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Brief report

A novel glucokinase deletion (p.Lys32del) and five previously described mutations co-segregate with the phenotype of mild familial hyperglycaemia (MODY2) in Brazilian families

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ABSTRACT

Six Brazilian families with mild familial hyperglycaemia have been screened for glucokinase (*GCK*) mutations. All had mutations that co-segregated with the phenotype. One of the mutations, the deletion 96_98delAAG (p.Lys32del), had not been previously described, reinforcing the worldwide prevalence of *GCK* MODY and widespread existence of undetected new mutations.

1. Introduction

Maturity-onset diabetes of the young (MODY) is the most common form of monogenic diabetes, being responsible for around 5% of all cases of diabetes [1]. Low prevalence of monogenic diabetes caused by glucokinase (*GCK*) mutations, also known as MODY2, has been previously reported in Brazilian individuals [2–4]. In these studies, patients had usually been recruited using classical MODY criteria (early-onset familial diabetes), which may yielded a higher frequency of mutations in *HNF1A* and other transcription factors, as seen in other populations [2,5,6]. Clinical strategy for screening of *GCK* mutations is now firmly established and sets MODY2 apart from other MODY subtypes as a clinical syndrome of mild non-progressive hyperglycaemia (often in the non-diabetic range), that seldom requires medical treatment [7]. Differently from MODY due to transcription factors, *GCK* mutations have complete penetrance and exhibit little clinical variation. Diagnosis is most commonly made as incidental hyperglycaemia in children and adolescents.

Genetic variability among populations probably accounts for the differences in MODY2 in different countries, but *GCK* mutations seem to have worldwide prevalence [8]. There are

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Table 1 – Clinical characteristics of studied individuals.

Family	Patient	Gender	Age (years)	Age at diagnosis (years)	BMI (kg/m^2)	Fasting glucose (mg/dL)	HbA1c (%)	Mutation	Aminoacid substitution	Previous description
A	**Proband**	**Male**	**10**	**7**	**16.5**	**119**	**NA**	**c.952G>A**	**Gly318Arg (exon 8)**	Pruhova et al. [16]
	Mother	Female	NA	26[a]	25.6	108	NA	c.952G>A	Gly318Arg (exon 8)	
	Father	Male	NA	41	30.1	123	NA	None	None	
B	**Proband**	**Male**	**NA**	**3**	**21.4**	**134**	**NA**	**c.106C>T**	**Arg36Trp (exon 2)**	Miller et al. [15]
	Mother	Female	40	17[a]	29.3	NA	NA	c.106C>T	Arg36Trp (exon 2)	
	Maternal grandmother	Female	NA	45	27.5	NA	NA	None	None	
C	**Proband**	**Female**	**10**	**9**	**16.6**	**132**	**6.2**	**IVS5+1del33**	**579+1_579+32del (intron 5)**	Hager et al. [9]
	Sister	Female	14	14	19.1	133	6.1	IVS5+1del33	579+1_579+32del (intron 5)	
	Mother	Female	39	24[a]	25.1	NA	6.3	IVS5+1del33	579+1_579+32del (intron 5)	
	Maternal grandmother	Female	57	27	29.9	178	NA	IVS5+1del33	579+1_579+32del (intron 5)	
D	**Proband**	**Female**	**6**	**4**	**NA**	**106**	**6.3**	**c.96_98delAAG**	**Lys32del (exon 2)**	New mutation
	Mother	Female	42	18	22.1	113	6.2	c.96_98delAAG	Lys32del (exon 2)	
	Maternal aunt	Female	48	19	26.5	108	6.3	c.96_98delAAG	Lys32del (exon 2)	
	Cousin	Female	17	13	26.4	111	NA	c.96_98delAAG	Lys32del (exon 2)	
	Cousin	Female	19	13	24.5	NA	NA	c.96_98delAAG	Lys32del (exon 2)	
	Maternal grandfather	Male	79	60	26.9	135	NA	c.96_98delAAG	Lys32del (exon 2)	
E	**Proband**	**Male**	**11**	**10**	**14.4**	**124**	**6.4**	**c.866A>G**	**Try289Cys (exon 8)**	Osbak et al. [8]
	Sister	Female	6	6	NA	121	6.4	c.866A>G	Try289Cys (exon 8)	
	Father	Male	42	33	34.2	136	6.7	c.866A>G	Try289Cys (exon 8)	
F	**Proband**	**Female**	**11**	**1**	**27.42**	**116**	**6.8**	**c.206C>G**	**Ser69Stop (exon 2)**	Della Manna et al. [18]
	Mother	Female	43	28	35.5	NA	NA	c.206C>G	Ser69Stop (exon 2)	
	Father	Male	45	39	38	NA	NA	None	None	

Proband's data are in bold. NA: not available.

[a] Hyperglycaemia diagnosed during pregnancy.