Vitamin D receptors and hyperparathyroidism

To the editor — Carling and colleagues report that the frequency of the vitamin D_3 receptor (VDR) genotype *bb* in Caucasian patients with primary hyperparathyroidism (HPT) is higher than that in control subjects[1]. They speculate that reduced VDR expression in parathyroid glands may impede adequate suppression by vitamin D_3 in subjects with the genotype *bb* and may contribute to parathyroid tumorigenesis in those subjects.

We have analyzed the frequency of *Bsm*I and *Apa*I polymorphism in intron 8 of the *VDR* gene, in 22 Japanese patients with HPT (46–80 years old) and generation-matched control subjects. Peripheral leukocyte DNA was amplified using the polymerase chain reaction (PCR) and the products digested with *Bsm*I or *Apa*I (ref. 2, 3). Genotype *bb* was found in 18 of the 22 patients with HPT (82%) and in 70 of the 92 control subjects (76%), revealing no significant difference. We found that the frequency of the *b* allele in Japanese subjects was much higher than that in Caucasians reported elsewhere[4,5]. Genotypes *aa* and *Aa* (*Apa*I polymorphism) were found in 13 and 8 of the 22 HPT patients, respectively. Those *aa* and *Aa* genotypes accounted for 31 and 31 of the 65 control subjects, respectively, and again, the frequency was not significantly different between HPT patients and controls. In Japan, the frequency of the *a* allele also seems higher than that in Caucasians[3].

The prevalence of HPT in Japanese is about 1% (ref. 6), comparable to that in Caucasians. As calcium intake or duration of sun exposure could also influence vitamin D–parathyroid hormone axis, the effect of the *VDR* gene polymorphisms on parathyroid tumorigenesis may be a little different among various ethnic groups.

Finally, Howard and colleagues report that suppression of parathyroid hormone secretion by active vitamin D_3 administration is less effective in subjects with the genotype *BB* (ref. 7) and Dawson-Hughes and colleagues demonstrated decreased calcium absorption rates with a low-calcium diet, in the *BB* subjects[8]. These results conflict with the idea that decreased expression of *VDR* in the *bb* subjects may impair the effect of vitamin D_3. Further functional analyses of the effects of *VDR* genotypes are necessary to clarify the exact relationship between *VDR* polymorphisms and HPT.

SHOICHIRO NAGASAKA[1], SAN-E ISHIKAWA[1], HANA MATOBA[2], KEN KUBOTA[2], TORU MURAKAMI[2] & TOSHIKAZU SAITO[1]

[1]*Division of Endocrinology and Metabolism*
Department of Medicine, Jichi Medical School
3311-1 Yakushiji, Minamikawachi
Tochigi 329-04, Japan
[2]*Department of Medicine*
Tokyo Metropolitan Komagome Hospital
Tokyo 113, Japan

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The greatest threat of all

To the editor — Your editorial (*Nature Medicine* **1**, 1221; 1995) points to 29 new or reemerging diseases during the past two decades and the international efforts to establish a global information infrastructure and global alert network. Undoubtedly, studies of the physiology, genetics and pathogenesis of these microbes should be initiated and pursued vigorously. However, it is also essential that the potential impact of global climate and environmental changes is taken seriously.

Even modest temperature changes can influence the distribution and abundance of vectors and intermediate hosts[1], and recent events have demonstrated that the performance of labile viral vaccines and other therapeutics can be suboptimal in developing countries[2] where refrigeration facilities may be poor and temperature fluctuations extreme. The potential impact of global climate changes on vaccine potency in the field could be minimized by first assessing the detailed environmental characteristics of various locations and then selecting products that can withstand these conditions. The development and availability of fully stabilized products would also be invaluable.

Basic laboratory research alone fails to take account of the influence the environment may have on our attempts to better treat and manage the threat of emerging diseases.

SUBHASH C. ARYA
Center for Logistical Research and Innovation
M-122, Greater Kailash-II
New Delhi, India 110048

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