

Supplemental Table 1: Genetics in subjects with lipodystrophy and *INSR* pathogenic variants

Subject	Diagnosis	Affected Gene	Homozygous vs. Heterozygous	Transcript (NM_####)	rs number ¹	cDNA	Protein
NIH-97	FPL	Unknown					
NIH-104	FPL	Unknown					
NIH-105	FPL	Unknown					
NIH-532	FPL	Unknown					
NIH-109	FPL	Unknown					
NIH-106	FPL	<i>PPARG</i>	Heterozygous			c.1313A>C	p.Q438P
NIH-508	FPL	<i>PPARG</i>	Heterozygous				p.K395R
NIH-103	FPL	<i>LMNA</i>	Heterozygous		rs57920071	c.1444C>T	p.R482W
NIH-107	FPL	<i>LMNA</i>	Heterozygous		rs57920071	c.1444C>T	p.R482W
NIH-581	FPL	<i>LMNA</i>	Heterozygous		rs11575937	c.1445G>A	p.R482Q
NIH-108	CGL	<i>BSCL2</i>	Homozygous	Transcript 1 (NM_001122955)	rs1064797076	c.844_854del; c. 652_662del	p.A282Wfs*32; p.A218Wfs*32
NIH-113	CGL	<i>AGPAT2</i>	Homozygous	Transcript 1 (NM_006412.3)	rs606231168	c.493-1G>C	Not known
NIH-115	CGL	<i>AGPAT2</i>	Homozygous	Transcript 1 (NM_006412.3)	rs764260414; rs606231168	c.299G>A; c.493-1G>C	p.S100N; Not known
NIH-116	CGL	<i>BSCL2</i>	Compound heterozygous	Transcript 1 (NM_001122955)	NA	c.489-2A>C c.213-1336 c.294+1921 delinsCA	Not known; p.T72Cfs*2
T405	RMS	<i>INSR</i>	Homozygous	NM_000208.4	rs749094324	c.659C>T	p.P220L
T406	RMS	<i>INSR</i>	Homozygous	NM_000208.4	rs749094324	c.659C>T	p.P220L
T410	RMS	<i>INSR</i>	Compound heterozygous	NM_000208.4	rs749713053; N/A	c.407T>G g.26624_26625del	p.L136R 2bp intronic deletion
T416	RMS (1)	<i>INSR</i>	Compound heterozygous	NM_000208.4	N/A; rs761203947	c.90C>A c.712G>A	p.Y30X p.E238K
T418	RMS	<i>INSR</i>	Compound heterozygous	NM_000208.4	N/A	c.1904C>T N/A	p.S635L exon 9-10 deletion
T427	Type A	<i>INSR</i>	Heterozygous	NM_000208.4	N/A	c.3167G>T	p.V1056G
T428	Type A	<i>INSR</i>	Heterozygous	NM_000208.4	N/A	c.3167G>T	p.V1056G

¹<https://www.ncbi.nlm.nih.gov/snp>

FPL, Familial Partial Lipodystrophy; CGL, Congenital Generalized Lipodystrophy; RMS, Rabson Mendenhall Syndrome; Type A, Type A insulin resistance

- Kim D, Cho SY, Yeau SH, Park SW, Sohn YB, Kwon MJ, et al. Two novel insulin receptor gene mutations in a patient with Rabson-Mendenhall syndrome: the first Korean case confirmed by biochemical, and molecular evidence. *Journal of Korean medical science*. 2012;27(5):565-8.

Supplemental Table 2: Sensitivity Analyses

	<i>INSR</i>	LD	T2D	Ob		Overall P	<i>INSR</i> vs LD	<i>INSR</i> vs T2D	<i>INSR</i> vs Ob	LD vs T2D	LD vs Ob	T2D vs Ob
Age (yr)	21.9 ± 6	37.2 ± 17.2	13.9 ± 2.5	15.3 ± 1.8	Unadjusted	<0.0001	0.023	0.48	0.65	0.0001	0.0004	0.99
		44.4 ± 14.1			No GL	<0.0001	<0.0001	0.25	0.43	<0.0001	<0.0001	0.99
Weight (kg)	48.4 ± 23.5	70.3 ± 18.0	107.1 ± 31.4	95.4 ± 19.3	Unadjusted	<0.0001	0.19	<0.0001	0.0020	0.0036	0.085	0.72
					Age-adjusted	<0.0001	0.81	<0.0001	0.0004	0.0004	0.0078	0.63
		78.9 ± 12.9			No GL	0.0001	0.047	<0.0001	0.0019	0.050	0.42	0.71
Height (cm)	155.7 ± 7.1	168.2 ± 9.1	159.6 ± 12.0	163.3 ± 11.5	Unadjusted	0.055	0.054	0.87	0.48	0.21	0.70	0.87
					Age-adjusted	0.2	0.23	0.78	0.39	0.79	0.99	0.89
		169.9 ± 7.1			No GL	0.033	0.030	0.86	0.45	0.12	0.49	0.86
Body mass index (kg/m²)	19.6 ± 8.4	24.6 ± 4.9	41.4 ± 7.9	35.6 ± 5.5	Unadjusted	<0.0001	0.37	<0.0001	0.0002	<0.0001	0.0030	0.29
					Age-adjusted	<0.0001	0.97	<0.0001	<0.0001	<0.0001	0.0003	0.20
		27.2 ± 3.0			No GL	<0.0001	0.098	<0.0001	0.0002	0.0002	0.042	0.27
Fat mass (kg)	11.9 ± 12.8	16.9 ± 10.4	50.4 ± 16.0	39.1 ± 9.2	Unadjusted	<0.0001	0.81	<0.0001	0.0007	<0.0001	0.0013	0.24
					Age-adjusted	<0.0001	0.99	<0.0001	0.0001	<0.0001	0.0002	0.16
		21.7 ± 8.1			No GL	<0.0001	0.35	<0.0001	0.0006	<0.0001	0.022	0.22
Fat free mass (kg)	36.5 ± 11.1	53.4 ± 10.2	56.7 ± 16.7	56.3 ± 13.4	Unadjusted	0.013	0.034	0.018	0.025	0.93	0.96	0.99
					Age-adjusted	0.005	0.30	0.0054	0.0089	0.35	0.41	0.99
		57.2 ± 9.2			No GL	0.0092	0.014	0.020	0.028	0.99	0.99	0.99
Hemoglobin A1c (%)	8.2 ± 2.8	8.4 ± 1.9	7.4 ± 0.9	N/A	Unadjusted	0.47	0.97	0.69		0.45		
					Age-adjusted	0.3	0.83	0.58		0.32		
		7.6 ± 1.6			No GL	0.68	0.81	0.66		0.95		
Fasting glucose (mg/dl)	120 ± 70	159 ± 55	126.8 ± 31.9	90.7 ± 5.7	Unadjusted	0.022	0.31	0.99	0.64	0.40	0.014	0.42
					Age-adjusted	0.03	0.21	1	0.54	0.29	0.019	0.44
		149 ± 46			No GL	0.063	0.53	0.99	0.57	0.68	0.04	0.34

	<i>INSR</i>	LD	T2D	Ob		Overall P	<i>INSR</i> vs LD	<i>INSR</i> vs T2D	<i>INSR</i> vs Ob	LD vs T2D	LD vs Ob	T2D vs Ob
Fasting insulin (mcU/ml) (log-transformed)	129.0 [81.5-1000]	33.1 [18.3-54.6]	47.8 [34.7-65.8]	17.6 [12.5-26.1]	Unadjusted	<0.0001	0.0002	0.0070	<0.0001	0.70	0.34	0.078
					Age-adjusted	<0.0001	0.0039	0.0038	<0.0001	1	0.16	0.08
		29.0 [18.6-40.4]			No GL	<0.0001	0.0002	0.0062	<0.0001	0.59	0.51	0.07
Insulin dose among insulin users (U/kg/day)	22.9 ± 21.3	2.6 ± 1.9	none	none	Unadjusted	0.012						
					Age-adjusted	0.03						
		2.3 ± 1.4			No GL	0.041						
# antidiabetic medications	2.3 ± 1.0	1.8 ± 1.1	none	none	Unadjusted	0.33						
					Age-adjusted	0.20						
		1.7 ± 1.3			No GL	0.32						
Cholesterol (mg/dl)	145 ± 25	189 ± 64	N/A	N/A	Unadjusted	0.10						
					Age-adjusted	0.2						
		195 ± 71			No GL	0.096						
Triglyceride (mg/dl) (log transformed)	60 [38-79]	423 [214-1080]	N/A	N/A	Unadjusted	<0.0001						
					Age-adjusted	<0.0001						
		636 ± 538			No GL	<0.0001						
HDL (mg/dl)	64 ± 14	27 ± 6	N/A	N/A	Unadjusted	<0.0001						
					Age-adjusted	<0.0001						
		29 ± 6			No GL	<0.0001						
LDL (mg/dl) (log-transformed)	71 [60-86]	71 [60-78]	N/A	N/A	Unadjusted	0.99						
					Age-adjusted	0.74						
		70 [60-78]			No GL	0.95						
# Lipid lowering medications	0.1 ± 0.4	1.5 ± 1.0	none	none	Unadjusted	0.0018						
					Age-adjusted	0.023						
		1.8 ± 0.8			No GL	0.0001						

	<i>INSR</i>	LD	T2D	Ob		Overall P	<i>INSR</i> vs LD	<i>INSR</i> vs T2D	<i>INSR</i> vs Ob	LD vs T2D	LD vs Ob	T2D vs Ob
Plasma Glycerol (ug/mL) (log-transformed)	10.0 [8.3-11.6]	5.6 [4.3-8.3]	7.1 [6.8-8.4]	5.1 [4.4-6.2]	Unadjusted	0.012	0.066	0.68	0.013	0.46	0.69	0.12
					Age-adjusted	0.01	0.11	0.48	0.014	0.83	0.82	0.22
		5.2 [4.3-7.8]			No GL	0.013	0.065	0.71	0.017	0.40	0.87	0.13
Glycerol R_a (umol/kg FM/min)	36.6 ± 19.9	20.9 ± 18.3	5.7 ± 1.2	4.9 ± 1.2	Unadjusted	0.0002	0.096	0.0006	0.0006	0.072	0.066	0.99
					Age-adjusted	<0.0001	0.83	<0.0001	<0.0001	0.0004	0.0004	1
		10.5 ± 4.6			No GL	<0.0001	<0.0001	<0.0001	<0.0001	0.67	0.58	0.99
Glycerol R_a (umol/kg FFM/min)	7.3 ± 3.1	4.2 ± 2.2	5.0 ± 1.0	3.5 ± 1.3	Unadjusted	0.0045	0.011	0.12	0.004	0.82	0.82	0.42
					Age-adjusted	0.0054	0.064	0.098	0.0037	0.99	0.68	0.44
		4.0 ± 2.5			No GL	0.0062	0.014	0.14	0.0067	0.71	0.96	0.46
Glycerol R_a (umol/kg/min)	6.0 ± 2.8	3.3 ± 1.6	2.6 ± 0.5	2.0 ± 0.6	Unadjusted	0.0001	0.0039	0.0009	0.0001	0.76	0.26	0.84
					Age-adjusted	<0.0001	0.055	0.0004	<0.0001	0.32	0.091	0.86
		2.8 ± 1.6			No GL	0.0001	0.0013	0.0010	0.0002	0.99	0.70	0.84
Palmitate R_a (umol/kg FM/min) (log-transformed)	19.3 [6.9-21.0]	8.5 [6.4-17.7]	N/A	N/A	Unadjusted	0.55						
					Age-adjusted	0.6						
		7.5 [5.8-8.7]			No GL	0.10						
Palmitate R_a (umol/kg FFM/min) (log-transformed)	3.1 [2.1-4.0]	2.5 [1.8-3.0]	N/A	N/A	Unadjusted	0.34						
					Age-adjusted	0.50						
		2.4 [1.8-2.6]			No GL	0.33						
Palmitate R_a (umol/kg/min) (log-transformed)	2.6 [1.8-3.3]	2.0 [1.4-2.3]	N/A	N/A	Unadjusted	0.37						
					Age-adjusted	0.70						
		1.9 [1.2-2.0]			No GL	0.24						

	<i>INSR</i>	LD	T2D	Ob		Overall P	<i>INSR</i> vs LD	<i>INSR</i> vs T2D	<i>INSR</i> vs Ob	LD vs T2D	LD vs Ob	T2D vs Ob
Plasma Palmitate (ug/ml)	40.6 ± 16.0	37.7 ± 15.8	49.7 ± 6.5	30.6 ± 8.3	Unadjusted	0.032	0.96	0.50	0.44	0.14	0.60	0.021
					Age-adjusted	0.042	1	0.65	0.37	0.68	0.45	0.024
		35.9 ± 14.2			No GL	0.015	0.85	0.43	0.37	0.073	0.78	0.012
Plasma total free fatty acid (uEq/L)	0.62 ± 0.22	0.42 ± 0.22	0.71 ± 0.11	0.32 ± 0.13	Unadjusted	0.0004	0.12	0.76	0.015	0.0071	0.60	0.0008
					Age-adjusted	0.0007	0.45	0.94	0.0067	0.27	0.23	0.0008
		0.40 ± 0.26			No GL	0.0007	0.12	0.78	0.021	0.012	0.83	0.0014
Hepatic Glucose Production (umol/kg/min)	17.6 ± 6.4	17.2 ± 4.9	8.4 ± 2.6	8.1 ± 1.4	Unadjusted	<0.0001	0.99	0.0008	0.0008	0.0002	0.0002	0.99
					Age-adjusted	<0.0001	0.71	<0.0001	<0.0001	<0.0001	<0.0001	1
		14.8 ± 2.5			No GL	<0.0001	0.38	<0.0001	<0.0001	0.0021	0.0018	0.99
Hepatic Glucose Production (umol/kg_FFM/min)	21.7 ± 6.2	22.0 ± 4.9	15.8 ± 4.3	13.8 ± 2.7	Unadjusted	0.0007	0.99	0.081	0.014	0.021	0.0023	0.82
					Age-adjusted	0.0008	0.86	0.040	0.0068	0.011	0.0016	0.84
		20.5 ± 4.3			No GL	0.0033	0.95	0.064	0.0098	0.12	0.18	0.80
Fractional Gluconeogenesis (%)	77.1 ± 9.4	55.4 ± 11.5	59.1 ± 5.9	52.2 ± 11.9	Unadjusted	0.0001	0.0003	0.0065	0.0002	0.84	0.89	0.51
					Age-adjusted	<0.0001	0.0001	0.019	0.0005	0.34	0.98	0.45
		56.7 ± 12.6			No GL	0.0004	0.0021	0.0085	0.0003	0.96	0.79	0.53
Absolute Gluconeogenesis (umol/kg/min)	14.3 ± 5.6	9.7 ± 2.6	5.1 ± 1.2	4.3± 0.5	Unadjusted	<0.0001	0.010	<0.0001	<0.0001	0.0055	0.0015	0.95
					Age-adjusted	<0.0001	0.070	<0.0001	<0.0001	0.012	0.0038	0.96
		8.7 ± 2.5			No GL	<0.0001	0.0038	<0.0001	<0.0001	0.062	0.021	0.95
Absolute Gluconeogenesis (umol/kg_FFM/min)	17.6 ± 6.0	12.4 ± 3.6	9.5 ± 1.9	7.3 ± 1.1	Unadjusted	<0.0001	0.019	0.0004	<0.0001	0.21	0.011	0.58
					Age-adjusted	<0.0001	0.043	0.0008	<0.0001	0.50	0.076	0.59
		12.2 ± 4.3			No GL	<0.0001	0.031	0.0009	<0.0001	0.41	0.045	0.62

	<i>INSR</i>	LD	T2D	Ob		Overall P	<i>INSR</i> vs LD	<i>INSR</i> vs T2D	<i>INSR</i> vs Ob	LD vs T2D	LD vs Ob	T2D vs Ob
Absolute Glycogenolysis (umol/kg/min)	3.3 ± 1.6	7.5 ± 3.6	3.4 ± 1.5	3.8 ± 1.6	Unadjusted	0.0005	0.0047	0.99	0.97	0.0027	0.012	0.98
					Age-adjusted	<0.0001	<0.0001	0.85	0.99	<0.0001	<0.0001	0.92
		6.1 ± 2.2			No GL	0.0053	0.015	0.99	0.92	0.012	0.056	0.94
Absolute Glycogenolysis (umol/kg FFM/min)	4.1 ± 1.9	9.5 ± 3.9	6.3 ± 2.6	6.5 ± 2.7	Unadjusted	0.0046	0.0036	0.50	0.44	0.10	0.16	0.99
					Age-adjusted	0.0004	0.0002	0.82	0.69	0.0055	0.0097	0.99
		8.3 ± 3.1			No GL	0.030	0.016	0.38	0.32	0.37	0.49	0.99
Lactate (mg/dl)	0.96 ± 0.10	1.57 ± 0.51	1.28 ± 0.36	0.90 ± 0.20	Unadjusted	0.0006	0.0067	0.34	0.97	0.29	0.0010	0.13
					Age-adjusted	0.0001	0.0009	0.62	0.82	0.040	0.0002	0.13
		1.47 ± 0.40			No GL	0.0009	0.011	0.19	0.95	0.54	0.0016	0.049
Hepatic Triglyceride Content (%) (log-transformed)	0.5 [0.1-0.5]	10.6 [2.8-17.1]	N/A	N/A	Unadjusted	<0.0001						
					Age-adjusted	<0.0001						
		10.7 [2.8-13.6]			No GL	0.0001						
Beta-hydroxybutyrate (mmol/L) (log-transformed)	0.73 [0.44-1.26]	0.35 [0.28-0.43]	0.10 [0.08-0.11]	0.11 [0.10-0.13]	Unadjusted	<0.0001	0.0004	<0.0001	<0.0001	<0.0001	0.0001	0.89
					Age-adjusted	<0.0001	0.0004	<0.0001	<0.0001	0.0028	0.013	0.91
		0.39 [0.30-0.44]			No GL	<0.0001	0.0035	<0.0001	<0.0001	<0.0001	<0.0001	0.87
Alanine (μmol/L)	570 ± 263	463 ± 125	410 ± 81	319 ± 58	Unadjusted	0.017	0.42	0.17	0.011	0.85	0.15	0.60
					Age-adjusted	0.036	0.34	0.26	0.02	0.99	0.56	0.59
		452 ± 141			Unadj. No GL	0.028	0.45	0.20	0.017	0.94	0.31	0.63

Comparisons of continuous outcomes between subjects with *INSR* pathogenic variants, lipodystrophy, type 2 diabetes, and obesity were performed using mixed models with post-hoc pairwise comparisons and Tukey correction for multiplicity. Sensitivity analyses were conducted for each model with the addition of age as a covariate and excluding patients with generalized lipodystrophy. P-values for statistical comparisons in which the results of the sensitivity analysis differed from the primary analysis (i.e. crossed the threshold of P=0.05) are indicated in bold font. Due to differences in body composition between groups, variables normalized to measures of body size or composition (Glycerol R_a, Palmitate R_a, hepatic glucose production, gluconeogenesis, glycogenolysis), sensitivity analyses of these variables normalized to alternate measures of body composition (e.g. fat mass, fat free mass, total body mass) are presented. Data are presented as mean ± SD or median (25-75th centile) based on distribution. Non-normally distributed variables were log-transformed prior to analyses as noted.

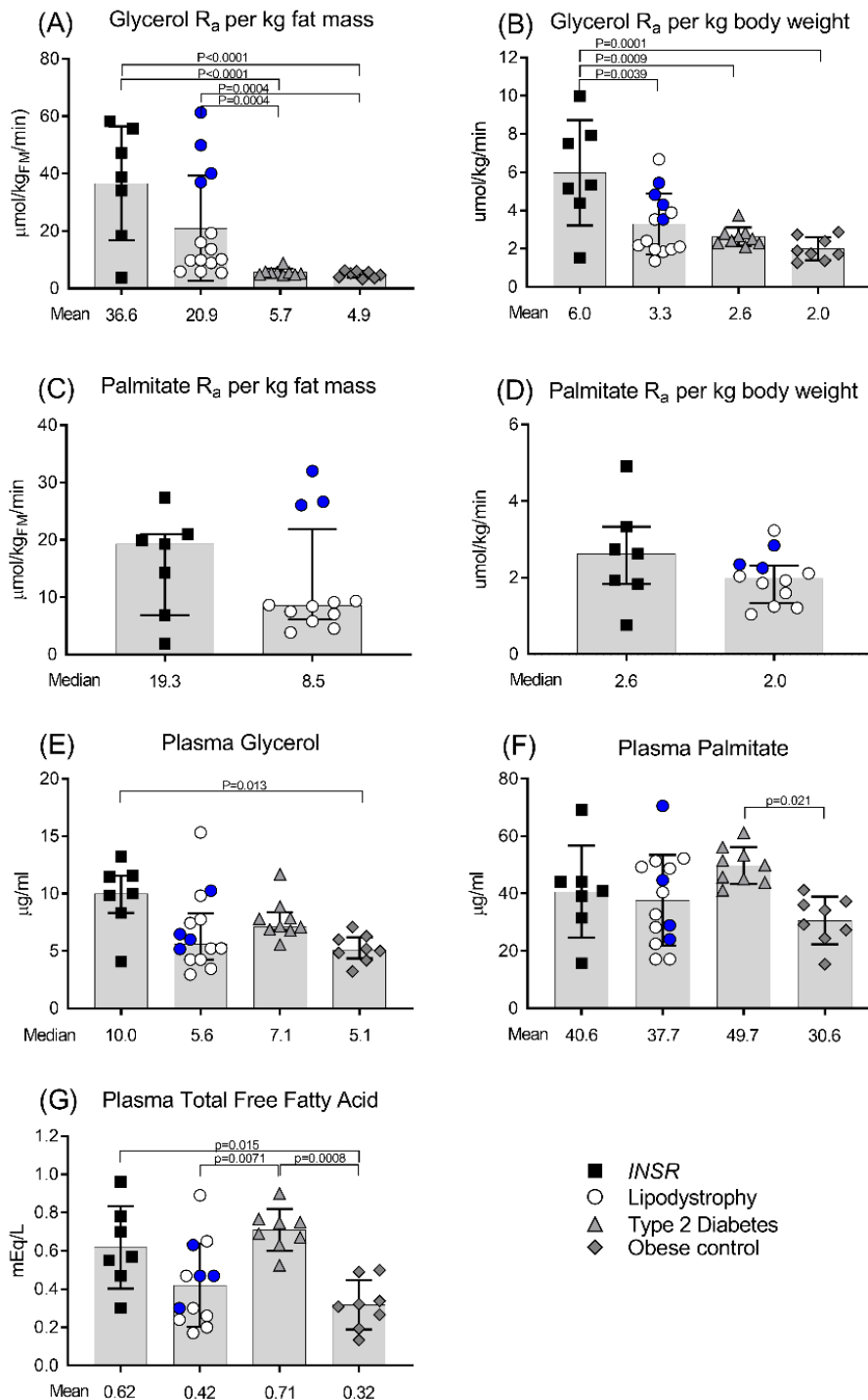
INSR, pathogenic variant in the insulin receptor; LD, lipodystrophy; T2D, type 2 diabetes; Ob, obesity; GL, generalized lipodystrophy; FM, fat mass; FFM, fat free mass; R_a, rate of appearance

Supplemental Table 3: Medication use and glucose and lipid measurements in individual subjects with lipodystrophy and *INSR* pathogenic variants

Group	ID	Diabetes Drugs	Insulin dose (units/kg/day)	Glucose R _a (μmol/kg/min)	HbA1c	Lipid Drugs	TG (mg/dL)
LD	NIH-103	None	0	11.9	5.4	Fenofibrate	239
LD	NIH-104	Metformin, Insulin	88	17.8	8.5	Fenofibrate, Atorvastatin,	216
LD	NIH-105	Metformin, Pioglitazone, Insulin	248	15.3	8.8	Fenofibrate, Rosuvastatin, Omega-3-acid ethyl esters	1581
LD	NIH-106	Insulin, Exenatide, Metformin, Pioglitazone	450	14.9	7.1	Fenofibrate, Rosuvastatin, Omega-3-acid ethyl esters	209
LD	NIH-107	Metformin, Sitagliptin, Insulin	137.5	16.9	9.2	Rosuvastatin	192
LD	NIH-108	Metformin	0	20.5	9.2	None	254
LD	NIH-109	Metformin	0	10.7	6.1	Fenofibrate, Icosopent ethyl	386
LD	NIH-113	Metformin, Insulin	320	25.9	11.3	Gemfibrozil	529
LD	NIH-115	Glyburide, Insulin, Metformin	15	18.7	10.8	Fenofibrate, Atorvastatin	460
LD	NIH-116	Metformin, Insulin	118	27.7	9.5		686
LD	NIH-97	Metformin, Insulin	190	13.7	8.5	Fenofibrate	1089
LD	NIH-508	Metformin	0	17.9	8.7	Atorvastatin	173
LD	NIH-532	Metformin, Insulin	100	15.9	8.8	Fenofibrate, Rosuvastatin	1204
LD	NIH-581	None	0	12.7	5	Fenofibrate, Icosopent ethyl	1077
<i>INSR</i>	T405	Metformin, Insulin, Metreleptin	300	16.0	8.5	None	91
<i>INSR</i>	T406	Metformin, Insulin, Metreleptin	1500	22.9	9.8	None	60
<i>INSR</i>	T410	Metformin, Metreleptin	0	24.7	7.8	None	25
<i>INSR</i>	T416	Metformin, Insulin, Metreleptin	90	17.9	7.1	None	38
<i>INSR</i>	T418	Metformin, Insulin, Metreleptin	1500	22.7	13.3	None	73
<i>INSR</i>	T427	Metformin	0	10.5	4.8	None	57
<i>INSR</i>	T428	Metformin	0	8.3	5.8	None	79

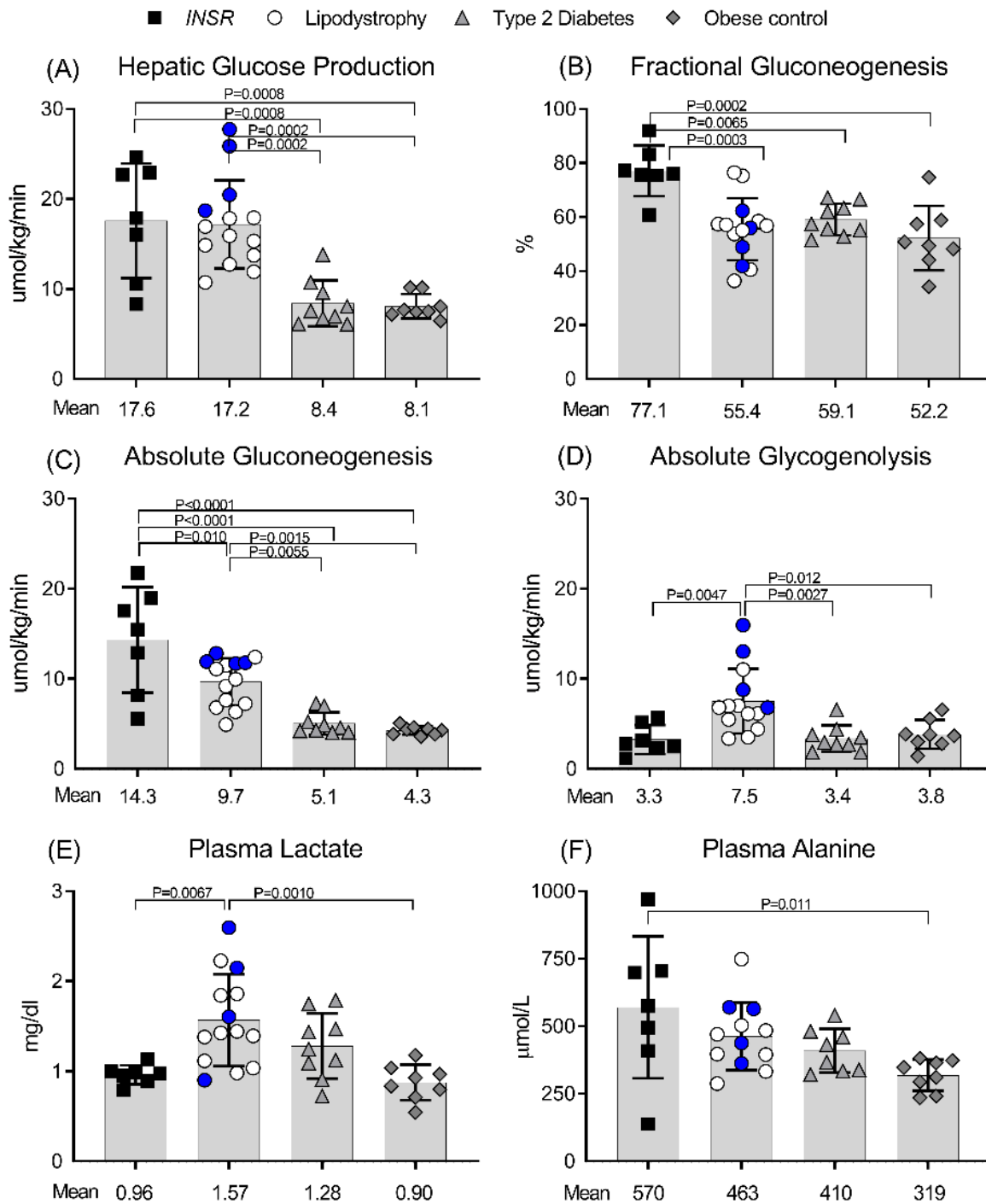
LD, lipodystrophy; *INSR*, pathogenic variant in the insulin receptor; R_a, rate of appearance

Supplemental Figure 1



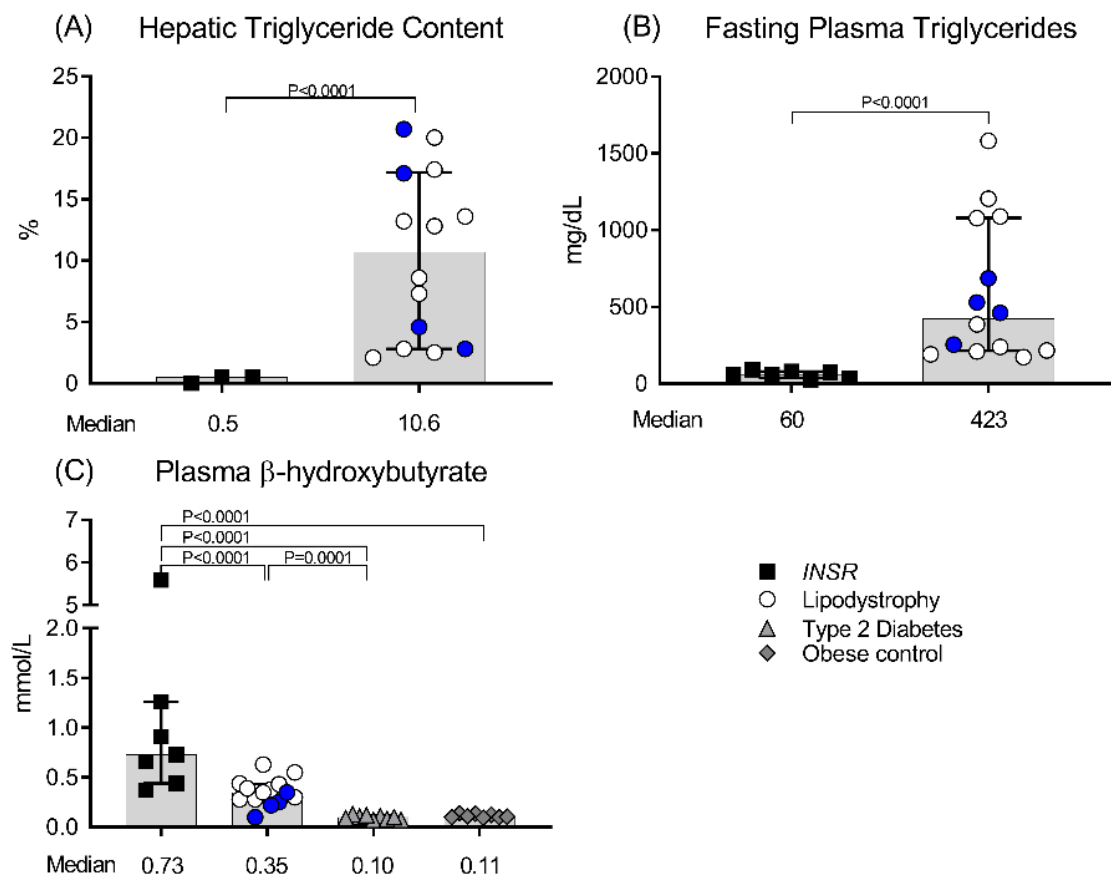
Supplemental Figure 1 Legend: Lipolysis was measured as glycerol rate of appearance (R_a) per kg of fat mass (A), a measure of adipose tissue lipolysis, and glycerol R_a per kg of body weight (B), a measure of total body lipolysis. Glycerol R_a per fat mass was elevated in subjects with *INSR* pathogenic variants (black squares) and lipodystrophy (partial lipodystrophy: white circles; generalized lipodystrophy: blue circles) compared to type 2 diabetes (gray triangles), or obesity (gray diamonds). However, patients with generalized lipodystrophy, who have very low fat mass, were outliers in this analysis, suggesting that this is not a valid measure of adipose lipolysis in this population, as most lipolysis may be extra-adipose. When glycerol R_a was normalized to total body weight (B), subjects with generalized lipodystrophy were no longer outliers, and only subjects with *INSR* pathogenic variants had elevated lipolysis compared to all other groups. Similarly, for measurements of free fatty acid (FFA) turnover assessed as palmitate R_a normalized to fat mass (C), subjects with generalized lipodystrophy were outliers. They were not outliers when palmitate R_a was normalized to total body weight (D). Subjects with generalized lipodystrophy were not outliers for any measurement that was not normalized to fat mass, including plasma glycerol (E), plasma palmitate (F), and plasma total FFA (G). Statistical comparisons were performed using mixed models with post-hoc pairwise comparisons and Tukey correction for multiplicity.

Supplemental Figure 2



Supplemental Figure 2 Legend: Hepatic glucose production (A), fractional gluconeogenesis (B), absolute gluconeogenesis (C), absolute glycogenolysis (D), plasma lactate (E), and plasma alanine (F) in subjects with *INSR* pathogenic variants (black squares), lipodystrophy (partial lipodystrophy: white circles, generalized lipodystrophy: blue circles), type 2 diabetes (gray triangles), and obesity (gray diamonds). Subjects with generalized lipodystrophy had higher hepatic glucose production, absolute gluconeogenesis, and absolute glycogenolysis compared to those with partial lipodystrophy, but exclusion of subjects with generalized lipodystrophy did not meaningfully affect results of between group comparisons on sensitivity analyses (Supplemental Table 2). Subjects with generalized lipodystrophy were not outliers for other outcomes. Statistical comparisons were performed using mixed models with post-hoc pairwise comparisons and Tukey correction for multiplicity.

Supplemental Figure 3



Supplemental Figure 3 Legend: Hepatic triglyceride content (A), plasma triglycerides (B), and plasma β -hydroxybutyrate (C) in subjects with *INSR* pathogenic variants (black squares), lipodystrophy (partial lipodystrophy: white circles, generalized lipodystrophy: blue circles), type 2 diabetes (gray triangles), and obesity (gray diamonds). Subjects with generalized lipodystrophy were not outliers for these outcomes. Statistical comparisons were performed using mixed models with post-hoc pairwise comparisons and Tukey correction for multiplicity.