Ubiquitin and dementia

SIR—Gallo and Anderton¹ draw attention to the demonstration by ubiquitin immunocytochemistry of ubiquitin-immunoreactive intraneuronal inclusions in the major neurodegenerative disorders, including Alzheimer's, Parkinson's and motor neuron diseases.

We wish to make two additional points. First, we believe that diffuse Lewy body disease can be added to Gallo and Anderton's table of common neurological diseases characterized by the presence of ubiquitinated filamentous inclusion bodies. We and others have recently shown that ubiquitin immunocytochemistry, coupled with classical neuropathological techniques, reveals diffuse Lewy body disease as a common cause of dementia^{2,4}—it accounts for 15–27 per cent of cases of dementia in hospital necropsies, whereas it was previously considered rare. We have also used ubiquitin immunocytochemistry to study the disorder quantitatively, and have shown that severity of dementia is related to the density of cortical inclusions but not to measures of sub-cortical pathology⁵.

Second, ubiquitinated filamentous inclusions are not confined to neurons but also occur in astrocytomas and, outside the nervous system, in alcoholic liver disease, a myopathy⁶ and in some viral diseases⁷. Many (but not all) of these inclusions contain intermediate filaments^{1,6}. The significance of this last observation could relate to the cell stress or 'heat-shock' response. It is well known that

experimental chemical and thermal stresses cause specific, reversible intermediate-filament collapse in various cell types⁸. We have recently shown⁹ that the expression of a human polyubiquitin gene is increased in spinal cord and brain in motor neuron disease. Polyubiquitin genes are inducible by heat shock and are essential for cell survival¹⁰.

R. J. MAYER

M. LANDON

F. J. DOHERTY

Department of Biochemistry,

J. S. LOWE

G. P. REYNOLDS

Department of Pathology,

E. J. BYRNE

Department of Health Care of the Elderly,
University of Nottingham Medical School,
Nottingham NG7 2UH, UK

G. G. LENNOX

D. JEFFERSON

R. B. GODWIN-AUSTEN

Department of Neurology,
Queens Medical Centre,
Nottingham NG7 2UH, UK

1. Gallo, J.-M. & Anderton, B.H. *Nature* **337**, 687 (1989).
2. Lennox, G. *et al.* *Lancet*, 323–324 (1989).
3. Lennox, G. *et al.* *J. Neurol. neurosurg. Psych.* **52**, 67–71 (1989).
4. Perry, R. H. *et al.* *Lancet*, 166 (1989).
5. Lennox, G. *et al.* in *Neural Mechanisms in Disorders of Movement* (eds Crossman, A.R. & Sambrook, J.) 265–268 (Libbey, London, 1989).
6. Lowe, J. *et al.* *J. Path.* **155**, 9–15 (1988).
7. Mayer, R.J. *et al.* *Biochem. Soc. Symp.* **55**, 193 (1989).
8. Mathews, M.B. & Feramisco, J.R. *Cold Spring Harbor Symp. quant. Biol.* **46**, 985–996 (1981).
9. Heggie, P. *et al.* *Neurosci. Lett.* (in the press).
10. Finley, D., Ozkaynak, E. & Varshavsky, A. *Cell* **48**, 1035–1046 (1989).

Silica polymorphs

SIR—In the contents panel of *Nature* of 18 May 1989, an explanation of a paper¹ on zeolite is accompanied by a figure that is, in fact, taken from our paper² in the same issue on new crystal structures of silica (SiO₂). Curiously, this inadvertent association reminds us of a notion that has

been at the back of our minds for some time—namely, that silica, which has typical framework structures comprising networks of tightly bound units (SiO₄ tetrahedra in this case), could assume open crystal structures that are reminiscent of zeolites.

As an old example³, melanophlogite, which is mentioned in a standard textbook

MIRAGE or no mirage?

SIR—Brenner *et al.*¹ doubt the potential of the Mössbauer-isotope-based method of cancer therapy we described² because of their calculation that several greys of low-energy gamma rays would be necessary to achieve the same effect by conventional mechanisms that we achieved with 10⁻⁵ Gy of resonant Mössbauer radiation. There are three reasons for this incongruity. First, although the cross-sections are small for all atoms found in tissue, so that most of the gamma rays are absorbed by water molecules and produce random transient free radicals, the Mössbauer cross-section for ⁵⁷Fe (with resonant 14.4-keV gamma rays) is about 100,000 times larger.

Considering the abundance of water molecules and ⁵⁷Fe atoms in these cells, and considering the cross-sections of water and ⁵⁷Fe, we estimate that about half of the gamma photons will be absorbed by ⁵⁷Fe atoms. Second, the strategic position of the ⁵⁷Fe atoms (bonded to molecules that are intercalated in the DNA), makes absorption by ⁵⁷Fe atoms much more effective than absorption by random water molecules. Third, gamma-photon absorption by ⁵⁷Fe produces an Auger cascade, of about eight high-LET electrons, and a highly-charged iron atom, within a femtosecond. Based on our results and on the results of radiolabelling experiments with a similar mechanism, we estimate the relative cell-killing efficiency of our MIRAGE processes compared with the conventional radiotherapy processes at about 10⁵ to 1.

Humm³ points out that ⁵⁷Fe would only be useful for superficial lesions and has asked for a control experiment at a Doppler shift well off the Mössbauer peak. In response to the former, we observe that it would be possible to use Mössbauer isotopes with more penetrating gamma

by Wells⁴, is thought to have a silicon framework of chlorine hydrate structure⁵, as shown in the figure. Although this particular polymorph could be an impure phase of silica containing some elements such as sulphur or carbon, it serves to indicate that silica and related compounds could assume more polymorphs than currently expected.

HIDEO AOKI

SHINJI TSUNEYUKI

Department of Physics,
University of Tokyo,
Hongo, Tokyo 113, Japan

1. Anderson, M.W. & Kilnowski, J. *Nature* **339**, 200–203 (1989).
2. Tsuneyuki, S. *et al.* *Nature* **339**, 209–211 (1989).
3. Zak, L. *Amer. Mineralogist* **57**, 779–796 (1972).
4. Wells, A.F. *Structural Inorganic Chemistry* 5th edn Ch. 23 (Oxford University Press, 1984).
5. Pauling, L. & Marsh, R.E. *Proc. natn. Acad. Sci. U.S.A.* **38**, 112–119 (1952).