Scrapie agent unlike viruses in size and susceptibility to inactivation by ionizing or ultraviolet radiation

SIR—The validity of using ionizing radiation for estimating the biologically effective sizes of macromolecule might appear to be called into question by Rohwer[1]. His Fig. 4, showing very little correlation between inactivation dose and molecular weight (MW), purports to be based on a "literature search". That search evidently led him for the most part only to secondary, in some instances tertiary, sources (13 out of 24 references for inactivation doses are from Kaplan and Moses[2], who had made use of a previous compilation by Terzi[3]). Some of the references are wrong—always a pitfall when these are taken from another paper without a check; and many of the "inactivation doses" used in Rohwer's figure were from experiments that were quite unsuitable for yielding data from which MWs could be calculated. The requirements for the application of "target theory"[4] are: (1) that the test macromolecules should be irradiated dry; (2) that oxygen should be present; (3) that temperatures should not be so low that charge migration is prevented; (4) that the radiation dosimetric methods should be fully reliable. Reasons for these minimal requirements have been given elsewhere[5].

Our estimate[6] of the MW of the scrapie agent, about 1.5×10^5, was based on the Lea theory[4], which, in our experience, has proved a reliable guide, of great predictive value. There is a good match between target theory and independent estimates of MWs of proteins and virus nucleic acid cores, over a range of 5×10^4 to 10^8 (refs 5, 7, 8, 9). Almost all the significant departures from the Lea theory[4] displayed in Rohwer's figure can be explained. For most of them, Kaplan and Moses[2] were used as the source for inactivation dose; they will be referred to as K & M in the following few examples:

Newcastle disease virus. Inactivation dose too low to fit the Lea theory. K & M cited Rubin and Temin[10], who irradiated the virus in suspension, so radiolysis products of water would have contributed to the inactivation.

Yellow fever virus. Molecular weight too low, about one-tenth of what we[7] took from our independent source[11]. Rohwer's source[12] makes no mention of the MW of this virus.

Vaccinia. D_{37} incorrectly quoted by Rohwer from K & M who cited McCrea[13] incorrectly. McCrea's Fig. 4 gives D_{37} as 2.9×10^4 r. Even this may be an overestimate, since the material was evidently irradiated *in vacuo*.

Shope papilloma. D_{37} plotted as too high to fit the Lea theory. K & M's source is Syverton *et al.*[14], who gave the dose for "total inactivation"—an unknown multiple of the inactivation dose, which will deliver an average of one "hit" per macromolecule, and therefore, because of the random nature of the ionizing events, will leave a fraction e^{-1} of the irradiated population biologically active.

The need for brevity inhibits enumeration of all the errors included in Rohwer's Fig. 4. But perhaps he may now be stimulated to make a more thorough literature search, paying attention to the validity of the sources cited for MWs as well as to the experimental details of studies yielding "inactivation doses" for viruses. He would find it of assistance also to include in his review of molecular weights versus inactivation doses some reliable results on proteins, inactivation doses for some of them being less than for the scrapie agent[8,15].

Rohwer states that the "small size ... inferred from scrapie's resistance to inactivation by ionizing radiation established and continues to foster expectations of an unconventional structure". He failed to refer to the studies which so strikingly confirmed those expectations, namely the completely unvirus-like UV action spectrum of the scrapie agent[16,17].

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● A reply from Rohwer may appear in a later issue.

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Accretion of the China blocks

IN their discussion of the assembly of the China blocks, Lin, Fuller and Zhang remark that they have "no detailed palaeomagnetic results from Middle Triassic to Lower Jurassic" for the South China block and the North China block, which prevents accurate timing of the amalgamation of these blocks. Palaeontological data provided by recent Thai-French work in northeastern Thailand may be of interest in this regard, as they give a latest possible date for the establishment of a land connection between Indochina and Laurasia and, indirectly, for the accretion of the South China and North China blocks.

Among the continental vertebrates found in the late Triassic (Norian) Huai Hin Lat Formation of northeastern Thailand, the lungfish *Ptychoceratodus* cf. *szechuanensis* is closely related to a form from South China[2]; this is in agreement with the reconstruction by Lin, Fuller and Zhang which shows the Indochina block attached to South China as early as the Permian.

Furthermore, other vertebrates from the Huai Hin Lat Formation, such as phytosaurs[3], turtles[4] and stegocephalian amphibians[5], show remarkable affinities with forms from the classical late Triassic localities of Germany. These resemblances show that by late Triassic times, the Indochina block had already been "colonized" by a Laurasian land vertebrate fauna[6]. These vertebrates must have reached the Indochina block via the South China block and the North China block, which itself had become accreted to the Russia/Siberia block in the late Permian according to Lin, Fuller and Zhang[1].

There is no other plausible faunal interchange route between Europe and South-East Asia for Laurasian land vertebrates in the early Mesozoic. Therefore, it can be concluded that the South China block and the North China block had probably become accreted by the beginning of the late Triassic. This is in agreement with Lin, Fuller and Zhang's suggestion[1] that "amalgamation occurred during the Triassic Indosinian orogeny", but available palaeontological data from Thailand would not preclude an even earlier accretion.

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