strated here between our predictions based on parameters fixed in 1985 and recent government data fully justifies our 2% accuracy. If the CEGB is able to produce quantitative information to support its assertion[17] that our calculations are "incorrect" it should do so in the normal scientific manner.

The CEGB response also put great emphasis on the statements made by ministers to parliament. The "encapsulation" of these[18] is that made by Mr Moore on 4 February 1983 (ref. 19) in which he said that "no plutonium produced in any of the CEGB's nuclear power stations has ever been used for military purposes. . . ." Yet in April 1986 the prime minister was only prepared to confirm this assurance for the period since 1979[7]. Energy ministers have repeatedly refused to say whether or not the earlier Moore statement is valid. The government assurance on which the CEGB relied in their response to our paper no longer appears valid for the first 16 years of CEGB Magnox operation.

Clarification by government and industry of the past history of civil plutonium production and end use, which can be done without compromising national security[16], is now urgently necessary for the following reasons:

(1) Our original conclusion that more than 2 tonnes of civil plutonium are unaccounted for, over and above that known to be in the United States, is now strengthened by the tests described here.

(2) Important assurances about civil plutonium made to parliament and to the Sizewell Inquiry have, in effect, been invalidated by statements from the prime minister.

(3) The rounding of the recent plutonium production figures to the nearest 50 kg (equivalent to 10 warheads per station per year) in no way meets the Sizewell Inquiry inspector's request for "full and accurate" records[11]. Such accurate records are unlikely to be provided until the past history is clarified.

(4) The Magnox reactors are approaching the end of their working life. In their shut-down phase they will produce large quantities of military quality plutonium, as they did in their early years. It is essential that before then plutonium production data is published in sufficient detail to allay suspicions of diversion.

(5) Publication of plutonium production figures in greater detail would be a better demonstration to the rest of the world that the United Kingdom is complying with the ideals of the non-proliferation treaty.

K.W.J. BARNHAM
Blackett Laboratory,
Imperial College,
Prince Consort Road,
London SW7 2BZ, UK

D. HART
Scientists Against Nuclear Arms,
1 Mill Cottages,
Burford Road,
Black Bourton OX8 2PF, UK

J. NELSON
Department of Physics,
University of Bristol,
Bristol BS8 1TL, UK

R.A. STEVENS
Unicam Corporation,
Aptos,
California 95003, USA

1. Barnham, K.W.J., Hart, D., Nelson, J., Stevens, R.A. *Nature* **317**, 213–217 (1985).
2. *Hansard* 15-4-86, Col 330, and 18-4-86, Col 525.
3. *Hansard* 24-7-87, Col 515.
4. *Hansard* 26-6-86, Col 269.
5. *Hansard* 10-7-86, Col 238.
6. *Hansard* 23-7-87, Col 368.
7. *Hansard* 16-12-87, Col 517.
8. *Hansard* 21-7-86, Col 10.
9. *Hansard* 14-4-86, Col 264.
10. Sizewell Inquiry Transcript, Day 67, p.49D (1983).
11. Department of Energy, Sizewell B Public Inquiry, Summary of Conclusions and Recommendations, Recommendation 13b, C109 (1986).
12. Department of Energy News Release No 181, 16-12-87.
13. Ashford, J. *Electrical Power Engineer*, p.163 (July, 1984).
14. Sizewell Inquiry Transcript, Day 193, p.14H (1984).
15. Broom, T. *Nature* **318**, 406 (1985)
16. Barnham, K.W.J. *et al. Nature* **320**, 9 (1986).
17. Broadcast by Lord Marshall Thames Television, TV-EYE, 20-3-86.
18. Sizewell Inquiry Transcript, Day 67, p.36A (1983).
19. *Hansard* 4-2-83, Col 206.

HLA antigens and insulin-dependent diabetes

SIR—Klitz states (*Nature* **333**, 402; 1988) that the HLA class II DQ β-chain residue 57 correlation[1] does not take into account the complexity[2] of the association of HLA class II antigens with insulin-dependent diabetes mellitus (IDDM). On the contrary, this correlation explains most of these complexities: of 17 common Caucasian DR–DQ haplotypes, 16 are consistent with the view that predisposing haplotypes encode a non-charged amino acid at position 57 of the DQ β-chain and non-predisposing (neutral or negative association) ones encode Asp 57.

The exception is DR7, which is associated with a DQ β-chain that has Ala at position 57 and therefore should be positively associated with IDDM, but instead is neutral. This may be explained by the presence of the DR7 DQ α-chain, which is found only on DR7 haplotypes[3]. In a recent model of class II structure[3], it is suggested that β-chain Asp 57 forms a salt bridge with α-chain Arg 79, occluding one end of the putative antigen-binding site. If this interaction is important in DQ Asp 57-associated IDDM resistance, variation in the α-chain, as well as the β-chain, would affect disease susceptibility[1,3–5]. In support of this, DR3,4 individuals are at the greatest risk for IDDM[6], implying that disease susceptibility is encoded by two different and complementing genes on the DR3 and DR4 haplotypes[5]. We have proposed[5] that, in addition to the DQ Asp 57-negative status of DR3 haplotypes, the DR3 DQ α-chain also contributes to IDDM susceptibility, by forming a hybrid molecule with a DR4 DQ β-chain. DQ_α and DQ_β genes are therefore primary IDDM susceptibility genes which encode a number of distinct DQ molecules that regulate autoimmunity to differing degrees, producing the observed "scale of susceptibility".

More than 90 per cent of Caucasian sporadic[1] and familial (P. Morel *et al.*, manuscript in preparation) IDDM patients possess two DQ Asp 57-negative alleles. This includes DR4/X (X is not DR3 or DR4) patients. We suggest that DR4 is not dominant' but is increased in frequency because it is associated with the most predisposing DQ Asp 57-negative molecule (DQw3.2).

The three additional points raised by Klitz are also inaccurate: (1) the DR7 DQ α-chain is not shared by DR4 haplotypes[1]; (2) we emphasized that 10 per cent of the patients studied had one DQ Asp 57 allele, implying that DQ Asp 57-mediated resistance was not complete and susceptibility could not be 'strictly recessive'[1,5]; (3) we did not exclude a role for DR in IDDM. The experiment by Nishimoto *et al.*[7] is equivocal because an IDDM resistance gene from the B6 mouse strain may have been present on the same chromosome into the $I\text{–}E_\alpha$ transgene had inserted. Wicker *et al.* have demonstrated a role for the *I–A* region in IDDM regardless of *I–E* expression[8]. Non-obese diabetic mice directly transgenic for *I–A* and *I–E* genes will be required to determine more precisely the role of class II in IDDM.

Recent studies of HLA antigens and IDDM in different ethnic groups support a DQ correlation[9–11] (J. A. T., unpublished data). Other genes and environmental factors are likely to be involved in IDDM because only 2 per cent of DQ Asp 57-negative individuals develop the disease. But the DQ correlation is compelling and indicates a major role for DQ in IDDM. It is also subject to experimental verification.

JOHN A. TODD
JOHN I. BELL
Nuffield Departments of Clinical Medicine and Surgery,
John Radcliffe Hospital,
Oxford OX3 9DU, UK

HUGH O. MCDEVITT
Departments of Medicine and Medical Microbiology,
Stanford University of Medicine,
Stanford, California 94305, USA

1. Todd, J. A., Bell, J. I. & McDevitt, H. O. *Nature* **329**, 599–604 (1987).
2. Louis, E. J. & Thomson, G. *Diabetes* **35**, 958–963 (1986).
3. Brown, J. H. *et al. Nature* **332**, 845–850 (1988).
4. Germain, R. N. & Malissen, B. *A. Rev. Immun.* **4**, 281–315 (1986).
5. Todd, J. A., Bell, J. I. & McDevitt, H. O. *Trends Genet.* **4** 129–134 (1988).
6. Svejgaard, A., Platz, P. & Ryder, L. P. *Immun. Rev.* **70** 193–218 (1983).
7. Nishimoto, H. *et al. Nature* **328**, 432–434 (1987).
8. Wicker, L. S. *et al. J. exp. med.* **165**, 1639–1654 (1987).
9. Todd, J. A. *et al. Science* **240**, 1003–1009 (1988).
10. Kohonen-Corish, M. R. J., Serjeantson, S. W., Lee, H. K & Zimmet, P. *Disease Markers* **5**, 153–164 (1987).
11. Fletcher, J. *et al. Diabetologia* (in the press.)