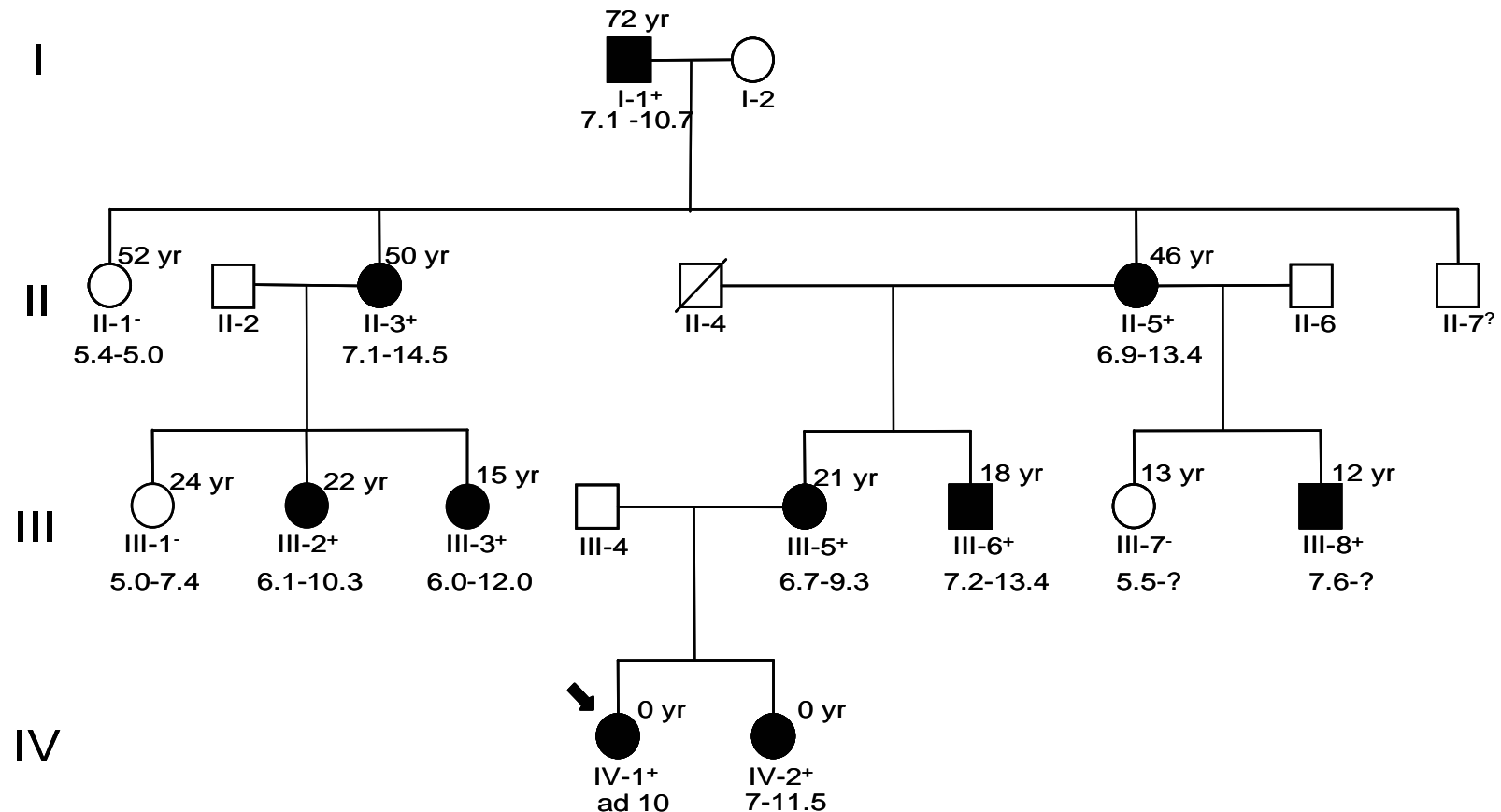


Online Appendix Figure A1



The pedigree shows the segregation of G261R mutation in the glucokinase gene in four generations of the family. Filled symbols indicate diabetes and non-filled symbols normal or unknown glucose tolerance. The age at investigation is given in the upper right hand side corner of the symbols, and the fasting and 2-hour plasma glucose below the symbols, except in the subject IV-1. Carrier status is given after the subjects identification (+=carrier, -= non-carrier, ?= not tested). Among the mutations carriers, the HbA1c range was 5.4 – 6.6%, BMI 19.8 – 29.5 kg/m² (in adults), S-triglycerides 0.39 – 1.27 mmol/l, S-HDL-cholesterol 0.92 – 1.51 mmol/l, and s-LDL cholesterol 2.2 – 4.31 mmol/l. The blood pressure was normal except for subject I1 (170/83 mmHg).

Table A1

	<i>n</i>	<i>K_{cat}</i>		<i>Glucose S_{0.5}</i>		<i>AI</i>		<i>n_H</i>	<i>ATP-K_m</i>
		a	EC ₅₀ ($\mu\text{mol/l}$)	b	EC ₅₀ ($\mu\text{mol/l}$)	g	EC ₅₀ ($\mu\text{mol/l}$)	$^c n_H / ^a n_H$	$^c \text{ATP}_{km} / ^a \text{ATP}_{km}$
GK-WT	3	1.51±0.06	0.73±0.14	4.35±0.06	0.87±0.06	19.6±1.33	6.73±0.71	1.13±0.02	0.91±0.05
GK-G261R	2	1.4 (1.48; 1.32)	0.6 (0.86; 0.34)	4.3 (4.04; 4.56)	0.58 (0.68; 0.48)	20.6 (17.4; 23.7)	14.2 (10.2; 1.23)	1.22 (1.20; 1.23)	1.15 (1.04; 1.25)

Results of the studies on the effect of GKA on GK-WT and mutant GK-G261R. Data for GK-WT are mean of three independent analyses. Data for GK-G261R are the result of two expressions, the means and the individual data are shown. α , β and γ represent the maximal fold drug effect on k_{cat} , glucose affinity and activity index respectively. *EC50 values are the half-maximal drug concentrations for the effect on α , β and γ , c and a refer to control and activated enzyme, respectively.