**Table 1.** Nitrogen transfer from leucine to alanine in superfused extensor digitorum longus (EDL) muscles from fasted and diabetic rats

| Group | Intramuscular pool (μmol/g wet wt muscle) | | EDL rate of release (μmol · 2 h$^{-1}$ · g$^{-1}$) | | N transfer from Leu to Ala (μmol · 2 h$^{-1}$ · g$^{-1}$) |
|---|---|---|---|---|---|
| | Total alanine ($M_T$) | [$^{15}$N]alanine ($M_L$) | Total alanine ($R_T$) | [$^{15}$N]alanine ($R_L$) | [$^{15}$N]alanine ($M_L + R_L$) |
| Control | 2.46 ± 0.01 | 0.79 ± 0.05 | 1.80 ± 0.07 | 0.74 ± 0.04 | 1.53 ± 0.04 |
| Diabetes | 2.73 ± 0.14 | 1.10 ± 0.07[a] | 2.15 ± 0.10[a] | 0.88 ± 0.14 | 1.97 ± 0.15[a,c] |
| Fasting | 1.11 ± 0.14[a,b] | 0.55 ± 0.03[a,b] | 2.44 ± 0.10[a] | 0.94 ± 0.14 | 1.49 ± 0.15 |

Values are given as means ± SEM ($n = 4$ to 8, no. of experiments/treatment group); [a] $p < 0.05$ significantly different from control rats, [b] $p < 0.05$ significantly different from diabetic rats, [c] $p < 0.05$ significantly different from fasted rats. $^{15}$N/$^{1}$H NMR, GC-MS and aminoacid measurements were made at the end of 2 h-superfusion experiments. $M_T$, intramuscular pool of total alanine; $M_L$, intramuscular pool of labelled alanine; $R_T$, release of total alanine from muscle; $R_L$, release of labelled alanine from muscle. N transfer from Leu to Ala was calculated as the sum of intramuscular [$^{15}$N]alanine ($M_L$) and the rate of [$^{15}$N]alanine released from muscle ($R_L$)

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# Hyperexcitability to sulphonylurea in MODY3

Dear Sir,

The genotypes of maturity-onset diabetes of the young (MODY) have, to some extent, specific phenotypic expression. Mutations in glucokinase (MODY2) are associated with impaired glucose tolerance or mild diabetes mellitus [1]. Mutations in the hepatocyte nuclear factor-1alpha gene (MODY3) [2] are, on the other hand, associated with a high prevalence of overt diabetes, resulting in chronic vascular complications [3]. Several years ago we described a large Norwegian family with MODY, in which there was a particular high frequency of severe eye complications. Five patients were blind, two showed proliferative retinopathy, and one patient had simplex retinopathy and cataract [4]. Whereas the diabetic subjects of this family were characterized by an almost abolished insulin response to oral glucose, several patients showed a remarkable sensitivity to sulphonylurea, with symptoms of hypoglycaemia 60–90 min after as little as 0.5 mg glibenclamide orally. The response to glibenclamide was not tested in glucose-tolerant subjects of the family. These observations were striking enough to be taken as part of the phenotypic expression in this family. At the time of publication the gene defect was unknown. Genotyping of this family now reveals that the mutated gene is HNF-1 alpha (MODY3), with mutation P291 fsinsC in exon 4 (the mutational hot spot), see Figure 1. This is the first MODY3 family observed in Norway. Recently, Hansen et al. [5] presented evidence of hyperexcitability to tolbutamide and glucagon in a glucose-tolerant subject with a MODY3 mutation. The authors speculated that such a hyperexcitability might be characteristic of the early stages in the pathogenesis of MODY3. It should be noted that the sulphonylurea hypersensitivity observed by us, was present in diabetic subjects after they had had the disease for several years. More work is obviously needed to establish if an abnormally sensitive sulphonylurea receptor is an element of the pathogenesis in some families with MODY3.

Yours sincerely


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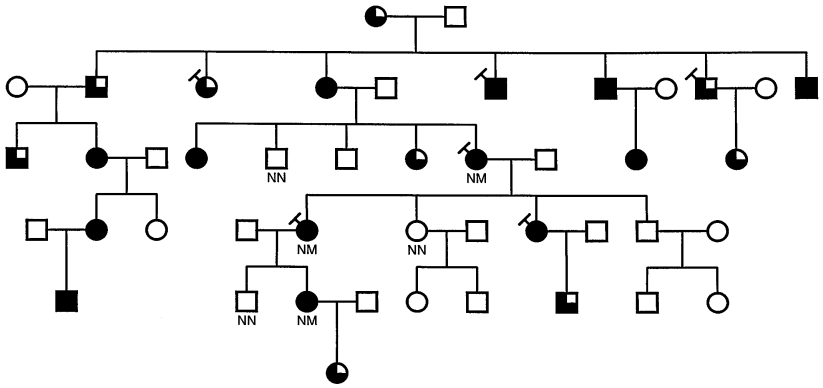


**Fig. 1.** A Norwegian family with MODY3. The pedigree has been reported previously [4]. Investigated subjects are marked with: male (■); female (●). Suspected diabetic or impaired glucose tolerant family members are denoted by: male (◨); female (◔). Normal or suspected normal family members are male (□); female (○). Six subjects were investigated by DNA analysis, and genotype was determined as previously described [6]. The mutation P291 fsinsC in exon 4 of the HNF-1 alpha gene (MODY3) was identified in one allele in three affected members and was not found in three unaffected subjects. The genotypes of these subjects are indicated: N, normal allele; M, p291 fsinsC allele. Six affected subjects had hypoglycaemic symptoms after small doses of glibenclamide (side cross). The family is currently under further investigation

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*Erratum*

# A. D. Liese et al.: "Familial components of the multiple metabolic syndrome: the ARIC study"

Diabetologia (1997) 40: 963–970

Page 964, Subjects and methods, Study design – para 2, lines 4, 7, 8 and 10 should read "greater than or equal to", rather than only "greater than".