		Fasting 12h				Refeeding 4h				
		WT		***L-Sin3a/b***		**WT**		***L-Sin3a/b***		**Statistical analysis**
Insulin	**ug/l**	0.67 ± 0.03	N=8	0.72 ± 0.06	N=7	1.15 ± 0.11	N=8	**2.10 ± 0.29**	N=8	*** WT vs *L-Sin3a/b* in refed mice; *** Fast vs Refed in *L-Sin3a/b*
Glucose	**mg/dl**	90 ± 3	N=10	93 ± 3	N=8	168 ± 6	N=10	163 ± 9	N=8	*** Fast vs Refed in iWT and iL-Sin3a/b
FFA	**umol/l**	811 ± 86	N=10	**612 ± 76**	N=8	351 ± 31	N=10	397 ± 53	N=8	*** Fast vs Refed in WT
TG	**mg/dl**	98 ± 4	N=10	93 ± 5	N=8	121 ± 9	N=10	**205 ± 37**	N=8	** WT vs *L-Sin3a/b* in refed; *** Fast vs Refed in *L-Sin3a/b*
Cholesterol	**mg/dl**	131 ± 14.5	N=10	**193 ± 22**	N=8	142 ± 11	N=10	**236 ± 35**	N=8	** WT vs *L-Sin3a/b* in refed
Ketone	**umol/l**	1259 ± 80	N=10	**924 ± 63**	N=8	227 ± 42	N=10	**149 ± 15**	N=8	*** WT vs *L-Sin3a/b* Fast; *** Fast vs Refed in WT and in *L-Sin3a/b*
Total Bile Acid	**umol/l**	-		-		3.6 ± 1.2	N=5	**32.1 ± 1.8**	N=5	***
Alk. Phos.	**U/l**	91 ± 12	N=8	**380 ± 101**	N=7	-		-		**
GGT	**U/l**	2.4 ± 0.6	N=8	2.5 ± 0.2	N=11	-		-		
AST(SGOT)	**U/l**	110 ± 16	N=8	**324 ± 57**	N=9	-		-		**
ALT(SGPT)	**U/l**	50 ± 7	N=8	**241 ± 57**	N=10	-		-		**
Amylase	**U/l**	2389 ± 232	N=6	2186 ± 176	N=9	-		-		
BUN	**mg/dl**	31 ± 1	N=8	37 ± 5	N=10	-		-		
Phosphorus	**mg/dl**	10.6 ± 0.7	N=8	10.7 ± 0.9	N=10	-		-		
Calcium	**mg/dl**	10.4 ± 0.4	N=8	10.6 ± 0.5	N=10	-		-		
Albumin	**g/dl**	3.49 ± 0.07	N=8	3.4 ± 0.3	N=10	-		-		
Cholesterol	**mg/dl**	110 ± 4	N=8	**235 ± 50**	N=10	-		-		*
Uric Acid	**mg/dl**	1.3 ± 0.1	N=8	1.1 ± 0.1	N=10	-		-		
CPK	**U/l**	410 ± 101	N=8	502 ± 124	N=10	-		-		
Creatinine	**mg/dl**	<0.19	N=8	<0.19	N=10	-		-		
Total Bilirubin	**mg/dl**	0.08 ± 0.01	N=8	**0.13 ± 0.01**	N=10	-		-		**
Total Protein	**g/dl**	5.1 ± 0.3	N=8	5.2 ± 0.4	N=10	-		-		
Globulin	**g/dl**	1.9 ± 0.1	N=7	2.0 ± 0.3	N=9	-		-		
Bun/Creat	**-**	164 ± 5	N=8	195 ± 26	N=10	-		-		
Alb/Glob	**-**	1.87 ± 0.11	N=7	3.67 ± 1.64	N=9	-		-		

Table S1. Relative to Figure 5. Blood analysis in WT *vs. L-Sin3a/b* (constitutive KO) in fasting *vs.* refeeding conditions. FFA=Free Fatty Acid; TG=Triglyceride; GGT= Gamma-Glutamyl Transferase; AST= Aspartate transaminase; ALT= Alanine transaminase; BUN= Blood Urea Nitrogen; CPK= Creatine phosphokinase.

		Fasting 12h				Refeeding 4h				
		WT		**iL-*Sin3a/b***		**WT Refed**		**iL-*Sin3a/b***		**Statistical analysis**
Insulin	**ug/l**	0.78 ± 0.14	N=6	0.70 ± 0.07	N=7	2.16 ± 0.18	N=6	1.79 ± 0.36	N=5	** Fast vs Refed in iWT and iL-*Sin3a/b*
Glucose	**mg/dl**	120 ± 8	N=6	**89 ± 3**	N=7	155 ± 6	N=9	**136 ± 5**	N=9	** iWT vs iL-*Sin3a/b* in Fast; * iWT vs iL-*Sin3a/b* in Refed; *** Fast vs Refed in iWT and iL-*Sin3a/b*
FFA	**umol/l**	394 ± 51	N=6	500 ± 35	N=7	112 ± 19	N=9	132 ± 21	N=9	*** Fast vs Refed in iWT and iL-*Sin3a/b*
TG	**mg/dl**	94 ± 13	N=6	**78 ± 9**	N=7	117 ± 14	N=9	100 ± 9	N=9	NS
Cholesterol	**mg/dl**	97 ± 6	N=6	**63± 6**	N=7	99 ± 2	N=9	**80 ± 4**	N=9	* Fast vs Refed in iL-*Sin3a/b;* *** iWT vs iL-*Sin3a/b* in Fast; ** iWT vs iL-*Sin3a/b* in refed
Ketone	**umol/l**	579 ± 131	N=6	458 ± 73	N=7	150 ± 10	N=9	183 ± 15	N=9	*** Fast vs Refed in iWT + ** Fast vs Refed in iL-*Sin3a/b*
Alk. Phos.	**U/l**	59 ± 4	N=7	**92 ± 13**	N=9	-		-		NS
GGT	**U/l**	1.7 ± 0.6	N=7	0.9 ± 0.4	N=9	-		-		
AST(SGOT)	**U/l**	147 ± 23	N=7	**407 ± 54**	N=8	-		-		**
ALT(SGPT)	**U/l**	62 ± 9	N=7	**275 ± 87**	N=7	-		-		*
Amylase	**U/l**	1922 ± 134	N=7	2138 ± 127	N=7	-		-		
BUN	**mg/dl**	31 ± 2	N=7	38 ± 4	N=9	-		-		
Phosphorus	**mg/dl**	9.5 ± 0.5	N=7	10.7 ± 1.1	N=9	-		-		
Calcium	**mg/dl**	10.4 ± 0.5	N=7	10.7 ± 0.6	N=9	-		-		
Albumin	**g/dl**	3.3 ± 0.1	N=7	3.7 ± 0.3	N=9	-		-		
Cholesterol	**mg/dl**	90 ± 6	N=7	**70 ± 6**	N=9	-		-		*
Uric Acid	**mg/dl**	1.1 ± 0.1	N=7	1.5 ± 0.2	N=9	-		-		
CPK	**U/l**	399 ± 90	N=7	**624 ± 56**	N=6	-		-		NS
Creatinine	**mg/dl**	0.2 ± 0.003	N=7	0.21 ± 0.02	N=9	-		-		
Total Bilirubin	**mg/dl**	0.08 ± 0.02	N=7	**0.12 ± 0.02**	N=9	-		-		NS
Total Protein	**g/dl**	5.2 ± 0.1	N=7	5.3 ± 0.1	N=9	-		-		
Globulin	**g/dl**	1.9 ± 0.1	N=7	2.0 ± 0.1	N=8	-		-		
Bun/Creat	**-**	160 ± 11	N=7	189 ± 22	N=9	-		-		
Alb/Glob	**-**	1.78 ± 0.18	N=7	1.70 ± 0.13	N=8	-		-		

Table S2. Relative to Figure 6. Blood analysis in WT *vs.* iL-*Sin3a/b* (induced KO) in fasting *vs.* refeeding conditions. FFA=Free Fatty Acid; TG=Triglyceride; GGT= Gamma-Glutamyl Transferase; AST= Aspartate transaminase; ALT= Alanine transaminase; BUN= Blood Urea Nitrogen; CPK= Creatine phosphokinase.

Compound	hFoxO1 (IC_{50})	hFoxA2 (IC_{50})	hFoxO3 (IC_{50})	mFoxO1 (IC_{50})
1	2.59	>50	>50	2.52
2	1.53	>50	1.36	1.92
3	0.68	>50	n.a.	n.a.
4	5.09	>50	n.a.	n.a.
5	2.56	2.88	n.a.	n.a.
6	3.39	n.d.	3.95	n.a.
7	0.83	n.d.	1.1	n.a.
8	2.91	31	3.03	2.64
9	0.04	>50	9.17	0.04
10	0.21	>50	0.03	0.14
11	0.49	2.29	0.71	0.54
12	1.9	11.2	0.84	0.6
13	1.9	>50	5.61	1.56

Table S3. Relative to Figure 7. Reporter gene assay IC_{50} values (µM) for compound 1-13. h = human; m = mouse; n.a. = Not analyzed; n.d. = Not determined due to irregular curve shape at the highest concentrations tested.

Compound	Tolerated p.o. dose (µmol/kg)	C_{max} (µM)	$T_{1/2}$ (h)	T_{max} (h)	mFoxO1 IC_{50} (µM)	Fraction unbound (%)	C_{max} u / mFoxO1 IC_{50}
8	25	4.5	1.3	0.17	2.5	52	0.94
9	100	0.034	2.5	0.67	0.041	0.4	0.003
13	50	7.3	1.3	0.33	1.6	16	0.73

Table S4. Relative to Figure7. Pharmacokinetics of compound 8, 9 and 13 *in vivo* in mice. Data are average means (*n*=3).