whereas the abundant silicate of the refractory planets and of stony meteorites indicates formation under conditions in which this ratio was greater than one[6]. Accordingly, the bolide responsible for the K/T event is unlikely to have been an asteroid, but seems more likely to have been a comet from the remote outer Solar System.

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Peptides bound to MHC

SIR — A. Y. Rudensky *et al.*[1] describe sequence determinations of sets of naturally processed peptides eluted from immunoaffinity-purified murine MHC class II molecules. The authors claim that only about six different peptides would represent most MHC-bound material. Crucial to this claim are quantitative data on the yield of the various peptides, relative to each other as well as relative to the amount of MHC-protein used as a source. Unfortunately, no such data are given[1], challenging readers to make their own estimation.

The 400–500 μg purified MHC-protein used as a source (see Fig. 1 legend of ref. 1) correspond to about 7 nmol. Consequently, one would expect a similar amount of about 7 nmol peptide to be released from this MHC preparation, which corresponds to about 10 μg peptide, assuming an average relative molecular mass of about 1,500 (Table 1 of ref. 1). If, as Rudensky *et al.* suggest, only six peptides together represent 50–70% of all material, any one dominant peptide should yield approximately 1 μg. In our experience, such an amount of peptide would yield peaks on an HPLC trace taken at 210 nm that are at least 20 times higher than those illustrated in their paper (Fig. 1*b*). Even peptide losses during Centricon filtration of up to 80% would still not explain the extremely poor yield of peptides as suggested by the minute peaks that were apparently found.

Because of the lack of data on the yield of the peptides involved, this consideration seems to suggest that the analysis described by Rudensky *et al.* actually deals with a tiny fraction, perhaps only the most loosely bound, of the peptides that were originally bound to the MHC preparation. Any far-reaching conclusions based on only a few per cent of the MHC-bound peptides seems inappropriate.

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JANEWAY *ET AL.* REPLY — van Noort correctly points out that yields of peptides eluted from MHC class II molecules reported in our paper[1] are not quantitative. We believe that some weakly bound peptides are lost in early phases of MHC class II purification and concentration, and that a significant amount of material may be lost in acetonitrile precipitation, whereas some of the strongly bound peptide may be lost, as van Noort suggests, during Centricon filtration. We have now documented that individual HPLC peaks contain, in addition to the dominant peptide, small amounts of other peptides. Using electrospray ionization tandem mass spectroscopy, D. Hunt and colleagues (personal communication) now find many peptides of different molecular mass at very low concentrations in a single HPLC peak. Thus, our techniques may underrepresent the complexity of peptides associated with MHC class II molecules.

Nevertheless, we do not believe that these considerations undermine the validity of the argument about the complexity of self peptides made in the manuscript[2] accompanying ref. 1, which van Noort ignores. In this paper, we used the Y–A*e* antibody[3] to identify a subset of MHC class II molecules that bind a single peptide derived from the I–E α-chain. This antibody binds 12% of MHC class II molecules on B cells, macrophages and dendritic cells[3] from strain B10.A(5R) and an equivalent number on B cells from B6 mice (I–E α and Y–A*e* negative) transgenic for the I–E α-gene. Recent studies (A.Y.R. *et al.*, manuscript submitted) show that this peptide can occur in different length forms, eluting in distinct HPLC peaks, but that T cells cannot distinguish this variability. Thus, one-eighth of $I\text{-}A^b$ molecules in this strain are occupied by one peptide. This peptide binds strongly to $I\text{-}A^b$ molecules as well as to $I\text{-}A^d$ molecules (A. Sette, personal communication). The yield of this peptide from LB27.4 cells was proportional to its surface abundance[1,2].

Finally, the crucial argument in our paper is based on peptide:MHC density requirements determined by other authors[4,5]. Our data simply limit the complexity of self imposed by these considerations even further. We have never claimed, as van Noort states, that only six peptides are bound to MHC class II molecules; indeed, we have data that disprove this notion (A.Y.R., manuscript submitted). Thus, whether or not our peptide yields are quantitative, we believe that immunological self is of limited complexity, and that this has important implications for self tolerance. Similar arguments have been made for MHC class I molecules (D. Wiley, personal communication).

It is important that van Noort's correct identification of the nonquantitative nature of our peptide elution strategy is not confounded with his subsequent surmises, which ignore essential data obtained independently of this technique.

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Crystal faces

SIR — J. A. D. Dickson[1] claims to be the first to report crystallographically controlled isotope fractionation of stoichiometric ions in his study of natural calcite, where he found a fractionation of the carbon and oxygen isotopes under the crystallographically differing faces of crystals. But our study[2] on natural amethyst showed that the $^{18}O/^{16}O$ ratio increases in the order *z*-sector, *r*-sector, *m*-sector of quartz. In a subsequent paper[3] on natural smoky quartz, we confirmed the order *r*-sector, *m*-sector.

The sampling methods used by Dickson and by us on crystals of 3–7-cm size are different. Dickson scraped material from the external surfaces of the crystals, which he admits causes sampling errors due to isotope mantle zoning, whereas we took the samples from polished slices of the crystals, where the boundaries between the differently coloured sectors are visible. This enabled us to compare samples from the same range of mantle zones. For millimetre-sized crystals, Dickson took samples from slices with mantle and sector zoning, as we did for our larger crystals, but he could not identify the faces belonging to these sectors.

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