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<110> BISSIG , Karl-Dimiter
 <120> HUMAN LIVER CHIMERIC NON-HUMAN ANIMAL WITH DEFICIENT P450
 OXIDOREDUCTASE AND METHODS OF USING SAME
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 <150> US 62/355,102
 <151> 2016-06-27
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 <151> 2017-05-23
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<210> 29
<211> 369
<212> PRT
<213> Homo sapiens

<400> 29

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
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Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp
35 40 45

Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
50 55 60

Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65 70 75 80

Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn
85 90 95

Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr
100 105 110

Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe
115 120 125

Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln
130 135 140

Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu
145 150 155 160

Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn
165 170 175

Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp
180 185 190

Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe
195 200 205

Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg
210 215 220

Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp

225		230		235		240
Ser His Pro Ile	His Trp Gly Ser Asn Thr	Ser Lys Glu Asn Pro Phe				
	245	250		255		
Leu Phe Ala Leu Glu Ala Val Val Ile Ser Val Gly Ser Met Gly Leu						
	260	265		270		
Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu Arg Thr Met Pro						
	275	280		285		
Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val Thr Glu Tyr His						
	290	295		300		
Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys Gly Leu Ala Glu Ser						
305	310	315		320		
Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu Val Ser Glu Ile Pro						
	325	330		335		
Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn						
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Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu						
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Thr

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 <211> 1663
 <212> DNA
 <213> Mus musculus

<400> 30	
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<210> 31
 <211> 369
 <212> PRT
 <213> Mus musculus

<400> 31

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			20					25					30		

Asn	Glu	Asp	Ile	Lys	Ala	Asp	Leu	Ile	Leu	Thr	Ser	Thr	Ala	Pro	Glu
		35					40					45			

His	Leu	Ser	Ala	Pro	Thr	Leu	Pro	Leu	Pro	Glu	Val	Gln	Cys	Phe	Val
	50					55					60				

Phe	Asn	Ile	Glu	Tyr	Met	Asn	Cys	Thr	Trp	Asn	Ser	Ser	Ser	Glu	Pro
65					70				75					80	

Gln	Ala	Thr	Asn	Leu	Thr	Leu	His	Tyr	Arg	Tyr	Lys	Val	Ser	Asp	Asn	85	90	95	
Asn	Thr	Phe	Gln	Glu	Cys	Ser	His	Tyr	Leu	Phe	Ser	Lys	Glu	Ile	Thr	100	105	110	
Ser	Gly	Cys	Gln	Ile	Gln	Lys	Glu	Asp	Ile	Gln	Leu	Tyr	Gln	Thr	Phe	115	120	125	
Val	Val	Gln	Leu	Gln	Asp	Pro	Gln	Lys	Pro	Gln	Arg	Arg	Ala	Val	Gln	130	135	140	
Lys	Leu	Asn	Leu	Gln	Asn	Leu	Val	Ile	Pro	Arg	Ala	Pro	Glu	Asn	Leu	145	150	155	160
Thr	Leu	Ser	Asn	Leu	Ser	Glu	Ser	Gln	Leu	Glu	Leu	Arg	Trp	Lys	Ser	165	170	175	
Arg	His	Ile	Lys	Glu	Arg	Cys	Leu	Gln	Tyr	Leu	Val	Gln	Tyr	Arg	Ser	180	185	190	
Asn	Arg	Asp	Arg	Ser	Trp	Thr	Glu	Leu	Ile	Val	Asn	His	Glu	Pro	Arg	195	200	205	
Phe	Ser	Leu	Pro	Ser	Val	Asp	Glu	Leu	Lys	Arg	Tyr	Thr	Phe	Arg	Val	210	215	220	
Arg	Ser	Arg	Tyr	Asn	Pro	Ile	Cys	Gly	Ser	Ser	Gln	Gln	Trp	Ser	Lys	225	230	235	240
Trp	Ser	Gln	Pro	Val	His	Trp	Gly	Ser	His	Thr	Val	Glu	Glu	Asn	Pro	245	250	255	
Ser	Leu	Phe	Ala	Leu	Glu	Ala	Val	Leu	Ile	Pro	Val	Gly	Thr	Met	Gly	260	265	270	
Leu	Ile	Ile	Thr	Leu	Ile	Phe	Val	Tyr	Cys	Trp	Leu	Glu	Arg	Met	Pro	275	280	285	
Pro	Ile	Pro	Pro	Ile	Lys	Asn	Leu	Glu	Asp	Leu	Val	Thr	Glu	Tyr	Gln	290	295	300	
Gly	Asn	Phe	Ser	Ala	Trp	Ser	Gly	Val	Ser	Lys	Gly	Leu	Thr	Glu	Ser	305	310	315	320
Leu	Gln	Pro	Asp	Tyr	Ser	Glu	Arg	Phe	Cys	His	Val	Ser	Glu	Ile	Pro	325	330	335	

Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Gly Ser Pro Cys Ser
 340 345 350

Leu His Ser Pro Tyr Trp Pro Pro Pro Cys Tyr Ser Leu Lys Pro Glu
 355 360 365

Ala

<210> 32
 <211> 2457
 <212> DNA
 <213> Homo sapiens

<400> 32
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<210> 33
<211> 527
<212> PRT
<213> Homo sapiens

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<400> 33

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Pro Gly Phe Ser Leu Met Asn Phe Asp Gly Gln Val Phe Phe Phe Gly
20          25          30

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Gln Lys Gly Trp Pro Lys Arg Ser Cys Pro Thr Gly Val Phe His Leu
35          40          45

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Asp Val Lys His Asn His Val Lys Leu Lys Pro Thr Ile Phe Ser Lys
50          55          60

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Asp Ser Cys Tyr Leu Pro Pro Leu Arg Tyr Pro Ala Thr Cys Thr Phe
65          70          75          80

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Lys Gly Ser Leu Glu Ser Glu Lys His Gln Tyr Ile Ile His Gly Gly
 85 90 95

Lys Thr Pro Asn Asn Glu Val Ser Asp Lys Ile Tyr Val Met Ser Ile
 100 105 110

Val Cys Lys Asn Asn Lys Lys Val Thr Phe Arg Cys Thr Glu Lys Asp
 115 120 125

Leu Val Gly Asp Val Pro Glu Ala Arg Tyr Gly His Ser Ile Asn Val
 130 135 140

Val Tyr Ser Arg Gly Lys Ser Met Gly Val Leu Phe Gly Gly Arg Ser
 145 150 155 160

Tyr Met Pro Ser Thr His Arg Thr Thr Glu Lys Trp Asn Ser Val Ala
 165 170 175

Asp Cys Leu Pro Cys Val Phe Leu Val Asp Phe Glu Phe Gly Cys Ala
 180 185 190

Thr Ser Tyr Ile Leu Pro Glu Leu Gln Asp Gly Leu Ser Phe His Val
 195 200 205

Ser Ile Ala Lys Asn Asp Thr Ile Tyr Ile Leu Gly Gly His Ser Leu
 210 215 220

Ala Asn Asn Ile Arg Pro Ala Asn Leu Tyr Arg Ile Arg Val Asp Leu
 225 230 235 240

Pro Leu Gly Ser Pro Ala Val Asn Cys Thr Val Leu Pro Gly Gly Ile
 245 250 255

Ser Val Ser Ser Ala Ile Leu Thr Gln Thr Asn Asn Asp Glu Phe Val
 260 265 270

Ile Val Gly Gly Tyr Gln Leu Glu Asn Gln Lys Arg Met Ile Cys Asn
 275 280 285

Ile Ile Ser Leu Glu Asp Asn Lys Ile Glu Ile Arg Glu Met Glu Thr
 290 295 300

Pro Asp Trp Thr Pro Asp Ile Lys His Ser Lys Ile Trp Phe Gly Ser
 305 310 315 320

Asn Met Gly Asn Gly Thr Val Phe Leu Gly Ile Pro Gly Asp Asn Lys
 325 330 335

Gln Val Val Ser Glu Gly Phe Tyr Phe Tyr Met Leu Lys Cys Ala Glu
340 345 350

Asp Asp Thr Asn Glu Glu Gln Thr Thr Phe Thr Asn Ser Gln Thr Ser
355 360 365

Thr Glu Asp Pro Gly Asp Ser Thr Pro Phe Glu Asp Ser Glu Glu Phe
370 375 380

Cys Phe Ser Ala Glu Ala Asn Ser Phe Asp Gly Asp Asp Glu Phe Asp
385 390 395 400

Thr Tyr Asn Glu Asp Asp Glu Glu Asp Glu Ser Glu Thr Gly Tyr Trp
405 410 415

Ile Thr Cys Cys Pro Thr Cys Asp Val Asp Ile Asn Thr Trp Val Pro
420 425 430

Phe Tyr Ser Thr Glu Leu Asn Lys Pro Ala Met Ile Tyr Cys Ser His
435 440 445

Gly Asp Gly His Trp Val His Ala Gln Cys Met Asp Leu Ala Glu Arg
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Thr Leu Ile His Leu Ser Ala Gly Ser Asn Lys Tyr Tyr Cys Asn Glu
465 470 475 480

His Val Glu Ile Ala Arg Ala Leu His Thr Pro Gln Arg Val Leu Pro
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Ile Leu Thr Pro Ala Lys Lys Ser Phe Leu Arg Arg Leu Phe Asp
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<210> 34

<211> 3393

<212> DNA

<213> Mus musculus

<400> 34

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agtgaaaagt gaaatatgaa catgagctca gacaaagggt tgggactatc actctcaagg 3300
aggctctact gctaagtcct gaactgcttt cacatgaata cagaaattat aacaaaaaat 3360
atgtaatcaa taaaaagaaa actttcatat tcc 3393

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<210> 35
<211> 527
<212> PRT
<213> Mus musculus

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<400> 35
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Met Ser Leu Gln Met Val Thr Val Gly His Asn Ile Ala Leu Ile Gln
1           5           10           15

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Pro Gly Phe Ser Leu Met Asn Phe Asp Gly Gln Val Phe Phe Phe Gly
          20           25           30

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Gln Lys Gly Trp Pro Lys Arg Ser Cys Pro Thr Gly Val Phe His Phe
35           40           45

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Asp Ile Lys Gln Asn His Leu Lys Leu Lys Pro Ala Ile Phe Ser Lys
50           55           60

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Asp	Ser	Cys	Tyr	Leu	Pro	Pro	Leu	Arg	Tyr	Pro	Ala	Thr	Cys	Ser	Tyr	65	70	75	80
Lys	Gly	Ser	Ile	Asp	Ser	Asp	Lys	His	Gln	Tyr	Ile	Ile	His	Gly	Gly	85	90	95	
Lys	Thr	Pro	Asn	Asn	Glu	Leu	Ser	Asp	Lys	Ile	Tyr	Ile	Met	Ser	Val	100	105	110	
Ala	Cys	Lys	Asn	Asn	Lys	Lys	Val	Thr	Phe	Arg	Cys	Thr	Glu	Lys	Asp	115	120	125	
Leu	Val	Gly	Asp	Val	Pro	Glu	Pro	Arg	Tyr	Gly	His	Ser	Ile	Asp	Val	130	135	140	
Val	Tyr	Ser	Arg	Gly	Lys	Ser	Met	Gly	Val	Leu	Phe	Gly	Gly	Arg	Ser	145	150	155	160
Tyr	Met	Pro	Ser	Thr	Gln	Arg	Thr	Thr	Glu	Lys	Trp	Asn	Ser	Val	Ala	165	170	175	
Asp	Cys	Leu	Pro	His	Val	Phe	Leu	Ile	Asp	Phe	Glu	Phe	Gly	Cys	Ala	180	185	190	
Thr	Ser	Tyr	Ile	Leu	Pro	Glu	Leu	Gln	Asp	Gly	Leu	Ser	Phe	His	Val	195	200	205	
Ser	Ile	Ala	Arg	Asn	Asp	Thr	Val	Tyr	Ile	Leu	Gly	Gly	His	Ser	Leu	210	215	220	
Ala	Ser	Asn	Ile	Arg	Pro	Ala	Asn	Leu	Tyr	Arg	Ile	Arg	Val	Asp	Leu	225	230	235	240
Pro	Leu	Gly	Thr	Pro	Ala	Val	Asn	Cys	Thr	Val	Leu	Pro	Gly	Gly	Ile	245	250	255	
Ser	Val	Ser	Ser	Ala	Ile	Leu	Thr	Gln	Thr	Asn	Asn	Asp	Glu	Phe	Val	260	265	270	
Ile	Val	Gly	Gly	Tyr	Gln	Leu	Glu	Asn	Gln	Lys	Arg	Met	Val	Cys	Ser	275	280	285	
Leu	Val	Ser	Leu	Gly	Asp	Asn	Thr	Ile	Glu	Ile	Ser	Glu	Met	Glu	Thr	290	295	300	
Pro	Asp	Trp	Thr	Ser	Asp	Ile	Lys	His	Ser	Lys	Ile	Trp	Phe	Gly	Ser	305	310	315	320

Asn Met Gly Asn Gly Thr Ile Phe Leu Gly Ile Pro Gly Asp Asn Lys
325 330 335

Gln Ala Met Ser Glu Ala Phe Tyr Phe Tyr Thr Leu Arg Cys Ser Glu
340 345 350

Glu Asp Leu Ser Glu Asp Gln Lys Ile Val Ser Asn Ser Gln Thr Ser
355 360 365

Thr Glu Asp Pro Gly Asp Ser Thr Pro Phe Glu Asp Ser Glu Glu Phe
370 375 380

Cys Phe Ser Ala Glu Ala Thr Ser Phe Asp Gly Asp Asp Glu Phe Asp
385 390 395 400

Thr Tyr Asn Glu Asp Asp Glu Asp Asp Glu Ser Val Thr Gly Tyr Trp
405 410 415

Ile Thr Cys Cys Pro Thr Cys Asp Val Asp Ile Asn Thr Trp Val Pro
420 425 430

Phe Tyr Ser Thr Glu Leu Asn Lys Pro Ala Met Ile Tyr Cys Ser His
435 440 445

Gly Asp Gly His Trp Val His Ala Gln Cys Met Asp Leu Glu Glu Arg
450 455 460

Thr Leu Ile His Leu Ser Glu Gly Ser Asn Lys Tyr Tyr Cys Asn Glu
465 470 475 480

His Val Gln Ile Ala Arg Ala Leu Gln Thr Pro Lys Arg Asn Pro Pro
485 490 495

Leu Gln Lys Pro Pro Met Lys Ser Leu His Lys Lys Gly Ser Gly Lys
500 505 510

Val Leu Thr Pro Ala Lys Lys Ser Phe Leu Arg Arg Leu Phe Asp
515 520 525

<210> 36
<211> 1810
<212> DNA
<213> Homo sapiens

<400> 36
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cgcacgccac cttaggcccg cagccgtgcc ggggtgctctt cagcatgtcc ttcacccgg 180

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gcgacccaag	accgaggata	ggtgtggcca	ttggcgacca	gatcctggac	ctcagcatca	300
tcaagcacct	ctttactggg	cctgtcctct	ccaaacacca	ggatgtcttc	aatcagccta	360
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agaacttgct	gtctgtgagc	caagccaggc	tcagagatga	caccgaactt	cggaagtgtg	480
cattcatctc	ccaggcttct	gccacgatgc	accttccagc	caccatagga	gactacacag	540
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ctctcgggcc	attccttggg	aagagtthttg	ggaccactgt	ctctccgtgg	gtgggtgccc	960
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aaggaatgag	ccaggcgggt	accatatgca	agtccaatth	taagtacatg	tactggacga	1140
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<210> 37
 <211> 419
 <212> PRT
 <213> Homo sapiens
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Gly	Val	Ala	Ile	Gly	Asp	Gln	Ile	Leu	Asp	Leu	Ser	Ile	Ile	Lys	His	35	40	45	
Leu	Phe	Thr	Gly	Pro	Val	Leu	Ser	Lys	His	Gln	Asp	Val	Phe	Asn	Gln	50	55	60	
Pro	Thr	Leu	Asn	Ser	Phe	Met	Gly	Leu	Gly	Gln	Ala	Ala	Trp	Lys	Glu	65	70	75	80
Ala	Arg	Val	Phe	Leu	Gln	Asn	Leu	Leu	Ser	Val	Ser	Gln	Ala	Arg	Leu	85	90	95	
Arg	Asp	Asp	Thr	Glu	Leu	Arg	Lys	Cys	Ala	Phe	Ile	Ser	Gln	Ala	Ser	100	105	110	
Ala	Thr	Met	His	Leu	Pro	Ala	Thr	Ile	Gly	Asp	Tyr	Thr	Asp	Phe	Tyr	115	120	125	
Ser	Ser	Arg	Gln	His	Ala	Thr	Asn	Val	Gly	Ile	Met	Phe	Arg	Asp	Lys	130	135	140	
Glu	Asn	Ala	Leu	Met	Pro	Asn	Trp	Leu	His	Leu	Pro	Val	Gly	Tyr	His	145	150	155	160
Gly	Arg	Ala	Ser	Ser	Val	Val	Val	Ser	Gly	Thr	Pro	Ile	Arg	Arg	Pro	165	170	175	
Met	Gly	Gln	Met	Lys	Pro	Asp	Asp	Ser	Lys	Pro	Pro	Val	Tyr	Gly	Ala	180	185	190	
Cys	Lys	Leu	Leu	Asp	Met	Glu	Leu	Glu	Met	Ala	Phe	Phe	Val	Gly	Pro	195	200	205	
Gly	Asn	Arg	Leu	Gly	Glu	Pro	Ile	Pro	Ile	Ser	Lys	Ala	His	Glu	His	210	215	220	
Ile	Phe	Gly	Met	Val	Leu	Met	Asn	Asp	Trp	Ser	Ala	Arg	Asp	Ile	Gln	225	230	235	240
Lys	Trp	Glu	Tyr	Val	Pro	Leu	Gly	Pro	Phe	Leu	Gly	Lys	Ser	Phe	Gly	245	250	255	

Thr Thr Val Ser Pro Trp Val Val Pro Met Asp Ala Leu Met Pro Phe
 260 265 270

Ala Val Pro Asn Pro Lys Gln Asp Pro Arg Pro Leu Pro Tyr Leu Cys
 275 280 285

His Asp Glu Pro Tyr Thr Phe Asp Ile Asn Leu Ser Val Asn Leu Lys
 290 295 300

Gly Glu Gly Met Ser Gln Ala Ala Thr Ile Cys Lys Ser Asn Phe Lys
 305 310 315 320

Tyr Met Tyr Trp Thr Met Leu Gln Gln Leu Thr His His Ser Val Asn
 325 330 335

Gly Cys Asn Leu Arg Pro Gly Asp Leu Leu Ala Ser Gly Thr Ile Ser
 340 345 350

Gly Pro Glu Pro Glu Asn Phe Gly Ser Met Leu Glu Leu Ser Trp Lys
 355 360 365

Gly Thr Lys Pro Ile Asp Leu Gly Asn Gly Gln Thr Arg Lys Phe Leu
 370 375 380

Leu Asp Gly Asp Glu Val Ile Ile Thr Gly Tyr Cys Gln Gly Asp Gly
 385 390 395 400

Tyr Arg Ile Gly Phe Gly Gln Cys Ala Gly Lys Val Leu Pro Ala Leu
 405 410 415

Leu Pro Ser

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 <211> 1597
 <212> DNA
 <213> Mus musculus

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 aatctaaagg ccctcggcta gtctgacct tgcctaagc atagtcccgt tagccaaccc 180
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 gaggactccg actttcccat ccaaaacctg ccctatggtg ttttctccac tcaaagcaac 300
 ccaaagccac ggattggtgt agccatcggg gaccagatct tggacctgag tgtcattaaa 360
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aataacttca tgggtctggg tcaagctgca tggaaggagg caagagcatc cttacagaac	480
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ctgttgccaa attggctcca cttacctgtg ggataccatg gccgagcttc ctccattgtg	720
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cctgtgtatg gtgcctgcag actccttagac atggagttgg aaatggcttt cttcgtaggc	840
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gccctcatgc cttttgtggg gccaaacca aagcaggacc ccaagccctt gccatatctc	1080
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atgagccagg cggctaccat ctgcaggctt aactttaagc acatgtactg gaccatgctg	1200
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aagggaacaa aggccatcga tgtggagcag gggcagacca ggaccttcct gctggacggc	1380
gatgaagtca tcataacagg tcaactgccag ggggacggct accgtgttgg ctttggccag	1440
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<210> 39
 <211> 419
 <212> PRT
 <213> Mus musculus

<400> 39

Met	Ser	Phe	Ile	Pro	Val	Ala	Glu	Asp	Ser	Asp	Phe	Pro	Ile	Gln	Asn
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Leu	Pro	Tyr	Gly	Val	Phe	Ser	Thr	Gln	Ser	Asn	Pro	Lys	Pro	Arg	Ile
			20					25					30		

Gly	Val	Ala	Ile	Gly	Asp	Gln	Ile	Leu	Asp	Leu	Ser	Val	Ile	Lys	His
		35					40					45			

Leu	Phe	Thr	Gly	Pro	Ala	Leu	Ser	Lys	His	Gln	His	Val	Phe	Asp	Glu
	50					55					60				

Thr	Thr	Leu	Asn	Asn	Phe	Met	Gly	Leu	Gly	Gln	Ala	Ala	Trp	Lys	Glu	65	70	75	80
Ala	Arg	Ala	Ser	Leu	Gln	Asn	Leu	Leu	Ser	Ala	Ser	Gln	Ala	Arg	Leu	85	90	95	
Arg	Asp	Asp	Lys	Glu	Leu	Arg	Gln	Arg	Ala	Phe	Thr	Ser	Gln	Ala	Ser	100	105	110	
Ala	Thr	Met	His	Leu	Pro	Ala	Thr	Ile	Gly	Asp	Tyr	Thr	Asp	Phe	Tyr	115	120	125	
Ser	Ser	Arg	Gln	His	Ala	Thr	Asn	Val	Gly	Ile	Met	Phe	Arg	Gly	Lys	130	135	140	
Glu	Asn	Ala	Leu	Leu	Pro	Asn	Trp	Leu	His	Leu	Pro	Val	Gly	Tyr	His	145	150	155	160
Gly	Arg	Ala	Ser	Ser	Ile	Val	Val	Ser	Gly	Thr	Pro	Ile	Arg	Arg	Pro	165	170	175	
Met	Gly	Gln	Met	Arg	Pro	Asp	Asn	Ser	Lys	Pro	Pro	Val	Tyr	Gly	Ala	180	185	190	
Cys	Arg	Leu	Leu	Asp	Met	Glu	Leu	Glu	Met	Ala	Phe	Phe	Val	Gly	Pro	195	200	205	
Gly	Asn	Arg	Phe	Gly	Glu	Pro	Ile	Pro	Ile	Ser	Lys	Ala	His	Glu	His	210	215	220	
Ile	Phe	Gly	Met	Val	Leu	Met	Asn	Asp	Trp	Ser	Ala	Arg	Asp	Ile	Gln	225	230	235	240
Gln	Trp	Glu	Tyr	Val	Pro	Leu	Gly	Pro	Phe	Leu	Gly	Lys	Ser	Phe	Gly	245	250	255	
Thr	Thr	Ile	Ser	Pro	Trp	Val	Val	Pro	Met	Asp	Ala	Leu	Met	Pro	Phe	260	265	270	
Val	Val	Pro	Asn	Pro	Lys	Gln	Asp	Pro	Lys	Pro	Leu	Pro	Tyr	Leu	Cys	275	280	285	
His	Ser	Gln	Pro	Tyr	Thr	Phe	Asp	Ile	Asn	Leu	Ser	Val	Ser	Leu	Lys	290	295	300	
Gly	Glu	Gly	Met	Ser	Gln	Ala	Ala	Thr	Ile	Cys	Arg	Ser	Asn	Phe	Lys	305	310	315	320

His Met Tyr Trp Thr Met Leu Gln Gln Leu Thr His His Ser Val Asn
 325 330 335

Gly Cys Asn Leu Arg Pro Gly Asp Leu Leu Ala Ser Gly Thr Ile Ser
 340 345 350

Gly Ser Asp Pro Glu Ser Phe Gly Ser Met Leu Glu Leu Ser Trp Lys
 355 360 365

Gly Thr Lys Ala Ile Asp Val Glu Gln Gly Gln Thr Arg Thr Phe Leu
 370 375 380

Leu Asp Gly Asp Glu Val Ile Ile Thr Gly His Cys Gln Gly Asp Gly
 385 390 395 400

Tyr Arg Val Gly Phe Gly Gln Cys Ala Gly Lys Val Leu Pro Ala Leu
 405 410 415

Ser Pro Ala

<210> 40
 <211> 72
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic polynucleotide

<220>
 <221> misc_feature
 <223> II2-rg WT-guide RNA

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 ggttgattat ta 72

<210> 41
 <211> 17
 <212> DNA
 <213> Artificial Sequence

<220>
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<220>
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 <223> Il2-rg genomic deletion

<400> 41
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<210> 42
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<210> 43
 <211> 34
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 <213> Artificial Sequence

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 <220>
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 <223> Rag2 gene Deletion-1 guide RNA

 <400> 43
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<210> 44
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
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 <220>
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 <223> Rag2 genomic Deletion-2 guide RNA

 <400> 44
 ccagatacgg ccattcaacg gagc 24

<210> 45
 <211> 20
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<213> Artificial Sequence	
<220>	
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<210> 48	
<211> 52	
<212> DNA	
<213> Artificial Sequence	
<220>	
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<221> misc_feature	
<223> Fah genomic Deletion-1 guide RNA	
<400> 48	
gtgcccctga ttctgtttca gtgcattatg ttgggcatta tgttcagagg ca	52
<210> 49	
<211> 40	
<212> DNA	
<213> Artificial Sequence	
<220>	
<223> Synthetic polynucleotide	
<220>	
<221> misc_feature	
<223> Fah genomic Deletion-2 guide RNA	

<400> 49
gtgccccctga ttctgtttca gtgcattatg ttcagaggca

40

<210> 50
<211> 47
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Polypeptide

<220>
<221> misc_feature
<223> Il2rg-/- Del-1, Frame shift mutation from aminoacid 28

<400> 50

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Leu	Ala	Pro	Leu	Thr	Cys	Gly	Ile	Pro	Trp	Pro	Ser	Phe	Leu	His	Cys
			20					25					30		

Gly	Ile	Trp	Asn	Pro	Asp	Ser	Lys	Thr	His	Gly	Ala	Asp	Glu	Thr
		35					40					45		

<210> 51
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> Rag2-/- Del-1; Frame shift from aminoacid 143

<400> 51

Ile	Leu	Phe	Asn	Gly	Ala	Gln
1				5		

<210> 52
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Polypeptide

<220>
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<223> Rag2-/- Del-2; Frame shift from aminoacid 141

<400> 52

Ile Gln Arg Ser Ser Ile Asn Pro Pro
1 5

<210> 53
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Polypeptide

<220>
<221> MISC_FEATURE
<223> Rag2-/- Del-3; Frame shift from aminoacid 122

<400> 53

Ile Gln Arg Ser Ser Ile Asn Pro Pro
1 5

<210> 54
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> Rag2-/- Del-4; Frame shift from aminoacid 142

<400> 54

Thr Lys Lys Ala Leu Gly Lys Ser
1 5

<210> 55
<211> 47
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Polypeptide

<220>
<221> MISC_FEATURE
<223> Fah-/- Del-1; Frame shift from aminoacid 107

<400> 55

Leu Cys Trp His Tyr Val Gln Arg Gln Gly Glu Cys Ala Val Ala Lys
1 5 10 15

Leu Ala Pro Leu Thr Cys Gly Ile Pro Trp Pro Ser Phe Leu His Cys
20 25 30

Gly Ile Trp Asn Pro Asp Ser Lys Thr His Gly Ala Asp Glu Thr
35 40 45

<210> 56

<211> 40

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Polypeptide

<220>

<221> MISC_FEATURE

<223> Fah-/- Del-2; Frame shift from aminoacid 107

<400> 56

Leu Cys Ser Glu Ala Arg Arg Met Arg Cys Cys Gln Ile Gly Ser Thr
1 5 10 15

Tyr Leu Trp Asp Thr Met Ala Glu Leu Pro Pro Leu Trp Leu Glu Pro
20 25 30

Arg Phe Glu Asp Pro Trp Gly Arg
35 40