the livers of Z homozygotes. Polyacrylamide gel electrophoresis confirmed that the Z polymers, like the liver inclusion[10,11], are formed by non-covalent bonding and are readily dissociable to monomers in detergents in the absence of thiol reducing agents. The critical evidence comes from the electron microscopy of the polymers (Fig. 3). Incubation of Z antitryptin results, as predicted, in the formation of multiple bead-like polymers usually in filaments of 4–10 molecules. Examination of α_1-antitrypsin inclusions isolated from the liver of a Z homozygote shows that they are formed of a myriad tangle of filaments, identical in structure to those seen in incubated isolated Z antitrypsin. Confirmation of this identity is provided by circular dichroism measurements in the far ultraviolet (Fig. 3*c*); these show superimposable spectra for both the fragmented liver inclusions and the *in vitro* polymers. Furthermore, both have the profile predictable[4] for loop–sheet bonding, intermediate between that of intact (S) and cleaved (R) antitrypsin.

The polymerization of isolated Z antitrypsin was observed previously[12], as was the formation of intracellular aggregates[13], but as the latter report points out, these observations do not by themselves explain the features of the disease. The occurrence of aggregation in the endoplasmic reticulum and the fact that it involves only 85% of the Z antitrypsin both follow from the mechanism of loop–sheet intermolecular bonding. This will predictably occur as the point of greatest concentration is approached in the hepatocyte just before entry to the Golgi apparatus. Furthermore, our results show that loop–sheet polymerization is an equilibrium process and there will always be some monomers as well as polymers. This accounts for the secretion of some 15% of Z antitrypsin into the plasma as functional monomers, a level that is insufficient to protect the lungs against the proteolytic damage that leads to emphysema[2].

The findings also explain previous observations that the number and density of the liver inclusions vary considerably between individuals, and from time to time in a single individual. As is shown here, the formation of liver aggregates will be dependent on temperature and concentration. At times of stress the formation of inclusions in the hepatocyte will be likely to overwhelm the degradative mechanisms responsible for their turnover. Antitrypsin is an acute phase protein and as such undergoes a manifold increase in production in association with temperature increases of up to 41 °C during bouts of inflammation. These stresses must contribute to the variable severity of hepatocellular involvement in children. There is now strong evidence[14] to support earlier conclusions[2] that the liver disease of the homozygote is a direct consequence of antitrypsin accumulation and degradation in the hepatocyte. It follows that a first step in the prevention and amelioration of liver involvement in the Z homozygote infant should be the use of simple established therapies for the limitation of inflammation and pyrexia. In the longer term there is the challenging possibility of more specific interventions such as the delivery to the hepatocyte of engineered loop peptides specific to α_1-antitrypsin. □

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CORRECTIONS

Were small galaxies once the dominant cosmological population?

L. L. Cowie, A Songaila & E. M. Hu

Nature **354,** 460–461 (1991)

IN this Letter the K correction was applied with the wrong sign. This in no way affects the conclusions or discussion, but the values of the variable M_K which appear in the table and figure must be corrected accordingly. We are grateful to W. Sutherland and R. Kron for pointing out this mistake.

Indirect chemical effects of methane on climate warming

Jos Lelieveld & Paul J. Crutzen

Nature **355,** 339–342 (1992)

IN preparing this paper, a typographical error in equation (4) has escaped our attention. The correct formulation is

$$G_{CO_2}(t) = -\frac{\partial}{\partial t} R_{CH_4}(t) \int_t^T f_{CO_2} R_{CO_2}(t'-t)\, dt' \qquad (4)$$

Close linkage of glucokinase locus on chromosome 7p to early-onset non-insulin-dependent diabetes mellitus

Ph. Froguel, M. Vaxillaire, F. Sun, G. Velho, H. Zouali, M. O. Butel, S. Lesage, N. Vionnet, K. Clément, F. Fougerousse, Y. Tanizawa, J. Weissenbach, J. S. Beckmann, G. M. Lathrop, Ph. Passa, M. A. Permutt & D. Cohen

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Genetically engineered alteration in the chilling sensitivity of plants

N. Murata, O. Ishizaki-Nishizawa, S. Higashi, H. Hayashi, Y. Tasaka & I. Nishida

Nature **356,** 710–713 (1992)

THIS Letter in the 23 April issue contains errors in the figure legends, involving the definition of parts *b*, *c* and *d*. Figure 1 legend should begin "Chilling-induced damage to the photosynthetic activity of leaves of transgenic plants. *a*, Transformant with pBI-121 (control; Clontech). *b*, Transformant with *pSQ*. *c*, Transformant with *pARA*. Methods. (The same as printed.)" Figure 2 legend should begin "Chilling-induced visible damage of transgenic plants. *a*, Wild type. *b*, Transformant with pBI-121 (control). *c*, Transformant with *pSQ*. *d*, Transformant with *pARA*." □