have found a mtDNA defect in 10.5 % of patients who had diabetes in combination with deafness. This high percentage confirms previous reports indicating that the prevalence of the 3243 nt mutation is increased in diabetic populations with sensory hearing loss [7, 8]. Until now, mitochondrial diabetes has probably been underestimated because of heteroplasmy and difficulty of searching for all mutations in the mitochondrial genome for each patient, despite the use of different techniques [9]. Moroever, it is likely that in some families, mitochondrial diabetes is secondary to mutations in nuclear genes coding for proteins belonging to the respiratory chain or important for the stability of the mitochondrial genome.

In conclusion, these results demonstrate that clinical criteria are most important to improve the detection of diabetes secondary to a respiratory chain defect. A mitochondrial origin might be evocated when diabetes is associated with other symptoms, especially with nerve deafness.

Yours sincerely,
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Effect of angiotensin II and bradykinin on insulin-stimulated tyrosine kinase activity of insulin receptor

Dear Sir,
Sechi et al. reported that angiotensin II (AII) infusion and captopril treatment did not affect insulin receptor binding and mRNA levels in the rat kidney [1]. This observation is an interesting counter evidence against the suggested role for AII in the modulation of renal sensitivity to insulin [2,3]. This animal study with renal insulin receptor, however, may not exclude the possibilities that: 1) AII may modulate the post-receptor transignalling steps; 2) rat kidney may not be the most ideal candidate organ for evaluating insulin action (sensitivity); and 3) one cannot exclude the possibility that modulation of the insulin sensitivity by captopril [4,5] might also be mediated by kinin [5]. We, therefore, measured the insulin receptor tyrosine kinase activity, the key step of post-insulin receptor transignalling pathway, in human adipocytes to assess whether AII and bradykinin (BK) would enhance the insulin action. AII receptors have been shown to exist in rat [6,7] and human adipocytes [6].

Adipocytes from surgically removed fat tissue were incubated with insulin to activate the receptor tyrosine kinase, with and without the presence of AII and BK. We observed that insulin increased the insulin receptor tyrosine kinase activity, measured according to the method by Klein et al. [8], in a dose-dependent manner (Fig. 1). Meanwhile, neither AII nor BK had an influence on the insulin-stimulated tyrosine kinase activity, even at the maximum concentration applied: 0.46 (saline), 0.44 (AII) and 0.43 (BK)fmolP · fmol $BA^{-1} \cdot min^{-1}$ (Fig. 1). These observations suggest that AII and BK have no effect on the insulin-stimulated insulin receptor tyrosine kinase activity in human adipocytes.

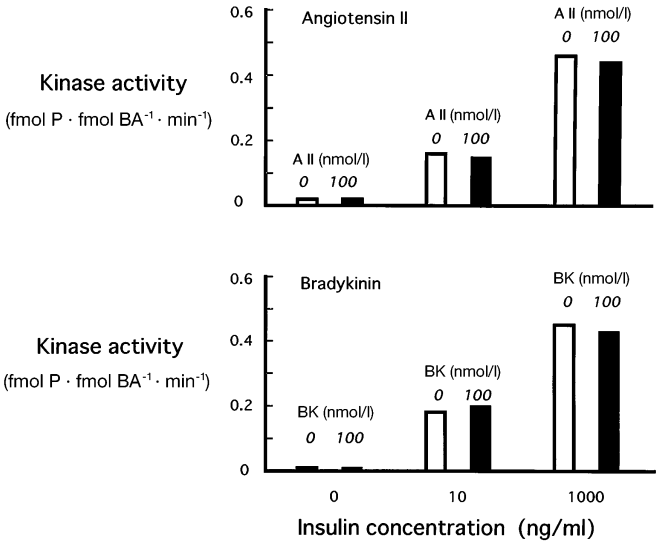

Fig. 1. Effect of angiotensin II (AII) (upper panel) and bradykinin (BK) (lower panel) on insulin receptor tyrosine kinase activity of human adipocytes. Cells were incubated with the indicated insulin concentration for 15 min at 37 °C, with and without AII or BK.

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Our preliminary results, together with the reported observations by Sechi et al. [1], provide some argument against a suggested role for AII in the modulation of insulin sensitivity.

Yours sincerely,
T. Baba, M. Drenckhan, S. Neugebauer, H. Klein

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Group specific component protein genotype is associated with NIDDM in Japan

Dear Sir,
Group specific component protein (Gc, vitamin D binding protein), which maps to chromosome 4q.12, has been reported to be associated with non-insulin-dependent diabetes mellitus (NIDDM) and glucose metabolism in some populations [1, 2]. However, the relationship between the Gc genotype and Japanese NIDDM has not been examined before. The aim of this study was to determine the association of the Gc genotype with NIDDM in Japanese patients.

We studied 208 NIDDM patients and 209 control subjects who showed normal glucose tolerance in a 75-g oral glucose tolerance test. Genetic polymorphisms at codon 335, 416, 420, and 429 were determined by polymerase chain reaction – restriction fragment length polymorphism (PCR-RFLP) analysis [3]. The Gc genotypes were also examined by the isoelectric focusing (IEF) technique. The distribution of the Gc genotypes, as shown in Table 1, indicated that the Gc 1F8/1F genotype was decreased in Japanese NIDDM patients compared to the control subjects (11.06% vs 19.14%, respectively, $p < 0.01$). The frequency of the Gc 1S/2 genotype was higher in NIDDM patients than in the control subjects (48.08% vs 27.75%, respectively, $p < 0.02$). The allele frequency of the 1F allele was significantly lower in NIDDM patients compared with control subjects (27.4% vs 41.15%, respectively, $p < 0.02$), and NIDDM showed a higher incidence of Gc 1S (34.62% vs 27.99%, respectively) and Gc 2 (36.3% vs 28.47%, respectively), although the differences were not statistically significant.

The present results suggest that the association of Gc and NIDDM is replicated in the Japanese population. One possible mechanism would be that Gc influences glucose metabolism by affecting the activity of vitamin D which might be correlated with glucose tolerance [4]. However, any direct involvement of vitamin D in insulin secretion and insulin resistance is still unclear. The other possibility is obviously that the association of Gc with NIDDM reflects the linkage of NIDDM with a hitherto unknown gene.

Table 1. The genotypes of group specific component protein in Japanese NIDDM patients and control subjects

Genotype	Diabetic patients		Control subjects		chi-square test
	N	(%)	N	(%)	
1A2/1F	0	0	5	2.39	NS
1A2/1S	2	0.96	0	0	NS
1A2/2	1	0.48	5	2.39	NS
1A3/1F	4	1.92	0	0	NS
1F/1F	23	11.06	40	19.14	$p < 0.01$
1F/1S	28	13.46	40	19.14	NS
1F/2	36	17.31	48	22.97	NS
1S/1S	7	3.37	9	4.31	NS
1S/2	101	48.08	58	27.75	$p < 0.02$
2/2	7	3.37	4	1.91	NS
total	208	100	209	100	

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Yours sincerely,
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