, centrilobular		[0]	[5]**
	+	0	0
	2+	0	4
	3+	0	1
Increased, mitosis		[0]	[1]
	+-	0	1
Necrosis, focal		[1]	[2]
	+-	1	2

+-:Slight, +:Mild, 2+:Moderate, 3+:Severe

Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 6. Replicative DNA synthesis and mRNA expression levels of selected cell proliferation-related genes in hepatocytes from animals treated with NaPB for 7 days

Wistar Hannover rats			CD-1 mice			Chimeric mice			SCID mice			
	(n)	Fold		(n)	Fold		(n)	Fold		(n)	Fold	
<i>BrdU labeling index (%)</i>												
NaPB 0 ppm	1.4	± 0.92	(8)	1.0		1.7	± 1.32	(7)	1.0	3.9	± 2.79	
NaPB 500ppm	5.4	± 1.99	** (8)	3.9		9.9	± 5.29	** (8)	5.7	7.2	± 5.41	
NaPB 1000ppm	6.4	± 1.04	** (8)	4.6		21.8	± 6.10	** (8)	12.5	5.0	± 2.51	
NaPB 1500ppm	6.5	± 1.83	** (8)	4.7		31.1	± 7.55	** (7)	17.9	5.5 (2.3, 8.6)	(2)	
NaPB 2500ppm	6.1	± 2.85	** (8)	4.4		29.9	± 10.92	** (7)	17.2	#		
											ND	
<i>Ki67 mRNA expression level (relative expression of Gapdh mRNA)</i>												
NaPB 0 ppm	100	± 23	(6)	1.0		100	± 53	(6)	1.0	100	± 64	
NaPB 500ppm	133	± 26	(6)	1.3		227	± 114	(6)	2.3	25	± 16	
NaPB 1000ppm	148	± 36	(6)	1.5		312	± 109	*	(6)	3.1	38	± 29
NaPB 1500ppm	145	± 20	(6)	1.5		285	± 123	(6)	2.9	81 (57,104)	(2)	
NaPB 2500ppm	212	± 59	** (6)	2.1		271	± 204	(6)	2.7	#		
											ND	
<i>PCNA mRNA expression level (relative expression of Gapdh mRNA)</i>												
NaPB 0 ppm	100	± 19	(6)	1.0		100	± 7	(6)	1.0	100	± 31	
NaPB 500ppm	109	± 13	(6)	1.1		105	± 12	(6)	1.1	65	± 17	
NaPB 1000ppm	121	± 18	(6)	1.2		144	± 19	** (6)	1.4	71	± 14	
NaPB 1500ppm	120	± 12	(6)	1.2		122	± 20	(6)	1.2	93 (84,102)	(2)	
NaPB 2500ppm	137	± 15	** (6)	1.4		111	± 28	(6)	1.1	#		
											ND	
<i>Gadd45b mRNA expression level (relative expression of Gapdh mRNA)</i>												
NaPB 0 ppm	100	± 24	(6)	1.0		100	± 28	(6)	1.0	100	± 23	
NaPB 500ppm	431	± 106	*	4.3		464	± 210	*	(6)	4.6	90	± 71
NaPB 1000ppm	672	± 407	*	6.7		933	± 235	*	(6)	9.3	58	± 24
NaPB 1500ppm	885	± 303	*	8.9		1765	± 366	*	(6)	17.6	71 (79,63)	(2)
NaPB 2500ppm	943	± 219	*	(6)	9.4	2860	± 1820	*	(6)	28.6	#	
											ND	
<i>Mdm2 mRNA expression level (relative expression of Gapdh mRNA)</i>												
NaPB 0 ppm	100	± 27	(6)	1.0		100	± 12	(6)	1.0	100	± 20	
NaPB 500ppm	121	± 17	(6)	1.2		93	± 11	(6)	0.9	94	± 21	
NaPB 1000ppm	145	± 18	** (6)	1.4		106	± 15	(6)	1.1	90	± 24	
NaPB 1500ppm	159	± 21	** (6)	1.6		109	± 14	(6)	1.1	66 (49,83)	(2)	
NaPB 2500ppm	174	± 22	** (6)	1.7		98	± 20	(6)	1.0	#		
											ND	

Results are presented as mean±SD.

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Values significantly different from control (0 ppm) are: *p<0.05 and **p<0.01.

Supplementary Table 7-1. Levels of liver metabolites in animals treated with NaPB for 7 days.

#	Metabolites	Wistar Hannover rats treated with 2500 ppm NaPB		CD-1 mice treated with 2500 ppm NaPB		Chimeric mice treated with 1000 ppm NaPB	
		Fold change	p value	Fold change	p value	Fold change	p value
1	pyruvic acid ‡	0.67	0.04*	1.04	0.91	0.78	0.44
2	lactic acid ‡	0.81	0.08	1.10	0.61	0.79	0.34
3	glycolic acid	2.29	0.00*	1.91	0.18	5.00	0.03*
4	alanine ‡	1.35	0.02*	1.21	0.10	0.95	0.94
5	hydroxylamine	1.09	0.11	1.03	0.61	0.97	0.50
6	sarcosine ‡	1.63	0.35	1<	0.36	N.D.	-
7	2-hydroxyglycolic acid	1.32	0.14	0.98	0.83	N.D.	-
8	β-hydroxybutyric acid ‡	1.30	0.06	1.11	0.66	1.36	0.56
9	valine ‡	1.32	0.07	1.30	0.03*	1.40	0.13
10	urea (2TMS)	0.92	0.48	0.89	0.46	1.32	0.24
11	phosphoric acid ‡	1.06	0.31	0.80	0.25	0.97	0.83
12	glycerol ‡	0.90	0.41	0.75	0.10	0.82	0.10
13	isoleucine ‡	5.24	0.01*	1.13	0.61	1.25	0.33
14	proline ‡	2.00	0.07	1.45	0.10	1.15	0.54
15	glycine ‡	1.23	0.01*	0.64	0.00*	0.76	0.69
16	succinic acid ‡	0.87	0.23	0.97	0.93	0.82	0.44
17	glyceric acid	1.17	0.11	1.21	0.44	1.05	0.57
18	uracil ‡	0.97	0.93	0.61	0.54	0.89	0.59
19	fumaric acid ‡	1.00	1.00	0.87	0.42	1.06	0.98
20	serine ‡	2.22	0.08	1.18	0.27	0.75	0.48
21	threonine (3TMS) ‡	2.12	0.06	1.15	0.45	0.96	1.00
22	(S)-3,4-dihydroxybutanoic acid	1.47	0.18	1.14	0.57	1.05	0.39
23	β-alanine ‡	1.35	0.55	0.00	0.20	0.72	0.20
24	aminomalonic acid	1.46	0.01*	0.50	0.00*	0.98	0.71
25	malic acid ‡	1.00	1.00	0.83	0.33	1.02	0.84
26	D-threitol	0.89	0.32	0.79	0.04*	1.20	0.22
27	aspartic acid ‡	3.00	0.41	1.14	0.93	0.85	0.74
28	methionine ‡	2.39	0.04*	0.91	0.86	1.07	0.77
29	pyroglutamic acid	1.26	0.00*	1.23	0.10	0.82	0.32
30	threonic acid ‡	1.43	0.00*	1.24	0.19	1.39	0.09
31	2-hydroxyglutaric acid	1.64	0.10	1.93	0.20	1.00	0.83
32	α-ketoglutaric acid ‡	3.82	0.00*	0.00	0.08	0.86	0.52
33	glutamic acid ‡	2.94	0.00*	1.64	0.16	1.44	0.15
34	phenylalanine ‡	1.43	0.11	1.18	0.16	0.86	0.88
35	diphosphoric acid	1.08	0.89	2.74	0.19	1.32	0.14
36	asparagine ‡	2.19	0.04*	1.71	0.41	0.75	0.72
37	xylitol ‡	4.15	0.00*	11.92	0.00*	20.23	0.00*
38	lysine ‡	1.62	0.05	1.02	0.97	1.19	0.30
39	arabitol ‡	0.98	0.90	1.25	0.12	1.54	0.03*
40	putrescine	1.00	0.99	3.54	0.09	1<	0.37
41	glycerol 3-phosphate	0.00	0.35	0.60	0.05	N.D.	-
42	glutamine ‡	4.02	0.09	1.20	0.71	1.94	0.14
43	ethanolamine phosphate	1.21	0.08	0.98	0.88	1.06	0.66
44	3-phosphoglycerate ‡	0.95	0.82	N.D.	-	N.D.	-
45	ornithine ‡	2.07	0.01*	2.09	0.05	0.99	0.84
46	hypoxanthine ‡	N.D.	-	1.11	0.89	N.D.	-
47	citric acid ‡	0.89	0.14	0.97	0.87	0.75	0.31
48	1,5-Anhydroglucitol	1.50	0.05	1.10	0.45	0.78	0.40
49	myristic acid	0.92	0.59	0.75	0.03*	1.11	0.98
50	hippuric acid (1TMS) ‡	0.00	0.04*	0.12	0.41	N.D.	-
51	d-fructose ‡	0.74	0.04*	0.77	0.34	1.08	0.82
52	d-mannose ‡	1<	0.00*	1.61	0.57	1.16	0.90
53	gluconic acid (6-mr) ‡	0.85	0.45	1.75	0.23	1.00	0.88
54	d-glucose ‡ / d-galactose ‡	0.85	0.01*	1.01	0.99	1.14	0.64
55	gluconic acid (5-mr) ‡	0.96	0.77	0.88	0.47	1.11	0.60
56	3-Hydroxysebacic acid	2.16	0.15	1.67	0.31	1.13	0.72
57	p-hydroxyphenylpyruvic acid ‡	N.D.	-	N.D.	-	1.16	0.66
58	lysine (4TMS)	1.77	0.04*	0.87	0.63	1.29	0.27
59	sorbitol ‡	1.00	1.00	0.62	0.28	0.64	0.10
60	tyrosine ‡	1.81	0.04*	0.52	0.05	1.65	0.11
61	ascorbic acid ‡	0.95	0.57	0.80	0.17	N.D.	-
62	Indole-3-acetic acid ‡	0.91	0.77	0.38	0.58	N.D.	-
63	galactonic acid ‡	0.20	0.29	1.71	0.65	2.13	0.10
64	3-hydroxydodecanedioic acid	0.88	0.22	0.59	0.31	0.00	0.39
65	gluconic acid ‡	4.44	0.00*	0.80	0.54	0.80	0.87
66	pantothenic acid	0.00	0.00*	1<	0.36	0.89	0.90
67	glucaric acid ‡	2.97	0.00*	8.16	0.01*	3.65	0.02*
68	d-glucuronic acid ‡	0.80	0.13	1.07	0.53	1.16	0.83
69	xanthine ‡	N.D.	-	0.95	0.95	N.D.	-
70	palmitoleic acid	0.50	0.14	0.53	0.00*	1.63	0.59
71	palmitic acid ‡	0.96	0.74	0.77	0.01*	1.19	0.39
72	myo-inositol ‡	0.96	0.51	1.17	0.32	1.11	0.42
73	uric acid ‡	0.78	0.50	0.98	0.95	0.34	0.10
74	methyl stearate	1.42	0.21	1.06	0.76	1<	0.24
75	Indolelactic acid ‡	3.03	0.05	1.14	0.47	2.08	0.05
76	myo-Inositol diphosphate	1.45	0.05	0.96	0.78	1.55	0.06
77	eicosadienoic acid	0.97	0.86	0.90	0.43	1.25	0.19
78	3-hydroxy-2,3-didehydrosebacic acid	1.17	0.81	0.84	0.48	1.50	0.60
79	tryptophan ‡	1.31	0.18	0.71	0.12	0.86	0.69
80	oleic acid ‡	1.05	0.91	1.14	0.74	1.33	0.56
81	stearic acid ‡	1.00	0.98	1.02	0.70	1.04	0.55
82	pseudouridine ‡	1.12	0.34	1.05	0.75	1.00	0.40
83	arachidonic acid	0.88	0.18	0.67	0.02*	1.17	0.32
84	glycerol 1-myristate	0.96	0.59	0.92	0.55	0.95	0.42

Supplementary Table 7-1. Levels of liver metabolites in animals treated with NaPB for 7 days.

#	Metabolites	Wistar Hannover rats treated with 2500 ppm NaPB		CD-1 mice treated with 2500 ppm NaPB		Chimeric mice treated with 1000 ppm NaPB	
		Fold change	p value	Fold change	p value	Fold change	p value
85	myo-Inositol monophosphate	1.34	0.24	1.04	0.82	1.42	0.05
86	5-Hydroxy-L-tryptophan ‡	0.99	0.95	1<	0.36	N.D.	-
87	3-Hydroxy-2,3-didehydrosebacic acid	0.72	0.62	N.D.	-	N.D.	-
88	oleamide	N.D.	-	0.73	0.19	N.D.	-
89	serotonin ‡	N.D.	-	0.05	0.14	1.07	0.63
90	glycerol 2-palmitate	1.05	0.36	1.00	0.96	1.02	0.54
91	glycerol 1-palmitate	0.93	0.36	0.94	0.50	0.88	0.05
92	sucrose ‡	1.00	1.00	4.77	0.02*	1.23	0.52
93	glycerol 1-stearate	0.97	0.70	0.96	0.71	0.88	0.09
94	tocopherol ‡	1.37	0.00*	0.81	0.04*	1.42	0.02*
95	cholesterol ‡	1.54	0.00*	1.11	0.32	1.39	0.15

Values are represented as the fold change of the peak intensity of the NaPB treated compared with that of the control in each species. Punctuation marks (‡) indicate identified metabolites by using standard compounds. The others are putatively identified metabolites by matching NIST spectra (>70% identity). P values were calculated according to the Student's t-test. Values significantly different from control (0 ppm) are: *p<0.05. N.D. means peaks were not detected.

Supplementary Table 7-2. Levels of plasma metabolites in animals treated with NaPB for 7 days.

#	Metabolites	Wistar Hannover rats treated with 2500 ppm NaPB		CD-1 mice treated with 2500 ppm NaPB		Chimeric mice treated with 1000 ppm NaPB	
		Fold change	p value	Fold change	p value	Fold change	p value
1	pyruvic acid ‡	0.94	0.79	0.42	0.26	1.68	0.10
2	lactic acid ‡	1.00	0.97	1.31	0.01*	0.97	0.81
3	alanine ‡	0.85	0.52	0.74	0.01*	1.56	0.01*
4	hydroxylamine	1.11	0.44	0.89	0.25	0.99	0.70
5	sarcosine ‡	0.68	0.51	2.32	0.10	N.D.	-
6	2-hydroxyglycolic acid	2.90	0.00*	1.05	0.78	N.D.	-
7	B-hydroxybutyric acid ‡	0.76	0.12	1.41	0.07	0.85	0.61
8	valine ‡	0.94	0.86	0.71	0.12	1.37	0.15
9	urea (2TMS)	0.91	0.43	0.95	0.84	1.44	0.21
10	leucine ‡	0.98	0.95	0.80	0.85	N.D.	-
11	phosphoric acid ‡	0.71	0.00*	0.80	0.00*	0.90	0.27
12	glycerol ‡	0.89	0.49	0.89	0.13	0.79	0.16
13	isoleucine ‡	2.61	0.09	0.53	0.47	1.28	0.32
14	proline ‡	1.10	0.77	0.87	0.56	1.21	0.33
15	3-hydroxyacrylic acid ‡	0.23	0.30	1.90	0.58	N.D.	-
16	glycine ‡	1.11	0.44	0.68	0.00*	2.56	0.00*
17	succinic acid ‡	0.44	0.23	1.02	0.97	1.03	0.94
18	glyceric acid	0.78	0.59	0.50	0.51	0.80	0.49
19	Itaconic acid ‡	0.15	0.03*	0.00	0.11	1.60	0.21
20	uracil ‡	0.56	0.01*	0.91	0.64	1.57	0.14
21	fumaric acid ‡	0.48	0.00*	0.66	0.02*	0.74	0.10
22	serine ‡	1.22	0.54	0.88	0.57	1.21	0.52
23	threonine (3TMS) ‡	1.20	0.55	0.95	0.73	1.32	0.25
24	glutaric acid ‡	0.43	0.49	1.55	0.47	2.40	0.11
25	B-alanine ‡	1.22	0.19	0.82	0.61	1.23	0.17
26	aminomalonic acid	N.D.	-	N.D.	-	1.88	0.04*
27	malic acid ‡	0.47	0.00*	0.62	0.01*	0.82	0.07
28	aspartic acid ‡	0.89	0.77	0.44	0.03*	1.55	0.17
29	methionine ‡	0.98	0.97	0.64	0.09	1.50	0.19
30	pyroglutamic acid	0.66	0.01*	0.66	0.02*	1.86	0.00*
31	threonic acid ‡	2.89	0.01*	2.25	0.23	1.60	0.09
32	creatinine ‡	N.D.	-	N.D.	-	0.74	0.04*
33	cysteine ‡	3.70	0.10	1.02	0.97	5.57	0.02*
34	α-ketoglutaric acid ‡	0.37	0.04*	0.03	0.03*	0.93	0.90
35	glutamic acid ‡	1.37	0.45	0.60	0.04*	3.09	0.03*
36	phenylalanine ‡	1.03	0.93	0.61	0.06	1.53	0.14
37	diphosphoric acid	0.00	0.35	N.D.	-	1.20	0.62
38	asparagine ‡	1<	0.29	1.23	0.89	1.10	0.72
39	xylitol ‡	0.98	0.88	1.66	0.01*	1.48	0.08
40	lysine ‡	1.20	0.90	0.51	0.19	N.D.	-
41	arabitol ‡	0.49	0.01*	0.37	0.01*	0.64	0.49
42	putrescine	0.23	0.00*	0.39	0.03*	N.D.	-
43	glycerol 3-phosphate	2.83	0.00*	0.50	0.01*	0.88	0.69
44	ethanolamine phosphate	0.86	0.20	1.35	0.47	1.13	0.68
45	3-phosphoglycerate ‡	1.29	0.22	1.38	0.52	1.41	0.62
46	ornithine ‡	1.22	0.55	0.50	0.04*	1.33	0.57
47	hypoxanthine ‡	2.15	0.02*	0.83	0.07	0.77	0.29
48	citric acid ‡	N.D.	-	N.D.	-	4.43	0.10
49	dopamine ‡	0.46	0.06	0.76	0.81	N.D.	-
50	1,5-Anhydroglucitol	0.83	0.83	1.11	0.40	0.94	0.68
51	hippuric acid (1TMS) ‡	0.04	0.37	0.00	0.35	N.D.	-
52	d-fructose ‡	0.72	0.12	0.27	0.00*	0.93	0.68
53	d-mannose ‡	0.61	0.00*	0.38	0.00*	0.80	0.25
54	gluconic acid (6-mr) ‡	0.60	0.21	0.52	0.04*	0.90	0.68
55	d-glucose ‡ / d-galactose ‡	0.71	0.14	0.46	0.02*	0.84	0.14
56	gluconic acid (5-mr) ‡	0.49	0.02*	0.45	0.00*	0.90	0.26
57	3-Hydroxysebacic acid	0.26	0.21	0.90	0.93	0.92	0.41
58	p-hydroxyphenylpyruvic acid ‡	0.27	0.24	0.62	0.00*	0.86	0.22
59	lysine (4TMS)	1.08	0.81	0.38	0.00*	1.14	0.53
60	histidine ‡	1.08	0.91	0.29	0.08	N.D.	-
61	sorbitol ‡	0.66	0.11	0.50	0.07	0.69	0.28
62	tyrosine ‡	1.11	0.75	1.18	0.48	1.25	0.35
63	ascorbic acid ‡	0.85	0.62	0.92	0.82	1<	0.18
64	adrenaline ‡	1.69	0.47	0.24	0.03*	N.D.	-
65	galactonic acid ‡	0.38	0.01*	0.22	0.00*	2.00	0.38
66	3-hydroxydodecanoic acid	0.00	0.09	N.D.	-	1.10	0.60
67	gluconic acid ‡	0.49	0.04*	0.61	0.02*	0.47	0.01*
68	pantothenic acid	0.61	0.02*	0.98	0.97	1.09	0.65
69	glucaric acid ‡	2.15	0.00*	2.62	0.06	10.19	0.00*
70	d-glucuronic acid ‡	0.73	0.02*	1.08	0.74	0.87	0.29
71	xanthine ‡	1.52	0.12	0.47	0.01*	1.11	0.88
72	palmitic acid ‡	0.81	0.13	0.82	0.17	1.01	0.94
73	myo-inositol ‡	0.81	0.01*	0.81	0.08	0.83	0.21
74	uric acid ‡	0.38	0.09	N.D.	-	0.00	0.39
75	glycerol 3-phosphate	1.15	0.70	0.43	0.00*	0.65	0.00*
76	tryptophan ‡	0.78	0.32	0.62	0.12	1.21	0.70
77	stearic acid ‡	0.86	0.09	0.99	0.91	0.92	0.33
78	glycerol 1-myristate	0.25	0.21	1.30	0.18	1.03	0.80
79	myo-Inositol monophosphate	2.29	0.45	0.74	0.09	0.94	0.58
80	uridine	1.80	0.06	0.98	0.86	0.95	0.75
81	glycerol 2-palmitate	0.62	0.23	1.46	0.19	1<	0.03*
82	glycerol 1-palmitate	0.92	0.11	1.07	0.42	1.04	0.64
83	adenosine	1.10	0.95	0.55	0.61	1.10	0.75
84	maltose ‡ / turanose ‡	0.56	0.04*	0.46	0.00*	0.84	0.73
85	glycerol 1-stearate	0.92	0.16	1.06	0.55	1.04	0.69
86	AMP	1<	0.12	0.87	0.73	0.78	0.59

Values are represented as the fold change of the peak intensity of the NaPB treated compared with that of the control in each species. Punctuation marks (‡) indicate identified metabolites by using standard compounds. The others are putatively identified metabolites by matching NIST spectra (>70% identity). P values were calculated according to the Student's t-test. Values significantly different from control (0 ppm) are: *p<0.05. N.D. means peaks were not detected.

Supplementary Table 8-1. Up-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in WH rats and chimeric mice with human hepatocytes

Gene Name	Gene symbol	CD-1 micetreated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
		Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	
cytochrome P450, family 2, subfamily b, polypeptide 10	Cyp2b10	118.83	0.03	Cyp2b2	52.81	0.00	CYP2B6	7.15	0.00	
aldo-keto reductase family 1, member B7	Akr1b7	52.06	0.03	Akr1b7	2.51	0.09	ND			
sulfotransferase family 1E, member 1	Sult1e1	47.04	0.01	ste2	0.66	0.02	SULT1E1	0.62	0.06	
meiosis expressed gene 1	Meig1	45.38	0.00	Meig1	1.13	0.17	MEIG1	1.21	0.50	
glutathione S-transferase, mu 3	Gstm3	44.62	0.02	Gstm3	15.83	0.04	ND			
RIKEN cDNA 1810053B23 gene	1810053B23Rik	37.87	0.02	ND			ND			
microtubule associated monooxygenase, calponin and LIM domain containing 1	Mical1	37.04	0.05	Mical1	0.76	0.26	MICAL1	1.90	0.19	
predicted gene 3776	Gm3776	36.13	0.03	Gsta5	2.65	0.00	GSTA5	1.35	0.07	
cytochrome P450, family 2, subfamily b, polypeptide 9	Cyp2b9	30.26	0.05	Cyp2b3	0.66	0.00	ND			
cytochrome P450, family 2, subfamily a, polypeptide 4	Cyp2a4	17.94	0.04	Cyp2a3	0.56	0.19	CYP2A7	5.25	0.00	
glutathione S-transferase, alpha 2 (Yc2)	Gsta2	17.26	0.02	Gsta5	2.65	0.00	GSTA5	1.35	0.07	
fibronectin type III domain containing 5	Fndc5	15.08	0.05	ND			FNDC5	0.68	0.07	
predicted gene 10639	Gm10639	13.47	0.02	Gsta5	2.65	0.00	GSTA5	1.35	0.07	
glutathione S-transferase, mu 2	Gstm2	10.35	0.02	Gstm2	1.59	0.01	GSTM1	3.95	0.02	
RIKEN cDNA 5330417C22 gene	5330417C22Rik	9.99	0.00	ND			KIAA1324	1.24	0.30	
RIKEN cDNA 1700023F06 gene	1700023F06Rik	8.94	0.02	ND			ND			
orosomucoid 3	Orm3	8.06	0.00	Orm1	1.68	0.04	ORM2	0.90	0.34	
cytochrome P450, family 2, subfamily c, polypeptide 54	Cyp2c54	7.97	0.01	Cyp2c6v1	4.59	0.00	CYP2C19	2.22	0.00	
glutathione S-transferase, mu 1	Gstm1	7.75	0.01	Gstm1	2.79	0.00	GSTM5	1.29	0.47	
cytochrome P450, family 2, subfamily c, polypeptide 50	Cyp2c50	7.56	0.02	Cyp2c6v1	4.59	0.00	CYP2C19	2.22	0.00	
ATP-binding cassette, sub-family C (CFTR/MRP), member 4	Abcc4	7.35	0.05	Abcc4	1.60	0.01	ABCC4	1.88	0.12	
carbonyl reductase 3	Cbr3	7.30	0.05	Cbr3	0.77	0.14	CBR3	4.27	0.19	
trefoil factor 1	Tff1	7.24	0.00	Tff1	1.67	0.17	TFF1	0.98	0.94	
cytochrome P450, family 2, subfamily c, polypeptide 39	Cyp2c39	7.16	0.01	Cyp2c7	0.96	0.75	ND			
ribosomal protein S6 kinase, polypeptide 2	Rps6ka2	7.05	0.00	Rps6ka2	1.38	0.08	RPS6KA2	1.23	0.09	
glutathione S-transferase, theta 3	Gstt3	6.90	0.04	Gstt3	3.63	0.00	ND			
pancreatic lipase related protein 1	Pnliprp1	6.73	0.01	Pnliprp1	0.73	0.19	PNLIPRP1	0.62	0.51	
olfactory receptor 141	Olfr141	6.65	0.03	Olr516	1.22	0.02	ND			
tumor necrosis factor receptor superfamily, member 19	Tnfrsf19	6.56	0.01	ND			TNFRSF19	0.81	0.36	
tumor necrosis factor receptor superfamily, member 11a	Tnfrsf11a	6.30	0.02	Tnfrsf11a	1.57	0.56	TNFRSF11A	0.16	0.40	
BPI fold containing family B, member 6	Bpifb6	6.16	0.01	Bpifb6	1.63	0.08	BPIFB6	2.97	0.05	
sulfotransferase family 1D, member 1	Sult1d1	6.14	0.00	Sult1d1	1.04	0.77	ND			
cDNA sequence BC048507	BC048507	6.14	0.02	ND			ND			
sulfotransferase family 2A,	Sult2a7	6.04	0.02	ND			ND			
dehydroepiandrosterone (DHEA)-preferring, olfactory receptor 1257	Olfr1257	6.03	0.02	Olr722	1.15	0.16	ND			
RIKEN cDNA 4930415C11 gene	4930415C11Rik	5.91	0.01	ND			ND			
cytochrome P450, family 2, subfamily c, polypeptide 37	Cyp2c37	5.75	0.01	Cyp2c6v1	4.59	0.00	CYP2C19	2.22	0.00	
carboxylesterase 2C	Ces2c	5.66	0.00	Ces2c	15.29	0.00	ND			
carboxylesterase 2B	Ces2b	5.61	0.05	Ces2c	15.29	0.00	ND			
glutathione S-transferase, mu 4	Gstm4	5.52	0.02	Gstm4	2.02	0.02	GSTM4	1.12	0.33	
glutathione S-transferase, mu 5	Gstm5	5.50	0.00	Gstm5	1.33	0.43	GSTM3	1.22	0.10	
solute carrier family 10 (sodium/bile acid cotransporter family), member 7	Slc10a7	5.48	0.04	Slc10a7	1.09	0.48	SLC10A7	1.30	0.03	
olfactory receptor 704	Olfr704	5.45	0.03	Olr215	1.19	0.03	ND			
carboxylesterase 2A	Ces2a	5.32	0.01	ND			ND			
serine (or cysteine) peptidase inhibitor, clade A, member 6	Serpina6	5.07	0.05	Serpina6	0.94	0.64	SERPINA6	1.15	0.11	
expressed sequence C78653	C78653	5.00	0.02	ND			ND			
aldehyde dehydrogenase family 1, subfamily A7	Aldh1a7	4.60	0.03	Aldh1a7	24.30	0.14	ND			
topoisomerase (DNA) III alpha	Top3a	4.55	0.00	ND			TOP3A	1.06	0.65	
secretoglobin, family 1A, member 1 (uteroglobin)	Scgb1a1	4.20	0.00	Scgb1a1	0.81	0.06	SCGB1A1	1.05	0.64	
NACHT and WD repeat domain containing 1	Nwd1	4.14	0.01	ND			NWD1	0.56	0.05	
cytochrome P450 3A41-like	LOC101056526	4.09	0.02	ND			ND			
BPI fold containing family B, member 3	Bpifb3	4.08	0.04	Bpifb3	1.23	0.40	BPIFB3	3.18	0.11	
olfactory receptor 1384	Olfr1384	3.98	0.01	Olr1397	0.82	0.71	ND			
predicted gene 11567	Gm11567	3.96	0.01	ND			ND			
PRELI domain containing 2	Prelid2	3.94	0.02	Prelid2	0.83	0.34	PRELID2	0.51	0.07	
olfactory receptor 482	Olfr482	3.87	0.00	Olr255	0.37	0.22	ND			
late cornified envelope 11	Lce1i	3.80	0.03	ND			ND			
keratin 31	Krt31	3.76	0.01	Krt31	0.86	0.68	KRT31	2.38	0.06	

Supplementary Table 8-1. Up-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in WH rats and chimeric mice with human hepatocytes

Gene Name	Gene symbol	CD-1 micetreated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
		Fold change	p value		Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
olfactory receptor 1535	Olf1535	3.76	0.05	ND	S100a4	1.18	0.37	S100A4	0.92	0.78
RIKEN cDNA 2310081J21 gene	2310081J21Rik	3.74	0.02	ND	Nos1	1.12	0.20	NOS1	1.31	0.61
S100 calcium binding protein A4	S100a4	3.72	0.01	ND	Cox6a2	0.68	0.25	COX6A2	0.85	0.25
nitric oxide synthase 1, neuronal	Nos1	3.71	0.01	ND	Sncg	0.53	0.24	SNCG	0.72	0.36
cytochrome c oxidase subunit VIa polypeptide 2	Cox6a2	3.63	0.00	ND	Olf464	0.57	0.29	OR4D1	1.22	0.48
synuclein, gamma	Sncg	3.63	0.00	ND	Vmn2r4	0.36	0.07	ND	ND	ND
olfactory receptor 464	Olf464	3.62	0.02	ND	sushi domain containing 2	3.56	0.02	SUSD2	1.42	0.41
vomeronasal 2, receptor 4	Vmn2r4	3.58	0.04	ND	retinoic acid receptor responder (tazarotene induced) 1	3.55	0.02	RARRES1	0.96	0.94
sushi domain containing 2	Susd2	3.56	0.02	ND	MAD2 mitotic arrest deficient-like 1	3.54	0.01	Mad2l1	1.91	0.00
retinoic acid receptor responder (tazarotene induced) 1	Rarres1	3.55	0.02	ND	cell death-inducing DFFA-like effector c	3.52	0.01	Cidec	0.68	0.02
cytochrome c oxidase subunit VIa polypeptide 2	Cidec	3.52	0.01	ND	coiled-coil domain containing 93	3.51	0.00	Ccdc93	1.16	0.02
synuclein, gamma	Ccdc93	3.51	0.00	ND	RIKEN cDNA 1810055G02 gene	3.50	0.00	RGD1311946	1.16	0.62
olfactory receptor 464	RGD1311946	3.50	0.00	ND	microchidia 4	3.46	0.01	Morc4	1.88	0.39
vomeronasal 2, receptor 4	Morc4	3.46	0.01	ND	olfactory receptor 700	3.46	0.03	Olr208	3.93	0.35
sushi domain containing 2	Olr208	3.46	0.03	ND	sphingomyelin phosphodiesterase 3, neutral	3.41	0.03	Smpd3	0.73	0.02
retinoic acid receptor responder (tazarotene induced) 1	Smpd3	3.41	0.03	ND	olfactory receptor 868	3.39	0.00	Olr1179	1.33	0.27
cytochrome c oxidase subunit VIa polypeptide 2	Olr1179	3.39	0.00	ND	RIKEN cDNA 6330403A02 gene	3.38	0.00	ND	ND	ND
synuclein, gamma	6330403A02Rik	3.38	0.00	ND	protease, serine, 8 (prostasin)	3.36	0.04	Prss8	2.40	0.12
olfactory receptor 868	Prss8	3.36	0.04	ND	olfactory receptor 74	3.36	0.00	Olr604	1.15	0.16
RIKEN cDNA 6330403A02 gene	Olr604	3.36	0.00	ND	cytochrome P450, family 3, subfamily a, polypeptide 16	3.35	0.01	Cyp3a16	5.17	0.00
protease, serine, 8 (prostasin)	Cyp3a16	3.35	0.01	ND	serine (or cysteine) peptidase inhibitor, clade B, member 3C	3.35	0.00	Serpibn3c	ND	ND
olfactory receptor 74	Serpibn3c	3.35	0.00	ND	coiled-coil domain containing 85B	3.33	0.01	Ccdc85b	0.91	0.22
cytochrome P450, family 3, subfamily a, polypeptide 16	Ccdc85b	3.33	0.01	ND	retinol binding protein 1, cellular	3.27	0.02	Rbp1	0.88	0.10
serine (or cysteine) peptidase inhibitor, clade B, member 3C	Rbp1	3.27	0.02	ND	secretory leukocyte peptidase inhibitor	3.26	0.00	Slpi	ND	ND
coiled-coil domain containing 85B	Slpi	3.26	0.00	ND	RIKEN cDNA 4930474H20 gene	3.24	0.02	4930474H20Rik	ND	ND
retinol binding protein 1, cellular	4930474H20Rik	3.24	0.02	ND	peroxisomal biogenesis factor 11 gamma	3.22	0.00	Pex11c	1.27	0.01
secretory leukocyte peptidase inhibitor	Pex11c	3.22	0.00	ND	MAM domain containing 4	3.21	0.00	Mamdc4	0.94	0.63
RIKEN cDNA 4930474H20 gene	Mamdc4	3.21	0.00	ND	proteoglycan 4 (megakaryocyte stimulating factor, articular superficial zone protein)	3.20	0.00	Prg4	ND	ND
peroxisomal biogenesis factor 11 gamma	Prg4	3.20	0.00	ND	RIKEN cDNA 5830416P10 gene	3.18	0.01	5830416P10Rik	ND	ND
MAM domain containing 4	5830416P10Rik	3.18	0.01	ND	predicted gene 10065	3.17	0.00	Gm10065	ND	ND
proteoglycan 4 (megakaryocyte stimulating factor, articular superficial zone protein)	Gm10065	3.17	0.00	ND	trophinin	3.17	0.01	Tro	ND	ND
RIKEN cDNA 5830416P10 gene	Tro	3.17	0.01	ND	wingless-related MMTV integration site 7B	3.16	0.00	Wnt7b	0.88	0.74
predicted gene 10065	Wnt7b	3.16	0.00	ND	RIKEN cDNA 3300002P13 gene	3.16	0.01	3300002P13Rik	ND	ND
trophinin	3300002P13Rik	3.16	0.01	ND	predicted gene 10872	3.16	0.04	Gm10872	ND	ND
wingless-related MMTV integration site 7B	Gm10872	3.16	0.04	ND	RIKEN cDNA E030025P04 gene	3.15	0.01	E030025P04Rik	ND	ND
RIKEN cDNA 3300002P13 gene	E030025P04Rik	3.15	0.01	ND	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	3.13	0.01	Uchl3	1.23	0.02
predicted gene 10872	Uchl3	3.13	0.01	ND	ubiquitin-like domain containing CTD	3.08	0.02	Ublcp1	ND	ND
RIKEN cDNA E030025P04 gene	Ublcp1	3.08	0.02	ND	cathepsin L	3.06	0.05	Ctsl	1.64	0.00
ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	Ctsl	3.06	0.05	ND	ATPase, H ⁺ transporting, lysosomal V0 subunit	3.05	0.01	Atp6v0a1	1.33	0.00
ubiquitin-like domain containing CTD	Atp6v0a1	3.05	0.01	ND	guanylate binding protein 5	3.04	0.01	Gbp5	1.98	0.06
cathepsin L	Gbp5	3.04	0.01	ND	amylase 2a5	3.04	0.00	Amy2a5	0.05	0.28
ATPase, H ⁺ transporting, lysosomal V0 subunit	Amy2a5	3.04	0.00	ND	RIKEN cDNA 9430008C03 gene	3.04	0.01	9430008C03Rik	ND	ND
guanylate binding protein 5	9430008C03Rik	3.04	0.01	ND	cytochrome P450, family 3, subfamily a, polypeptide 41B	3.01	0.03	Cyp3a41b	5.17	0.00
amylase 2a5	Cyp3a41b	3.01	0.03	ND	epoxide hydrolase 1, microsomal	2.99	0.03	Ephx1	5.68	0.00
RIKEN cDNA 9430008C03 gene	Ephx1	2.99	0.03	ND	PDX1 C-terminal inhibiting factor 1	2.97	0.00	Pcf1f	0.96	0.64
cytochrome P450, family 3, subfamily a, polypeptide 41B	Pcf1f	2.97	0.00	ND	t-complex protein 10c	2.96	0.00	Tcp10c	0.62	0.33
epoxide hydrolase 1, microsomal	Tcp10c	2.96	0.00	ND	G protein-coupled receptor 37-like 1	2.95	0.04	Gpr37l1	1.21	0.04
PDX1 C-terminal inhibiting factor 1	Gpr37l1	2.95	0.04	ND	chromatin assembly factor 1, subunit B (p60)	2.95	0.01	Chaf1b	4.35	0.04
t-complex protein 10c	Chaf1b	2.95	0.01	ND	solute carrier family 38, member 6	2.94	0.01	Slc38a6	0.83	0.02
G protein-coupled receptor 37-like 1	Slc38a6	2.94	0.01	ND	F-box protein 39	2.94	0.01	Fbxo39	1.36	0.42
chromatin assembly factor 1, subunit B (p60)	Fbxo39	2.94	0.01	ND	F-box and leucine-rich repeat protein 20	2.91	0.02	Fbxl20	ND	ND
solute carrier family 38, member 6	Fbxl20	2.91	0.02	ND	RIKEN cDNA 1600029D21 gene	2.91	0.01	1600029D21Rik	1.04	0.75
F-box protein 39	1600029D21Rik	2.91	0.01	ND	predicted gene 1631	2.90	0.00	Gm1631	ND	ND
F-box and leucine-rich repeat protein 20	Gm1631	2.90	0.00	ND	cadherin 6	2.90	0.00	Cdh6	0.76	0.30
RIKEN cDNA 1600029D21 gene	Cdh6	2.90	0.00	ND	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2 6-sialyltransferase 6	2.90	0.00	St6galnac6	ND	ND
predicted gene 1631	St6galnac6	2.90	0.00	ND	mitochondrial ubiquitin ligase activator of NFKB 1	2.89	0.01	Mul1	1.42	0.02
cadherin 6	Mul1	2.89	0.01	ND	RIKEN cDNA 4933403O08 gene	2.89	0.02	4933403O08Rik	ND	ND
ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2 6-sialyltransferase 6	4933403O08Rik	2.89	0.02	ND	cartilage intermediate layer protein 2	2.88	0.02	Cilp2	0.75	0.25
mitochondrial ubiquitin ligase activator of NFKB 1	Cilp2	2.88	0.02	ND	Mab-21 domain containing 1	2.88	0.00	Mb21d1	ND	ND
RIKEN cDNA 4933403O08 gene	Mb21d1	2.88	0.00	ND	RIKEN cDNA F830115B05 gene	2.88	0.03	F830115B05Rik	ND	ND
cartilage intermediate layer protein 2	F830115B05Rik	2.88	0.03	ND	olfactory receptor 713	2.88	0.00	Olf713	1.67	0.23
Mab-21 domain containing 1	Olf713	2.88	0.00	ND	predicted gene 6436	2.87	0.01	Gm6436	ND	ND
RIKEN cDNA F830115B05 gene	Gm6436	2.87	0.01	ND	olfactory receptor 713	2.88	0.00	Olf227	1.67	0.23
olfactory receptor 713	Olf227	2.88	0.00	ND	predicted gene 6436	2.87	0.01	ND	ND	ND

Supplementary Table 8-1. Up-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in WH rats and chimeric mice with human hepatocytes

CD-1 micetreated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
pyrin domain containing 3	Pydc3	2.85	0.03	ND			ND		
CDK5 regulatory subunit associated protein 1-like	Cdkal1	2.85	0.01	ND			CDKAL1	0.81	0.24
RELT-like 2	Rell2	2.81	0.01	Rell2	1.18	0.27	RELL2	1.01	0.96
predicted gene 14635	Gm14635	2.81	0.01	ND			ND		
cytochrome P450, family 2, subfamily c, polypeptide 29	Cyp2c29	2.80	0.04	Cyp2c7	0.96	0.75	ND		
glucagon-like peptide 2 receptor	Glp2r	2.79	0.04	Glp2r	1.37	0.16	GLP2R	0.40	0.43
myosin VC	Myo5c	2.76	0.02	Myo5c	1.20	0.05	MYO5C	1.26	0.17
tribbles homolog 1 (<i>Drosophila</i>)	Trib1	2.71	0.04	Trib1	0.72	0.42	TRIB1	0.85	0.30
predicted gene 3448	Gm3448	2.71	0.00	ND			TCTE3	1.40	0.27
leucine-rich repeats and transmembrane domains	Lrtm1	2.71	0.05	ND			LRTM1	0.80	0.32
acyl-coenzyme A amino acid N-acyltransferase 2	Acnat2	2.71	0.04	Acnat2	0.41	0.03	ND		
RIKEN cDNA 6030443J06 gene	6030443J06Rik	2.70	0.02	ND			ND		
carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotate	Cad	2.69	0.00	Cad	0.96	0.84	CAD	1.32	0.17
triple functional domain (PTPRF interacting)	Trio	2.69	0.01	Trio	0.97	0.77	TRIO	1.03	0.82
carbonic anhydrase 10	Car10	2.67	0.01	ND			CA10	0.09	0.37
olfactory receptor 476	Olf476	2.67	0.00	Olr242	1.18	0.03	ND		
sortilin 1	Sort1	2.67	0.00	Sort1	1.39	0.18	SORT1	0.85	0.12
cell division cycle associated 8	Cdc8a	2.67	0.03	Cdc8a	3.09	0.00	CDC8A	1.26	0.12
transgelin 2	Tagln2	2.67	0.04	Tagln2	1.12	0.29	TAGLN2	1.28	0.15
defensin beta 11	Defb11	2.66	0.00	ND			ND		
MAS-related GPR, member B4	Mrgprb4	2.65	0.00	ND			ND		
phosphodiesterase 11A	Pde11a	2.65	0.00	Pde11a	1.62	0.06	PDE11A	0.37	0.27
olfactory receptor 458	Olf458	2.64	0.00	Olr801	1.31	0.32	ND		
interleukin 19	Il19	2.64	0.01	ND			IL19	2.24	0.23
RAD21-like (<i>S. pombe</i>)	Rad21l	2.64	0.02	Rad21l	1.12	0.10	RAD21L1	1.06	0.73
RIKEN cDNA 2310043M15 gene	2310043M15Rik	2.61	0.00	ND			ND		
calponin 2	Cnn2	2.61	0.01	ND			CNN2	1.23	0.04
calcium/calmodulin-dependent protein kinase II alpha	Camk2a	2.60	0.02	Camk2a	1.51	0.27	CAMK2A	0.82	0.64
Rac GTPase-activating protein 1	Racgap1	2.59	0.02	Racgap1	4.32	0.02	RACGAP1	1.10	0.80
vacuolar protein sorting 39 (yeast)	Vps39	2.58	0.00	Vps39	1.07	0.46	VPS39	0.80	0.06
RASD family, member 2	Rasd2	2.58	0.01	Rasd2	0.68	0.36	RASD2	1.18	0.75
growth factor independent 1B	Gfi1b	2.57	0.02	Gfi1b	1.21	0.03	GFI1B	0.67	0.23
angiomotin	Amot	2.53	0.04	Amot	0.80	0.65	AMOT	2.02	0.05
v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian)	Erbb2	2.53	0.00	Erbb2	2.63	0.32	ERBB2	0.70	0.00
RIKEN cDNA D930023I05 gene	D930023I05Rik	2.52	0.02	ND			ND		
glycerophosphocholine phosphodiesterase GDE1 homolog (<i>S. cerevisiae</i>)	Gpcpd1	2.52	0.00	Gpcpd1	1.08	0.16	GPCPD1	1.03	0.86
translocated promoter region	Tpr	2.52	0.01	Tpr	0.89	0.00	TPR	1.19	0.09
olfactory receptor 122	Olf122	2.50	0.00	Olr1696	0.41	0.20	ND		
transmembrane protein 86B	Tmem86b	2.50	0.04	Tmem86b	0.77	0.04	TMEM86B	1.11	0.13
rhabdoid tumor deletion region gene 1	Rtdr1	2.49	0.00	ND			ND		
ATPase, H+ transporting, lysosomal V0 subunit E	Atp6v0e	2.46	0.03	Atp6v0e1	0.95	0.54	ATP6V0E1	1.21	0.13
uridine-cytidine kinase 2	Uck2	2.46	0.00	Uck2	1.44	0.04	UCK2	1.21	0.17
Wiskott-Aldrich syndrome homolog (human)	Was	2.45	0.02	ND			WAS	1.19	0.74
glycosyltransferase-like domain containing 1	Gtdc1	2.44	0.01	Gtdc1	0.84	0.06	GTDC1	6.58	0.00
multiple C2 domains, transmembrane 2	Mctp2	2.43	0.04	Mctp2	1.62	0.09	MCTP2	0.87	0.75
phosphatidylserine synthase 2	Ptdss2	2.43	0.02	Ptdss2	1.42	0.00	PTDSS2	1.15	0.17
selectin, platelet (p-selectin) ligand	Selp1g	2.43	0.03	Selp1g	0.88	0.49	SEPLIG	0.57	0.30
Mpv17 transgene, kidney disease mutant-like	Mpv17l	2.42	0.04	Mpv17l	1.24	0.00	MPV17L	2.00	0.03
solute carrier organic anion transporter family, member 1a4	Slco1a4	2.42	0.01	Slco1a2	1.77	0.01	SLCO1A2	1.25	0.38
Bloom syndrome, RecQ helicase-like	Blm	2.41	0.01	ND			BLM	0.88	0.66
cytochrome b-5	Cyb5	2.40	0.04	Cyb5a	1.49	0.00	CYB5A	1.76	0.00
cytochrome P450, subfamily 3A, polypeptide 59	Cyp3a59	2.40	0.02	Cyp3a18	0.51	0.04	CYP3A43	1.08	0.74
S100 calcium binding protein A11 (calgizzarin)	S100a11	2.39	0.02	RGD1563581	0.96	0.77	S100A11	1.35	0.27
myosin XVI	Myo16	2.39	0.04	Myo16	1.15	0.11	MYO16	1.49	0.27
predicted pseudogene 6987	Gm6987	2.39	0.01	ND			ND		
RIKEN cDNA 9130409J20 gene	9130409J20Rik	2.38	0.00	ND			ND		
RIKEN cDNA 5330434G04 gene	5330434G04Rik	2.38	0.02	ND			ND		
NOP9 nucleolar protein	Nop9	2.37	0.04	Nop9	0.92	0.20	C14orf21	1.12	0.10
RIKEN cDNA 2610318M16 gene	2610318M16Rik	2.34	0.01	ND			ND		
ATP-binding cassette, sub-family C (CFTR/MRP), member 3	Abcc3	2.34	0.04	Abcc3	50.85	0.00	ABCC3	1.32	0.25
regulator of chromosome condensation 2	Rcc2	2.34	0.02	Rcc2	1.23	0.13	RCC2	1.31	0.39
transferrin receptor	Tfrc	2.33	0.00	Tfrc	1.73	0.20	TFRC	2.95	0.00
thiosulfate sulfurtransferase (rhodanese)-like domain containing 2	Tstd2	2.33	0.03	Tstd2	1.03	0.74	TSTD2	0.59	0.29

Supplementary Table 8-1. Up-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in WH rats and chimeric mice with human hepatocytes

CD-1 micetreated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
folate receptor 4 (delta)	Folr4	2.33	0.05	Folr4	0.60	0.08	FOLR4	1.23	0.68
N(alpha)-acetyltransferase 30, NatC catalytic	Naa30	2.32	0.00	Naa30	1.06	0.34	NAA30	0.90	0.45
synaptogyrin 4	Syngr4	2.32	0.00	Syngr4	1.15	0.10	SYNGR4	1.04	0.92
ADP-ribosylation factor-like 5C	Arl5c	2.32	0.00	Arl5c	0.79	0.19	ARL5C	1.00	1.00
glycogenin	Gyg	2.31	0.00	Gyg1	1.41	0.01	GYG1	1.41	0.05
expressed sequence BB287469	BB287469	2.31	0.02	ND	ND	ND	ND	ND	ND
regulating synaptic membrane exocytosis 1	Rims1	2.29	0.03	ND	ND	ND	ND	ND	ND
transmembrane protein 29	Tmem29	2.29	0.04	ND	ND	ND	ND	ND	ND
RIKEN cDNA 5730488B01 gene	5730488B01Rik	2.29	0.00	ND	ND	ND	ND	ND	ND
cytochrome P450, family 3, subfamily a,	Cyp3a11	2.29	0.04	Cyp3a23/3a1	5.17	0.00	CYP3A4	3.17	0.00
polvoepitide 11	Ggn	2.27	0.01	Ggn	1.58	0.09	GGN	0.82	0.25
killer cell lectin-like receptor subfamily A, member	Klra22	2.27	0.02	ND	ND	ND	ND	ND	ND
lysophosphatidylglycerol acyltransferase 1	Lpgat1	2.27	0.00	Lpgat1	0.94	0.43	LPGAT1	1.33	0.03
purinergic receptor P2X, ligand-gated ion	P2rx3	2.26	0.03	P2rx3	1.25	0.42	P2RX3	1.15	0.75
protein AHNAK2-like	LOC101055828	2.26	0.00	Ahnak2	0.85	0.25	AHNAK2	0.71	0.41
heat shock protein 70 family, member 13	Hspa13	2.25	0.00	Hspa13	0.96	0.52	HSPA13	1.49	0.08
FK506 binding protein 8	Fkbp8	2.24	0.02	Fkbp8	1.44	0.02	FKBP8	1.05	0.54
serlyl-aminoacyl tRNA synthetase 2	Sars2	2.24	0.03	Sars2	1.22	0.00	SARS2	0.80	0.23
RIKEN cDNA A330032P22 gene	A330032P22Rik	2.24	0.00	ND	ND	ND	ND	ND	ND
RIKEN cDNA 6330409D20 gene	6330409D20Rik	2.24	0.02	ND	ND	ND	ND	ND	ND
ST3 beta-galactoside alpha-2,3-sialyltransferase	St3gal5	2.24	0.04	St3gal5	0.90	0.36	ST3GAL5	0.94	0.53
luteinizing hormone beta	Lhb	2.23	0.02	Lhb	1.34	0.18	LHB	0.95	0.77
RIKEN cDNA 4930442P07 gene	4930442P07Rik	2.23	0.00	ND	ND	ND	ND	ND	ND
predicted gene 7634	Gm7634	2.23	0.02	ND	ND	ND	ND	ND	ND
histone cluster 2, H2be	Hist2h2be	2.22	0.00	Hist2h2be	1.39	0.21	HIST1H2BL	1.54	0.26
NADH dehydrogenase (ubiquinone) 1 alpha	Ndufa8	2.22	0.04	Ndufa8	0.78	0.01	NDUFA8	1.26	0.44
subcomplex, 8	Lix1l	2.22	0.00	ND	ND	ND	ND	ND	ND
cDNA sequence BC021614	BC021614	2.21	0.00	RGD1307603	0.65	0.00	ND	ND	ND
Sycp3 like X-linked	Slx	2.21	0.03	ND	ND	ND	ND	ND	ND
ATP/GTP binding protein 1	Agtpbp1	2.21	0.00	Agtpbp1	1.26	0.02	AGTPBP1	1.13	0.30
solute carrier family 20, member 1	Slc20a1	2.20	0.03	Slc20a1	1.03	0.73	SLC20A1	1.08	0.67
hemochromatosis	Hfe	2.19	0.05	ND	ND	ND	ND	ND	ND
B cell translocation gene 3	Btg3	2.19	0.01	Btg3	0.94	0.69	BTG3	1.10	0.67
RIKEN cDNA 1700010I14 gene	1700010I14Rik	2.19	0.03	MGC94891	1.08	0.46	C6orf118	0.82	0.58
RIKEN cDNA 5730409E04Rik gene	5730409E04Rik	2.19	0.00	RGD1563072	0.96	0.85	C1orf216	1.72	0.10
predicted gene 9372	Gm9372	2.19	0.00	ND	ND	ND	ND	ND	ND
membrane-associated ring finger (C3HC4) 10	10-Mar	2.19	0.04	ND	ND	ND	ND	ND	ND
dynein light chain Tctex-type 1C	Dynlt1c	2.18	0.04	Dynlt1	1.70	0.00	DYNLT1	1.14	0.10
CDC28 protein kinase 1b	Cks1b	2.18	0.01	Cks1b	1.19	0.09	CKS1B	0.90	0.38
vomeronasal 1 receptor 168	Vmn1r168	2.18	0.02	ND	ND	ND	ND	ND	ND
tetratricopeptide repeat domain 39B	Ttc39b	2.18	0.04	Ttc39b	1.07	0.25	TTC39B	1.15	0.37
M-phase phosphoprotein 10 (U3 small nucleolar	Mphosph10	2.17	0.01	Mphosph10	0.87	0.18	MPHOSPH10	1.19	0.08
ribonucleoprotein)									
predicted gene 10419	Gm10419	2.17	0.03	ND	ND	ND	ND	ND	ND
exportin, tRNA (nuclear export receptor for	Xpot	2.17	0.02	Xpot	1.10	0.06	XPOT	1.14	0.38
trace amine-associated receptor 4	Taar4	2.17	0.04	Taar4	1.17	0.05	ND	ND	ND
asparagine-linked glycosylation 2 (alpha-1,3-	Alg2	2.17	0.01	Alg2	1.07	0.79	ALG2	1.53	0.01
mannosyltransferase)									
prostaglandin E synthase	Ptges	2.16	0.01	Ptges	1.31	0.09	PTGES	0.97	0.93
actin, alpha 2, smooth muscle, aorta	Acta2	2.16	0.02	Actg2	0.58	0.36	ACTG2	0.68	0.42
thymus, brain and testes associated	Tbata	2.16	0.00	Tbata	0.70	0.43	C10orf27	0.86	0.59
zinc finger and BTB domain containing 14	Zbtb14	2.15	0.02	Zfp161	1.23	0.16	ZFP161	0.99	0.91
muscle glycogen phosphorylase	Pygm	2.14	0.01	Pygm	1.46	0.03	PYGM	1.37	0.31
olfactory receptor 67	Olr67	2.14	0.00	Olr128	2.27	0.06	ND	ND	ND
syndecan 4	Sdc4	2.14	0.00	Sdc4	0.78	0.02	SDC4	1.17	0.46
TGFB-induced factor homeobox 2-like, X-linked 2	Tgif2lx2	2.14	0.04	ND	ND	ND	ND	ND	ND
Sec24 related gene family, member D (S.	Sec24d	2.13	0.04	ND	ND	ND	SEC24D	1.31	0.05
MAD2 mitotic arrest deficient-like 2	Mad2l2	2.13	0.03	ND	ND	ND	MAD2L2	0.81	0.75
tumor suppressing subtransferable candidate 1	Tssc1	2.13	0.04	Tssc1	0.89	0.41	TSSC1	1.39	0.33
solute carrier family 35, member G1	Slc35g1	2.13	0.00	Slc35g1	1.44	0.08	SLC35G1	0.85	0.70
ATPase, H ⁺ transporting, lysosomal V1 subunit D	Atp6v1d	2.13	0.04	Atp6v1d	1.07	0.37	ATP6V1D	1.00	0.96
3-ketodihydroinositol reductase	Kdsr	2.13	0.01	Kdsr	1.17	0.07	KDSR	0.88	0.21
phospholipase A2, group IIE	Pla2g2e	2.13	0.04	Pla2g2e	1.05	0.77	PLA2G2E	0.78	0.38
serine (or cysteine) peptidase inhibitor, clade B,	Serpinb6c	2.13	0.00	ND	ND	ND	ND	ND	ND
member 6c									
protein phosphatase methylesterase 1	Ppme1	2.13	0.01	Ppme1	1.13	0.09	PPME1	1.44	0.05
TDP-glucose 4,6-dehydratase	Tgds	2.12	0.01	Tgds	1.13	0.12	TGDS	1.08	0.64
major urinary protein 6	Mup6	2.12	0.03	ND	ND	ND	ND	ND	ND
G protein-coupled receptor 30	Grp30	2.12	0.02	Gper	1.25	0.65	GPER	0.64	0.09
predicted gene 9868	Gm9868	2.12	0.01	ND	ND	ND	ND	ND	ND

Supplementary Table 8-1. Up-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in WH rats and chimeric mice with human hepatocytes

CD-1 micetreated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB				Chimeric mice treated with 1000 ppm NaPB				
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
sex comb on midleg-like 2 (Drosophila)	Scml2	2.11	0.02	ND			SCML2	1.07	0.64			
predicted gene 15032	Gm15032	2.11	0.03	ND			ND					
signal recognition particle 19	Srp19	2.11	0.02	Srp19	1.13	0.18	SRP19	1.72	0.00			
cytochrome c oxidase subunit Vlb polypeptide 2	Cox6b2	2.10	0.00	Cox6b2	0.94	0.63	COX6B2	1.85	0.08			
olfactory receptor 96	Olf96	2.10	0.05	Olr1743	1.29	0.06	OR11A1	1.07	0.71			
serum/glucocorticoid regulated kinase 1	Sgk1	2.09	0.00	Sgk1	0.63	0.04	SGK1	1.30	0.33			
BTB (POZ) domain containing 10	Btbd10	2.09	0.00	Btbd10	1.30	0.02	BTBD10	1.03	0.81			
RIKEN cDNA 5730422E09 gene	5730422E09Rik	2.09	0.01	ND			ND					
synaptonemal complex central element protein 2	Syce2	2.08	0.01	Syce2	1.59	0.15	SYCE2	1.20	0.49			
mitogen-activated protein kinase 1 interacting protein 1-like	Mapk1ip1l	2.08	0.03	Mapk1ip1l	0.90	0.11	MAPK1IP1L	1.05	0.61			
transmembrane protein 167	Tmem167	2.08	0.03	ND			TMEM167A	1.95	0.06			
RIKEN cDNA 1810044D09 gene	1810044D09Rik	2.08	0.03	ND			ND					
glutamate receptor, metabotropic 4	Grm4	2.07	0.02	Grm4	1.40	0.20	GRM4	0.94	0.88			
olfactory receptor 401	Olf401	2.06	0.00	Olr1511	1.14	0.13	ND					
protein transport protein Sec61 subunit beta-like	LOC101055909	2.06	0.01	Sec61b	1.12	0.12	SEC61B	1.35	0.02			
potassium voltage-gated channel, subfamily H (eaad-related), member 3	Kcnh3	2.05	0.01	Kcnh3	1.05	0.48	KCNH3	0.94	0.79			
predicted pseudogene 5478	Gm5478	2.05	0.01	ND			ND					
predicted gene 13194	Gm13194	2.05	0.05	RGD1564617	1.06	0.04	ND					
plexin A4	Plxna4	2.05	0.01	ND			PLXNA4	0.94	0.75			
lipase, family member N	Lipn	2.04	0.02	Lipn	2.00	0.16	LIPN	1.11	0.87			
RIKEN cDNA 1700028K03 gene	1700028K03Rik	2.04	0.03	LOC689986	1.07	0.75	C1orf146	0.40	0.49			
defensin, alpha, related sequence 12	Defa-rs12	2.04	0.04	ND			ND					
olfactory receptor 531	Olf531	2.04	0.03	Olr298	1.17	0.09	ND					
predicted gene 6570	Gm6570	2.03	0.03	ND			ND					
RIKEN cDNA 1700016H13 gene	1700016H13Rik	2.02	0.02	LOC498330	1.16	0.13	C4orf36	1.22	0.63			
predicted gene 13271	Gm13271	2.02	0.01	ND			ND					
predicted gene 6484	Gm6484	2.02	0.03	ND			C19orf80	0.93	0.75			
Casitas B-lineage lymphoma b	Cblb	2.02	0.04	Cblb	0.83	0.02	CBLB	1.03	0.79			
ribosomal protein L7A	Rpl7a	2.01	0.03	RGD1564370	1.12	0.06	ND					
lectin, galactoside-binding, soluble, 3 binding	Lgals3bp	2.01	0.02	Lgals3bp	1.18	0.37	LGALS3BP	1.02	0.86			
RIKEN cDNA 2010012O05 gene	2010012O05Rik	2.01	0.00	RGD1311783	0.81	0.00	C10orf32	0.90	0.17			
urotensin 2 receptor	Uts2r	2.00	0.01	Uts2r	0.73	0.70	UTS2R	0.79	0.49			
RIKEN cDNA A730028G07 gene	A730028G07Rik	2.00	0.00	ND			ND					
UBX domain protein 10	Ubxn10	2.00	0.03	Ubxn10	0.69	0.56	UBXN10	0.83	0.39			
Number of genes with significant alteration	286			21			16					

Data represent the expression ratio between control and NaPB treatment. Genes showing greater than 2 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in an experimental (treatment) arrays were chosen as up-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (greater than 2 fold, p<0.05). ND means "not determined".

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
hydroxy-delta-5-steroid dehydrogenase, 3 beta-Sp7 transcription factor 7	Hsd3b5 Sp7	0.03 0.07	0.00 0.00	Hsd3b5 Sp7	0.68 1.71	0.00 0.58	ND	SP7	1.08 0.72
olfactory receptor 176	Olfr176	0.08	0.01	ND			ND		
core-binding factor, runt domain, alpha subunit 2, translocated to, 3 (human)	Cbfa2t3	0.11	0.01	Cbfa2t3	0.75	0.23	CBFA2T3	0.73	0.13
spermatogenesis associated, serine-rich 2-like	Spats2l	0.13	0.01	Spats2l	0.76	0.02	SPATS2L	0.85	0.08
sushi domain containing 4	Susd4	0.13	0.03	Susd4	1.16	0.12	SUSD4	0.38	0.12
cyclin-dependent kinase 15	Cdk15	0.13	0.00	ND			CDK15	0.61	0.13
RIKEN cDNA A430048G15 gene	A430048G15Rik	0.14	0.00	ND			ND		
noggin	Nog	0.14	0.00	Nog	0.36	0.05	NOG	0.94	0.79
WD repeat domain 85	Wdr85	0.14	0.01	ND			WDR85	1.21	0.01
RIKEN cDNA 5330439K02 gene	5330439K02Rik	0.14	0.01	ND			ND		
olfactory receptor 139	Olfr139	0.15	0.01	ND			ND		
SPEG complex locus	Speg	0.15	0.01	Speg	1.23	0.37	SPEG	1.66	0.31
predicted gene 2447	Gm2447	0.15	0.00	ND			ND		
vomeronasal 2, receptor 56	Vmn2r56	0.16	0.02	Vom2r33	1.24	0.01	ND		
cDNA sequence BC089597	BC089597	0.16	0.01	Rdh16	0.28	0.04	RDH16	1.01	0.97
RIKEN cDNA 4930565B19 gene	4930565B19Rik	0.16	0.01	ND			ND		
dynamin 3, opposite strand	Dnm3os	0.16	0.02	ND			ND		
beaded filament structural protein 2, phakinin	Bfsp2	0.17	0.01	ND			BFSP2	1.88	0.40
malate dehydrogenase 1B, NAD (soluble)	Mdh1b	0.17	0.00	Mdh1b	0.90	0.71	MDH1B	0.77	0.25
olfactory receptor 324	Olfr324	0.17	0.00	Olr1431	2.05	0.06	ND		
developmental pluripotency associated 4	Dppa4	0.17	0.00	ND			ND		
recombination activating gene 2	Rag2	0.17	0.05	Rag2	1.15	0.14	RAG2	2.02	0.34
ORAI calcium release-activated calcium modulator 2	Orai2	0.17	0.00	Orai2	0.45	0.34	ORAI2	1.80	0.14
predicted gene 10827	Gm10827	0.18	0.01	ND			ND		
solute carrier family 24 (sodium/butassium/calcium exchanger), member C2	Slc24a3	0.18	0.01	Slc24a3	0.69	0.34	SLC24A3	1.68	0.36
calcium-dependent domain containing 4C	C2cd4c	0.18	0.01	C2cd4c	1.43	0.31	C2CD4C	0.95	0.88
transmembrane protein 130	Tmem130	0.18	0.01	Tmem130	1.29	0.11	TMEM130	1.00	1.00
somatostatin	Sst	0.18	0.00	Sst	1.42	0.19	SST	4.07	0.10
succinate receptor 1	Sucnr1	0.18	0.01	Sucnr1	1.30	0.03	SUCNR1	0.89	0.66
protein phosphatase 1, regulatory (inhibitor) subunit 3C	Ppp1r3c	0.18	0.00	Ppp1r3c	0.79	0.32	PPP1R3C	1.57	0.17
olfactory receptor 1109	Olfr1109	0.18	0.02	Olr541	0.50	0.45	ND		
predicted gene 10389	Gm10389	0.18	0.00	ND			ND		
prodynorphin	Pdyn	0.18	0.00	Pdyn	1.14	0.14	PDYN	2.54	0.42
predicted gene, 20822	Gm20822	0.19	0.00	ND			ND		
family with sequence similarity 5, member B	Fam5b	0.19	0.03	Fam5b	2.03	0.09	FAM5B	0.98	0.93
RIKEN cDNA 4930487D11 gene	4930487D11Rik	0.19	0.01	ND			ND		
olfactory receptor 248	Olfr248	0.19	0.00	ND			ND		
RIKEN cDNA 2810474O19 gene	2810474O19Rik	0.19	0.00	RGD1309621	0.70	0.03	C12orf35	0.82	0.20
AP2 associated kinase 1	Aak1	0.20	0.02	Aak1	1.35	0.08	AAK1	1.21	0.23
predicted gene 10325	Gm10325	0.20	0.01	ND			ND		
calcium/calmodulin-dependent protein kinase II, beta	Camk2b	0.20	0.03	Camk2b	0.62	0.24	CAMK2B	0.57	0.08
olfactory receptor 259	Olfr259	0.20	0.01	Olr542	0.55	0.44	ND		
vomeronasal 2, receptor 10	Vmn2r10	0.20	0.00	ND			ND		
insulin-like growth factor 2	Igf2	0.21	0.03	Igf2	0.62	0.28	IGF2	0.69	0.04
protein tyrosine phosphatase, receptor type, O	Ptpro	0.21	0.01	Ptpro	0.86	0.27	PTPRO	0.08	0.38
olfactory receptor 1222	Olfr1222	0.21	0.02	Olr679	1.21	0.02	ND		
hematopoietic cell transcript 1	Hemt1	0.22	0.01	Gml	5.49	0.42	GML	0.89	0.75
HECT domain containing 2	Hectd2	0.22	0.00	Hectd2	0.88	0.58	HECTD2	0.91	0.63
hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 2	Hsd3b2	0.22	0.01	ND			HSD3B1	0.44	0.08
olfactory receptor 100	Olfr100	0.22	0.03	ND			ND		
ephrin A5	Efna5	0.22	0.02	Efna5	0.28	0.00	EFNA5	0.75	0.58
vomeronasal 2, receptor 88	Vmn2r88	0.22	0.01	ND			ND		
serine (or cysteine) peptidase inhibitor, clade A (alpha-1 antitrypsin. antitrypsin). member 9	Serpina9	0.22	0.04	Serpina9	1.13	0.21	SERPINA9	1.48	0.41

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
potassium voltage-gated channel, Shal-related family, member 1	Kcnd1	0.23	0.02	Kcnd1	1.27	0.37	KCND1	0.97	0.89
sparc/osteonectin, cwcv and kazal-like domains proteoglycan 1	Spock1	0.23	0.01	Spock1	0.58	0.05	SPOCK1	0.91	0.63
steroidogenic acute regulatory protein	Star	0.23	0.02	Star	0.48	0.00	STAR	1.18	0.55
C1D nuclear receptor co-repressor	C1d	0.23	0.00	C1d	0.94	0.37	ND		
olfactory receptor 1316	Olfr1316	0.23	0.02	Olr788	2.24	0.21	ND		
solute carrier family 22 (organic anion transporter), member 7	Slc22a7	0.23	0.01	Slc22a7	0.66	0.00	SLC22A7	0.61	0.04
RIKEN cDNA 2810007J24 gene	2810007J24Rik	0.24	0.01	ND			ND		
zinc finger protein 619	Zfp619	0.24	0.00	ND			ZNF619	0.80	0.34
Na+/K+ transporting ATPase interacting 2	Nkain2	0.24	0.00	ND			NKAIN2	1.26	0.37
eukaryotic translation initiation factor 2C, 2	Eif2c2	0.24	0.00	Eif2c2	0.87	0.21	EIF2C2	1.41	0.00
zinc finger protein 536	Zfp536	0.24	0.03	Zfp536	1.32	0.52	ZNF536	1.44	0.10
sialic acid binding Ig-like lectin H	Siglech	0.24	0.01	Siglech	2.06	0.00	ND		
talin 2	Tln2	0.24	0.01	ND			TLN2	0.99	0.94
RIKEN cDNA 4933433G19 gene	4933433G19Rik	0.24	0.00	ND			ND		
defensin, alpha, related sequence 2	Defa-rs2	0.24	0.00	ND			ND		
nudix (nucleoside diphosphate linked moiety X)-type motif 7	Nudt7	0.24	0.00	Nudt7	0.76	0.08	NUDT7	1.13	0.48
RIKEN cDNA E330014E10 gene	E330014E10Rik	0.24	0.01	ND			ND		
ATPase, Ca++ transporting, plasma membrane peptidase M20 domain containing 2	Atp2b4	0.25	0.01	Atp2b4	3.81	0.05	ATP2B4	1.33	0.20
olfactory receptor 638	Pm20d2	0.25	0.01	Pm20d2	0.72	0.35	PM20D2	1.38	0.13
carboxylesterase 3B	Olfr638	0.25	0.01	Olr140	1.17	0.06	OR51Q1	1.67	0.42
coiled-coil domain containing 93	Ces3b	0.25	0.01	ND			CES3	0.56	0.00
VPS10 domain receptor protein SORCS 1	Ccdc93	0.26	0.00	Ccdc93	1.16	0.02	CCDC93	0.90	0.32
aldehyde oxidase 3	Sorcs1	0.26	0.02	Sorcs1	2.18	0.13	SORCS1	0.40	0.20
neurobeachin like 1	Aox3	0.26	0.00	Aox3	1.29	0.53	ND		
oxysterol binding protein-like 6	Nbeal1	0.26	0.02	Nbeal1-ps1	1.16	0.05	NBEAL1	1.14	0.32
minichromosome maintenance deficient 10 (S. cerevisiae)	Osbpl6	0.26	0.01	Osbpl6	1.15	0.15	OSBPL6	1.18	0.25
RIKEN cDNA 1700111N16 gene	Mcm10	0.26	0.01	Mcm10	0.36	0.08	MCM10	2.06	0.18
olfactory receptor 1276	1700111N16Rik	0.26	0.01	ND			ND		
predicted gene 1070	Olfr1276	0.26	0.01	Olr748	1.17	0.06	ND		
predicted gene 13399	Gm1070	0.27	0.00	ND			ND		
odorant binding protein 2A	Gm13399	0.27	0.01	ND			ND		
glycoprotein hormone alpha 2	Obp2a	0.27	0.04	Obp2a	1.09	0.46	OBP2B	1.14	0.56
leucine-rich repeat, immunoglobulin-like and transmembrane domains 1	Gpha2	0.27	0.01	Gpha2	1.10	0.57	GPHA2	1.05	0.90
leptin	Lrit1	0.27	0.01	Lrit1	2.81	0.18	LRIT1	0.87	0.81
ankyrin repeat domain 13 family, member D	Lep	0.27	0.00	Lep	0.70	0.15	LEP	2.56	0.27
parvalbumin	Ankrd13d	0.27	0.00	Ankrd13d	0.82	0.53	ANKRD13D	1.25	0.08
huntingtin-associated protein 1	Pvalb	0.27	0.01	Pvalb	1.60	0.22	PVALB	1.08	0.84
selectin, platelet	Hap1	0.27	0.00	Hap1	1.13	0.11	HAP1	0.87	0.53
neurotrophic tyrosine kinase, receptor, type 3	Selp	0.27	0.00	Selp	0.60	0.44	SELP	1.27	0.64
RIKEN cDNA D930048G16 gene	Ntrk3	0.27	0.00	Ntrk3	1.19	0.17	NTRK3	1.75	0.21
GS homeobox 2	D930048G16Rik	0.27	0.02	ND			ND		
RIKEN cDNA A330069K06 gene	Gsx2	0.27	0.00	Gsx2	1.31	0.31	GSX2	0.81	0.39
transmembrane protein 66	A330069K06Rik	0.28	0.00	ND			ND		
forkhead box M1	Tmem66	0.28	0.00	Tmem66	1.06	0.23	TMEM66	1.20	0.11
phosphofuran acidic cluster sorting protein 2	Foxm1	0.28	0.01	Foxm1	2.24	0.01	FOXM1	1.57	0.42
RIKEN cDNA D030024E09 gene	Pacs2	0.28	0.01	ND			PACS2	0.92	0.45
ski sarcoma viral oncogene homolog (avian) expressed sequence C88045	D030024E09Rik	0.28	0.01	ND			ND		
RIKEN cDNA B230303O12 gene	Ski	0.28	0.03	ND			SKI	0.73	0.40
RIKEN cDNA 4933439N14 gene	C88045	0.28	0.01	ND			ND		
olfactory receptor 1111	B230303O12Rik	0.28	0.03	ND			ND		
dual oxidase maturation factor 2	4933439N14Rik	0.28	0.01	ND			ND		
complement component 9	Olfr1111	0.28	0.04	Olr544	1.24	0.09	OR5AS1	1.11	0.77
predicted gene 11213	Duoxa2	0.28	0.03	Duoxa2	2.07	0.19	DUOXA2	0.65	0.20
	C9	0.28	0.01	C9	0.83	0.11	C9	0.79	0.09
	Gm11213	0.29	0.01	ND			ND		

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
polycystic kidney disease 1 like 3	Pkd1l3	0.29	0.01	ND			PKD1L3	1.40	0.06
crystallin, gamma F	Crygf	0.29	0.00	Crygf	1.96	0.05	ND		
predicted gene 10638	Gm10638	0.29	0.00	ND			ND		
olfactory receptor 103	Olfr103	0.29	0.01	Olr1734	2.17	0.11	ND		
olfactory receptor 576	Olfr576	0.29	0.00	Olr68	0.89	0.34	OR51A7	0.75	0.59
arylalkylamine N-acetyltransferase	Aanat	0.29	0.01	Aanat	0.43	0.41	AANAT	1.51	0.33
TAF6-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor transmembrane protein, adipocyte associated 1	Taf6l	0.29	0.03	Taf6l	0.96	0.66	TAF6L	0.99	0.91
killer cell lectin-like receptor, subfamily A, D-aspartate oxidase	Klra5	0.29	0.00	Ly49si2	0.77	0.34	ND		
olfactory receptor 868	Ddo	0.29	0.01	Ddo	1.44	0.16	DDO	0.83	0.18
predicted gene 6034	Gm6034	0.29	0.00	Olr1179	1.33	0.27	ND		
secretogranin V	Scg5	0.30	0.02	Scg5	1.41	0.15	SCG5	0.50	0.11
ubiquitin specific peptidase 43	Usp43	0.30	0.00	Usp43	0.70	0.38	USP43	0.85	0.39
guanine nucleotide binding protein, alpha stimulatory, olfactory type	Gnal	0.30	0.01	Gnal	0.90	0.21	GNAL	1.11	0.78
late cornified envelope 3B	Lce3b	0.30	0.02	ND			LCE3B	1.05	0.79
ribosomal protein L6	Rpl6	0.30	0.01	ND			RPL6	1.05	0.61
RIKEN cDNA 4930579C12 gene	4930579C12Rik	0.30	0.04	ND			ND		
olfactory receptor 74	Olfr74	0.30	0.00	Olr604	1.15	0.16	ND		
sex comb on midleg-like 4 (Drosophila)	Scml4	0.30	0.01	Scml4	0.72	0.04	SCML4	1.24	0.70
expressed sequence AU015791	AU015791	0.30	0.02	ND			ND		
angiogenin, ribonuclease A family, member 4	Ang4	0.30	0.01	ND			ND		
RIKEN cDNA 6430531B16 gene	6430531B16Rik	0.31	0.00	LOC680693	1.63	0.01	ND		
RIKEN cDNA D330025C20 gene	D330025C20Rik	0.31	0.05	ND			ND		
prosaposin-like 1	Psapl1	0.31	0.01	ND			PSAPL1	2.47	0.31
RIKEN cDNA C920008N22 gene	C920008N22Rik	0.31	0.00	ND			ND		
olfactory receptor 635	Olfr635	0.31	0.03	Olr140	1.17	0.06	OR51Q1	1.67	0.42
cadherin-related family member 4	Cdhr4	0.31	0.01	Cdhr4	1.15	0.12	CDHR4	0.73	0.60
cytochrome P450, family 2, subfamily c, polypeptide 67	Cyp2c67	0.31	0.04	Cyp2c13	0.64	0.00	ND		
RIKEN cDNA 8430408G22 gene	8430408G22Rik	0.31	0.03	LOC500300	0.76	0.48	C10orf10	1.19	0.81
H6 homeobox 1	Hmx1	0.32	0.00	Hmx1	1.03	0.76	HMX1	0.72	0.31
Fc receptor, IgE, low affinity II, alpha polypeptide	Fcer2a	0.32	0.00	Fcer2	0.51	0.07	FCER2	1.01	0.98
envoplakin	Evpl	0.32	0.02	Evpl	1.26	0.32	EVPL	0.89	0.36
phosphoinositide-3-kinase, class 2, beta	Pik3c2b	0.32	0.00	Pik3c2b	0.89	0.65	PIK3C2B	1.48	0.07
polypeptide olfactory receptor 1143	Olfr1143	0.32	0.01	Olr590	1.16	0.12	ND		
mitogen-activated protein kinase 11	Mapk11	0.32	0.00	Mapk11	1.22	0.22	MAPK11	0.88	0.53
isoprenoid synthase domain containing 3-hydroxy-3-methylglutaryl-Coenzyme A	Ispd	0.32	0.02	Ispd	1.17	0.04	ISPD	0.68	0.16
alanine-glyoxylate aminotransferase 2-like 1	Hmgcs2	0.32	0.01	Hmgcs2	0.70	0.00	HMGCS2	0.66	0.06
DNA (cytosine-5-)methyltransferase 3-like	Agxt2l1	0.32	0.00	ND			AGXT2L1	1.78	0.12
tripartite motif-containing 34A	Dnmt3l	0.32	0.02	Dnmt3l	1.52	0.26	DNMT3L	0.63	0.10
coiled-coil domain containing 135	Trim34a	0.32	0.04	ND			ND		
olfactory receptor 713	Ccdc135	0.32	0.00	Ccdc135	0.95	0.85	CCDC135	0.93	0.85
olfactory receptor 424	Olfr713	0.32	0.00	Olr227	1.67	0.23	OR10A5	1.47	0.57
cytochrome c oxidase assembly protein 17	Olfr424	0.32	0.04	Olr1593	1.40	0.29	ND		
predicted gene 15217	Cox17	0.32	0.00	Cox17	0.92	0.21	COX17	0.97	0.73
expressed sequence AW125646	Gm15217	0.32	0.01	ND			ND		
RIKEN cDNA 4930529M08 gene	AW125646	0.32	0.00	ND			ND		
RIKEN cDNA 2700046G09 gene	4930529M08Rik	0.32	0.00	ND			C20orf26	0.77	0.12
myosin, heavy polypeptide 2, skeletal muscle, predicted gene 16340	2700046G09Rik	0.32	0.01	ND			ND		
olfactory receptor 392	Myh2	0.32	0.02	Myh2	0.43	0.21	MYH2	1.92	0.48
roundabout homolog 3 (Drosophila)	Gm16340	0.33	0.01	ND			ND		
ADP-ribosylation factor-like 9	Olfr392	0.33	0.00	Olr1500	5.13	0.17	ND		
transmembrane protein 179B	Robo3	0.33	0.03	Robo3	1.16	0.06	ROBO3	1.03	0.92
WD repeat domain 52	Arl9	0.33	0.02	Arl9	0.15	0.41	ARL9	2.36	0.14
olfactory receptor 586	Tmem179b	0.33	0.00	Tmem179b	0.92	0.05	TMEM179B	1.05	0.58
	Wdr52	0.33	0.02	Wdr52	1.15	0.15	WDR52	1.74	0.11
	Olfr586	0.33	0.00	Olr72	1.14	0.13	OR51A2	0.76	0.62

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB				Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	
energy homeostasis associated	Enho	0.33	0.02	ND			ND			
olfactory receptor 215	Olfr215	0.33	0.00	Olr832	1.17	0.09	ND			
transmembrane channel-like gene family 6	Tmc6	0.34	0.01	ND			TMC6	1.56	0.05	
olfactory receptor 1106	Olfr1106	0.34	0.02	Olr539	1.13	0.15	ND			
RIKEN cDNA 4930519P11 gene	4930519P11Rik	0.34	0.03	ND			ND			
RIKEN cDNA 1810008I18 gene	1810008I18Rik	0.34	0.00	ND			ND			
polycystic kidney disease 1 like 2	Pkd1l2	0.34	0.03	ND			PKD1L2	3.12	0.34	
RIKEN cDNA A930009E08 gene	A930009E08Rik	0.34	0.00	ND			ND			
calcium channel, voltage-dependent, alpha 1F subunit	Cacna1f	0.34	0.01	Cacna1f	1.26	0.05	CACNA1F	0.80	0.54	
calcium channel, voltage-dependent, alpha 2/delta subunit 2	Cacna2d2	0.34	0.02	Cacna2d2	1.29	0.63	CACNA2D2	0.82	0.41	
acyl-Coenzyme A binding domain containing 4	Acb4	0.34	0.00	Acb4	0.81	0.14	ACBD4	0.76	0.08	
RIKEN cDNA 1700016K19 gene	1700016K19Rik	0.34	0.01	RGD1565611	1.22	0.33	C17orf97	0.92	0.75	
cDNA sequence BC048943	BC048943	0.34	0.03	RGD1305627	1.10	0.27	ND			
NLR family, pyrin domain containing 1C, pseudogene	Nlrp1c-ps	0.34	0.01	ND			ND			
protease, serine, 33	Prss33	0.34	0.02	Prss33	0.63	0.53	PRSS33	1.65	0.10	
RIKEN cDNA 9530046B11 gene	9530046B11Rik	0.34	0.03	ND			ND			
homeobox A4	Hoxa4	0.34	0.02	ND			HOXA4	0.47	0.21	
cDNA sequence BC024137	BC024137	0.34	0.03	ND			ND			
RIKEN cDNA 3110082I17 gene	3110082I17Rik	0.34	0.01	LOC498154	1.06	0.62	C7orf50	0.95	0.59	
meningioma 1	Mn1	0.34	0.01	Mn1	0.87	0.59	MN1	0.98	0.93	
murinoglobulin 1	Mug1	0.34	0.04	A1i3	0.91	0.07	ND			
kinase suppressor of ras 1	Ksr1	0.34	0.01	Ksr1	1.16	0.09	KSR1	0.40	0.34	
cyclin A1	Ccna1	0.34	0.01	Ccna1	1.42	0.23	CCNA1	0.77	0.38	
tetratricopeptide repeat domain 39C	Ttc39c	0.35	0.00	ND			TTC39C	1.41	0.03	
gamma-aminobutyric acid (GABA) A receptor, subunit epsilon	Gabre	0.35	0.03	Gabre	1.18	0.09	GABRE	2.46	0.11	
olfactory receptor 48	Olfr48	0.35	0.04	Olr721	1.15	0.18	ND			
G protein-coupled receptor 4	Gpr4	0.35	0.00	Gpr4	0.90	0.31	GPR4	1.10	0.76	
prolactin family 6, subfamily a, member 1	Prl6a1	0.35	0.01	Prl6a1	1.51	0.17	ND			
predicted gene 10866	Gm10866	0.35	0.00	ND			ND			
testis expressed gene 9	Tex9	0.35	0.02	ND			TEX9	1.49	0.37	
keratin 6B	Krt6b	0.35	0.00	ND			KRT6A	0.47	0.40	
otospiralin	Otos	0.35	0.01	Otos	0.61	0.03	OTOS	1.02	0.95	
tryptase beta 2	Tpsb2	0.35	0.03	Tpsb2	0.97	0.91	TPSAB1	0.03	0.39	
hydroxysteroid (17-beta) dehydrogenase 6	Hsd17b6	0.35	0.01	Hsd17b6	0.74	0.14	HSD17B6	0.95	0.76	
AF4/FMR2 family, member 3	Aff3	0.35	0.00	Aff3	0.79	0.66	AFF3	2.81	0.40	
cytochrome P450, family 2, subfamily u, polypeptide 1	Cyp2u1	0.35	0.01	Cyp2u1	0.81	0.14	CYP2U1	1.09	0.55	
cytochrome P450, family 7, subfamily b, polypeptide 1	Cyp7b1	0.35	0.00	Cyp7b1	0.54	0.03	CYP7B1	0.74	0.47	
dynein, axonemal, heavy chain 14	Dnahc14	0.35	0.05	ND			ND			
zinc finger protein 367	Zfp367	0.35	0.01	Zfp367	2.92	0.00	ZNF367	1.48	0.15	
epidermal growth factor receptor	Egfr	0.35	0.00	Egfr	0.69	0.00	EGFR	1.17	0.23	
neuropeptides B/W receptor 1	Npbwr1	0.35	0.02	Npbwr1	1.18	0.05	NPBWR1	1.34	0.48	
olfactory receptor 1307	Olfr1307	0.35	0.01	Olr780	1.20	0.04	ND			
GRB2 associated, regulator of MAPK1-like telomerase RNA component	Gareml	0.35	0.00	Gareml	2.22	0.31	ND			
chromobox 1	Cbx1	0.35	0.04	ND			ND			
family with sequence similarity 89, member A	Fam89a	0.35	0.02	Fam89a	0.61	0.21	FAM89A	1.48	0.01	
serine (or cysteine) peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 7	Serpina7	0.35	0.00	Serpina7	0.93	0.89	SERPINA7	0.96	0.71	
homeobox B6	Hoxb6	0.35	0.04	Hoxb6	1.07	0.72	HOXB6	0.60	0.34	
RIKEN cDNA 1700101E01 gene	1700101E01Rik	0.35	0.00	RGD1564114	1.21	0.48	C9orf171	1.68	0.38	
INO80 complex subunit E	Ino80e	0.35	0.03	Ino80e	1.23	0.05	INO80E	1.02	0.88	
RIKEN cDNA 1700110I01 gene	1700110I01Rik	0.36	0.01	ND			ND			
vomeronasal 2, receptor 59	Vmn2r59	0.36	0.01	ND			ND			
choline kinase alpha	Chka	0.36	0.03	Chka	1.03	0.78	CHKA	0.88	0.34	
RIKEN cDNA 4930405D01 gene	4930405D01Rik	0.36	0.05	ND			ND			
RIKEN cDNA 1810010D01 gene	1810010D01Rik	0.36	0.00	ND			ND			

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
sphingomyelin phosphodiesterase 1, acid	Smpd1	0.36	0.00	Smpd1	1.03	0.68	SMPD1	1.35	0.07
lysosomal biogenesis of lysosome-related organelles complex-1, subunit 3	Bloc1s3	0.36	0.01	Bloc1s3	1.13	0.67	BLOC1S3	1.27	0.31
carbonic anhydrase 11	Car11	0.36	0.02	Car11	0.69	0.02	CA11	1.23	0.55
butyrophilin-like 5	Btnl5	0.36	0.01	ND			ND		
adrenergic receptor, beta 3	Adrb3	0.36	0.02	Adrb3	1.51	0.16	ADRB3	1.52	0.13
glutathione S-transferase omega 2	Gsto2	0.36	0.00	Gsto2	1.18	0.29	GSTO2	0.83	0.24
dynein, axonemal, heavy chain 7A	Dnahc7a	0.36	0.01	ND			DNAH7	1.45	0.22
monoglyceride lipase	Mgll	0.36	0.00	Mgll	1.12	0.50	MGLL	1.08	0.62
cyclin Y-like 1	Ccnyl1	0.36	0.02	Ccnyl1	0.88	0.04	CCNYL1	0.97	0.76
leucine rich repeat containing 2	Lrrc2	0.36	0.00	Lrrc2	0.94	0.66	LRRC2	0.67	0.43
mucolipin 3	Mcoln3	0.36	0.01	Mcoln3	0.73	0.01	MCOLN3	0.67	0.12
secretoglobin, family 1A, member 1 (uteroglobin)	Scgb1a1	0.36	0.00	Scgb1a1	0.81	0.06	SCGB1A1	1.05	0.64
histocompatibility 2, class II antigen A, beta 1	H2-Ab1	0.36	0.00	RT1-Bb	1.17	0.62	HLA-DQB1	1.90	0.33
solute carrier family 28 (sodium-coupled nucleoside transporter), member 3	Slc28a3	0.36	0.05	Slc28a3	0.57	0.47	SLC28A3	1.00	0.99
predicted gene 2044	Gm2044	0.37	0.03	ND			ND		
arylacetamide deacetylase-like 3	Aadacl3	0.37	0.01	Aadacl3	0.53	0.18	AADACL3	0.93	0.68
non-protein coding RNA 86	Ncrna00086	0.37	0.02	ND			CXorf69	2.26	0.36
coiled coil domain containing 88A	Ccdc88a	0.37	0.00	Ccdc88a	0.67	0.08	CCDC88A	1.06	0.53
BTB (POZ) domain containing 10	Btbd10	0.37	0.01	Btbd10	1.30	0.02	BTBD10	1.03	0.81
serine/arginine-rich splicing factor 3	Srsf3	0.37	0.01	Srsf3	0.77	0.04	SRSF3	1.45	0.06
secretoglobin, family 2B, member 20	Scgb2b20	0.37	0.00	ND			ND		
cytochrome P450, family 2, subfamily c, polypeptide 68	Cyp2c68	0.37	0.01	Cyp2c13	0.64	0.00	ND		
APC membrane recruitment 3	Amer3	0.37	0.00	Amer3	2.31	0.25	FAM123C	1.05	0.84
purine-rich element binding protein G	Purg	0.37	0.01	ND			PURG	1.62	0.10
suppressor APC domain containing 2	Sapcd2	0.37	0.01	Sapcd2	2.50	0.01	C9orf140	1.47	0.32
vomeronasal 1 receptor 81	Vmn1r81	0.37	0.01	Vom1r47	1.17	0.07	ND		
NK1 transcription factor related, locus 1	Nkx1-1	0.37	0.00	ND			ND		
predicted gene 5237	Gm5237	0.37	0.01	ND			ND		
Eph receptor A8	Epha8	0.37	0.03	Epha8	1.55	0.16	EPHA8	1.36	0.58
5-hydroxytryptamine (serotonin) receptor 6	Htr6	0.37	0.01	Htr6	0.93	0.87	HTR6	2.12	0.12
vesicle-associated membrane protein 1	Vamp1	0.37	0.00	Vamp1	0.81	0.10	VAMP1	0.79	0.11
ankyrin repeat and SOCS box-containing 1	Asb1	0.38	0.04	Asb1	0.48	0.17	ASB1	1.26	0.01
solute carrier family 1 (glial high affinity glutamate transporter), member 2	Slc1a2	0.38	0.02	Slc1a2	0.46	0.01	SLC1A2	1.17	0.38
olfactory receptor 1131	Olfr1131	0.38	0.01	Olr575	1.35	0.13	ND		
ADP-ribosylhydrolase like 1	Adprhl1	0.38	0.01	Adprhl1	0.96	0.88	ADPRHL1	0.98	0.92
RIKEN cDNA 1110014L15 gene	1110014L15Rik	0.38	0.01	ND			ND		
RIKEN cDNA 4930466K18 gene	4930466K18Rik	0.38	0.01	ND			ND		
cytochrome P450, family 46, subfamily a, polypeptide 1	Cyp46a1	0.38	0.02	Cyp46a1	1.36	0.26	CYP46A1	1.30	0.62
olfactory receptor 1419	Olfr1419	0.38	0.01	ND			ND		
CAAX box 1A	Cxx1a	0.38	0.01	ND			FAM127C	3.86	0.40
RIKEN cDNA C130079G13 gene	C130079G13Rik	0.38	0.01	ND			ND		
predicted gene 2102	Gm2102	0.38	0.00	ND			ND		
Fraser syndrome 1 homolog (human)	Fras1	0.38	0.01	Fras1	0.41	0.10	FRAS1	0.51	0.56
Sad1 and UNC84 domain containing 1	Sun1	0.38	0.01	Sun1	2.05	0.47	SUN1	0.72	0.17
olfactory receptor 338	Olfr338	0.38	0.04	Olr399	0.54	0.25	ND		
doublecortin-like kinase 2	Dclk2	0.38	0.04	Dclk2	0.91	0.38	DCLK2	1.16	0.66
ankyrin and armadillo repeat containing	Ankar	0.39	0.05	Ankar	0.52	0.15	ANKAR	1.06	0.71
zinc finger and SCAN domain containing 4C	Zscan4c	0.39	0.01	ND			ND		
hydroxysteroid (17-beta) dehydrogenase 3	Hsd17b3	0.39	0.02	Hsd17b3	1.88	0.46	HSD17B3	1.31	0.03
serine (or cysteine) peptidase inhibitor, clade B, member 3C	Serpinb3c	0.39	0.02	ND			ND		
cDNA sequence AY074887	AY074887	0.39	0.02	ND			ND		
ATP-binding cassette, sub-family A (ABC1), member 8a	Abca8a	0.39	0.01	ND			ND		
solute carrier family 43, member 1	Slc43a1	0.39	0.04	Slc43a1	1.05	0.75	SLC43A1	1.35	0.37
PDZ and LIM domain 7	Pdlim7	0.39	0.01	ND			ND		

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
predicted gene 4559	Gm4559	0.39	0.02	ND			ND		
predicted gene 4956	Gm4956	0.39	0.05	ND			ND		
secretoglobin, family 1B, member 30	Scgb1b30	0.39	0.02	Scgb1b30	1.20	0.04	ND		
fibroblast growth factor 1	Fgf1	0.39	0.04	Fgf1	0.85	0.04	FGF1	0.87	0.57
GTPase, IMAP family member 4	Gimap4	0.39	0.03	Gimap4	0.86	0.58	GIMAP4	1.01	0.98
engrailed 2	En2	0.39	0.02	En2	0.73	0.48	EN2	0.93	0.69
guanylate cyclase activator 2a (guanylin)	Guca2a	0.39	0.03	Guca2a	1.32	0.15	GUCA2A	1.06	0.85
transient receptor potential cation channel, subfamily V, member 4	Trpv4	0.39	0.00	Trpv4	4.72	0.02	TRPV4	1.62	0.02
RIKEN cDNA 2610027K06 gene	2610027K06Rik	0.39	0.02	ND			ND		
TD and POZ domain containing 2	Tdpoz2	0.39	0.01	ND			ND		
kin of IRRE like (Drosophila)	Kirrel	0.39	0.03	Kirrel	1.91	0.07	KIRREL	1.62	0.29
RIKEN cDNA 5031425E22 gene	5031425E22Rik	0.39	0.03	ND			ND		
RIKEN cDNA 9330151L19 gene	9330151L19Rik	0.40	0.02	ND			ND		
TATA box binding protein-like 1	Tbpl1	0.40	0.01	Tbpl1	0.90	0.07	TBPL1	1.07	0.67
RIKEN cDNA 4930544I03 gene	4930544I03Rik	0.40	0.00	ND			ND		
NOL1/NOP2/Sun domain family, member 7	Nsun7	0.40	0.02	Nsun7	2.31	0.33	NSUN7	0.90	0.70
solute carrier organic anion transporter family, member 1a1	Slco1a1	0.40	0.02	Slco1a1	0.92	0.05	ND		
olfactory receptor 787	Olfr787	0.40	0.01	Olr943	2.15	0.45	ND		
predicted gene 14135	Gm14135	0.40	0.03	ND			ND		
claudin 4	Cldn4	0.40	0.00	Cldn4	2.10	0.12	CLDN4	1.74	0.01
small nucleolar RNA, H/ACA box 47	Snora47	0.40	0.00	ND			ND		
RIKEN cDNA 1700010I14 gene	1700010I14Rik	0.40	0.03	MGC94891	1.08	0.46	C6orf118	0.82	0.58
tripartite motif-containing 65	Trim65	0.40	0.01	ND			ND		
nuclear receptor co-repressor 1	Ncor1	0.40	0.03	ND			NCOR1	0.70	0.00
RIKEN cDNA 9430015G10 gene	9430015G10Rik	0.40	0.03	RGD1311517	1.87	0.06	C1orf159	0.94	0.67
RIKEN cDNA 4930448A20 gene	4930448A20Rik	0.40	0.04	ND			ND		
transmembrane protein 14A	Tmem14a	0.40	0.04	Tmem14a	0.27	0.43	TMEM14A	0.98	0.92
AT-hook transcription factor	Akna	0.40	0.01	Akna	1.27	0.07	AKNA	0.60	0.26
retinol binding protein 2, cellular	Rbp2	0.40	0.04	Rbp2	0.96	0.79	RBP2	3.43	0.08
zyg-II family member B, cell cycle regulator	Zyg11b	0.40	0.03	Zyg11b	1.08	0.55	ZYG11B	0.87	0.35
tubulin tyrosine ligase-like family, member 13	Ttll13	0.40	0.00	ND			TTLL13	0.70	0.34
apoptosis-inducing, TAF9-like domain 1	Apitd1	0.41	0.03	ND			APITD1	1.21	0.09
basic helix-loop-helix family, member e41	Bhlhe41	0.41	0.02	ND			BHLHE41	0.47	0.18
peptidoglycan recognition protein 2	Pglyrp2	0.41	0.01	ND			PGLYRP2	0.72	0.27
MAS-related GPR, member E	Mrgpre	0.41	0.02	Mrgpre	3.66	0.25	MRGPRE	1.33	0.59
H2.0-like homeobox	Hlx	0.41	0.01	Hlx	0.90	0.26	HLX	0.52	0.16
carboxylesterase 3A	Ces3a	0.41	0.01	ND			CES3	0.56	0.00
vomeronasal 1 receptor 217	Vmn1r217	0.41	0.02	ND			ND		
predicted gene 15386	Gm15386	0.41	0.02	Defb17	4.32	0.25	ND		
carbohydrate (chondroitin 6/keratan)	Chst3	0.41	0.00	Chst3	1.67	0.13	CHST3	1.57	0.52
sulfotransferase 3							ND		
RIKEN cDNA 8430428J23 gene	8430428J23Rik	0.41	0.01	ND			ND		
Rho guanine nucleotide exchange factor (GEF)	Arhgef33	0.41	0.02	ND			ND		
chymase 2, mast cell	Cma2	0.41	0.03	ND			ND		
zinc finger protein 846	Zfp846	0.41	0.01	Zfp846	1.03	0.72	ZNF846	0.88	0.45
RIKEN cDNA 2610035D17 gene	2610035D17Rik	0.41	0.01	ND			ND		
FAT tumor suppressor homolog 2 (Drosophila)	Fat2	0.41	0.00	Fat2	1.17	0.06	FAT2	0.82	0.72
zinc finger protein 503	Zfp503	0.41	0.01	Zfp503	0.77	0.03	ZNF503	1.17	0.51
cDNA sequence BC025933	BC025933	0.41	0.03	ND			ND		
olfactory receptor 794	Olfr794	0.41	0.02	Olr889	1.46	0.51	ND		
methyltransferase like 21C	Mettl21c	0.41	0.00	Mettl21c	1.11	0.29	METTL21C	0.97	0.88
islet cell autoantigen 1-like	Ica1l	0.41	0.01	Ica1l	9.96	0.41	ICA1L	0.54	0.54
solute carrier family 17 (sodium phosphate), member 2	Slc17a2	0.41	0.01	Slc17a2	0.71	0.02	SLC17A2	0.58	0.02
C-type lectin domain family 2, member e	Clec2e	0.41	0.00	Clec2h	0.60	0.13	ND		
prokineticin 1	Prok1	0.41	0.05	Prok1	1.53	0.21	PROK1	0.57	0.29
RIKEN cDNA 1700128E19 gene	1700128E19Rik	0.41	0.01	ND			ND		
polymeric immunoglobulin receptor	Pigr	0.41	0.01	Pigr	0.76	0.05	PIGR	2.16	0.20
NADPH oxidase 4	Nox4	0.41	0.04	Nox4	0.50	0.09	NOX4	0.71	0.12

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

Gene Name	CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB				Chimeric mice treated with 1000 ppm NaPB			
	Gene symbol	Fold change	p value		Gene symbol	Fold change	p value		Gene symbol	Fold change	p value	
family with sequence similarity 122, member C	Fam122c	0.41	0.01		Fam122c	1.22	0.21		ND			
bassoon	Bsn	0.41	0.02		Bsn	0.65	0.15		BSN	0.93	0.75	
COMM domain containing 7	Commd7	0.41	0.03		Commd7	0.96	0.29		COMMD7	1.02	0.81	
G6B protein	G6b	0.42	0.03		ND				ND			
microtubule-associated protein 6	Map6	0.42	0.04		Map6	0.57	0.07		MAP6	1.03	0.89	
S100 calcium binding protein A2	S100a2	0.42	0.00		ND				ND			
inositol 1,4,5-triphosphate receptor interacting protein-like 2	Itpripl2	0.42	0.04		Itpripl2	1.41	0.00		ITPRIP1L2	1.03	0.90	
ADP-ribosylation factor-like 4D	Arl4d	0.42	0.05		Arl4d	1.71	0.20		ARL4D	1.23	0.36	
transmembrane protein 40	Tmem40	0.42	0.01		Tmem40	1.99	0.07		TMEM40	0.81	0.46	
ankyrin repeat domain 45	Ankrd45	0.42	0.01		Ankrd45	0.82	0.52		ANKRD45	0.88	0.40	
coiled-coil domain containing 42B	Ccdc42b	0.42	0.03		Ccdc42b	1.30	0.12		CCDC42B	0.70	0.40	
protein phosphatase 1 (formerly 2C)-like	Ppm1l	0.42	0.01		Ppm1l	0.62	0.00		PPM1L	1.79	0.12	
ladybird homeobox homolog 1 (Drosophila)	Lbx1	0.42	0.03		Lbx1	1.14	0.14		LBX1	0.87	0.49	
olfactory receptor 521	Olf521	0.42	0.01		Olr37	1.28	0.63		ND			
aristaless-like homeobox 4	Alx4	0.42	0.01		Alx4	1.11	0.84		ALX4	0.94	0.83	
histocompatibility 2, class II antigen A, alpha	H2-Aa	0.42	0.04		RT1-Ba	1.22	0.67		HLA-DQA1	1.15	0.74	
collagen, type V, alpha 3	Col5a3	0.42	0.03		Col5a3	1.30	0.03		COL5A3	0.32	0.03	
Rho family GTPase 1	Rnd1	0.42	0.02		Rnd1	1.15	0.50		RND1	1.56	0.18	
RIKEN cDNA 1110017D15 gene	1110017D15Rik	0.42	0.02		RGD1561916	0.84	0.09		C9orf24	1.01	0.91	
aminoglycoside phosphotransferase domain containing 1	Agphd1	0.42	0.02		Agphd1	1.52	0.01		AGPHD1	1.12	0.52	
a disintegrin and metalloproteinase domain 26B	Adam26b	0.42	0.03		Adam34	1.17	0.06		ND			
regucalcin	Rgn	0.42	0.02		Rgn	0.43	0.00		RGN	0.86	0.25	
membrane-spanning 4-domains, subfamily A, member 10	Ms4a10	0.42	0.02		Ms4a10	1.22	0.47		MS4A10	1.28	0.59	
testis expressed 26	Tex26	0.42	0.04		Tex26	1.13	0.21		C13orf26	0.21	0.40	
actin, alpha 2, smooth muscle, aorta	Acta2	0.42	0.01		Actg2	0.58	0.36		ACTG2	0.68	0.42	
neurexophilin and PC-esterase domain family, member 5	Nxpe5	0.42	0.03		LOC680711	0.48	0.06		ND			
mutS homolog 3 (E. coli)	Msh3	0.42	0.02		Msh3	0.79	0.13		MSH3	1.14	0.32	
RIKEN cDNA 4933407O12 gene	4933407O12Rik	0.42	0.03		ND				ND			
angiogenin, ribonuclease A family, member 3	Ang3	0.42	0.02		ND				ND			
prostaglandin D2 synthase (brain)	Ptgds	0.42	0.01		Ptgds	1.53	0.22		PTGDS	1.16	0.37	
transmembrane protein 247	Tmem247	0.42	0.04		ND				LOC388946	1.09	0.85	
CD27 antigen	Cd27	0.42	0.02		Cd27	1.76	0.04		CD27	0.57	0.18	
potassium channel tetramerisation domain containing 14	Kctd14	0.43	0.01		Kctd14	1.40	0.17		KCTD14	1.08	0.67	
RIKEN cDNA 2500002B13 gene	2500002B13Rik	0.43	0.01		ND				ND			
predicted gene 9054	Gm9054	0.43	0.03		ND				ND			
cysteine-rich hydrophobic domain 1	Chic1	0.43	0.00		Chic1	1.28	0.08		CHIC1	0.72	0.11	
D-2-hydroxyglutarate dehydrogenase	D2hgdh	0.43	0.00		D2hgdh	1.19	0.08		D2HGDH	0.87	0.18	
RIKEN cDNA 4933421I07 gene	4933421I07Rik	0.43	0.00		ND				ND			
TBC1 domain family, member 21	Tbc1d21	0.43	0.01		Tbc1d21	1.17	0.09		TBC1D21	0.23	0.45	
soc-2 (suppressor of clear) homolog (C. elegans)	Shoc2	0.43	0.05		Shoc2	0.94	0.80		SHOC2	0.85	0.12	
betaine-homocysteine methyltransferase	Bhmt	0.43	0.01		Bhmt	0.83	0.05		BHMT	0.64	0.02	
transmembrane protein 107	Tmem107	0.43	0.00		Tmem107	2.62	0.04		TMEM107	1.15	0.52	
predicted gene 14340	Gm14340	0.43	0.00		ND				ND			
RAB interacting factor	Rabif	0.43	0.00		Rabif	0.83	0.00		RABIF	1.04	0.87	
tissue factor pathway inhibitor	Tfpi	0.43	0.04		Tfpi	1.33	0.11		TFPI	0.83	0.15	
RNA (guanine-7-) methyltransferase	Rnmt	0.43	0.02		Rnmt	1.60	0.26		RNMT	0.75	0.06	
family with sequence similarity 170, member B	Fam170b	0.43	0.01		ND				FAM170B	1.01	0.97	
GLI pathogenesis-related 2	Glipr2	0.43	0.00		Glipr2	1.58	0.17		GLIPR2	0.57	0.13	
chondroitin polymerizing factor 2	Chpf2	0.43	0.01		ND				ND			
dual oxidase maturation factor 1	Duoxa1	0.43	0.03		Duoxa1	1.52	0.00		DUOXA1	0.63	0.38	
WD repeat domain 92	Wdr92	0.44	0.00		ND				WDR92	0.96	0.56	
inter-alpha trypsin inhibitor, heavy chain 2	Itih2	0.44	0.01		ND				ITIH2	1.05	0.78	
phospholipase D family, member 4	Pld4	0.44	0.00		Pld4	0.83	0.10		PLD4	1.07	0.88	
RIKEN cDNA 9530034A14 gene	9530034A14Rik	0.44	0.00		ND				ND			
vomeronasal 1 receptor 173	Vmn1r173	0.44	0.04		ND				ND			
RIKEN cDNA 4930556A20 gene	4930556A20Rik	0.44	0.03		ND				ND			

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
CD79A antigen (immunoglobulin-associated	Cd79a	0.44	0.02	Cd79a	1.65	0.12	CD79A	1.07	0.81
cytochrome P450, family 2, subfamily e, polypeptide 1	Cyp2e1	0.44	0.04	Cyp2e1	0.64	0.00	CYP2E1	0.69	0.09
glycan 5	Gpc5	0.44	0.04	Gpc5	0.61	0.44	GPC5	0.43	0.15
anaphase promoting complex subunit 7	Anapc7	0.44	0.02	Anapc7	0.84	0.20	ANAPC7	1.05	0.66
proline-rich transmembrane protein 4	Prrt4	0.44	0.04	Prrt4	1.41	0.18	PRRT4	0.97	0.92
predicted gene 10857	Gm10857	0.44	0.01	ND			ND		
apolipoprotein E	Apoe	0.44	0.01	Apoe	0.87	0.14	APOE	1.11	0.45
protein associated with topoisomerase II homolog 1 (yeast)	Patl1	0.44	0.01	Patl1	0.92	0.37	PATL1	1.12	0.40
albumin	Alb	0.44	0.01	Alb	0.92	0.07	ALB	1.04	0.70
heat shock transcription factor 2 binding protein	Hsf2bp	0.44	0.03	Hsf2bp	2.16	0.11	HSF2BP	0.89	0.58
anaphase promoting complex subunit 1	Anapc1	0.44	0.04	Anapc1	1.10	0.51	ANAPC1	0.61	0.08
mitogen-activated protein kinase kinase kinase 3	Map3k3	0.44	0.03	Map3k3	0.81	0.00	MAP3K3	1.09	0.47
RIKEN cDNA 9930021J03 gene	9930021J03Rik	0.44	0.02	RGD1311595	0.84	0.41	KIAA2026	0.76	0.12
RNA binding motif, single stranded interacting protein	Rbms3	0.44	0.04	ND			RBMS3	1.47	0.02
HtrA serine peptidase 2	Htra2	0.44	0.04	Htra2	1.18	0.00	HTRA2	1.26	0.53
alcohol dehydrogenase 4 (class II), pi	Adh4	0.44	0.03	Adh4	1.27	0.15	ADH4	0.75	0.16
regulator of G-protein signaling 12	Rgs12	0.44	0.05	Rgs12	0.73	0.08	RGS12	1.12	0.32
RIKEN cDNA 4931408D14 gene	4931408D14Rik	0.45	0.03	ND			ND		
expressed sequence AI427809	AI427809	0.45	0.02	ND			ND		
expressed sequence AW549542	AW549542	0.45	0.03	ND			ND		
olfactory receptor 149	Olfr149	0.45	0.04	Olr1315	1.21	0.03	ND		
steroid 5 alpha-reductase 2	Srd5a2	0.45	0.01	Srd5a2	0.99	0.96	SRD5A2	0.59	0.17
expressed sequence AI593442	AI593442	0.45	0.02	ND			C11orf87	0.58	0.43
integrin alpha M	Itgam	0.45	0.02	Itgam	1.04	0.56	ITGAM	1.51	0.18
single-stranded DNA binding protein 1	Ssbp1	0.45	0.03	Ssbp1	0.96	0.36	SSBP1	1.03	0.74
expressed sequence AA684185	AA684185	0.45	0.01	ND			ND		
butyrophilin-like 9	Btnl9	0.45	0.00	ND			BTNL9	1.03	0.92
dopamine receptor D2	Drd2	0.45	0.04	Drd2	6.37	0.03	DRD2	0.80	0.38
cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	Chrnb2	0.45	0.03	Chrnb2	0.96	0.86	CHRNB2	0.79	0.40
transcription factor 19	Tcf19	0.45	0.01	Tcf19	2.91	0.02	TCF19	1.15	0.77
neutral sphingomyelinase (N-SMase) activation associated factor	Nsmaf	0.45	0.01	Nsmaf	1.11	0.32	NSMAF	1.03	0.87
zinc finger protein 11	Zfp11	0.45	0.00	ND			ZNF546	1.46	0.33
olfactory receptor 207	Olfr207	0.45	0.03	Olr1528	1.20	0.72	ND		
cyclin-dependent kinase 5, regulatory subunit 1 (p35)	Cdk5r1	0.45	0.01	Cdk5r1	1.18	0.27	CDK5R1	0.87	0.45
a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 synaptotagmin V	Adamts13	0.45	0.00	ND			ADAMTS13	1.23	0.14
olfactory receptor 441	Syt5	0.45	0.03	Syt5	0.91	0.41	SYT5	0.40	0.35
cytochrome C oxidase assembly factor 5	Olfr441	0.45	0.02	Olr186	1.14	0.18	OR2A2	0.92	0.82
predicted gene 14015	Coa5	0.45	0.04	Coa5	1.19	0.03	COA5	0.84	0.05
G patch domain containing 8	Gm14015	0.45	0.04	ND			ND		
insulin receptor substrate 2	Gpatch8	0.46	0.04	ND			ND		
mucin 20	Irs2	0.46	0.05	Irs2	0.93	0.70	IRS2	0.75	0.13
serine/threonine/tyrosine interaction protein	Muc20	0.46	0.03	Muc20	1.48	0.46	MUC20	0.81	0.36
protocadherin alpha subfamily C, 2	Styx	0.46	0.02	LOC689246	1.38	0.03	STYX	0.70	0.09
vomeronasal 2, receptor 11	Pcdhac2	0.46	0.00	Pcdhac2	1.12	0.79	PCDHAC2	0.95	0.84
protein kinase C, epsilon	Vmn2r11	0.46	0.00	Vomr73	1.43	0.03	ND		
inter-alpha trypsin inhibitor, heavy chain 1	Prkce	0.46	0.02	Prkce	1.13	0.25	PRKCE	0.67	0.26
ring finger protein 103	Itih1	0.46	0.01	Itih1	0.73	0.00	ITIH1	0.80	0.16
TLC domain containing 2	Rnf103	0.46	0.01	Rnf103	1.08	0.13	RNF103	1.01	0.96
olfactory receptor 730	Tlcd2	0.46	0.02	Tlcd2	2.02	0.05	TLCD2	1.32	0.04
predicted gene 10568	Olfr730	0.46	0.00	Olr1608	1.02	0.93	OR4K2	1.04	0.88
bone morphogenetic protein 4	Gm10568	0.46	0.00	ND			ND		
predicted gene 5935	Bmp4	0.46	0.01	Bmp4	0.63	0.12	BMP4	1.07	0.81
dual oxidase 2	Gm5935	0.46	0.02	ND			ND		
troponin I, skeletal, fast 2	Duo2	0.46	0.03	Duo2	1.24	0.28	DUOX2	2.19	0.34
	Tnni2	0.46	0.01	Tnni2	1.20	0.43	TNNI2	1.24	0.47

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
NSA2 ribosome biogenesis homolog (S. mutated in colorectal cancers)	Nsa2	0.46	0.00	ND			NSA2	0.93	0.52
RIKEN cDNA 0610008F07 gene expressed sequence AI606181	Mcc	0.46	0.02	ND			ND		
zinc finger protein 169	0610008F07Rik	0.46	0.00	ND			ND		
guanylate cyclase 1, soluble, beta 2	Al606181	0.46	0.01	ND			ND		
olfactory receptor 1128	Zfp169	0.46	0.01	Zfp169	0.94	0.78	ZNF169	0.91	0.59
regulator of G-protein signaling 9	Gucy1b2	0.46	0.04	Gucy1b2	0.80	0.08	ND		
solute carrier family 25 (mitochondrial carrier, phosphate carrier), member 25 predicted gene 5092	Olfr1128	0.46	0.01	ND			ND		
acetyl-Coenzyme A acetyltransferase 1	Rgs9	0.46	0.04	Rgs9	0.82	0.44	RGS9	0.59	0.14
predicted gene 5092	Slc25a25	0.46	0.00	Slc25a25	0.60	0.15	SLC25A25	0.86	0.55
UDP glycosyltransferases 3 family, polypeptide predicted gene 2694	Gm5092	0.47	0.01	ND			ND		
F-box and WD-40 domain protein 4	Acat1	0.47	0.01	Acat1	0.74	0.01	ACAT1	1.42	0.19
leucine rich repeat containing 18	Ugt3a1	0.47	0.01	Ugt3a2	0.88	0.39	UGT3A2	0.56	0.03
RIKEN cDNA A130042O14 gene	Gm2694	0.47	0.04	ND			ND		
tripartite motif-containing 9	Fbxw4	0.47	0.02	Fbxw4	0.81	0.01	FBXW4	0.85	0.25
insulin-like growth factor 1	Lrrc18	0.47	0.01	Lrrc18	0.93	0.75	LRRC18	0.66	0.46
protein tyrosine phosphatase, receptor type, N polypeptide 2	A130042O14Rik	0.47	0.04	ND			ND		
predicted gene 2814	Trim9	0.47	0.00	Trim9	1.16	0.08	TRIM9	0.44	0.12
RIKEN cDNA 4930413E15 gene	Igf1	0.47	0.03	Igf1	0.82	0.00	IGF1	0.61	0.06
spermatogenesis associated 2	Ptpn2	0.47	0.00	Ptpn2	1.11	0.37	PTPRN2	1.17	0.57
adenylate kinase 8	Gm2814	0.47	0.03	ND			ND		
G protein-coupled receptor 153	Spata2	0.47	0.02	Spata2	0.90	0.45	SPATA2	0.03	0.39
olfactory receptor 213	Ak8	0.47	0.01	Ak8	1.15	0.68	AK8	1.07	0.79
chymotrypsin-like	Gpr153	0.47	0.03	Gpr153	0.75	0.45	GPR153	1.56	0.49
potassium voltage-gated channel, shaker-related subfamily, member 5	Olfr213	0.47	0.00	ND			ND		
protein phosphatase 1K (PP2C domain)	Ctrl	0.47	0.00	Ctrl	0.67	0.22	CTRL	1.07	0.81
predicted gene 2085	Kcna5	0.47	0.02	Kcna5	1.41	0.28	KCNA5	1.07	0.78
DNA segment, Chr 4, ERATO Doi 58, expressed	Ppm1k	0.47	0.01	Ppm1k	0.63	0.01	PPM1K	0.74	0.34
serine (or cysteine) peptidase inhibitor, clade A (alpha-1 antiproteinase inhibitor, antitrypsin), member 11	Apoa1	0.47	0.03	ND			APOA1	1.21	0.31
neurotensin receptor 2	D4Ert58e	0.47	0.03	ND			ND		
hydroxyacid oxidase 1, liver	Serpina11	0.47	0.00	Serpina11	0.80	0.00	SERPINA11	1.36	0.00
solute carrier family 9 (sodium/hydrogen exchanger), member 2	Ntsr2	0.47	0.02	ND			NTSR2	1.00	0.99
solute carrier family 19 (thiamine transporter), member 2	Hao1	0.47	0.01	Hao1	0.53	0.01	HAO1	0.96	0.70
solute carrier family 18 (vesicular monoamine), member 3	Slc9a2	0.47	0.01	Slc9a2	8.67	0.40	SLC9A2	0.32	0.39
pseudouridylate synthase-like 1	Slc19a2	0.47	0.02	Slc19a2	0.91	0.58	SLC19A2	0.85	0.21
glial fibrillary acidic protein	Slc18a3	0.47	0.00	Slc18a3	1.05	0.64	SLC18A3	0.64	0.07
ubiquitin domain containing 1	Pusl1	0.47	0.01	Pusl1	1.21	0.02	PUSL1	1.02	0.89
predicted gene 8994	Gfap	0.47	0.04	Gfap	0.61	0.06	GFAP	1.18	0.67
RIKEN cDNA E330013P04 gene	Ubtd1	0.48	0.01	Ubtd1	0.82	0.04	UBTD1	1.21	0.03
ornithine aminotransferase	Gm8994	0.48	0.03	ND			ND		
chondroadherin-like	E330013P04Rik	0.48	0.03	ND			ND		
sulfatase 1	Oat	0.48	0.02	Oat	0.28	0.00	OAT	0.68	0.01
coiled-coil domain containing 48	Chadl	0.48	0.01	ND			ND		
EGF-like and EMI domain containing 1	Sulf1	0.48	0.00	Sulf1	1.97	0.16	SULF1	1.38	0.29
TAR (HIV) RNA binding protein 2	Ccdc48	0.48	0.02	Efcc1	2.10	0.06	ND		
complement component 8, alpha polypeptide	Egfem1	0.48	0.01	Egfem1	1.19	0.05	ND		
membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4)	Tarbp2	0.48	0.01	Tarbp2	1.03	0.46	TARBP2	1.06	0.56
transition protein 2	C8a	0.48	0.00	C8a	0.77	0.02	C8A	0.68	0.05
spectrin repeat containing, nuclear envelope 1	Mpp4	0.48	0.01	Mpp4	2.77	0.30	MPP4	0.70	0.29
predicted gene 3014	Tnp2	0.48	0.02	Tnp2	1.16	0.06	TNP2	1.04	0.84
RUN and SH3 domain containing 2	Syne1	0.48	0.04	ND			SYNE1	0.62	0.02
	Gm3014	0.48	0.00	ND			ND		
	Rusc2	0.48	0.01	ND			RUSC2	0.98	0.94

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
M-phase phosphoprotein 10 (U3 small nucleolar ribonucleoprotein)	Mphosph10	0.48	0.05	Mphosph10	0.87	0.18	MPHOSPH10	1.19	0.08
small nucleolar RNA, H/ACA box 74A	Snora74a	0.48	0.02	ND			ND		
transmembrane protein 116	Tmem116	0.48	0.01	Tmem116	2.40	0.04	TMEM116	1.19	0.15
peroxisome proliferator activated receptor alpha	Ppara	0.48	0.02	Ppara	0.90	0.68	PPARA	0.84	0.19
calcium channel, voltage-dependent, gamma subunit 7	Cacng7	0.48	0.04	Cacng7	2.38	0.02	CACNG7	1.06	0.87
lipoma HMGIC fusion partner-like 3	Lhfpl3	0.48	0.03	Lhfpl3	4.81	0.12	LHFPL3	0.39	0.46
RIKEN cDNA A430033K04 gene	A430033K04Rik	0.48	0.04	RGD1566386	0.63	0.28	ND		
hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 7	Hsd3b7	0.48	0.02	Hsd3b7	1.14	0.24	HSD3B7	0.82	0.25
4short chain dehydrogenase/reductase family 9C, member 7	Sdr9c7	0.48	0.00	Sdr9c7	0.77	0.06	SDR9C7	1.04	0.88
sorting nexin 22	Snx22	0.48	0.04	Snx22	1.04	0.66	SNX22	0.20	0.07
RAB22A, member RAS oncogene family	Rab22a	0.48	0.03	Rab22a	0.72	0.01	RAB22A	0.92	0.48
crystallin, gamma N	Crygn	0.48	0.05	Crygn	1.52	0.23	CRYGN	1.76	0.40
RIKEN cDNA 170010J08 gene	170010J08Rik	0.48	0.00	ND			ND		
oxytocin	Oxt	0.48	0.05	Oxt	0.85	0.15	OXT	0.92	0.53
spectrin repeat containing, nuclear envelope 2	Syne2	0.48	0.01	ND			SYNE2	0.82	0.30
golgi reassembly stacking protein 2	Gorasp2	0.48	0.01	Gorasp2	0.82	0.00	GORASP2	1.16	0.26
germinal center associated, signaling and coagulation factor XI	Gcsam	0.48	0.01	ND			GCET2	0.85	0.76
complement component 1, q subcomponent, alpha polypeptide	F11	0.49	0.02	F11	0.95	0.76	F11	1.12	0.21
zinc finger protein 352 pseudogene	C1qa	0.49	0.00	C1qa	0.88	0.29	C1QA	0.71	0.19
transferrin	Gm12633	0.49	0.05	ND			ND		
cDNA sequence BC029214	Trf	0.49	0.04	Tf	0.94	0.29	TF	1.08	0.73
solute carrier family 16 (monocarboxylic acid transporters), member 14	BC029214	0.49	0.01	RGD1306215	1.09	0.10	C9orf142	1.06	0.52
prostate androgen-regulated mucin-like protein 1	Slc16a14	0.49	0.05	Slc16a14	1.31	0.49	SLC16A14	0.59	0.07
keratin 86	Parm1	0.49	0.01	Parm1	0.78	0.21	PARM1	0.49	0.44
predicted gene 9992	Krt86	0.49	0.03	ND			KRT86	0.88	0.69
LIM domain only 7	Gm9992	0.49	0.03	ND			UNC93A	0.72	0.11
predicted gene 6936	Lmo7	0.49	0.00	Lmo7	0.78	0.14	LMO7	0.77	0.04
acyl-Coenzyme A dehydrogenase, short-branched chain ephrin A3	Gm6936	0.49	0.01	ND			ND		
oxysterol binding protein-like 1A	Acadsb	0.49	0.01	Acadsb	0.72	0.17	ACADSB	1.42	0.08
coiled coil domain containing 178	Efna3	0.49	0.01	ND			EFNA3	1.24	0.59
RIKEN cDNA 4933427G17 gene	Osbpl1a	0.49	0.01	ND			OSBPL1A	1.46	0.02
protein phosphatase 1, regulatory subunit 27	Ccdc178	0.49	0.03	Ccdc178	1.19	0.05	C18orf34	0.62	0.49
family with sequence similarity 46, member C	4933427G17Rik	0.49	0.00	ND			ND		
DNA methyltransferase (cytosine-5) 1	Ppp1r27	0.49	0.03	Ppp1r27	2.77	0.11	PPP1R27	1.73	0.11
mercaptopyruvate sulfurtransferase	Fam46c	0.49	0.01	ND			ND		
tetratricopeptide repeat domain 30A1	Dnmt1	0.49	0.00	Dnmt1	1.98	0.09	DNMT1	1.43	0.11
defender against cell death 1	Mpst	0.49	0.04	Mpst	0.88	0.10	MPST	0.89	0.41
complement component 1, s subcomponent	Ttc30a1	0.49	0.01	ND			TTC30A	0.81	0.45
discs, large homolog 1 (<i>Drosophila</i>)	Dad1	0.49	0.05	Dad1	1.02	0.83	DAD1	1.27	0.01
carboxylesterase 1E	C1s	0.49	0.01	C1s	0.86	0.24	C1S	0.85	0.22
ring finger protein 212	Dlg1	0.49	0.04	Dlg1	0.71	0.13	DLG1	1.17	0.16
tetratricopeptide repeat domain 28	Ces1e	0.49	0.01	Ces1e	1.07	0.29	ND		
vomeronasal 2, receptor 55	Rnf212	0.49	0.01	ND			ND		
predicted gene 7111	Ttc28	0.49	0.05	ND			ND		
family with sequence similarity 19, member A4	Vmn2r55	0.49	0.04	Vom2r33	1.24	0.01	ND		
nebulin	Gm7111	0.49	0.02	ND			ND		
DMRT-like family C1b	Fam19a4	0.50	0.02	Fam19a4	1.15	0.10	FAM19A4	0.48	0.19
DNA segment, Chr 11, Wayne State University	Neb	0.50	0.05	Neb	0.79	0.18	NEB	0.35	0.41
47. expressed	Dmrtc1b	0.50	0.01	Dmrtc1b	1.83	0.11	ND		
predicted gene 15056	D11Wsu47e	0.50	0.02	MGC95210	1.08	0.01	C17orf80	1.22	0.32
granzyme K	Defb52	0.50	0.02	Defb52	1.47	0.33	ND		
predicted gene 3161	Gzmk	0.50	0.01	Gzmk	0.81	0.36	GZMK	1.06	0.80
melanoma inhibitory activity 1	Gm15056	0.50	0.02	ND			ND		
	Mia1	0.50	0.01	Mia	1.32	0.36	MIA	2.58	0.03

Supplementary Table 8-2. Down-regulated genes by NaPB in CD-1 mice and correlation with expression alterations in Wistar Hannover rats and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
predicted gene 9963	Gm9963	0.50	0.02	ND			ND		
armadillo repeat gene deleted in velo-cardio-facial syndrome	Arvcf	0.50	0.00	ND			ARVCF	0.57	0.04
cyclin-dependent kinase 14	Cdk14	0.50	0.01	Cdk14	0.37	0.05	CDK14	0.94	0.54
transmembrane protein 255B	Tmem255b	0.50	0.01	ND			ND		
kallikrein B, plasma 1	Klkb1	0.50	0.02	Klkb1	1.29	0.60	KLKB1	0.64	0.09
signal sequence receptor, alpha	Ssr1	0.50	0.01	Ssr1	1.28	0.01	SSR1	1.78	0.00
complement component 6	C6	0.50	0.00	C6	1.09	0.54	C6	0.62	0.06
melanoma antigen, family B, 1	Mageb1	0.50	0.02	ND			MAGEB4	0.93	0.77
zinc finger protein 384	Zfp384	0.50	0.00	Zfp384	1.12	0.51	ZNF384	0.94	0.49
Number of genes with significant alteration	560			7			1		

Data represent the expression ratio between control and NaPB treatment. Genes showing less than 0.5 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in the baseline (control) arrays were chosen as down-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (less than 0.5 fold, p<0.05). ND means "not determined".

Supplementary Table 8-3. Up-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 micetreated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
cytochrome P450, family 2, subfamily b, polypeptide 21	Cyp2b21	141.34	0.00	Cyp2b23	1.10	0.74	ND		
hypothetical protein LOC498152	LOC498152	116.37	0.00	ND			ND		
DNA-damage-inducible transcript 4-like	Ddit4l	105.18	0.01	Ddit4l	1.48	0.46	DDIT4L	0.95	0.83
cytochrome P450, family 2, subfamily b, polypeptide 2	Cyp2b2	52.81	0.00	Cyp2b10	118.83	0.03	CYP2B6	7.15	0.00
ATP-binding cassette, subfamily C (CFTR/MRP), member 3	Abcc3	50.85	0.00	Abcc3	2.34	0.04	ABCC3	1.32	0.25
UDP glucuronosyltransferase 2 family, polypeptide B7	Ugt2b7	34.53	0.01	ND			UGT2B7	1.35	0.05
glutathione peroxidase 2	Gpx2	21.44	0.01	Gpx2	1.30	0.28	GPX2	6.15	0.00
aldehyde dehydrogenase 1 family, member A1	Aldh1a1	17.99	0.00	Aldh1a1	2.11	0.11	ALDH1A1	1.58	0.01
Shc SH2-domain binding protein 1	Shcbp1	16.86	0.02	Shcbp1	1.20	0.74	SHCBP1	1.39	0.59
glutathione S-transferase mu 3	Gstm3	15.83	0.04	Gstm3	44.62	0.02	ND		
carboxylesterase 2C	Ces2c	15.29	0.00	Ces2c	5.66	0.00	ND		
ubiquitin-conjugating enzyme E2T (putative)	Ube2t	15.25	0.02	Ube2t	2.09	0.18	UBE2T	1.32	0.43
cytochrome P450, family 2, subfamily c, polypeptide 24	Cyp2c24	15.02	0.00	ND			ND		
similar to K04F10.2	LOC361646	12.10	0.00	D430042O09R	0.86	0.13	KIAA0556	0.95	0.84
SPC25, NDC80 kinetochore complex component, homolog (S. cerevisiae)	Spc25	11.06	0.02	Spc25	1.81	0.23	SPC25	0.43	0.39
cytoskeleton associated protein 2	Ckap2	10.95	0.03	Ckap2	1.28	0.58	CKAP2	0.65	0.10
epithelial cell transforming sequence 2 oncogene	Ect2	10.38	0.03	Ect2	2.53	0.07	ECT2	0.92	0.83
aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)	Akr7a3	10.31	0.00	ND			AKR7A3	0.75	0.11
dual specificity phosphatase 13	Dusp13	10.30	0.01	ND			ND		
ribonucleotide reductase M2	Rrm2	8.79	0.02	Rrm2	7.49	0.10	RRM2	0.74	0.68
cell division cycle associated 3	Cdca3	8.69	0.02	Cdca3	10.82	0.19	CDCA3	1.22	0.54
BRCA1 associated RING domain 1	Bard1	8.67	0.02	Bard1	0.77	0.19	BARD1	0.96	0.92
testis expressed 36	Tex36	8.54	0.01	Tex36	1.02	0.97	C10orf122	0.77	0.37
similar to F-box only protein 27	RGD1563982	8.35	0.00	ND			ND		
cyclin A2	Ccna2	8.32	0.02	Ccna2	2.22	0.20	CCNA2	1.20	0.77
DEP domain containing 1	Depdc1	8.29	0.03	Depdc1a	0.78	0.45	DEPDC1	1.52	0.30
growth arrest and DNA-damage-inducible, beta	Gadd45b	8.26	0.00	Gadd45b	10.08	0.07	GADD45B	0.74	0.15
kinetochore-localized astrin/SPAG5 binding	Knstrn	8.25	0.01	Knstrn	1.50	0.20	C15orf23	1.29	0.10
kinetochore associated 1	Kntc1	8.23	0.01	ND			ND		
forkhead box N4	Foxn4	8.12	0.05	Foxn4	1.26	0.53	FOXN4	7.88	0.18
diaphanous homolog 3 (Drosophila)	Diaph3	7.94	0.01	Diaph3	1.19	0.64	DIAPH3	1.30	0.34
centromere protein W	Cenpw	7.91	0.03	Cenpw	1.40	0.20	CENPW	1.24	0.58
spindle and kinetochore associated complex subunit 1	Ska1	7.83	0.03	Ska1	0.69	0.11	SKA1	2.77	0.38
somatomedin B and thrombospondin, type 1 domain containing	Sbspon	7.77	0.00	Sbspon	0.66	0.17	C8orf84	0.81	0.66
cyclin-dependent kinase 1	Cdk1	7.70	0.01	Cdk1	0.88	0.31	CDK1	1.26	0.69
non-SMC condensin I complex, subunit G	Ncapg	7.32	0.04	ND			NCAPG	0.99	0.99
chemokine (C-X-C motif) ligand 9	Cxcl9	7.02	0.00	Cxcl9	0.86	0.32	CXCL9	4.82	0.38
PDZ binding kinase	Pbk	6.92	0.04	Pbk	1.31	0.39	PBK	1.36	0.65
cyclin B1	Ccnb1	6.87	0.02	Ccnb1	2.12	0.06	CCNB1	1.65	0.39
UDP glucuronosyltransferase 2 family, polypeptide B1	Ugt2b1	6.67	0.00	Ugt2b1	1.84	0.16	UGT2B4	1.60	0.00
RAD51 homolog (S. cerevisiae)	Rad51	6.58	0.04	Rad51	0.90	0.72	RAD51	1.26	0.46
centromere protein T	Cenpt	6.28	0.02	Cenpt	0.84	0.76	CENPT	1.48	0.10
cyclin B2	Ccnb2	6.23	0.01	Ccnb2	2.37	0.16	CCNB2	1.49	0.54
NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae)	Nuf2	6.21	0.05	Nuf2	2.12	0.35	NUF2	0.99	0.99
non-SMC condensin I complex, subunit H	Ncaph	6.06	0.03	Ncaph	0.58	0.13	NCAPH	0.80	0.63
alpha-1-B glycoprotein	A1bg	5.97	0.03	A1bg	0.78	0.53	A1BG	0.71	0.05
solute carrier family 22 (organic anion transporter) member 13	Slc22a13	5.77	0.00	Slc22a13	0.64	0.25	SLC22A13	1.46	0.43
epoxide hydrolase 1, microsomal (xenobiotic) protein regulator of cytokinesis 1	Ephx1	5.68	0.00	Ephx1	2.99	0.03	EPHX1	2.47	0.00
cytochrome P450, family 26, subfamily a, polypeptide 1	Prc1	5.67	0.01	Prc1	2.60	0.22	PRC1	1.24	0.68
triggering receptor expressed on myeloid cells-like 4	Treml4	5.63	0.03	Treml4	0.95	0.81	TREML4	1.04	0.85
polo-like kinase 4	Plk4	5.62	0.00	Plk4	0.43	0.46	PLK4	0.74	0.58
E2F1-inducible gene	LOC303566	5.62	0.01	BC030867	1.25	0.21	C17orf53	0.84	0.62
kinesin family member 20A	Kif20a	5.55	0.01	Kif20a	1.58	0.19	KIF20A	1.29	0.70
G protein-coupled receptor kinase 5	Grk5	5.53	0.02	Grk5	0.73	0.29	GRK5	1.41	0.15
glutamate receptor, ionotropic, N-methyl D-aspartate 2C	Grin2c	5.49	0.01	Grin2c	1.03	0.93	GRIN2C	0.21	0.35

Supplementary Table 8-3. Up-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 micetreated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
ATP-binding cassette, subfamily B (MDR/TAP), member 1B	Abcb1b	5.46	0.02	Abcb1b	0.86	0.70	ND		
hypothetical protein LOC685203	LOC685203	5.41	0.01	ND			ND		
transglutaminase 4 (prostate)	Tgm4	5.31	0.01	Tgm4	1.24	0.24	TGM4	1.18	0.56
Ttk protein kinase	Ttk	5.24	0.01	Ttk	0.96	0.88	TTK	1.17	0.86
cytochrome P450, family 3, subfamily a, polypeptide 23/polypeptide 1	Cyp3a23/3a1	5.17	0.00	Cyp3a16	3.35	0.01	CYP3A4	3.17	0.00
kinesin family member 22	Kif22	5.12	0.01	Kif22	2.04	0.27	KIF22	0.93	0.78
sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferrina.	Sult2a2	4.99	0.02	Sult2a6	8.06	0.09	ND		
NS5A (hepatitis C virus) transactivated protein 9	Ns5atp9	4.91	0.05	2810417H13Ri	0.50	0.01	KIAA0101	1.19	0.70
ubiquitin-conjugating enzyme E2C	Ube2c	4.80	0.03	Ube2c	2.15	0.05	UBE2C	1.54	0.49
CUB and Sushi multiple domains 1	Csmd1	4.76	0.02	Csmd1	0.51	0.14	CSMD1	0.45	0.09
NDC80 homolog, kinetochore complex component (<i>S. cerevisiae</i>)	Ndc80	4.66	0.03	Ndc80	1.07	0.75	NDC80	0.96	0.92
cytochrome P450, family 2, subfamily C, polypeptide 6, variant 1	Cyp2c6v1	4.59	0.00	Cyp2c54	7.97	0.01	CYP2C19	2.22	0.00
budding uninhibited by benzimidazoles 1	Bub1b	4.58	0.02	Bub1b	1.22	0.69	BUB1B	1.01	0.98
homolog beta (yeast)									
minichromosome maintenance complex component 6	Mcm6	4.57	0.02	Mcm6	2.48	0.15	MCM6	1.20	0.56
polo-like kinase 1	Plk1	4.57	0.01	Plk1	4.13	0.20	PLK1	0.72	0.60
amyloid beta (A4) precursor protein	App	4.54	0.00	App	1.14	0.55	APP	1.29	0.14
nucleolar and spindle associated protein 1	Nusap1	4.52	0.01	Nusap1	1.20	0.47	NUSAP1	1.13	0.77
kallikrein related-peptidase 11	Klk11	4.50	0.00	Klk11	1.30	0.60	KLK11	0.77	0.37
centrosomal protein 55	Cep55	4.49	0.01	Cep55	1.93	0.30	CEP55	1.87	0.33
family with sequence similarity 83, member D	Fam83d	4.48	0.00	ND			FAM83D	1.15	0.73
sperm associated antigen 5	Spag5	4.41	0.01	Spag5	0.84	0.55	SPAG5	1.80	0.11
sarcoglycan, gamma (dystrophin-associated glycoprotein)	Sgcg	4.39	0.02	Sgcg	1.65	0.13	SGCG	0.95	0.83
chromatin assembly factor 1, subunit B (p60)	Chaf1b	4.35	0.04	Chaf1b	2.95	0.01	CHAF1B	1.50	0.37
lipoprotein lipase	Lpl	4.35	0.00	Lpl	1.64	0.09	LPL	0.05	0.40
Rac GTPase-activating protein 1	Racgap1	4.32	0.02	Racgap1	2.59	0.02	RACGAP1	1.10	0.80
carboxylesterase 2J	Ces2j	4.31	0.00	ND			ND		
carboxylesterase 2A	Ces2a	4.24	0.00	ND			ND		
kinesin family member 18B	Kif18b	4.24	0.02	Kif18b	0.84	0.31	KIF18B	0.58	0.10
zinc finger, DHHC-type containing 2	Zdhhc2	4.23	0.00	Zdhhc2	0.38	0.05	ZDHHC2	1.20	0.33
lipocalin 5	Lcn5	4.21	0.04	Lcn5	1.11	0.80	ND		
minichromosome maintenance complex component 5	Mcm5	4.14	0.02	Mcm5	2.92	0.18	MCM5	1.31	0.23
Max dimerization protein 3	Mxd3	4.10	0.02	Mxd3	1.01	0.98	MXD3	1.13	0.50
FERM and PDZ domain containing 1	Frmfd1	3.99	0.01	Frmfd1	0.86	0.56	FRMPD1	1.45	0.28
hypothetical protein LOC680955	LOC680955	3.95	0.00	1700067P10Ri	0.59	0.02	ND		
kinesin family member 11	Kif11	3.95	0.00	Kif11	1.42	0.26	KIF11	0.87	0.80
cytochrome P450, family 2, subfamily c, polypeptide 12	Cyp2c12	3.94	0.00	ND			ND		
minichromosome maintenance complex component 3	Mcm3	3.92	0.01	Mcm3	1.60	0.12	MCM3	1.20	0.51
centromere protein Q	Cenpq	3.86	0.02	Cenpq	0.56	0.08	CENPQ	1.08	0.08
kinesin family member C1	Kifc1	3.86	0.03	Kifc5b	0.70	0.36	KIFC1	1.14	0.82
rCG29620-like	LOC100361147	3.81	0.00	ND			ND		
chloride channel, voltage-sensitive 1	Clcn1	3.79	0.02	Clcn1	0.64	0.13	CLCN1	0.94	0.76
phosphoserine aminotransferase 1	Psat1	3.71	0.01	Psat1	0.72	0.22	PSAT1	0.70	0.18
cancer susceptibility candidate 5	Casc5	3.65	0.04	Casc5	1.49	0.34	CASC5	0.60	0.32
glutathione S-transferase, theta 3	Gstt3	3.63	0.00	Gstt3	6.90	0.04	ND		
vascular endothelial growth factor B	Vegfb	3.62	0.04	ND			ND		
ssu-2 homolog	Ssuh2	3.62	0.00	ND			ND		
DEAH (Asp-Glu-Ala-His) box polypeptide 33	Dhx33	3.61	0.00	Dhx33	0.71	0.23	DHX33	0.99	0.93
asparagine synthetase (glutamine-hydrolyzing) galanin-like peptide	Asns	3.53	0.01	Asns	1.02	0.95	ASNS	1.56	0.20
budding uninhibited by benzimidazoles 1 homolog (yeast)	Galp	3.52	0.01	Galp	1.18	0.06	GALP	1.01	0.98
ATP-binding cassette, sub-family B (MDR/TAP), member 1A	Abcb1a	3.50	0.00	Abcb1a	1.12	0.34	ABCB1	1.88	0.00
metallothionein 2A	Mt2a	3.50	0.01	Mt2	11.01	0.40	MT1E	0.56	0.09
neurexin 1	Nrxn1	3.49	0.00	Nrxn1	1.40	0.19	NRXN1	0.61	0.35
hypothetical protein LOC100362769	LOC100362769	3.43	0.01	ND			ND		
XK, Kell blood group complex subunit-related family, member 5	Xkr5	3.43	0.03	Xkr5	0.67	0.06	XKR5	0.86	0.54
stathmin 1	Stmn1	3.42	0.00	Stmn1	2.99	0.05	STMN1	1.14	0.74

Supplementary Table 8-3. Up-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 micetreated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
carboxylesterase 2I	Ces2i	3.41	0.00	ND			ND		
discs, large (Drosophila) homolog-associated protein 5	Dlgap5	3.41	0.01	Dlgap5	1.48	0.16	DLGAP5	1.42	0.61
pannexin 2	Panx2	3.38	0.00	Panx2	1.51	0.34	PANX2	1.27	0.05
testis specific X-linked gene	Tsx	3.37	0.03	Tsx	1.36	0.46	ND		
ubiquitin D	Ubd	3.36	0.00	Ubd	0.84	0.45	UBD	1.94	0.46
acyl-CoA synthetase medium-chain family member 2A	Acsm2a	3.36	0.04	Acsm2	2.06	0.29	ACSM2A	0.61	0.12
pirin (iron-binding nuclear protein)	Pir	3.34	0.00	Pir	1.62	0.05	PIR	2.11	0.01
AT rich interactive domain 3A (Bright like) similar to stathmin 1/oncoprotein 18)	Arid3a	3.33	0.00	ND			ND		
antigen identified by monoclonal antibody Ki-67	RGD1565395	3.31	0.02	ND			ND		
GINS complex subunit 1 (Psf1 homolog)	Mki67	3.31	0.02	Mki67	2.96	0.19	MKI67	1.62	0.20
phospholipase A2, group XIIA	Gins1	3.27	0.01	Gins1	0.89	0.51	GINS1	0.90	0.69
protein kinase, membrane associated	Pla2g12a	3.22	0.00	Pla2g12a	2.89	0.06	PLA2G12A	0.77	0.13
tyrosine/threonine 1	Pkmyt1	3.21	0.00	Pkmyt1	1.20	0.68	PKMYT1	1.09	0.55
protein phosphatase 2, regulatory subunit A, DSN1, MIND kinetochore complex component, homolog (S. cerevisiae)	Ppp2r1b	3.17	0.00	Ppp2r1b	0.88	0.54	PPP2R1B	0.84	0.20
rhotekin	Dsn1	3.15	0.01	Dsn1	1.33	0.26	DSN1	1.04	0.85
camello-like 3	Rtkn	3.12	0.01	Rtkn	0.77	0.49	RTKN	1.60	0.02
growth differentiation factor 15	Cml3	3.12	0.01	ND			ND		
cell division cycle associated 8	Gdf15	3.10	0.01	Gdf15	8.95	0.09	GDF15	0.83	0.82
Fanconi anemia, complementation group B	Cdca8	3.09	0.00	Cdca8	2.67	0.03	CDCA8	1.26	0.67
malic enzyme 1, NADP(+)-dependent, cytosolic epithelial cell adhesion molecule	Fancb	3.09	0.02	Fancb	1.18	0.36	FANCB	0.67	0.27
kinesin family member 20B	Me1	3.06	0.01	Me1	1.86	0.27	ME1	4.59	0.00
olfactory receptor 1411	Epcam	3.06	0.00	Epcam	1.19	0.48	EPCAM	0.96	0.86
stonin 1	Kif20b	3.05	0.01	Kif20b	1.59	0.30	KIF20B	0.66	0.40
sulfiredoxin 1	Olr1411	3.05	0.00	ND			ND		
SPC24, NDC80 kinetochore complex component, homolog (S. cerevisiae).	Stron1	3.04	0.03	ND			ND		
cell division cycle 45 homolog (S. cerevisiae)	Spc24-ps1	3.03	0.00	Srxn1	2.54	0.14	SRXN1	2.36	0.01
tribbles homolog 3 (Drosophila)	Spc24	3.03	0.00	Srxn1	2.53	0.10	SPC24	1.72	0.23
claudin 23	Trib3	3.01	0.02	Trib3	1.73	0.11	TRIB3	0.63	0.12
inner centromere protein	Cldn23	2.96	0.01	Cldn23	1.03	0.76	CLDN23	0.90	0.26
zinc finger protein 367	Incnep	2.94	0.02	Incnep	2.08	0.14	INCENP	1.56	0.02
meiotic nuclear divisions 1 homolog (S. cerevisiae)	Zfp367	2.92	0.00	Zfp367	0.35	0.01	ZNF367	1.48	0.15
transcription factor 19	Mnd1	2.92	0.00	Mnd1	0.85	0.47	MND1	0.81	0.69
nucleolar protein 3 (apoptosis repressor with CARD domain)	Tcf19	2.91	0.02	Tcf19	0.45	0.01	TCF19	1.15	0.77
cytidine deaminase	Nol3	2.89	0.00	Nol3	1.20	0.27	NOL3	1.49	0.02
cardiotrophin-like cytokine factor 1	Cda	2.88	0.00	Cda	1.09	0.62	CDA	1.23	0.17
ASF1 anti-silencing function 1 homolog B (S. cerevisiae)	Clcf1	2.87	0.01	Clcf1	1.50	0.11	CLCF1	1.64	0.12
vomeronasal 2 receptor, 51	Asf1b	2.87	0.02	Asf1b	2.46	0.05	ASF1B	1.00	1.00
ATPase, H ⁺ transporting, lysosomal V1 subunit	Vom2r51	2.86	0.04	Vmn2r26	0.24	0.34	ND		
ras-like protein family member 10B-like	Atp6v1g3	2.83	0.02	Atp6v1g3	1.57	0.02	ATP6V1G3	1.00	1.00
testicular haploid expressed gene	LOC100912246	2.82	0.00	ND			ND		
dCMP deaminase	Theg	2.81	0.04	Theg	1.05	0.76	THEG	1.61	0.18
annexin A7	Dctd	2.80	0.02	Dctd	0.77	0.41	DCTD	0.75	0.05
glutathione S-transferase mu 1	Anxa7	2.79	0.01	Anxa7	1.63	0.02	ANXA7	1.30	0.03
uridine phosphorylase 2	Gstm1	2.79	0.00	Gstm1	7.75	0.01	GSTM5	1.29	0.47
similar to Carboxylesterase 2	Upp2	2.76	0.03	Upp2	1.32	0.39	UPP2	2.34	0.25
dual specificity phosphatase 8	RGD1564578	2.75	0.00	ND			ND		
matrix metallopeptidase 12	Dusp8	2.74	0.00	ND			DUSP8	0.67	0.05
metallothionein 1a	Mmp12	2.74	0.04	Mmp12	0.74	0.22	MMP12	0.86	0.51
coiled-coil domain containing 69	Mt1a	2.73	0.01	Mt1	9.31	0.39	MT1F	0.34	0.17
mesenchyme homeobox 2	Ccdc69	2.72	0.01	Ccdc69	1.66	0.30	ND		
activating transcription factor 3	Meox2	2.71	0.00	Meox2	1.50	0.26	MEOX2	2.02	0.08
NAD(P)H dehydrogenase, quinone 1	Atf3	2.71	0.02	Atf3	1.41	0.20	ATF3	0.73	0.34
PQ loop repeat containing 3	Nqo1	2.68	0.01	Nqo1	0.88	0.77	NQO1	19.22	0.01
myotubularin related protein 11	Pqlc3	2.68	0.00	Pqlc3	0.88	0.47	PQLC3	0.78	0.04
glutathione S-transferase alpha 5	Mtrmr11	2.68	0.04	Mtrmr11	0.90	0.51	MTMR11	1.10	0.68
transglutaminase 1 (K polypeptide epidermal type I, protein-glutamine-gamma-chemokine (C-C motif) ligand 2	Gsta5	2.65	0.00	Gm10639	13.47	0.02	GSTA5	1.35	0.07
glutathione S-transferase alpha 2	Tgm1	2.65	0.04	Tgm1	0.73	0.26	TGM1	0.78	0.15
period circadian clock 3	Ccl2	2.63	0.01	Ccl2	1.55	0.14	CCL13	1.19	0.56
serine carboxypeptidase 1	Gsta2	2.62	0.00	Gm10639	13.47	0.02	GSTA5	1.35	0.07
CTF18, chromosome transmission fidelity factor 18 homolog (S. cerevisiae)	Per3	2.62	0.00	Per3	1.46	0.12	PER3	0.54	0.25
Scpep1	Scpep1	2.61	0.01	Scpep1	0.90	0.63	SCPEP1	1.66	0.02
Chtf18	Chtf18	2.59	0.02	Chtf18	1.86	0.14	CHTF18	0.90	0.61

Supplementary Table 8-3. Up-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
sodium channel, nonvoltage-gated 1 alpha	Scnn1a	2.58	0.00	Scnn1a	0.33	0.09	SCNN1A	0.69	0.15
similar to Tie6 protein	RGD1561530	2.58	0.00	ND			ND		
NIPA-like domain containing 2	Nipal2	2.57	0.01	Nipal2	0.85	0.37	NIPAL2	1.38	0.22
G protein-coupled receptor 64	Gpr64	2.57	0.03	Gpr64	2.96	0.20	GPR64	2.18	0.18
olfactory receptor 1415	Olr1415	2.56	0.00	Olf332	1.66	0.27	ND		
inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma	Ikbkg	2.56	0.00	Ikbkg	2.14	0.18	IKBKG	1.60	0.03
tumor suppressor candidate 3	Tusc3	2.55	0.00	Tusc3	1.00	0.99	TUSC3	1.12	0.40
cyclin E1	Ccne1	2.54	0.05	Ccne1	1.60	0.03	CCNE1	1.16	0.41
Rho GTPase activating protein 11A	Arhgap11a	2.53	0.03	Arhgap11a	0.73	0.22	ARHGAP11A	1.35	0.28
similar to transcription factor 19	LOC678775	2.51	0.00	ND			ND		
carbonic anhydrase 2	Ca2	2.51	0.00	Car2	1.43	0.22	CA2	0.86	0.13
extra spindle pole bodies homolog 1 (S. transmembrane protein 179	Esp1	2.51	0.03	Esp1	0.89	0.75	ESPL1	0.87	0.60
family with sequence similarity 72, member A	Tmem179	2.50	0.04	ND			ND		
DnaJ (Hsp40) homolog, subfamily B, member 3	Fam72a	2.49	0.02	Fam72a	1.69	0.22	FAM72A	1.23	0.60
HAUS augmin-like complex, subunit 1	Dnajb3	2.49	0.00	Dnajb3	0.44	0.40	HAUS1	0.97	0.78
suppressor APC domain containing 2	Sapcd2	2.46	0.01	Sapcd2	0.37	0.01	C9orf140	1.47	0.32
aldehyde oxidase 1	Aox1	2.46	0.03	Aox1	1.65	0.30	AOX1	2.52	0.00
GLIS family zinc finger 1	Glis1	2.45	0.01	Glis1	0.98	0.92	GLIS1	1.31	0.33
armadillo repeat containing 12	Armc12	2.44	0.03	Armc12	1.15	0.55	C6orf81	0.97	0.94
IQ motif containing GTPase activating protein 3	Iqgap3	2.43	0.05	Iqgap3	0.93	0.61	IQGAP3	1.88	0.16
P450 (cytochrome) oxidoreductase	Por	2.43	0.00	Por	7.74	0.08	POR	1.80	0.01
insulinoma-associated 1	Insm1	2.43	0.00	Insm1	0.76	0.55	INSM1	0.18	0.40
cell division cycle associated 7	Cdca7	2.42	0.00	Cdca7	0.90	0.84	ND		
ELOVL fatty acid elongase 6	Elov6	2.42	0.04	Elov6	5.78	0.08	ELOVL6	2.85	0.03
cytochrome P450, family 1, subfamily a, polypeptide 1	Cyp1a1	2.41	0.05	Cyp1a1	0.95	0.91	CYP1A1	2.49	0.03
E2F transcription factor 1	E2f1	2.41	0.02	E2f1	1.00	0.98	E2F1	1.35	0.36
similar to Glutathione S-transferase 8 (GST 8-8)	RGD1564906	2.41	0.00	Gsta4	1.68	0.06	ND		
(Chain 8) (GST class-alpha) transmembrane protein 116	Tmem116	2.40	0.04	Tmem116	0.48	0.01	TMEM116	1.19	0.15
discs, large (Drosophila) homolog-associated protein 2	Dlgap2	2.39	0.00	Dlgap2	1.41	0.40	DLGAP2	0.99	0.97
Cd276 molecule	Cd276	2.38	0.00	Cd276	0.79	0.52	CD276	0.91	0.50
glutathione reductase	Gsr	2.38	0.00	Gsr	1.63	0.17	GSR	1.30	0.05
baculoviral IAP repeat-containing 5	Birc5	2.37	0.02	ND			ND		
defective in sister chromatid cohesion 1 homolog (S. cerevisiae)	Dsccl1	2.35	0.04	Dsccl1	1.34	0.27	DSCC1	1.85	0.24
HIV-1 Tat interactive protein 2	Htatip2	2.35	0.01	Htatip2	2.48	0.06	HTATIP2	2.29	0.00
sphingosine-1-phosphate lyase 1	Sgpl1	2.33	0.00	Sgpl1	1.97	0.18	SGPL1	0.92	0.48
similar to Expressed sequence AI788959	RGD1559459	2.33	0.00	ND			UGT2B11	1.09	0.44
BR serine/threonine kinase 2	Brsk2	2.32	0.04	Brsk2	1.19	0.22	BRSK2	1.24	0.53
trophinin associated protein	Troap	2.32	0.02	Troap	1.18	0.29	TROAP	1.30	0.50
solute carrier family 39 (metal ion transporter), member 5	Slc39a5	2.32	0.00	Slc39a5	1.18	0.57	SLC39A5	0.83	0.30
similar to Hypothetical protein LOC73072	RGD1566084	2.31	0.02	BC068157	0.80	0.38	FLJ22184	0.69	0.41
glutamate receptor interacting protein 2	Grip2	2.29	0.01	Grip2	0.52	0.09	GRIP2	0.04	0.39
leucine rich repeat containing 51	Lrrc51	2.29	0.00	Lrrc51	2.16	0.02	ND		
dopa decarboxylase (aromatic L-amino acid decarboxylase)	Ddc	2.29	0.00	Ddc	0.66	0.19	DDC	0.95	0.81
sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferring, NK3 homeobox 1	Sult2a6	2.28	0.02	Sult2a6	8.06	0.09	ND		
frizzled family receptor 6	Nkx3-1	2.28	0.00	Nkx3-1	0.83	0.38	NKX3-1	1.26	0.08
cyclin-dependent kinase-like 2 (CDC2-related kinase)	Fzd6	2.28	0.03	Fzd6	0.66	0.12	FZD6	0.76	0.15
transmembrane protein 171	Tmem171	2.26	0.01	Tmem171	1.04	0.88	TMEM171	1.03	0.91
elongation factor RNA polymerase II-like 3	Eif3	2.26	0.04	Eif3	0.82	0.67	ELL3	1.45	0.12
forkhead box M1	Foxm1	2.24	0.01	Foxm1	0.28	0.01	FOXM1	1.57	0.42
microsomal glutathione S-transferase 2	Mgst2	2.24	0.00	Mgst2	1.00	1.00	MGST2	0.89	0.10
hypothetical protein LOC690422	LOC690422	2.23	0.01	4930427A07Ri	1.11	0.48	C14orf80	1.38	0.21
perilipin 3	Plin3	2.22	0.00	Plin3	1.02	0.92	PLIN3	0.84	0.01
heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	Hs3st3a1	2.21	0.02	Hs3st3a1	1.15	0.61	HS3ST3A1	0.96	0.89
tonsoku-like, DNA repair protein	Tonsl	2.21	0.00	Tonsl	0.89	0.31	TONSL	1.85	0.28
similar to 1190005I06Rik protein	RGD1309651	2.20	0.03	1190005I06Rik	1.48	0.02	C16orf74	0.91	0.74
UDP-glucose 6-dehydrogenase	Ugdh	2.19	0.00	Ugdh	3.05	0.10	UGDH	3.30	0.00
p53 E3 ubiquitin protein ligase	Mdm2	2.19	0.00	Mdm2	1.53	0.05	MDM2	1.42	0.05
tubulin, beta 6 class V	Tubb6	2.18	0.01	Tubb6	1.61	0.13	TUBB6	1.78	0.36
RAD51 associated protein 1	Rad51ap1	2.18	0.01	Rad51ap1	1.11	0.80	RAD51AP1	0.90	0.82

Supplementary Table 8-3. Up-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
HECT and RLD domain containing E3 ubiquitin protein ligase family member 6	Herc6	2.17	0.03	Herc6	1.12	0.77	HERC6	0.53	0.08
ectonucleotide pyrophosphatase/phosphodiesterase 5	Enpp5	2.17	0.03	Enpp5	1.46	0.27	ENPP5	0.77	0.17
A kinase (PRKA) anchor protein 5	Akap5	2.17	0.01	Akap5	1.28	0.33	AKAP5	1.29	0.29
olfactory receptor 862	Olr862	2.17	0.00	Olr1335	1.24	0.50	ND	ND	
similar to CG7194-PA	LOC682147	2.15	0.00	ND			ND	ND	
thymidylate synthetase	Tyms	2.14	0.00	Tyms	1.39	0.33	TYMS	1.26	0.64
repetin	Rptn	2.14	0.04	Rptn	1.29	0.55	RPTN	1.02	0.94
vav 2 guanine nucleotide exchange factor	Vav2	2.13	0.00	Vav2	0.59	0.01	VAV2	1.37	0.35
similar to TDPOZ3	RGD1563667	2.11	0.03	ND			ND	ND	
kinesin family member 23	Kif23	2.10	0.01	Kif23	0.57	0.12	KIF23	0.97	0.95
olfactory receptor 1206	Olr1206	2.10	0.04	Olr884	1.59	0.22	ND	ND	
WD repeat domain 31	Wdr31	2.10	0.00	Wdr31	1.25	0.33	WDR31	0.94	0.69
GINS complex subunit 2 (Psf2 homolog)	Gins2	2.10	0.01	Gins2	1.29	0.22	GINS2	0.83	0.53
UDP-N-acetylglucosamine pyrophosphorylase 1-like 1	Uap1l1	2.09	0.02	Uap1l1	1.40	0.19	UAP1L1	0.77	0.59
bone morphogenetic protein 7	Bmp7	2.09	0.00	Bmp7	1.20	0.23	BMP7	1.43	0.20
poly (ADP-ribose) polymerase 1	Parp1	2.08	0.00	Parp1	1.28	0.42	PARP1	1.42	0.01
similar to Protein C10orf11 homolog	LOC681383	2.08	0.01	1700112E06Ri	1.26	0.52	C10orf11	0.68	0.05
membrane metallo-endopeptidase	Mme	2.07	0.02	Mme	0.59	0.24	MME	1.05	0.71
mature T-cell proliferation 1	Mtcp1	2.06	0.01	Mtcp1	0.69	0.10	MTCP1	0.32	0.42
tetratricopeptide repeat domain 8	Ttc8	2.06	0.00	Ttc8	1.24	0.32	TTC8	0.90	0.33
nerve growth factor receptor (TNFRSF16)	Ngfrap1	2.05	0.03	Ngfrap1	1.13	0.40	NGFRAP1	0.90	0.38
associated protein 1									
cytochrome P450 2C26-like	LOC100912265	2.05	0.02	ND			ND	ND	
UDP glucuronosyltransferase 2 family, polypeptide B10	Ugt2b10	2.05	0.00	Ugt2b34	4.20	0.07	UGT2B10	1.18	0.22
sterile alpha motif domain containing 4A	Samd4a	2.04	0.00	Samd4	0.84	0.34	SAMD4A	1.15	0.46
pleckstrin 2	Plek2	2.04	0.04	Plek2	0.75	0.18	PLEK2	1.18	0.61
glutathione S-transferase alpha 4	Gsta4	2.03	0.00	Gsta4	1.68	0.06	ND	ND	
growth arrest specific 7	Gas7	2.03	0.04	Gas7	1.82	0.05	GAS7	0.42	0.19
protein kinase C, delta binding protein	Prkcdbp	2.03	0.01	Prkcdbp	0.89	0.23	PRKCDBP	1.07	0.60
glutathione S-transferase mu 4	Gstm4	2.02	0.02	Gstm4	5.52	0.02	GSTM4	1.12	0.33
TLC domain containing 2	Tlcd2	2.02	0.05	Tlcd2	0.46	0.02	TLCD2	1.32	0.04
zinc finger protein 780B	Zfp780b	2.02	0.00	Zfp626	1.52	0.17	ND	ND	
POU class 1 homeobox 1	Pou1f1	2.02	0.04	Pou1f1	1.44	0.30	POU1F1	1.13	0.55
phospholipase A2, group IID	Pla2g2d	2.02	0.02	Pla2g2d	0.92	0.83	PLA2G2D	1.04	0.94
adenosine A1 receptor	Adora1	2.01	0.00	Adora1	1.20	0.56	ADORA1	0.70	0.46
apelin	Apln	2.01	0.04	Apln	0.79	0.33	APLN	0.60	0.46
chromatin assembly factor 1, subunit A (p150)	Chaf1a	2.01	0.01	Chaf1a	0.89	0.60	CHAF1A	0.54	0.34
CDC42 effector protein (Rho GTPase binding) 5	Cdc42ep5	2.00	0.00	Cdc42ep5	0.49	0.16	CDC42EP5	0.85	0.54
solute carrier family 35, member E3	Slc35e3	2.00	0.00	Slc35e3	0.87	0.41	SLC35E3	0.81	0.04
Number of genes with significant alteration	274			16			15		

Data represent the expression ratio between control and NaPB treatment. Genes showing greater than 2 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in an experimental (treatment) arrays were chosen as up-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (greater than 2 fold, p<0.05). ND means "not determined".

Supplementary Table 8-4. Down-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
serine/threonine-protein kinase NIM1	Nim1	0.18	0.00	Nim1	1.19	0.71	NIM1	0.93	0.84
period circadian clock 2	Per2	0.20	0.04	Per2	1.66	0.30	PER2	0.53	0.25
meiosis specific with OB domains	Meiob	0.20	0.02	Meiob	0.62	0.15	ND		
aryl hydrocarbon receptor nuclear translocator-similar to OX-2 membrane glycoprotein precursor (MRC OX-2 antigen) (CD200 antigen)	Arntl2	0.22	0.02	ND			ND		
similar to Wolf-Hirschhorn syndrome candidate 1	LOC685767	0.22	0.02	Gm609	0.94	0.85	ND		
protein isoform 3	RGD1565590	0.22	0.01	ND			ND		
synaptotagmin-like 5	Syt15	0.22	0.00	Syt15	0.96	0.92	SYTL5	0.67	0.51
flavin containing monooxygenase 1	Fmo1	0.24	0.00	Fmo1	1.89	0.14	FMO1	2.22	0.03
glucokinase	Gck	0.24	0.03	Gck	1.65	0.20	GCK	0.68	0.07
neural cell adhesion molecule 2	Ncam2	0.25	0.04	Ncam2	1.29	0.50	NCAM2	0.96	0.85
teneurin transmembrane protein 2	Tenm2	0.25	0.01	Tenm2	1.18	0.40	ODZ2	0.84	0.30
collagen, type XXVII, alpha 1	Col27a1	0.25	0.05	Col27a1	0.55	0.04	COL27A1	1.27	0.36
flavin containing monooxygenase 2	Fmo2	0.25	0.00	Fmo2	2.03	0.05	FMO2	1.05	0.87
TSC22 domain family, member 1	Tsc22d1	0.26	0.00	Tsc22d1	0.64	0.03	TSC22D1	0.88	0.46
outer dense fiber of sperm tails 3B	Odf3b	0.26	0.00	Odf3b	0.52	0.03	ODF3B	1.64	0.19
retinol dehydrogenase 16 (all-trans)	Rdh16	0.28	0.04	Rdh16	0.56	0.01	RDH16	1.01	0.97
hydroxyacid oxidase 2 (long chain)	Hao2	0.28	0.00	Hao2	4.31	0.07	HAO2	0.52	0.11
RGM domain family, member A	Rgma	0.28	0.03	Rgma	1.21	0.29	RGMA	0.19	0.44
ornithine aminotransferase	Oat	0.28	0.00	Oat	0.48	0.02	OAT	0.68	0.01
ephrin A5	Efna5	0.28	0.00	Efna5	0.22	0.02	EFNA5	0.75	0.58
apolipoprotein A-IV	Apoa4	0.28	0.00	ND			ND		
hydroxy-delta-5-steroid dehydrogenase, 3 beta-and steroid delta-isomerase 6	Hsd3b6	0.29	0.00	Hsd3b1	0.80	0.64	HSD3B2	1.33	0.54
Purkinje cell protein 4-like 1	Pcp4l1	0.30	0.02	Pcp4l1	0.53	0.10	ND		
sprouty homolog 4 (Drosophila)	Spry4	0.30	0.00	Spry4	1.17	0.74	SPRY4	1.08	0.86
2'-5' oligoadenylate synthetase 1E	Oas1e	0.31	0.04	Oas1e	0.62	0.10	ND		
cholesterol 25-hydroxylase	Ch25h	0.31	0.02	Ch25h	1.23	0.64	CH25H	0.88	0.54
solute carrier family 13 (sodium/sulfate symporters), member 4	Slc13a4	0.31	0.00	Slc13a4	1.14	0.66	SLC13A4	1.10	0.74
troponin C type 2 (fast)	Tnnc2	0.31	0.01	Tnnc2	1.04	0.70	TNNC2	1.36	0.07
transducin-like enhancer of split 3 (E(sp1) homolog). Drosophila)	Tle3	0.32	0.00	Tle3	1.05	0.66	TLE3	1.20	0.27
solute carrier family 34 (sodium phosphate), member 2	Slc34a2	0.32	0.05	Slc34a2	1.86	0.08	SLC34A2	0.06	0.37
glutamate-ammonia ligase	Glul	0.32	0.01	Ccdc92	0.65	0.19	CCDC92	0.81	0.07
src-related kinase lacking C-terminal regulatory tyrosine and N-terminal myristylation sites	Srms	0.33	0.00	Srms	0.69	0.11	SRMS	1.09	0.81
regulator of G-protein signaling 7 binding protein	Rgs7bp	0.33	0.01	Rgs7bp	1.37	0.14	RGS7BP	0.30	0.06
megalencephalic leukoencephalopathy with subcortical cysts 1	Mlc1	0.33	0.01	Mlc1	1.71	0.10	MLC1	1.67	0.03
Eph receptor A4	Epha4	0.34	0.05	Epha4	0.51	0.49	EPHA4	0.75	0.14
delta-like 1 (Drosophila)	Dll1	0.34	0.01	Dll1	1.87	0.15	DLL1	1.43	0.30
gap junction protein, alpha 5	Gja5	0.34	0.04	Gja5	1.46	0.20	GJA5	0.61	0.31
ATP-binding cassette, subfamily B (MDR/TAP), member 9	Abcb9	0.34	0.00	Abcb9	0.95	0.78	ABCB9	1.25	0.46
laminin, beta 3	Lamb3	0.35	0.01	Lamb3	0.93	0.64	LAMB3	1.23	0.08
hypothetical protein LOC690126	LOC690126	0.36	0.00	ND			ND		
noggin	Nog	0.36	0.05	Nog	0.14	0.00	NOG	0.94	0.79
POM121 transmembrane nucleoporin-like 2	Pom121l2	0.36	0.00	ND			ND		
carbonic anhydrase 3	Car3	0.36	0.01	Car3	0.91	0.81	CA3	0.74	0.32
discoidin domain receptor tyrosine kinase 2	Ddr2	0.37	0.04	Ddr2	0.54	0.50	DDR2	1.17	0.51
carbonic anhydrase 1	Car1	0.37	0.00	Car1	1.95	0.03	CA1	0.85	0.72
granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	Gzmb	0.37	0.02	ND			ND		
liver-expressed antimicrobial peptide 2	Leap2	0.37	0.05	Leap2	2.18	0.15	LEAP2	0.88	0.47
Jun dimerization protein 2	Jdp2	0.38	0.03	Jdp2	1.44	0.48	JDP2	1.19	0.31
neurotrophin 3	Ntf3	0.38	0.03	Ntf3	1.19	0.46	NTF3	0.90	0.70
somatostatin receptor 3	Sstr3	0.38	0.01	Sstr3	1.18	0.33	SSTR3	1.10	0.73
nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	Nfkbid	0.38	0.01	Nfkbid	1.11	0.44	NFKBIZ	0.84	0.59
Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6	Arhgef6	0.38	0.00	Arhgef6	1.14	0.63	ARHGEF6	0.87	0.54
Cd200 molecule	Cd200	0.38	0.00	Cd200	1.21	0.21	CD200	0.38	0.27
ATP-binding cassette, subfamily C (CFTR/MRP), member 9	Abcc9	0.38	0.05	Abcc9	0.88	0.50	ABCC9	0.53	0.09
claudin 1	Cldn1	0.39	0.01	Cldn1	0.53	0.11	CLDN1	0.64	0.02
PTK6 protein tyrosine kinase 6	Ptk6	0.39	0.00	Ptk6	0.88	0.49	PTK6	0.61	0.03
GIMAP family P-loop NTPase domain containing phytanoyl-CoA 2-hydroxylase	Gimd1	0.39	0.03	Gm5549	1.09	0.57	ND		
syntaxis 1B	Phyh	0.39	0.02	Phyh	0.63	0.04	PHYH	0.72	0.11
	Stx1b	0.39	0.02	Stx1b	1.33	0.10	STX1B	0.96	0.89

Supplementary Table 8-4. Down-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
olfactory receptor 59	Olr59	0.40	0.01	Olf78	1.50	0.23	OR51E2	0.47	0.15
growth differentiation factor 10	Gdf10	0.40	0.01	Gdf10	0.72	0.24	GDF10	0.93	0.81
SH3 and cysteine rich domain 3	Stac3	0.40	0.02	Stac3	1.00	0.98	STAC3	1.27	0.33
FERM domain containing 4B	Frmd4b	0.40	0.01	Frmd4b	1.71	0.03	FRMD4B	0.84	0.14
tenascin XA, pseudogene 1	Tnxa-ps1	0.41	0.00	ND			ND		
acyl-coenzyme A amino acid N-acyltransferase 2	Acnat2	0.41	0.03	Acnat2	2.71	0.04	ND		
transmembrane protein 26	Tmem26	0.42	0.00	Tmem26	1.06	0.89	TMEM26	3.46	0.12
abhydrolase domain containing 2	Abhd2	0.42	0.00	Abhd2	0.91	0.79	ABHD2	0.73	0.31
similar to RIKEN cDNA 3110035E14	RGD1561849	0.42	0.02	3110035E14Ri	0.89	0.65	C8orf46	0.68	0.09
phosphatidylinositol-4-phosphate 3-kinase, catalytic subunit two 2 gamma	Pik3c2g	0.42	0.00	Pik3c2g	1.36	0.36	PIK3C2G	0.87	0.15
fibronectin 1	Fn1	0.42	0.00	Fn1	0.99	0.96	FN1	1.43	0.01
disabled homolog 1 (Drosophila)	Dab1	0.43	0.01	Dab1	0.77	0.21	DAB1	1.01	0.96
TLR4 interactor with leucine-rich repeats	Tril	0.43	0.04	Tril	0.72	0.19	TRIL	0.79	0.55
solute carrier family 25, member 34	Slc25a34	0.43	0.00	Slc25a34	0.60	0.02	SLC25A34	0.77	0.08
regucalcin (senescence marker protein-30)	Rgn	0.43	0.00	Rgn	0.42	0.02	RGN	0.86	0.25
forkhead box A3	Foxa3	0.43	0.01	Foxa3	0.61	0.10	FOXA3	0.84	0.34
RAB11 family interacting protein 4 (class II)	Rab11fip4	0.44	0.01	Rab11fip4	0.57	0.02	RAB11FIP4	1.04	0.76
stefin A2-like 3	Stfa2l3	0.44	0.03	Stfa2	1.12	0.65	ND		
transcription factor 24	Tcf24	0.44	0.00	ND			TCF24	0.08	0.39
beta-site APP cleaving enzyme 1	Bace1	0.44	0.02	Bace1	0.80	0.12	BACE1	1.11	0.45
NLR family, pyrin domain containing 3	Nlrp3	0.45	0.01	Nlrp3	0.55	0.13	NLRP3	1.21	0.72
zinc finger, DHHC-type containing 23	Zdhhc23	0.45	0.00	Zdhhc23	2.29	0.09	ZDHHC23	2.39	0.01
integral membrane transport protein UST5r	Ust5r	0.45	0.05	Slc22a30	0.37	0.06	SLC22A9	0.69	0.05
fer-1-like 5 (C. elegans), pseudogene 1	Fer1l5-ps1	0.45	0.00	ND			FER1L5	0.80	0.48
anthrax toxin receptor 1	Antxr1	0.45	0.02	Antxr1	0.81	0.23	ANTXR1	1.16	0.56
beta-carotene oxygenase 2	Bco2	0.45	0.02	Bco2	0.50	0.14	BCO2	1.02	0.91
retinoblastoma 1	Rb1	0.45	0.02	Rb1	1.57	0.27	RB1	1.07	0.34
sushi, nidogen and EGF-like domains 1	Sned1	0.45	0.01	ND			ND		
sortilin-related VPS10 domain containing	Sorcs2	0.45	0.00	Sorcs2	2.06	0.08	SORCS2	0.55	0.08
killer cell lectin-like receptor subfamily G, thymidine phosphorylase	Klrg1	0.46	0.00	Klrg1	0.91	0.79	KLRG1	0.93	0.59
inhibin beta-A	Tymp	0.46	0.00	Tymp	0.63	0.06	TYMP	1.03	0.86
similar to Sulfotransferase K1 (rSULT1C2)	Inhba	0.46	0.00	Inhba	1.01	0.95	INHBA	0.69	0.02
solute carrier family 1 (glial high affinity glutamate transporter), member 2	RGD1559960	0.46	0.01	ND			SULT1C2	5.36	0.00
FK506 binding protein 10	Slc1a2	0.46	0.01	Slc1a2	0.38	0.02	SLC1A2	1.17	0.38
cytochrome P450, family 4, subfamily a, polvoepoxide 1	Fkbp10	0.46	0.01	Fkbp10	1.03	0.89	FKBP10	1.24	0.58
progestin and adipoQ receptor family member ATP-binding cassette, subfamily A (ABC1), member 9	Cyp4a1	0.47	0.00	Cyp4a10	0.57	0.27	CYP4A11	0.73	0.04
cryptochrome 1 (photolyase-like)	Paqr7	0.47	0.01	Paqr7	0.60	0.02	PAQR7	2.36	0.00
SRY (sex determining region Y)-box 7	Abca9	0.47	0.01	Abca9	0.81	0.33	ABCA9	0.74	0.45
apolipoprotein L 9a	Cry1	0.47	0.05	Cry1	0.73	0.17	CRY1	1.05	0.87
dual specificity phosphatase 7	Sox7	0.47	0.04	Sox7	0.94	0.86	SOX7	1.16	0.60
steroidogenic acute regulatory protein	Apol9a	0.47	0.01	ND			ND		
similar to CG1998-PA	Dusp7	0.48	0.04	Dusp7	1.20	0.37	DUSP7	1.46	0.27
lin-7 homolog a (C. elegans)	Star	0.48	0.00	Star	0.23	0.02	STAR	1.18	0.55
RAS, dexamethasone-induced 1	LOC691221	0.48	0.00	ND			C5orf4	0.85	0.26
protoenin	Lin7a	0.48	0.00	Lin7a	0.67	0.50	LIN7A	1.35	0.05
progestin and adipoQ receptor family member IX	Rasd1	0.48	0.01	Rasd1	1.65	0.21	RASD1	1.40	0.21
platelet derived growth factor receptor, beta	Prtg	0.48	0.00	Prtg	0.88	0.54	PRTG	1.00	0.99
hypothetical LOC498316	Paqr9	0.48	0.00	Paqr9	0.80	0.41	PAQR9	0.80	0.34
sulfotransferase family 2A, dehydroepiandrosterone (DHEA)-preferring	Pdgfrb	0.48	0.00	Pdgfrb	1.90	0.22	PDGFRB	1.23	0.66
solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	Slc13a3	0.49	0.00	Slc13a3	1.28	0.37	SLC13A3	0.87	0.50
upper zone of growth plate and cartilage matrix associated	Ucma	0.49	0.01	Ucma	1.43	0.36	UCMA	1.46	0.51
prospero homeobox 1	Prox1	0.49	0.04	Prox1	0.74	0.26	PROX1	0.94	0.63
olfactory receptor 1352	Olr1352	0.49	0.02	Olf1410	0.82	0.31	ND		
N-myc downstream regulated gene 4	Ndrg4	0.49	0.05	Ndrg4	0.90	0.67	NDRG4	0.56	0.06
Eph receptor B3	Ephb3	0.49	0.01	Ephb3	0.84	0.20	EPHB3	0.87	0.65
neurexin 3	Nrxn3	0.50	0.01	Nrxn3	0.66	0.05	ND		
olfactory receptor 1605	Olr1605	0.50	0.02	ND			OR2T2	1.07	0.77
G protein-coupled receptor 135	Gpr135	0.50	0.03	Gpr135	1.52	0.32	GPR135	1.65	0.15
Number of genes with significant alteration	119			6			0		

Supplementary Table 8-4. Down-regulated genes by NaPB in Wistar Hannover rats and correlation with expression alterations in CD-1 mice and chimeric mice with human hepatocytes

Wistar Hannover rats treated with 2500 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value

Data represent the expression ratio between control and NaPB treatment. Genes showing less than 0.5 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in the baseline (control) arrays were chosen as down-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (less than 0.5 fold, p<0.05). ND means "not determined".

Supplementary Table 8-5. Up-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Chimeric mice treated with 1000 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
HCC-related HCC-C11_v3	LOC100131726	27.67	0.01	ND			ND		
aldo-keto reductase family 1, member B10 (aldose reductase)	AKR1B10	26.44	0.02	Akr1b10	1.60	0.03	Akr1b10	0.93	0.87
aldo-keto reductase family 1, member B15	AKR1B15	22.98	0.03	Akr1b8	1.29	0.08	Akr1b8	2.53	0.05
NAD(P)H dehydrogenase, quinone 1	NQO1	19.22	0.01	Nqo1	0.88	0.77	Nqo1	2.68	0.01
aldo-keto reductase family 1, member B1 (aldose reductase)	AKR1B1	11.36	0.02	Akr1b3	1.26	0.23	Akr1b1	0.92	0.17
HEAT repeat containing 7B1	HEATR7B1	10.19	0.01	Mroh2a	1.89	0.05	ND		
F-box and WD repeat domain containing 10	FBXW10	9.68	0.01	Fbxw10	1.54	0.18	ND		
low density lipoprotein receptor class A domain containing 1	LDLRAD1	8.29	0.01	Ldlrad1	1.84	0.12	Ldlrad1	2.37	0.50
calcium binding tyrosine-(Y)-phosphorylation regulated	CABYR	7.79	0.01	Cabyr	0.55	0.02	ND		
tsukushi small leucine rich proteoglycan homolog (Xenopus laevis)	TSKU	7.60	0.00	Tsku	2.72	0.11	Tsku	2.15	0.08
cytochrome P450, family 2, subfamily B, polypeptide 6	CYP2B6	7.15	0.00	Cyp2b10	118.83	0.03	Cyp2b2	52.81	0.00
glycosyltransferase-like domain containing 1	GTDC1	6.58	0.00	Gtdc1	2.44	0.01	Gtdc1	0.84	0.06
secreted phosphoprotein 1	SPP1	6.29	0.01	Spp1	1.10	0.66	Spp1	1.88	0.18
glutathione peroxidase 2 (gastrointestinal)	GPX2	6.15	0.00	Gpx2	1.30	0.28	Gpx2	21.44	0.01
cytochrome P450, family 2, subfamily A, polypeptide 13	CYP2A13	5.83	0.00	Cyp2a4	17.94	0.04	Cyp2a3	0.56	0.19
chitinase 3-like 1 (cartilage glycoprotein-39)	CHI3L1	5.43	0.04	Chi3l1	1.18	0.61	Chi3l1	0.90	0.59
sulfotransferase family, cytosolic, 1C, member 2	SULT1C2	5.36	0.00	ND			RGD1559960	0.46	0.01
interleukin 17D	IL17D	5.27	0.04	Il17d	1.27	0.36	Il17d	1.14	0.35
cytochrome P450, family 2, subfamily A, polypeptide 7	CYP2A7	5.25	0.00	Cyp2a4	17.94	0.04	Cyp2a3	0.56	0.19
cytochrome P450, family 2, subfamily G, polypeptide 1 pseudogene	CYP2G1P	5.05	0.00	ND			ND		
serpin peptidase inhibitor, clade B (ovalbumin), member 9	SERPINB9	4.94	0.00	Serpibn9	0.70	0.16	Serpibn9	1.23	0.03
glutathione S-transferase mu 2 (muscle)	GSTM2P1	4.93	0.02	ND			ND		
pseudoogene 1	SEC14L4	4.70	0.00	Sec14l4	0.74	0.21	Sec14l4	0.93	0.77
malic enzyme 1, NADP(+) -dependent, cytosolic	ME1	4.59	0.00	Me1	1.86	0.27	Me1	3.06	0.01
potassium channel tetramerisation domain containing 15	KCTD15	4.47	0.01	Kctd15	0.89	0.58	Kctd15	1.25	0.09
guanylate cyclase 2E	GUCY2E	4.35	0.00	ND			ND		
UDP glucuronosyltransferase 1 family, polypeptide A8	UGT1A8	4.25	0.00	ND			ND		
tescalcin	TESC	4.25	0.04	Tesc	1.16	0.54	Tesc	0.65	0.44
UDP glucuronosyltransferase 1 family, polypeptide A6	UGT1A6	4.19	0.00	Ugt1a6b	1.82	0.06	Ugt1a6	1.98	0.00
F-box protein 15	FBXO15	4.16	0.02	ND			Fbxo15	0.96	0.79
neuropeptide W	NPW	4.13	0.02	Npw	0.95	0.88	Npw	1.07	0.71
gamma-glutamyltransferase 3 pseudogene	GGT3P	4.12	0.00	ND			ND		
cytochrome P450, family 26, subfamily A, polypeptide 1	CYP26A1	4.04	0.01	Cyp26a1	2.47	0.11	Cyp26a1	5.64	0.01
tripartite motif containing 16-like	TRIM16L	4.00	0.02	ND			ND		
glutathione S-transferase mu 1	GSTM1	3.95	0.02	Gstm2	10.35	0.02	Gstm2	1.59	0.01
transmembrane protein 233	TMEM233	3.93	0.01	Tmem233	1.03	0.82	ND		
histidine decarboxylase	HDC	3.89	0.03	Hdc	1.89	0.10	Hdc	1.68	0.07
G protein-coupled receptor, family C, group 5, member B	GPRC5B	3.84	0.04	Gprc5b	0.85	0.60	Gprc5b	1.22	0.83
gamma-glutamyltransferase light chain 1	GGTLC1	3.72	0.00	ND			ND		
heat shock 70kDa protein 1A	HSPA1A	3.70	0.03	Hspa1a	1.08	0.84	Hspa1b	1.15	0.06
left-right determination factor 1	LEFTY1	3.68	0.01	Lefty1	1.39	0.51	Lefty1	1.34	0.21
glutathione S-transferase pi 1	GSTP1	3.64	0.00	ND			Gstp1	2.41	0.05
gamma-glutamyltransferase 1	GGT1	3.62	0.00	ND			ND		
keratin 23 (histone deacetylase inducible)	KRT23	3.62	0.04	Krt23	0.84	0.67	Krt23	0.53	0.30
tetraspanin 8	TSPAN8	3.58	0.00	Tspan8	0.92	0.78	Tspan8	0.75	0.35
glutathione S-transferase mu 2 (muscle)	GSTM2	3.53	0.04	Gstm7	0.80	0.01	Gstm7	1.14	0.32
wingless-type MMTV integration site family, member 5B	WNT5B	3.49	0.00	Wnt5b	1.41	0.20	Wnt5b	1.62	0.24
chemokine (C-X-C motif) receptor 3	CXCR3	3.46	0.04	Cxcr3	1.07	0.78	Cxcr3	1.08	0.62
Nmra-like family domain containing 1	LOC344887	3.39	0.00	ND			ND		
cytoplasmic polyadenylation element binding protein 3	CPEB3	3.34	0.02	Cpeb3	1.08	0.34	Cpeb3	0.82	0.11
UDP-glucose 6-dehydrogenase	UGDH	3.30	0.00	Ugdh	3.05	0.10	Ugdh	2.19	0.00
dynein, axonemal, heavy chain 12	DNAH12	3.29	0.01	ND	0.77	0.09	Dnah12	0.53	0.35
aldo-keto reductase family 1, member D1 (delta 4-3-ketosteroid-5-beta-reductase)	AKR1D1	3.29	0.01	Akr1d1	2.37	0.11	Akr1d1	1.14	0.31

Supplementary Table 8-5. Up-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Chimeric mice treated with 1000 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
WAS/WASL interacting protein family, member 3	WIPF3	3.28	0.04	Wipf3	0.65	0.14	Wipf3	0.76	0.23
aldo-keto reductase family 1, member C1	AKR1C1	3.27	0.00	Akr1c21	0.61	0.15	Akr1c2	0.92	0.69
(dihydrodiol dehydrogenase 1; 20-alpha (3-alpha)-hydroxysteroid dehydrogenase)									
chromosome 6 open reading frame 7	C6orf7	3.25	0.01	ND			ND		
DnaJ (Hsp40) homolog, subfamily A, member 4	DNAJA4	3.25	0.02	Dnaja4	1.45	0.02	Dnaja4	0.74	0.04
tumor necrosis factor (ligand) superfamily, member 14	TNFSF14	3.23	0.03	Tnfsf14	0.92	0.61	Tnfsf14	1.29	0.52
armadillo repeat containing 9	ARMC9	3.18	0.01	Armc9	0.80	0.63	ND		
cytochrome P450, family 3, subfamily A, polypeptide 4	CYP3A4	3.17	0.00	Cyp3a16	3.35	0.01	Cyp3a23/3a1	5.17	0.00
Rho guanine nucleotide exchange factor (GEF) angiotensin I converting enzyme (peptidyl-dipeptidase A) 2	ARHGEF17	3.14	0.02	Arhgef17	1.01	0.99	ND		
cytochrome P450, family 3, subfamily A, polypeptide 7	ACE2	3.12	0.00	Ace2	1.27	0.14	Ace2	1.19	0.64
organic solute transporter beta	CYP3A7	3.10	0.00	Cyp3a13	3.71	0.22	Cyp3a9	1.87	0.03
neuromedin U receptor 2	OSTBETA	3.04	0.04	Slc51b	0.77	0.26	Slc51b	1.11	0.34
dedicator of cytokinesis 11	NMUR2	3.00	0.00	Nmur2	1.48	0.22	Nmur2	1.13	0.19
transferrin receptor (p90, CD71)	DOCK11	2.98	0.00	Dock11	1.23	0.31	Dock11	5.44	0.20
glycican 3	TFRC	2.95	0.00	Tfrc	2.33	0.00	Tfrc	1.73	0.20
contactin associated protein-like 2	GPC3	2.92	0.01	Gpc3	0.75	0.19	Gpc3	0.85	0.54
gamma-glutamyltransferase light chain 2	CNTNAP2	2.92	0.02	Cntnap2	0.34	0.08	ND		
ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	GGTLC2	2.90	0.00	ND			ND		
heat shock protein 90kDa alpha (cytosolic), class A member 2	UCHL1	2.90	0.00	Uchl1	1.52	0.27	Uchl1	1.19	0.10
coiled-coil domain containing 3	HSP90AA2	2.88	0.02	ND			ND		
ELOVL fatty acid elongase 6	CCDC3	2.87	0.04	Ccdc3	0.73	0.15	Ccdc3	0.80	0.21
transketolase	ELOVL6	2.85	0.03	Elov6	5.78	0.08	Elov6	2.42	0.04
polycystic kidney disease 2-like 1	TKT	2.84	0.01	Tkt	1.58	0.23	Tkt	1.95	0.00
acyl-CoA synthetase long-chain family member 4	PKD2L1	2.83	0.02	Pkd2l1	0.85	0.52	Pkd2l1	1.14	0.13
complement factor H-related 5	ACSL4	2.82	0.01	Acs4	1.17	0.65	Acs4	1.05	0.30
heat shock 105kDa/110kDa protein 1	CFHR5	2.82	0.00	ND			ND		
leptin receptor overlapping transcript	HSPH1	2.78	0.03	Hspf1	1.57	0.36	Hspf1	0.71	0.05
HECT, C2 and WW domain containing E3	LEPROT	2.76	0.01	ND			ND		
ubiquitin protein ligase 2	HECW2	2.74	0.01	Hebw2	1.67	0.03	Hebw2	0.50	0.08
AF4/FMR2 family, member 3	AFF3	2.74	0.02	ND			ND		
Rho family GTPase 2	RND2	2.73	0.03	Rnd2	1.84	0.00	Rnd2	0.66	0.02
chromosome 12 open reading frame 5	C12orf5	2.71	0.03	9630033F20Ri	1.66	0.23	LOC502894	1.33	0.01
aminolevulinate, delta-, synthase 1	ALAS1	2.71	0.02	Alas1	4.06	0.12	ND		
aldo-keto reductase family 1, member C-like 1	AKR1CL1	2.70	0.00	ND			ND		
RNA binding protein with multiple splicing 2	RPBMS2	2.69	0.00	Rpbms2	0.89	0.62	Rpbms2	0.87	0.26
angiominot like 1	AMOTL1	2.68	0.02	Amotl1	0.48	0.12	ND		
solute carrier family 2 (facilitated glucose transporter), member 1	SLC2A1	2.67	0.05	Slc2a1	0.97	0.89	Slc2a1	1.13	0.36
chitinase, acidic	CHIA	2.58	0.00	Chia	0.88	0.68	Chia	1.15	0.10
chromosome 7 open reading frame 49	C7orf49	2.57	0.03	3110062M04Ri	0.81	0.19	LOC500077	85.05	0.39
aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	AKR1C3	2.55	0.00	Akr1c18	0.74	0.36	Akr1c3	0.53	0.00
galactose-3-O-sulfotransferase 1	GAL3ST1	2.55	0.00	Gal3st1	0.24	0.44	ND		
TBC1 domain family, member 8B (with GRAM domain)	TBC1D8B	2.54	0.02	Tbc1d8b	0.73	0.08	ND		
long intergenic non-protein coding RNA 319	LINC00319	2.54	0.01	ND			ND		
FIC domain containing	FICD	2.53	0.05	Ficd	1.21	0.50	Ficd	1.24	0.20
chromosome 21 open reading frame 56	C21orf56	2.53	0.02	Spatc1l	0.65	0.07	Spatc1l	7.07	0.41
muscle RAS oncogene homolog	Mras	2.52	0.03	Mras	1.74	0.10	Mras	1.44	0.02
aldehyde oxidase 1	AOX1	2.52	0.00	Aox1	1.65	0.30	Aox1	2.46	0.03
CAP-GLY domain containing linker protein family, member 4	CLIP4	2.51	0.00	Clip4	0.81	0.32	Clip4	0.57	0.19
solute carrier family 2 (facilitated glucose transporter), member 12	SLC2A12	2.50	0.02	Slc2a12	0.85	0.36	Slc2a12	0.75	0.42
cytochrome P450, family 1, subfamily A, polypeptide 1	CYP1A1	2.49	0.03	Cyp1a1	0.95	0.91	Cyp1a1	2.41	0.05
chromosome 1 open reading frame 106	C1orf106	2.48	0.01	5730559C18Ri	1.22	0.66	RGD1311892	1.44	0.20
epoxide hydrolase 1, microsomal (xenobiotic)	EPHX1	2.47	0.00	Ephx1	2.99	0.03	Ephx1	5.68	0.00
semaphorin 7A, GPI membrane anchor (John Milton Haagen blood group)	SEMA7A	2.46	0.03	Sema7a	0.85	0.80	Sema7a	0.76	0.38
long intergenic non-protein coding RNA 152	LINC00152	2.45	0.03	ND			ND		
tetraspanin 3	TSPAN3	2.42	0.01	Tspan3	1.21	0.22	Tspan3	1.02	0.80
methyltransferase like 7B	METTL7B	2.41	0.04	Mettl7b	1.41	0.26	Mettl7b	0.85	0.27

Supplementary Table 8-5. Up-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Chimeric mice treated with 1000 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
vault RNA 1-3	VTRNA1-3	2.39	0.05	ND			ND		
zinc finger, DHHC-type containing 23	ZDHHC23	2.39	0.01	Zdhhc23	2.29	0.09	Zdhhc23	0.45	0.00
Rho guanine nucleotide exchange factor (GEF) nuclear receptor subfamily 6, group A, member 1	ARHGEF37	2.39	0.00	Arhgef37	0.73	0.24	Arhgef37	1.42	0.25
nuclear receptor subfamily 6, group A, member 1	NR6A1	2.39	0.01	Nr6a1	1.28	0.44	Nr6a1	3.04	0.02
serum/glucocorticoid regulated kinase 2	SGK2	2.39	0.02	Sgk2	0.69	0.23	Sgk2	0.56	0.05
FK506 binding protein 11, 19 kDa	FKBP11	2.39	0.02	Fkbp11	1.14	0.48	Fkbp11	1.52	0.02
sulfiredoxin 1	SRXN1	2.36	0.01	Srxn1	2.54	0.14	Srxn1	3.04	0.00
progestin and adiponQ receptor family member	PAQR7	2.36	0.00	Paqr7	0.60	0.02	Paqr7	0.47	0.01
chromosome 11 open reading frame 96	C11orf96	2.36	0.04	Gm13889	1.20	0.15	RGD1564664	0.88	0.41
solute carrier family 29 (nucleoside transporters), member 4	SLC29A4	2.35	0.00	Slc29a4	0.37	0.15	Slc29a4	1.28	0.18
protamine 1	PRM1	2.34	0.01	ND			ND		
integrin, alpha 7	ITGA7	2.34	0.01	Itga7	0.74	0.16	Itga7	0.71	0.33
dynein, light chain, roadblock-type 2	DYNLRB2	2.31	0.01	Dynlrb2	0.51	0.24	Dynlrb2	0.35	0.11
EPH receptor B4	EPHB4	2.31	0.00	Ephb4	0.85	0.05	ND		
potassium channel, subfamily V, member 2	KCNV2	2.31	0.01	Kcnv2	0.75	0.19	Kcnv2	0.56	0.03
degenerative spermatocyte homolog 1, lipid desaturase (Drosophila)	DEGS1	2.30	0.00	Degs1	0.84	0.42	Degs1	1.24	0.01
HIV-1 Tat interactive protein 2, 30kDa	HTATIP2	2.29	0.00	Htatip2	2.48	0.06	Htatip2	2.35	0.01
lipoma HMGIC fusion partner-like 2	LHFPL2	2.27	0.01	Lhfpl2	0.69	0.28	Lhfpl2	0.94	0.46
uridine phosphorylase 1	UPP1	2.27	0.04	Upp1	1.33	0.35	Upp1	0.84	0.11
chemokine (C-C motif) ligand 3	CCL3	2.26	0.05	ND			ND		
chromosome 1 open reading frame 70	C1orf70	2.26	0.04	Tmem240	0.83	0.05	ND		
ladinin 1	LAD1	2.26	0.03	Lad1	0.94	0.82	Lad1	1.03	0.95
tubulin, alpha 4a	TUBA4A	2.25	0.02	Tuba4a	1.21	0.62	Tuba4a	0.81	0.31
muscle, skeletal, receptor tyrosine kinase	MUSK	2.25	0.04	Musk	0.84	0.35	Musk	1.26	0.23
heat shock protein 90kDa alpha (cytosolic), class B member 2, pseudogene	HSP90AB2P	2.24	0.02	ND			ND		
numb homolog (Drosophila)-like	NUMBL	2.24	0.00	Numb1	0.86	0.62	Numbl	1.41	0.15
mucin 22	MUC22	2.24	0.02	ND			ND		
cytochrome P450, family 2, subfamily C, polypeptide 8	CYP2C8	2.24	0.01	Cyp2c65	2.51	0.12	Cyp2c79	1.91	0.08
long intergenic non-protein coding RNA 204B	LINC00204B	2.23	0.02	ND			ND		
cytochrome P450, family 2, subfamily C, polypeptide 19	CYP2C19	2.22	0.00	Cyp2c54	7.97	0.01	Cyp2c6v1	4.59	0.00
flavin containing monooxygenase 1	FMO1	2.22	0.03	Fmo1	1.89	0.14	Fmo1	0.24	0.00
solute carrier family 27 (fatty acid transporter), member 2	SLC27A2	2.21	0.01	Slc27a2	0.78	0.13	Slc27a2	0.97	0.62
thyroglobulin	TG	2.20	0.03	Tg	0.88	0.54	Tg	0.81	0.22
solute carrier family 5 (sodium/glucose cotransporter). member 11	SLC5A11	2.20	0.01	Slc5a11	1.62	0.12	Slc5a11	1.17	0.06
pecanex-like 2 (Drosophila)	PCNXL2	2.19	0.02	Pcnxl2	1.29	0.11	Pcnxl2	1.83	0.02
heat shock protein 90kDa alpha (cytosolic), class A member 1	HSP90AA1	2.19	0.00	Hsp90aa1	1.38	0.43	Hsp90aa1	0.90	0.51
dapper, antagonist of beta-catenin, homolog 2 (<i>Xenopus laevis</i>)	DACT2	2.18	0.02	Dact2	0.90	0.73	Dact2	1.40	0.01
paternally expressed 3	PEG3	2.17	0.05	Peg3	1.74	0.13	ND		
MCF2L antisense RNA 1 (non-protein coding)	MCF2L-AS1	2.17	0.02	ND			ND		
transmembrane emp24 protein transport domain containing 6	TMED6	2.17	0.02	Tmed6	0.56	0.19	Tmed6	0.47	0.31
potassium large conductance calcium-activated channel, subfamily M, alpha member 1	KCNMA1	2.15	0.03	Kcnma1	0.81	0.28	Kcnma1	2.09	0.04
olfactory receptor, family 5, subfamily E, member 1 pseudo gene	OR5E1P	2.15	0.02	ND			ND		
ADP-ribosyltransferase 5	ART5	2.15	0.00	Art5	0.81	0.14	Art5	2.42	0.36
vault RNA 2-1	VTRNA2-1	2.15	0.01	ND			ND		
anthrax toxin receptor 2	ANTXR2	2.14	0.00	Antxr2	0.79	0.26	ND		
transmembrane 4 L six family member 1	TM4SF1	2.13	0.04	Tm4sf1	1.77	0.08	Tm4sf1	0.90	0.49
BMP and activin membrane-bound inhibitor homolog (<i>Xenopus laevis</i>)	BAMBI	2.13	0.03	Bambi	0.72	0.23	Bambi	0.85	0.60
KIAA1549	KIAA1549	2.12	0.03	D630045J12Ri	0.69	0.42	RGD1306271	1.60	0.10
dipeptidyl-peptidase 9	DPP9	2.12	0.00	Dpp9	0.72	0.08	Dpp9	0.88	0.15
DENN/MADD domain containing 2D	DENNND2D	2.11	0.00	Dennnd2d	1.52	0.04	Dennd2d	1.99	0.00
pirin (iron-binding nuclear protein)	PIR	2.11	0.01	Pir	1.62	0.05	Pir	3.34	0.00
ATP-binding cassette, sub-family B (MDR/TAP), member 6	ABCB6	2.11	0.01	Abcb6	1.11	0.58	Abcb6	1.27	0.01
diacylglycerol O-acyltransferase 1	DGAT1	2.10	0.01	Dgat1	0.56	0.46	Dgat1	0.94	0.39
interleukin 1, beta	IL1B	2.10	0.04	Il1b	1.67	0.15	Il1b	0.69	0.05
transmembrane protein 54	TMEM54	2.08	0.02	Tmem54	0.83	0.48	Tmem54	10.32	0.40
transmembrane protein 164	TMEM164	2.08	0.02	Tmem164	1.69	0.32	Tmem164	1.07	0.56
heme oxygenase (decycling) 1	HMOX1	2.07	0.03	Hmox1	0.70	0.06	Hmox1	1.57	0.04
chromosome 5 open reading frame 30	C5orf30	2.07	0.00	D1ertd622e	1.34	0.15	RGD1562136	1.41	0.10

Supplementary Table 8-5. Up-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Chimeric mice treated with 1000 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB		
Gene Name	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value
ATP-binding cassette, sub-family C (CFTR/MRP), member 2	ABCC2	2.07	0.00	Abcc2	2.49	0.13	ND		
glycoprotein (transmembrane) nmb	GPNMB	2.06	0.04	Gpnmb	0.82	0.26	Gpnmb	1.54	0.02
mitochondrial fission process 1	MTFP1	2.06	0.04	Mtfp1	1.89	0.11	Mtfp1	0.98	0.82
signal transducer and activator of transcription 4	STAT4	2.04	0.04	Stat4	0.81	0.66	Stat4	0.62	0.05
zinc finger protein 300 pseudogene 1	ZNF300P1	2.03	0.00	ND			ND		
vault RNA 1-2	VTRNA1-2	2.03	0.04	ND			ND		
24-dehydrocholesterol reductase	DHCR24	2.02	0.00	Dhcr24	1.82	0.09	Dhcr24	1.39	0.00
MPV17 mitochondrial membrane protein-like	MPV17L	2.00	0.03	Mpv17l	2.42	0.04	Mpv17l	1.24	0.00
Number of genes with significant alteration		174		10			17		

Data represent the expression ratio between control and NaPB treatment. Genes showing greater than 2 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in an experimental (treatment) arrays were chosen as up-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (greater than 2 fold, p<0.05). ND means "not determined".

Supplementary Table 8-6. Down-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Gene Name	Chimeric mice treated with 1000 ppm NaPB				CD-1 mice treated with 2500 ppm NaPB				Wistar Hannover rats treated with 2500 ppm NaPB			
	Gene symbol	Fold change	p value		Gene symbol	Fold change	p value		Gene symbol	Fold change	p value	
achaete-scute complex homolog 1 (Drosophila)	ASCL1	0.11	0.03		Ascl1	1.70	0.02		Ascl1	0.93	0.26	
T-box 15	TBX15	0.15	0.01		Tbx15	1.03	0.94		Tbx15	1.99	0.19	
lensin, lens protein with glutamine synthetase domain	LGSN	0.16	0.00		Lgsn	0.62	0.06		Lgsn	0.26	0.13	
phenylethanolamine N-methyltransferase	PNMT	0.16	0.04		Pnmt	0.99	0.95		ND			
dynein, axonemal, heavy chain 6	DNAH6	0.20	0.00		Dnah6	3.73	0.41		Dnahc6	1.14	0.13	
myelin transcription factor 1	MYT1	0.20	0.00		Myt1	0.81	0.23		Myt1	1.22	0.03	
titin-cap (telethonin)	TCAP	0.21	0.03		Tcap	1.17	0.56		ND			
trefol factor 3 (intestinal)	TFF3	0.22	0.00		Tff3	0.50	0.15		Tff3	0.20	0.30	
steroid sulfatase (microsomal), isozyme S	STS	0.23	0.01		ND				Sts	0.85	0.18	
ret proto-oncogene	RET	0.24	0.00		Ret	0.69	0.12		Ret	2.32	0.02	
leucine-rich, glioma inactivated 1	LG11	0.27	0.02		Lgi1	1.13	0.72		Lgi1	0.53	0.26	
glial cell derived neurotrophic factor	GDNF	0.28	0.01		Gdnf	0.75	0.18		Gdnf	0.47	0.31	
forkhead box P3	FOXP3	0.30	0.00		Foxp3	1.01	0.96		Foxp3	1.57	0.00	
Mov10l1, Moloney leukemia virus 10-like 1, homolog (mouse)	MOV10L1	0.30	0.04		Mov10l1	0.64	0.43		ND			
SP140 nuclear body protein	SP140	0.31	0.03		Sp140	1.22	0.24		Sp140	1.08	0.17	
cerebellin 4 precursor	CBLN4	0.32	0.02		Cbln4	0.85	0.37		Cbln4	1.47	0.06	
HemK methyltransferase family member 1	HEMK1	0.32	0.01		Hemk1	1.09	0.78		Hemk1	1.22	0.01	
collagen, type V, alpha 3	COL5A3	0.32	0.03		Col5a3	0.42	0.03		Col5a3	1.30	0.03	
GRB2-related adaptor protein	GRAP	0.33	0.01		Grap	0.93	0.82		Grap	1.11	0.49	
Rho guanine nucleotide exchange factor (GEF) metallothionein 1M	ARHGEF26	0.33	0.02		Arhgef26	0.77	0.41		Arhgef26	0.76	0.22	
multiple EGF-like-domains 6	MEGF6	0.34	0.05		Megf6	1.09	0.78		Megf6	1.03	0.85	
secretagogin, EF-hand calcium binding protein	SCGN	0.34	0.02		Scgn	1.09	0.79		Scgn	1.17	0.04	
metallothionein 1E	MT1E	0.34	0.05		ND				ND			
wingless-type MMTV integration site family, member 11	WNT11	0.36	0.02		Wnt11	0.90	0.50		Wnt11	1.18	0.57	
RAS-like, family 11, member B	RASL11B	0.36	0.02		Rasl11b	1.93	0.09		Rasl11b	0.52	0.05	
dual specificity phosphatase 1	DUSP1	0.38	0.03		Dusp1	0.67	0.20		Dusp1	0.41	0.12	
tropomodulin 1	TMOD1	0.38	0.00		Tmod1	0.69	0.08		Tmod1	0.87	0.52	
arrestin domain containing 4	ARRDC4	0.38	0.01		Arrdc4	0.51	0.06		Arrdc4	1.51	0.21	
latent transforming growth factor beta binding protein 1	LTBP1	0.39	0.01		Ltp1	1.12	0.33		Ltp1	0.64	0.01	
FERM domain containing 7	FRMD7	0.39	0.03		ND				Frmd7	1.13	0.21	
Tctex1 domain containing 1	TCTEX1D1	0.39	0.01		Tctex1d1	1.59	0.24		Tctex1d1	1.21	0.04	
inhibin, beta E	INHBE	0.39	0.00		Inhbe	0.83	0.34		Inhbe	0.64	0.00	
arginine vasopressin receptor 1A	AVPR1A	0.39	0.03		Avpr1a	0.48	0.14		Avpr1a	0.56	0.01	
coiled-coil domain containing 68	CCDC68	0.39	0.03		Ccdc68	0.81	0.54		Ccdc68	1.54	0.16	
cytidine monophospho-N-acetylneurameric acid hydroxylase, pseudogene	CMAHP	0.40	0.02		ND				ND			
gamma-aminobutyric acid (GABA) B receptor, 2	GABBR2	0.40	0.02		Gabbr2	0.74	0.14		Gabbr2	1.86	0.04	
peptidase inhibitor 15	P115	0.40	0.04		Pi15	1.38	0.42		Pi15	2.09	0.27	
carbonic anhydrase XIV	CA14	0.41	0.00		Car14	1.09	0.77		ND			
angiopeitin-like 4	ANGPTL4	0.41	0.01		Angptl4	0.43	0.22		Angptl4	1.30	0.51	
arrestin domain containing 2	ARRDC2	0.41	0.03		Arrdc2	0.53	0.15		Arrdc2	1.24	0.35	
tripartite motif containing 29	TRIM29	0.42	0.02		ND				Trim29	1.16	0.10	
complement component 5a receptor 1	C5AR1	0.42	0.04		C5ar1	1.21	0.53		ND			
nuclear pore complex interacting protein related gene	LOC100132247	0.42	0.04		ND				ND			
adenylate cyclase 1 (brain)	ADCY1	0.42	0.01		Adcy1	0.77	0.18		Adcy1	1.72	0.12	
lymphocyte cytosolic protein 1 (L-plastin)	LCP1	0.42	0.01		Lcp1	0.81	0.70		Lcp1	1.28	0.07	
syntabulin (syntaxin-interacting)	SYBU	0.42	0.00		Sybu	1.47	0.35		Sybu	2.15	0.31	
sodium channel, voltage-gated, type IX, alpha subunit	SCN9A	0.43	0.00		Scn9a	0.89	0.73		Scn9a	0.64	0.45	
chromosome 9 open reading frame 72	C9orf72	0.43	0.03		3110043O21Ri	0.85	0.51		RGD1359108	1.17	0.25	
POU class 6 homeobox 1	POU6F1	0.43	0.00		Pou6f1	0.81	0.67		Pou6f1	0.86	0.55	
activating transcription factor 5	ATF5	0.43	0.00		Atf5	0.66	0.14		Atf5	0.54	0.00	
calmodulin-like 4	CALML4	0.43	0.03		Calml4	1.56	0.04		Calml4	0.93	0.16	
KIAA1984	KIAA1984	0.44	0.05		4921530D09Ri	0.42	0.24		LOC499754	1.19	0.04	
lipase, endothelial	LIPG	0.44	0.02		Lipg	1.11	0.81		Lipg	1.11	0.21	
leucine rich repeat containing 17	LRRC17	0.44	0.01		ND				Lrrc17	1.13	0.25	
golgi autoantigen, golgin subfamily a, 6	LOC645752	0.45	0.01		ND				ND			
pseudogene												
B lymphoid tyrosine kinase	BLK	0.45	0.01		Blk	1.12	0.76		Blk	0.69	0.01	
trigger transposable element derived 7	TIGD7	0.45	0.02		ND				ND			
ERBB receptor feedback inhibitor 1	ERRFI1	0.45	0.01		Errfi1	0.62	0.28		Errfi1	0.67	0.06	
chemokine (C-C motif) ligand 18 (pulmonary and activation-regulated)	CCL18	0.45	0.00		ND				ND			
chromosome 1 open reading frame 21	C1orf21	0.45	0.02		1700025G04Ri	0.84	0.58		RGD1309104	0.81	0.29	
G0/G1switch 2	G0S2	0.45	0.05		G0s2	1.08	0.66		G0s2	0.63	0.07	
ret finger protein-like 4A	RFPL4A	0.46	0.05		ND				ND			

Supplementary Table 8-6. Down-regulated genes by NaPB in chimeric mice with human hepatocytes and correlation with expression alterations in CD-1 mice and Wistar Hannover rats

Gene Name	Gene symbol	Chimeric mice treated with 1000 ppm NaPB			CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB		
		Fold change	p value	Gene symbol	Fold change	p value	Gene symbol	Fold change	p value	
leucine rich repeat containing 31	LRRC31	0.46	0.02	ND			Lrrc31	1.52	0.02	
solute carrier family 23 (nucleobase transporters), member 3	SLC23A3	0.46	0.03	Slc23a3	1.23	0.57	Slc23a3	1.03	0.97	
tenascin R (restrictin, janusin)	TNR	0.46	0.00	Tnr	1.04	0.93	Tnr	2.85	0.25	
NLR family, apoptosis inhibitory protein	NAIP	0.46	0.02	ND			ND			
chromosome 2 open reading frame 54	C2orf54	0.46	0.02	2310007B03Ri	0.67	0.25	RGD1563692	1.34	0.50	
torsin family 3, member A	TOR3A	0.46	0.00	Tor3a	1.73	0.09	Tor3a	0.78	0.57	
CXXC finger protein 4	CXXC4	0.47	0.01	Cxxc4	0.67	0.08	Cxxc4	0.86	0.47	
transforming growth factor, beta receptor III	TGFBR3	0.47	0.03	Tgfb3	1.08	0.76	Tgfb3	0.53	0.13	
chromosome 1 open reading frame 186	C1orf186	0.47	0.03	ND			ND			
dopamine beta-hydroxylase (dopamine beta-monooxygenase)	DBH	0.47	0.02	Dbh	0.95	0.86	Dbh	1.19	0.04	
prolyl 4-hydroxylase, alpha polypeptide I	P4HA1	0.47	0.01	P4ha1	0.84	0.20	P4ha1	1.16	0.06	
sperm associated antigen 1	SPAG1	0.47	0.02	Spag1	0.97	0.92	Spag1	1.29	0.06	
fyn-related kinase	FRK	0.47	0.00	Frk	1.55	0.23	Frk	0.83	0.11	
major facilitator superfamily domain containing transmembrane protein 63A	MFSD2A	0.48	0.03	Mfsd2a	1.87	0.26	Mfsd2a	0.28	0.10	
cadherin-related family member 2	TMEM63A	0.48	0.00	Tmem63a	0.62	0.07	Tmem63a	1.06	0.33	
putative caspase-14-like protein	CASP14L	0.48	0.02	ND			ND			
protein tyrosine phosphatase, non-receptor type	PTPN9	0.48	0.00	Ptpn9	1.03	0.89	Ptpn9	0.84	0.48	
nucleolar protein 4	NOL4	0.48	0.02	Nol4	0.59	0.28	Nol4	1.15	0.11	
RAS (RAD and GEM)-like GTP binding 2	REM2	0.49	0.04	Rem2	1.22	0.53	Rem2	0.88	0.36	
steroid-5-alpha-reductase, alpha polypeptide 1	SRD5A1	0.49	0.03	ND			ND			
(3-oxo-5-alpha-steroid delta 4-dehydrogenase	HPGDS	0.49	0.02	Hpgds	1.15	0.70	Hpgds	0.87	0.13	
hematopoietic prostaglandin D synthase	C6orf123	0.49	0.00	ND			ND			
chromosome 6 open reading frame 123	KCND3	0.49	0.00	Kcnd3	2.02	0.12	Kcnd3	0.82	0.19	
potassium voltage-gated channel, Shal-related subfamily, member 3	FAM107A	0.50	0.04	Fam107a	0.82	0.55	Fam107a	2.01	0.38	
family with sequence similarity 107, member A	LINC00324	0.50	0.01	ND			ND			
long intergenic non-protein coding RNA 324	AIFM2	0.50	0.03	Aifm2	1.11	0.59	Aifm2	0.84	0.11	
apoptosis-inducing factor, mitochondrion-associated 2										
Number of genes with significant alteration	90			1			0			

Data represent the expression ratio between control and NaPB treatment. Genes showing greater than 2 for the ratio and less than 0.05 for the p-value, and "1 (present)" for Detection Call in an experimental (treatment) arrays were chosen as up-regulated genes. Genes with alteration were listed in order of larger alteration. Shadow means significant alteration (greater than 2 fold, p<0.05). ND means "not determined".

Supplementary Table 9. Up- or Down-regulated cell proliferation related genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Acer2	1.76	0.02	Acer2	0.63	0.03	ACER2	0.89	0.67
Acvr1b	0.50	0.04	Acvr1b	1.20	0.52	ACVR1B	1.59	0.05
Acvrl1	1.09	0.69	Acvrl1	0.81	0.01	ACVRL1	1.81	0.30
Adm	1.56	0.02	Adm	0.77	0.08	ADM	0.89	0.40
Adora1	1.20	0.56	Adora1	2.01	0.00	ADORA1	0.70	0.46
Adrb2	2.15	0.05	Adrb2	0.91	0.53	ADRB2	0.66	0.03
Agt	1.00	0.97	Agt	0.80	0.02	AGT	0.60	0.00
Ahsg	0.99	0.96	Ahsg	0.69	0.00	AHSG	0.83	0.10
Akirin2	0.87	0.32	Akirin2	0.91	0.30	AKIRIN2	1.94	0.03
Aldh3a1	1.05	0.89	Aldh3a1	1.27	0.03	ALDH3A1	0.82	0.75
Anxa7	1.63	0.02	Anxa7	2.79	0.01	ANXA7	1.30	0.03
Apbb2	0.48	0.16	Apbb2	0.78	0.04	APBB2	0.67	0.01
Apln	0.79	0.33	Apln	2.01	0.04	APLN	0.60	0.46
Apobec1	0.65	0.49	Apobec1	1.35	0.02	APOBEC1	1.00	0.99
Appl1	1.50	0.16	Appl1	1.56	0.02	APPL1	1.21	0.10
Appl2	0.92	0.65	Appl2	1.27	0.03	APPL2	1.53	0.01
Atf3	1.41	0.20	Atf3	2.71	0.02	ATF3	0.73	0.34
Avpr1a	0.48	0.14	Avpr1a	0.56	0.01	AVPR1A	0.39	0.03
Avpr2	1.24	0.38	Avpr2	1.42	0.05	AVPR2	0.74	0.29
Axin2	1.60	0.02	Axin2	0.52	0.01	AXIN2	0.80	0.16
B4galt1	1.14	0.44	B4galt1	0.78	0.03	B4GALT1	0.89	0.34
Bambi	0.72	0.23	Bambi	0.85	0.60	BAMBI	2.13	0.03
Bcl2l1	0.81	0.29	Bcl2l1	0.82	0.01	BCL2L1	1.11	0.19
BeCN1	1.99	0.43	BeCN1	0.84	0.03	BECN1	1.04	0.74
Bid	1.26	0.52	Bid	1.10	0.34	BID	1.42	0.00
Bmp2	0.55	0.05	Bmp2	0.91	0.04	BMP2	1.10	0.72
Bmp4	0.46	0.01	Bmp4	0.63	0.12	BMP4	1.07	0.81
Bop1	0.99	0.96	Bop1	0.95	0.56	BOP1	1.33	0.05
Btc	1.08	0.85	Btc	4.62	0.33	BTC	0.66	0.05
Btg1	1.37	0.24	Btg1	0.63	0.02	BTG1	0.78	0.21
Carm1	0.84	0.18	Carm1	1.14	0.02	CARM1	1.06	0.66
Cav2	0.56	0.06	Cav2	1.33	0.38	CAV2	0.67	0.01
Ccdc85b	3.33	0.01	Ccdc85b	0.91	0.22	CCDC85B	0.88	0.50
Ccdc88a	0.37	0.00	Ccdc88a	0.67	0.08	CCDC88A	1.06	0.53
Ccdc92	0.65	0.19	Glul	0.32	0.01	CCDC92	0.81	0.07
Cd74	0.52	0.00	Cd74	1.15	0.61	CD74	1.87	0.26
Cd81	0.97	0.87	Cd81	0.84	0.01	CD81	0.74	0.08
Cda	1.09	0.62	Cda	2.88	0.00	CDA	1.23	0.17
Cdc20	6.05	0.20	Cdc20	1.91	0.01	CDC20	1.06	0.88
Cdca7	0.90	0.84	Cdca7	2.42	0.00	CDCA7	1.74	0.07
Cdca7l	1.30	0.41	Cdca7l	1.98	0.00	CDCA7L	0.83	0.44
Cdhr2	0.86	0.64	Cdhr2	1.85	0.03	CDHR2	0.48	0.04
Cdk2	0.56	0.03	Cdk2	0.91	0.29	CDK2	1.22	0.08
Cdkn1b	0.84	0.40	Cdkn1b	1.08	0.47	CDKN1B	1.19	0.05
Cdkn2aip	1.26	0.32	Cdkn2aip	0.83	0.01	CDKN2AIP	0.85	0.07
Cdkn2b	0.77	0.45	Cdkn2b	1.41	0.02	CDKN2B	0.68	0.09
Cep120	1.91	0.42	Cep120	1.33	0.02	CEP120	0.78	0.10
Cgref1	1.69	0.01	Cgref1	1.37	0.56	CGREF1	1.87	0.14
Cherp	1.03	0.85	Cherp	0.83	0.03	CHERP	0.66	0.05
Cib1	1.25	0.31	Cib1	0.89	0.02	CIB1	1.07	0.57
Cited2	0.69	0.11	Cited2	0.59	0.01	CITED2	1.24	0.32
Clcf1	1.50	0.11	Clcf1	2.87	0.01	CLCF1	1.64	0.12
Clu	1.21	0.19	Clu	1.30	0.00	CLU	0.90	0.34

Supplementary Table 9. Up- or Down-regulated cell proliferation related genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Cntf	1.13	0.71	Cntf	0.80	0.01	CNTF	0.62	0.34
Col18a1	0.71	0.03	Col18a1	0.78	0.01	COL18A1	0.77	0.18
Col4a3bp	1.36	0.03	Col4a3bp	0.93	0.62	COL4A3BP	0.93	0.43
Creb3	0.94	0.71	Creb3	1.19	0.01	CREB3	1.30	0.01
Crim1	1.24	0.38	Crim1	0.65	0.00	CRIM1	0.11	0.40
Crip2	1.19	0.50	Crip2	0.80	0.00	CRIP2	0.86	0.37
Crlf3	0.79	0.26	Crlf3	0.84	0.03	CRLF3	1.19	0.45
Csf1r	0.69	0.04	Csf1r	0.85	0.26	CSF1R	1.68	0.02
Csk	0.90	0.81	Csk	0.88	0.04	CSK	1.06	0.67
Ctgf	1.20	0.45	Ctgf	0.63	0.05	CTGF	0.72	0.45
Cth	1.25	0.43	Cth	1.18	0.04	CTH	0.77	0.34
Ctnnb1	1.40	0.03	Ctnnb1	0.91	0.40	CTNNB1	1.09	0.26
Cul1	0.76	0.02	Cul1	0.87	0.06	CUL1	0.78	0.06
Dab2	0.69	0.28	Dab2	0.79	0.00	DAB2	0.99	0.93
Dbh	0.95	0.86	Dbh	1.19	0.04	DBH	0.47	0.02
Dcbld2	0.86	0.62	Dcbld2	0.74	0.03	DCBLD2	1.33	0.05
Dcun1d3	1.01	0.98	Dcun1d3	0.83	0.36	DCUN1D3	0.82	0.03
Ddr2	0.54	0.50	Ddr2	0.37	0.04	DDR2	1.17	0.51
Dhcr24	1.82	0.09	Dhcr24	1.39	0.00	DHCR24	2.02	0.00
Dhcr7	1.49	0.21	Dhcr7	1.45	0.03	DHCR7	0.90	0.61
Dlc1	0.75	0.14	Dlc1	0.70	0.02	DLC1	0.90	0.79
Dnaja3	1.55	0.08	Dnaja3	1.22	0.05	DNAJA3	0.88	0.16
Dnajb2	1.47	0.10	Dnajb2	0.89	0.04	DNAJB2	1.32	0.05
Dnajc2	1.43	0.01	Dnajc2	1.11	0.19	DNAJC2	1.05	0.64
Dpp4	0.79	0.09	Dpp4	1.24	0.01	DPP4	1.66	0.14
Drd2	0.45	0.04	Drd2	6.37	0.03	DRD2	0.80	0.38
Dusp22	1.09	0.40	Dusp22	0.78	0.03	DUSP22	1.04	0.71
E2f3	3.07	0.06	E2f3	1.17	0.01	E2F3	1.48	0.15
Eapp	1.15	0.38	Eapp	0.88	0.03	EAPP	0.96	0.72
Eef1e1	1.16	0.65	Eef1e1	1.29	0.01	EEF1E1	1.35	0.07
Egfr	0.35	0.00	Egfr	0.69	0.00	EGFR	1.17	0.23
Egln3	3.79	0.13	Egln3	1.65	0.04	EGLN3	0.71	0.07
Eid2	3.58	0.40	Eid2	0.86	0.03	EID2	1.09	0.49
Eif2ak1	0.97	0.76	Eif2ak1	0.82	0.01	EIF2AK1	1.61	0.08
Enpep	0.78	0.20	Enpep	0.71	0.02	ENPEP	1.19	0.23
Enpp1	0.81	0.37	Enpp1	0.77	0.01	ENPP1	0.88	0.37
Entpd5	2.31	0.10	Entpd5	1.81	0.00	ENTPD5	1.63	0.00
Epcam	1.19	0.48	Epcam	3.06	0.00	EPCAM	0.96	0.86
Erbb2	2.53	0.00	Erbb2	2.63	0.32	ERBB2	0.70	0.00
Fam107a	0.82	0.55	Fam107a	2.01	0.38	FAM107A	0.50	0.04
Fbp1	0.88	0.57	Fbp1	0.81	0.01	FBP1	0.93	0.33
Fgf1	0.39	0.04	Fgf1	0.85	0.04	FGF1	0.87	0.57
Fgf6	1.84	0.05	Fgf6	2.79	0.18	FGF6	2.20	0.24
Fgfr1	0.85	0.44	Fgfr1	0.81	0.05	FGFR1	2.04	0.08
Fgfr2	0.57	0.02	Fgfr2	0.68	0.12	FGFR2	0.73	0.10
Fgfr3	0.77	0.27	Fgfr3	0.62	0.00	FGFR3	0.77	0.17
Fgfr4	0.74	0.04	Fgfr4	0.75	0.00	FGFR4	0.95	0.56
Fktn	0.66	0.07	Fktn	0.78	0.01	FKTN	0.84	0.22
Fntb	0.79	0.50	Fntb	1.15	0.41	FNTB	1.25	0.01
Foxa3	0.61	0.10	Foxa3	0.43	0.01	FOXA3	0.84	0.34
Foxk1	0.63	0.29	Foxk1	0.79	0.18	FOXK1	0.57	0.02
Foxm1	0.28	0.01	Foxm1	2.24	0.01	FOXM1	1.57	0.42
Foxo3	0.85	0.34	Foxo3	0.64	0.34	FOXO3	0.66	0.04

Supplementary Table 9. Up- or Down-regulated cell proliferation related genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Foxo4	0.64	0.01	Foxo4	1.11	0.16	FOXO4	1.39	0.15
Foxp3	1.01	0.96	Foxp3	1.57	0.00	FOXP3	0.30	0.00
Gab2	0.75	0.26	Gab2	1.21	0.64	GAB2	1.64	0.01
Gabbr1	2.12	0.13	Gabbr1	0.83	0.02	GABBR1	2.52	0.10
Gdf2	0.62	0.06	Gdf2	0.77	0.01	GDF2	1.10	0.88
Ghrh	0.37	0.05	Ghrh	1.36	0.00	GHRH	1.38	0.56
Gja1	0.75	0.21	Gja1	0.65	0.00	GJA1	0.88	0.27
Gli1	0.92	0.71	Gli1	1.42	0.42	GLI1	0.78	0.02
Gnai2	1.07	0.72	Gnai2	1.10	0.01	GNAI2	1.44	0.27
Gnat1	0.98	0.97	Gnat1	0.68	0.02	GNAT1	1.54	0.48
Gnl3	1.06	0.82	Gnl3	1.28	0.02	GNL3	1.23	0.14
Hcls1	0.71	0.00	Hcls1	1.07	0.63	HCLS1	1.21	0.53
Hdac1	0.71	0.17	Hdac1	0.84	0.05	HDAC1	1.12	0.65
Hes5	1.82	0.04	Hes5	0.96	0.91	HES5	0.53	0.20
Hipk2	0.63	0.07	Hipk2	0.74	0.01	HIPK2	0.74	0.00
Hlcs	0.65	0.04	Hlcs	1.17	0.66	HLCS	1.19	0.23
Hlx	0.41	0.01	Hlx	0.90	0.26	HLX	0.52	0.16
Hmga1	0.73	0.02	Hmga1	0.69	0.40	HMGA1	1.33	0.11
Hnf4a	1.20	0.16	Hnf4a	1.48	0.00	HNF4A	0.97	0.85
Hoxb4	1.21	0.70	Hoxb4	0.70	0.01	HOXB4	0.86	0.68
Hsd3b7	0.48	0.02	Hsd3b7	1.14	0.24	HSD3B7	0.82	0.25
Htra1	0.84	0.50	Htra1	0.74	0.00	HTRA1	1.21	0.07
Hyal1	0.66	0.09	Hyal1	0.73	0.01	HYAL1	1.05	0.70
Icm1	1.70	0.09	Icm1	0.85	0.03	ICMT	1.18	0.50
Igf1	0.47	0.03	Igf1	0.82	0.00	IGF1	0.61	0.06
Igfbp4	0.82	0.13	Igfbp4	0.89	0.15	IGFBP4	0.64	0.02
Il1b	1.67	0.15	Il1b	0.69	0.05	IL1B	2.10	0.04
Inhba	1.01	0.95	Inhba	0.46	0.00	INHBA	0.69	0.02
Insr	0.65	0.06	Insr	0.80	0.05	INSR	1.15	0.70
Irf6	0.71	0.17	Irf6	0.92	0.83	IRF6	0.70	0.05
Irs2	0.46	0.05	Irs2	0.93	0.70	IRS2	0.75	0.13
Jag2	1.46	0.55	Jag2	1.59	0.02	JAG2	0.67	0.18
Jtb	0.90	0.69	Jtb	0.88	0.01	JTB	1.08	0.46
Kctd11	0.57	0.04	Kctd11	1.21	0.28	KCTD11	1.07	0.57
Kdr	1.35	0.17	Kdr	0.74	0.00	KDR	0.96	0.78
Kifap3	1.09	0.78	Kifap3	1.34	0.00	KIFAP3	0.92	0.48
Klf10	1.64	0.11	Klf10	0.93	0.69	KLF10	0.58	0.04
Lbx1	0.42	0.03	Lbx1	1.14	0.14	LBX1	0.87	0.49
Lep	0.27	0.00	Lep	0.70	0.15	LEP	2.56	0.27
Lipg	1.11	0.81	Lipg	1.11	0.21	LIPG	0.44	0.02
Lrp1	1.78	0.03	Lrp1	0.61	0.00	LRP1	1.16	0.22
Lrp2	1.36	0.38	Lrp2	0.66	0.00	LRP2	0.90	0.66
Lrp5	0.96	0.86	Lrp5	0.56	0.00	LRP5	1.04	0.52
Lyn	0.76	0.34	Lyn	0.79	0.12	LYN	1.19	0.03
Mab21l2	0.70	0.05	Mab21l2	0.61	0.02	MAB21L2	0.86	0.65
Mad2l2	2.13	0.03	Mad2l2	1.54	0.01	MAD2L2	0.81	0.75
Mafg	0.78	0.33	Mafg	1.20	0.04	MAFG	1.16	0.10
Map2k1	1.02	0.96	Map2k1	0.85	0.03	MAP2K1	0.87	0.59
Mbd2	0.82	0.04	Mbd2	1.12	0.01	MBD2	1.32	0.31
Mdm4	0.76	0.21	Mdm4	0.82	0.04	MDM4	1.41	0.06
Mif	1.25	0.25	Mif	1.22	0.02	MIF	1.21	0.07
Mki67	2.96	0.19	Mki67	3.31	0.02	MKI67	1.62	0.20
Mul1	2.89	0.01	Mul1	1.42	0.02	MUL1	1.18	0.11

Supplementary Table 9. Up- or Down-regulated cell proliferation related genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Mvd	1.22	0.49	Mvd	1.84	0.03	MVD	1.30	0.45
Myd88	1.14	0.22	Myd88	0.91	0.09	MYD88	0.74	0.03
Myh10	0.70	0.22	Myh10	1.25	0.01	MYH10	0.64	0.05
Myo16	2.39	0.04	Myo16	1.15	0.11	MYO16	1.49	0.27
Nacc1	0.91	0.63	Nacc1	1.52	0.13	NACC1	1.51	0.02
Nanog	0.69	0.04	Nanog	4.94	0.36	NANOG	0.71	0.37
Nasp	1.74	0.04	Nasp	0.81	0.63	NASP	0.93	0.43
Nfib	0.67	0.16	Nfib	0.75	0.02	NFIB	1.14	0.54
Nkx2-6	0.68	0.02	Nkx2-6	1.25	0.17	NKX2-6	0.95	0.84
Nkx3-1	0.83	0.38	Nkx3-1	2.28	0.00	NKX3-1	1.26	0.08
Nme6	1.49	0.10	Nme6	1.25	0.02	NME6	1.01	0.92
Nodal	0.51	0.04	Nodal	1.95	0.08	NODAL	80.74	0.37
Nos3	1.92	0.01	Nos3	0.75	0.00	NOS3	1.01	0.95
Notch1	0.83	0.54	Notch1	0.75	0.00	NOTCH1	0.79	0.22
Nox4	0.41	0.04	Nox4	0.50	0.09	NOX4	0.71	0.12
Npm1	1.49	0.03	Npm1	1.28	0.00	NPM1	1.22	0.16
Nppa	1.49	0.04	Nppa	1.31	0.01	NPPA	1.15	0.63
Odc1	2.03	0.15	Odc1	1.14	0.05	ODC1	1.58	0.02
Osgin1	0.56	0.16	Osgin1	1.54	0.04	OSGIN1	0.85	0.52
Pbrm1	0.76	0.01	Pbrm1	0.85	0.04	PBRM1	1.16	0.23
Pdgfra	1.65	0.14	Pdgfra	0.69	0.00	PDGFRA	1.33	0.47
Pdgfrb	1.90	0.22	Pdgfrb	0.48	0.00	PDGFRB	1.23	0.66
Pdpn	0.64	0.04	Pdpn	1.17	0.14	PDPN	1.77	0.46
Pelo	1.86	0.10	Pelo	1.75	0.00	PELO	1.41	0.02
Pemt	0.82	0.38	Pemt	0.77	0.02	PEMT	0.85	0.36
Pes1	1.37	0.29	Pes1	1.16	0.03	PES1	1.08	0.28
Pggt1b	0.91	0.53	Pggt1b	0.86	0.04	PGGT1B	0.87	0.25
Phb	1.69	0.09	Phb	1.28	0.01	PHB	1.07	0.55
Pou1f1	1.44	0.30	Pou1f1	2.02	0.04	POU1F1	1.13	0.55
Pparg	1.16	0.25	Pparg	1.85	0.01	PPARG	1.66	0.12
Ppp1r8	0.80	0.01	Ppp1r8	1.14	0.09	PPP1R8	0.85	0.05
Ppp2r5c	1.92	0.04	Ppp2r5c	0.89	0.02	PPP2R5C	1.11	0.59
Ppt1	1.06	0.80	Ppt1	1.31	0.03	PPT1	1.16	0.38
Prdx1	1.47	0.23	Prdx1	1.33	0.00	PRDX1	1.40	0.01
Prdx3	1.47	0.15	Prdx3	1.26	0.00	PRDX3	0.90	0.37
Prok1	0.41	0.05	Prok1	1.53	0.21	PROK1	0.57	0.29
Prox1	0.74	0.26	Prox1	0.49	0.04	PROX1	0.94	0.63
Psrc1	0.91	0.74	Psrc1	1.29	0.02	PSRC1	0.96	0.87
Pten	0.85	0.54	Pten	0.90	0.28	PTEN	0.80	0.01
Ptges	2.16	0.01	Ptges	1.31	0.09	PTGES	0.97	0.93
Pth1r	0.93	0.24	Pth1r	0.73	0.02	PTH1R	1.06	0.78
Ptk2b	1.20	0.02	Ptk2b	0.77	0.03	PTK2B	0.90	0.60
Ptpn6	1.06	0.70	Ptpn6	1.06	0.02	PTPN6	1.20	0.44
Ptprk	1.29	0.14	Ptprk	0.65	0.00	PTPRK	0.76	0.09
Ptpru	0.79	0.10	Ptpru	1.74	0.00	PTPRU	1.12	0.45
Pura	0.67	0.00	Pura	1.05	0.51	PURA	1.05	0.70
Rac2	1.42	0.03	Rac2	1.04	0.79	RAC2	1.22	0.57
Raf1	0.98	0.92	Raf1	1.54	0.00	RAF1	0.80	0.05
Rap1b	1.01	0.92	Rap1b	0.89	0.02	RAP1B	0.89	0.24
Rara	0.79	0.15	Rara	0.81	0.04	RARA	0.63	0.06
Rarg	0.63	0.20	Rarg	0.71	0.01	RARG	1.06	0.62
Rb1	1.57	0.27	Rb1	0.45	0.02	RB1	1.07	0.34
Rbbp7	1.36	0.29	Rbbp7	1.20	0.00	RBBP7	1.13	0.19

Supplementary Table 9. Up- or Down-regulated cell proliferation related genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Rnf187	0.98	0.90	Rnf187	0.77	0.02	RNF187	1.03	0.76
Rogdi	0.44	0.06	Rogdi	1.04	0.64	ROGDI	1.40	0.02
Ros1	1.91	0.04	Ros1	1.17	0.05	ROS1	1.20	0.57
Rpl23a	1.30	0.31	Rpl23a	1.22	0.02	RPL23A	1.43	0.01
Rps15a	1.30	0.33	Rps15a	1.24	0.01	RPS15A	0.83	0.27
Rps4x	1.18	0.43	Rps4x	1.42	0.00	RPS4X	1.06	0.83
Rps6ka2	7.05	0.00	Rps6ka2	1.38	0.08	RPS6KA2	1.23	0.09
Rxra	0.77	0.07	Rxra	0.68	0.00	RXRA	0.72	0.02
Sbds	1.40	0.05	Sbds	0.93	0.33	SBDS	1.11	0.26
Sfn	0.54	0.02	Sfn	1.05	0.84	SFN	1.35	0.18
Skap2	1.20	0.41	Skap2	0.84	0.04	SKAP2	0.99	0.95
Smad4	0.71	0.10	Smad4	1.06	0.25	SMAD4	0.74	0.05
Smarca4	1.39	0.13	Smarca4	0.86	0.03	SMARCA4	1.07	0.45
Sox7	0.94	0.86	Sox7	0.47	0.04	SOX7	1.16	0.60
Sparc	1.80	0.09	Sparc	0.90	0.03	SPARC	0.79	0.39
Sphk2	1.16	0.54	Sphk2	0.91	0.16	SPHK2	0.66	0.02
Sra1	0.98	0.93	Sra1	0.84	0.02	SRA1	0.96	0.74
Srk2	0.88	0.46	Srk2	1.21	0.02	SRPK2	0.93	0.60
Stat4	0.81	0.66	Stat4	0.62	0.05	STAT4	2.04	0.04
Stat5a	1.10	0.63	Stat5a	0.72	0.01	STAT5A	0.97	0.85
Stk3	1.13	0.62	Stk3	1.18	0.02	STK3	0.85	0.30
Sts	0.78	0.38	Sts	0.85	0.18	STS	0.23	0.01
Taf6	0.84	0.47	Taf6	1.08	0.05	TAF6	1.26	0.02
Tbrg1	1.28	0.12	Tbrg1	1.25	0.02	TBRG1	1.24	0.26
Tbx2	1.53	0.11	Tbx2	0.72	0.00	TBX2	0.59	0.11
Tes	0.33	0.07	Tes	1.45	0.00	TES	1.61	0.03
Tesc	1.16	0.54	Tesc	0.65	0.44	TESC	4.25	0.04
Tfap4	0.88	0.44	Tfap4	1.70	0.01	TFAP4	0.78	0.40
Tgfa	0.78	0.16	Tgfa	1.36	0.01	TGFA	0.65	0.27
Tgfb1	0.71	0.05	Tgfb1	0.85	0.11	TGFB1	1.11	0.65
Tgfb2	0.85	0.38	Tgfb2	0.52	0.00	TGFB2	1.14	0.71
Tgfb3	0.68	0.02	Tgfb3	1.19	0.44	TGFB3	0.39	0.29
Tgfbr1	2.03	0.13	Tgfbr1	0.81	0.00	TGFBR1	1.42	0.02
Tgfbr2	1.47	0.02	Tgfbr2	1.10	0.31	TGFBR2	0.76	0.04
Tgif1	0.66	0.02	Tgif1	1.20	0.48	TGIF1	1.07	0.79
Tlx1	1.38	0.05	Tlx1	1.53	0.23	TLX1	0.56	0.17
Tns3	0.58	0.03	Tns3	1.11	0.15	TNS3	0.91	0.51
Ube2a	1.31	0.19	Ube2a	0.84	0.02	UBE2A	1.13	0.31
Uchl1	1.52	0.27	Uchl1	1.19	0.10	UCHL1	2.90	0.00
Uhrf2	0.89	0.51	Uhrf2	1.05	0.36	UHRF2	1.24	0.04
Vegfa	0.73	0.19	Vegfa	0.80	0.02	VEGFA	1.34	0.03
Wnt11	0.90	0.50	Wnt11	1.18	0.57	WNT11	0.36	0.02
Xrcc5	1.18	0.29	Xrcc5	1.32	0.01	XRCC5	0.72	0.47
Zeb1	0.48	0.22	Zeb1	0.88	0.00	ZEB1	0.83	0.06

Data represent the expression ratio between control and NaPB treatment as "fold change". Blue shadow means statistically significant alteration (p<0.05).

Supplementary Table 10. CAR target genes in CD-1 mice, WH rats, and chimeric mice with human hepatocytes

CD-1 mice treated with 2500 ppm NaPB			Wistar Hannover rats treated with 2500 ppm NaPB			Chimeric mice treated with 1000 ppm NaPB		
Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value	Gene Symbol	Fold change	p value
Insig1	0.97	0.94	Insig1	0.58	0.11	INSIG1	0.54	0.11
Thrsp	3.32	0.11	Thrsp	0.73	0.18	THRSP	0.81	0.54
			Abcg2	0.65	0.00	ABCG2	1.42	0.23
Cyp1a1	0.95	0.91	Cyp1a1	2.41	0.05	CYP1A1	2.49	0.03
Cyp24a1	0.30	0.28	Cyp24a1	1.18	0.04	CYP24A1	2.55	0.12
Cyp2b10	118.83	0.03	Cyp2b2	52.81	0.00	CYP2B6	7.15	0.00
Cyp2c54	7.97	0.01	Cyp2c6v1	4.59	0.00	CYP2C19	2.22	0.00
Cyp2c65	2.51	0.12	Cyp2c79	1.91	0.08	CYP2C8	2.24	0.01
Cyp3a16	3.35	0.01	Cyp3a23/3a1	5.17	0.00	CYP3A4	3.17	0.00
Cyp3a13	3.71	0.22	Cyp3a9	1.87	0.03	CYP3A7	3.10	0.00
			Cyp7a1	0.30	0.05	CYP7A1	0.92	0.80
Sult2a1	88.94	0.12	Sult2a1	0.49	0.01	SULT2A1	1.11	0.53
Ugt1a6b	1.82	0.06	Ugt1a6	1.98	0.00	UGT1A6	4.19	0.00

Data represent the expression ratio between control and NaPB treatment as "fold change". Blue shadow means statistically significant alteration ($p<0.05$). CAR target genes were from MetaCore. Of these genes, data to be found in at least two species among rat, mice and chimeric mice were shown.