FOR ONLINE APPENDIX ONLY

ONLINE APPENDIX TABLE 1: GLUCOKINASE MUTATIONS DETECTED IN THE

PARTICIPANTS

GCK MUTATION	SUBJECTS (N)
c.292C>T (Q98X)	2
c.483+1_483+2delGT	1
c.483+2_483+16del	1
c.523G>A (G175R)*	5
c.571C>T (R191W)	3
c.676G>A (V226M)	2
c.680-2A>T	3
c.731delT (V244fsdelT)	1
c.781G>A (G261R)	3
c.898G>A (E300K)	1
c.898G>C (E300Q)	8
c.1007C>T (S336L)	1
c.1240A>G (K414E)	2

*Mutation detected in two different kindred

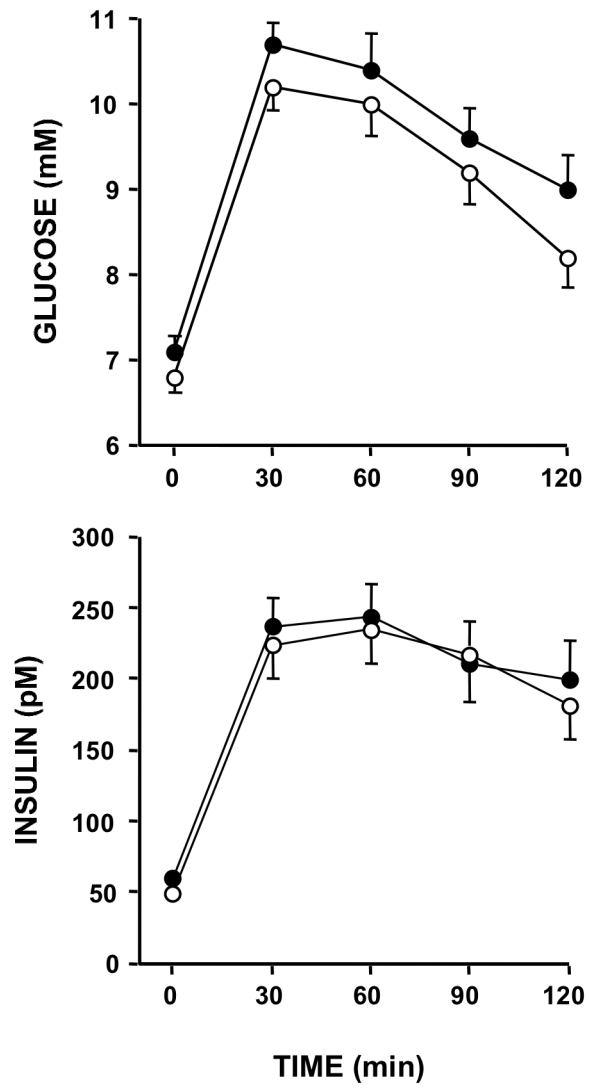ONLINE APPENDIX TABLE 2: CLINICAL PROFILE OF MODY2 SUBJECTS ACCORDING TO GLUCOSE TOLERANCE EVOLUTION DURING FOLLOW-UP

	Glucose Tolerance ($AUC_{glucose}$)		p
	Stable	Deteriorated	
n	16	17	
Sex (M/F)	44% / 56%	53% / 47%	0.73
Duration of follow-up (years)	8 ± 1	14 ± 2	0.007
Age at 2nd OGTT (years)	27 ± 4	38 ± 4	0.02
ΔBMI (z score differences)	0.10 ± 0.17	0.37 ± 0.16	0.28
$\Delta AUC_{glucose}$ (%)	-8 ± 2	21 ± 3	<0.0001
$\Delta AUC_{insulin}$ (%)*	-3 ± 11	23 ± 10	0.09
ΔHOMA%B (%)*	6 ± 10	16 ± 10	0.49
ΔHOMA%S (%)*	18 ± 15	-27 ± 12	0.04
Systolic Blood Pressure (mmHg)†	119 ± 3	124 ± 4	0.33
Diastolic Blood Pressure (mmHg)†	77 ± 3	76 ± 2	0.57
Creatinine Clearance (ml/min)†	89 ± 8	93 ± 8	0.85
Triglycerides (mmol/l)†	0.97 ± 0.10	1.27 ± 0.19	0.21
LDL-cholesterol (mmol/l)†	3.11 ± 0.20	3.93 ± 0.18	0.009
HDL-cholesterol (mmol/l)†	1.49 ± 0.20	1.38 ± 0.12	0.62
Proteinuria (n)†,‡	0	0	-
Proliferative Retinopathy (n)†	0	1	-

Data expressed as Mean ± SEM. Statistics are Fisher's exact test (sex) and analyses of variance performed with log-transformed data when adequate. *Comparison adjusted by sex and age at follow-up. †Values at 2nd OGTT. ‡Proteinuria tested by strips (lower limit of detection: ~250 mg/l). Δ: difference between the values at 2nd and 1st OGTTs, expressed
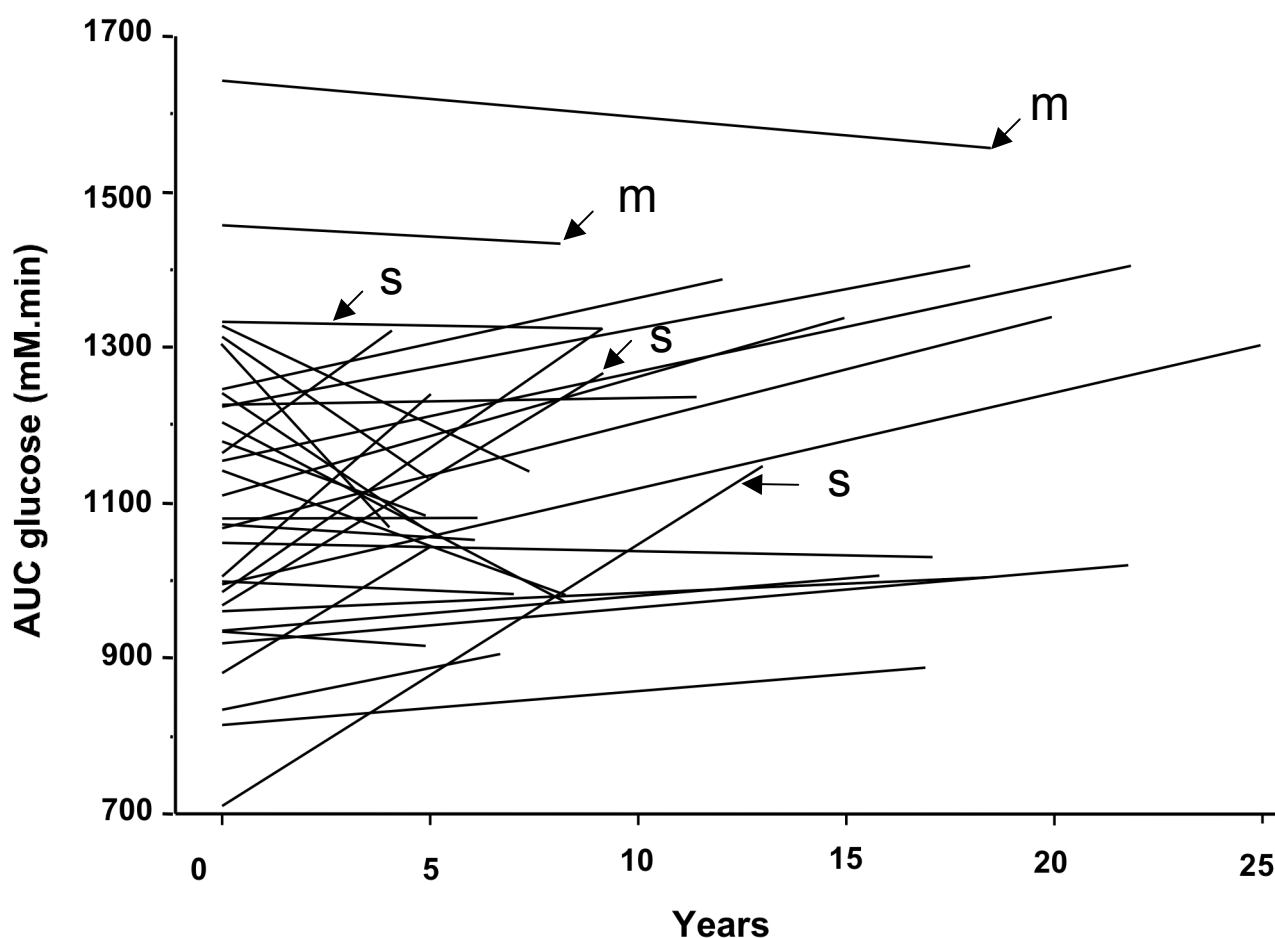
as a percent of the value at 1st OGTT, except for ∆BMI expressed as Z-score differences.

AUC: area under the curve.

FIGURES

Online Appendix Figure 1. Plasma glucose and insulin levels during oral glucose tolerance tests (OGTT) in MODY2 subjects. Open circles: 1st OGTT; closed circles: 2nd OGTT. Data expressed as mean ± SEM.

Online Appendix Figure 2. Evolution of glucose tolerance during the follow-up period. Glucose tolerance is expressed as the area under the curve relating glucose levels and time during oral glucose tolerance tests (AUC_{glu}). Lines connect values for the same individual at 1st and 2nd OGTT. Arrows indicate subjects receiving metformin (m) or sulfonylurea (s) at follow-up. Subjects receiving sulfonylurea had decreased insulin secretion (HOMA%B 26%, 33% and 73%) with preserved insulin sensitivity (HOMA%S 140%, 207%, 125%), while subjects receiving metformin had preserved insulin secretion (HOMA%B 110%, 102%) with decreased insulin sensitivity (HOMA%S 25%, 44%) at the second OGTT.