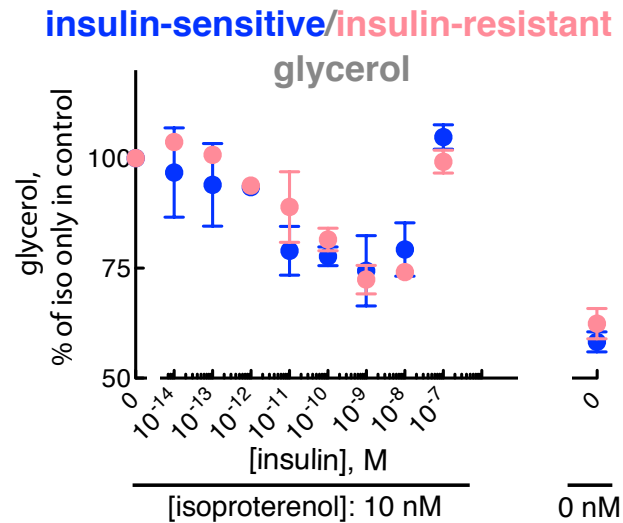**Inhibition of mTORC1 does not affect control of lipolysis by isoproterenol or insulin.**
Adipocytes were pre-incubated without (blue) or with 50 nM rapamycin (cyan) for 60 min, when indicated concentration of insulin was added and cells incubated for 15 min before incubation with 10 nM isoproterenol (iso) for another 10 min. Cells were then separated from medium and fatty acids (n=7) (**a**) and glycerol (n=7) (**b**) were determined in the medium. cAMP (n=3) (**c**) and the phosphorylation of HSL (n=4) (**d**), S6K1(n=3) (**e**) and PKB at Ser[473] (n=4) (**f**) were determined in the cells. Representative immunoblots of one experiment are shown.
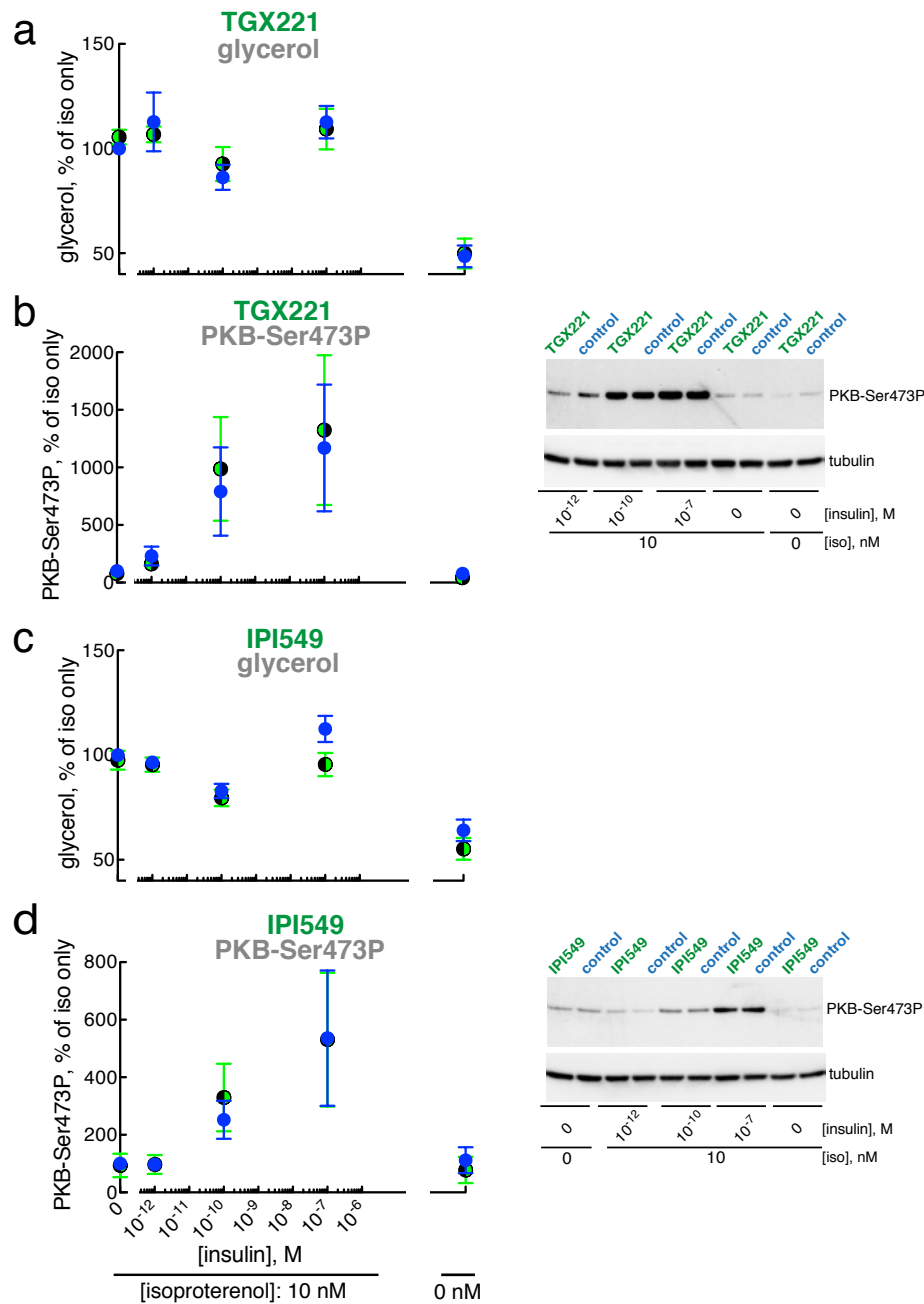
Effect of PI3K-inhibitors TGX221 and IPI549 on lipolysis.

Adipocytes were pre-incubated without (blue) or with inhibitors of PI3K (green/black) for 30 min: 10 μM TGX221 (inhibitor of PI3Kβ) (n=4) (**a,b**) or 1 μM IPI549 (inhibitor of PI3Kγ) (n=4) (**c,d**). Then the indicated concentration of insulin was added and cells incubated for 15 min before incubation with 10 nM isoproterenol (iso) for another 10 min. Cells were then separated from medium and glycerol released to the medium (**a,c**) and the phosphorylation of PKB at Ser[473] (**b,d**) in the cells were determined. Representative immunoblots of one experiment are shown.

insulin-sensitive/insulin-resistant
glycerol

glycerol, % of iso only in control

[insulin], M

[isoproterenol]: 10 nM   0 nM

Control of lipolysis in insulin-sensitive and insulin-resistant non-diabetic non-obese control subjects.

Adipocytes from non-diabetic insulin sensitive subjects (HOMA-IR average 0.91, range 0.33-1.45; QUICKI average 0.40, range 0.36-0.47) (n=22, blue symbols) or from non-diabetic insulin resistant subjects (HOMA-IR average 3.20, range 2.24-5.00; QUICKI average 0.32, range 0.30-0.34) (n=17, pink symbols). The cells were incubated with the indicated concentration of insulin for 15 min, when 10 nM isoproterenol was added and cells incubated for another 10 min. Cells were then separated from medium and glycerol was determined in the medium.

Clinical data of subjects (female) analysed in Figure 14.

Blood was sampled after overnight fasting and values refer to concentration in plasma or serum (insulin). g, glycerol; f, fatty acid; h, HSL phosphorylation; c, cAMP; p, HSL protein. BMI, body mass index; TAG, triacylglycerol; chol, cholesterol; LDL, low density lipoprotein; HDL, high density lipoprotein.

a. Non-obese, non-diabetic subjects

subject #	analyses	age years	BMI kg/m^2	TAG mM	chol mM	LDLchol mM	HDLchol mM	glucose mM	insulin mIU/L
1	g,h	46	24	0.94	4	2.5	1.1	5.7	5.6
2	g,f,h	74	28	1.8	6.8	4.1	1.8	6.8	11
3	g,f,h	53	24	1.1	4.5	2.3	1.7	5.6	5.5
4	g,f,h	86	25	1.2	3.1	1.8	0.76	7.1	3.5
5	g,f,h	66	24	0.54	4.1	2.1	1.7	4.9	2.0
6	f,h	63	27	2.9	5.2	2.4	1.6	6.8	13
7	f	78	23	1.2	6	3.7	1.7	7.5	4.9
8	g,f,h	62	18	0.99	2.6	1.6	0.52	7.3	6.9
9	h	44	26	2.2	4.7	2.2	1.5	5.0	3.5
10	h	81	27	1.1	4.4	2.8	1.2	5.6	4.4
11	c	75	29	2.8	4.1	1.8	1.1	8.7	22
12	c	69	28	3	5.2	3.1	0.82	6.2	2.3
13	c	65	20	1.1	5.4	3.2	1.7	5	1.9
14	c	71	23	1.4	6.5	4.3	1.6	6.5	5.4
15	c	78	28	1.0	5.8	4.2	1.1	6.3	10
16	c	60	22	3.0	6.6	4.2	1.1	6.1	14
17	c	40	28	0.92	3.1	1.8	0.82	5.3	4.7
18	p	71	22	1.5	3.2	1.7	0.83	5.4	1.9
19	p	65	28	2.5	3.7	1.0	1.5	6.6	5.5
20	p	73	20	1.0	4.0	2.1	1.4	7.6	2.4
21	p	44	20	0.79	2.6	1.0	1.3	6.8	6.2
22	p	47	21	5.3	4.2	-	0.56	4.8	2.4
23	p	45	21	1.1	4.1	2.2	1.4	5.8	3.6
24	p	49	26	1.6	3.5	1.3	1.4	6.8	9.1
25	p	49	28	0.88	4.2	2.3	1.5	5.8	3.9
26	p	47	25	1.0	4.5	3.3	0.77	4.9	2.4
27	p	34	26	1.2	4.3	2.4	1.3	5.1	1.6

b. Obese, diabetic subjects

subject #	analyses	age years	BMI kg/m²	TAG mM	chol mM	LDLchol mM	HDLchol mM	glucose mM	insulin mIU/L	diabetes-treatment
1	g,f,h	70	36	2.1	6	4.0	1.1	8.4	69	metformin
2	g,f,h,c	45	32	4.1	4.8	-	0.8	7	5.9	diet
3	g,f,h,c	75	31	1.6	2.5	1.0	0.8	9	12	metformin
4	g,f,h,c	68	28	1.7	3.6	1.6	1.2	6.3	6.7	metformin
5	g,f,h,c	77	28	2.7	5.9	3.7	1.0	9.5	10	metformin
6	g,f,h,c,p	71	40	4.1	4.6	-	0.9	12.3	30	insulin
7	g,f,h,c,p	65	33	2.8	4.3	1.8	1.2	11.8	17	glipizide metformin
8	c,p	61	35	2.2	2.7	1.1	0.7	5.4	13	dulaglutide metformin
9	c,p	83	36	1.4	3.0	1.4	1.0	10	6.0	glipizide sitagliptin
10	c,p	66	38	3.5	5.2	2.8	0.8	10.7	39	sitagliptin
11	c,p	75	35	2.4	2.8	0.8	1.0	6.5	6.8	diet
12	p	65	37	2.7	5.7	3.5	1.0	10.4	173	-
13	p	45	38	1.2	4.6	3.2	0.9	6.4	8.7	-
14	p	72	31	2.4	3.1	0.8	1.1	7.6	7.2	-
15	p	65	43	2.7	4.5	2.4	0.9	8.5	15	-

Characteristics of subjects (female) analysed in Figure S3.

	insulin sensitive (*n=22*)		insulin resistant (*n=17*)	
	mean	*range*	*mean*	*range*
age, years	59	30-86	66	43-80
BMI, kg/m²	23	18-27	24	18-28
QUICKI	0.40	0.36-0.47	0.32	0.30-0.34
HOMA-IR	0.91	0.33-1.45	3.20	2.24-5.00