

apo-metalloproteins was supported by K. Lerch and by U. Weser and H. Hartmann (University of Tübingen). They showed reconstitution of different copper-dependent apoproteins with *Neurospora* and yeast copper-metallothionein respectively. However, no single function can be ascribed to metallothionein. M. Webb and K. Cain (MRC Toxicology Unit, Carshalton) demonstrated that in rats the protein can act as a mobile zinc and copper reserve in maintaining homeostasis or as a control agent for zinc and copper uptake in fetal and neonatal life stages. The detoxication role for controlling cadmium and mercury may well be a carry-over of this fetal mechanism into adult life.

Introducing the topic of metallothionein biosynthesis, R. Palmiter and D. Durham (University of Seattle) described experiments carried out on mouse metallothionein gene structure. Recombinant cDNA and genomic clones corresponding to mouse metallothionein-1 have been isolated and characterized. The DNA sequence indicates that this gene spans 1,100 base pairs with two intervening sequences (see Palmiter *Nature* 292; 267, 1981). The gene is regulated at the transcriptional level by heavy metals and less efficiently by glucocorticoid hormones both *in vivo* and in isolated cell lines.

Several cell lines that were selected for resistance to cadmium were shown to have amplified their metallothionein genes, allowing enhanced synthesis of this metal-binding protein. In an elegant study using DNA recombinant techniques, the regulatory portion of the mouse metallothionein gene was fused to the structural gene of thymidine kinase, rendering this enzyme inducible by Cd<sup>2+</sup>. Furthermore, evidence was presented that the inducibility of the mouse metallothionein gene is controlled by DNA methylation.

The application of high-pressure liquid chromatography to the assessment of homogeneity, structural investigations and the isolation of fragments from enzymatic and chemical cleavage of metallothioneins was described by K.J Wilson (University of Zurich). Other communications emphasized the importance of these metalloproteins in the homeostatic control of specific metals not only in mammalian species but also in yeasts, marine arthropods, crustaceans, eels and sea-birds. From the significant developments that were reported in all fields it seems that the elucidation of the mechanisms of synthesis, degradation, gene regulation and of the structural arrangements at the metal-binding sites of the metallothioneins is 'just around the corner'.

## Treating urea cycle defects

from Vicente Rubio and Santiago Grisolia

THERE is much interest in the treatment of inborn errors of the urea cycle. As pointed out by Smith<sup>1</sup> in her excellent review, the prospects for patients with deficiencies of this cycle are far better now than in the recent past. Therefore, we regret her omission of *N*-acetylglutamate synthetase deficiency and of *N*-carbamoyl glutamate as a therapeutic agent for this condition.

*N*-acetylglutamate, synthesized by *N*-acetylglutamate synthetase, is the physiological activator of mitochondrial carbamoyl phosphate synthetase. Deficiency of *N*-acetylglutamate synthetase should induce hyperammonaemia. The deficiency cannot be treated by administration of *N*-acetylglutamate because this compound is deacylated by cytosolic deacylases and it does not permeate the mitochondrial membrane. However, carbamoyl phosphate synthetase is also activated by analogues of *N*-acetylglutamate, such as *N*-carbamoyl glutamate<sup>2</sup>, which is resistant to deacylases and which, when injected into rats, can be found in the mitochondrial matrix of liver cells<sup>3</sup>.

Therefore, it is not surprising that

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Bachmann *et al.*<sup>4</sup>, who recently described the first case of hyperammonaemia due to *N*-acetylglutamate synthetase deficiency, found that *N*-carbamoyl glutamate is indeed extremely effective in the treatment of this condition.

As indicated by Smith, increases in the levels of *N*-acetylglutamate leading to greater activation of carbamoyl phosphate synthetase may improve control of ammonia levels in ornithine carbamoyl transferase, arginosuccinate synthetase and arginosuccinate lyase deficiencies and in partial defects of carbamoyl phosphate synthetase. Thus, although *N*-carbamoyl glutamate should be regarded as the specific treatment for *N*-acetylglutamate synthetase deficiency, its efficacy in these conditions should also be tested. *N*-carbamoyl glutamate may also be useful for patients with propionic or methylmalonic acidaemias, for which decreased levels of *N*-acetylglutamate are postulated as a cause for the hyperammonaemia associated with these syndromes.

1. Smith, I. *Nature, News and Views* 291, 378 (1981).
2. Grisolia, S. & Cohen, P. P. *J. Biol. Chem.* 198, 561 (1952).
3. Rubio, V. & Grisolia, S. *Enzyme* (in the press).
4. Bachmann, C. *et al. New Engl. J. Med.* 304, 543 (1980).



### 100 years ago

#### THE COMET OF 25 JUNE

THE appearance of a large comet has afforded an opportunity of adding to our knowledge of these bodies by applying to it a new means of research. Owing to the recent progress in photography it was to be hoped that photographs of the comet and even of its spectrum might be obtained and peculiarities invisible to the eye detected.

It was obvious that if the comet could be photographed by less than an hour's exposure there would be a chance of obtaining a photograph of the spectrum of the coma, especially as it was probable that its ultra-violet region consisted of but few lines. In examining my photographs of the spectrum of the voltaic arc, a strong band or group of lines was found above H, and on the hypothesis that the incandescent vapour of a carbon compound exists in comets, this band might be photographed in their spectrum.

Accordingly at the first attempt a photograph of the nucleus and part of the envelopes was obtained in seventeen minutes, on the night of June 24, through breaks in the clouds. On succeeding occasions, when an exposure of 162 minutes was given, the tail impressed itself to an extent of nearly ten degrees in length.

I next tried by interposing a direct-vision prism between the sensitive plate and the object-glass to secure a photograph which would show the continuous spectrum of the nucleus and the banded spectrum of the coma. After an exposure of eighty-three minutes a strong picture of the spectrum of the nucleus, coma, and part of the tail was obtained, but the banded spectrum was overpowered by the continuous spectrum.

I then applied the two-prism spectroscopy used for stellar spectrum photography, anticipating that, although the diminution of light would be serious after passing through the slit, two prisms, and two object-glasses, yet the advantage of being able to have a juxtaposed comparison-spectrum would make the attempt desirable, and, moreover, the continuous spectrum being more weakened than the banded by the increased dispersion, the latter would become more distinct. Three photographs of the comet's spectrum have been taken with this arrangement with exposures of 180 minutes, 196 minutes, and 228 minutes, and with a comparison spectrum on each. The continuous spectrum of the nucleus was plainly seen while the photography was in progress. For the present it suffices to say that the most striking feature is a heavy band above H which is divisible into lines, and in addition two faint bands, one between G and h, and another between h and H. I was very careful to stop the exposures before dawn, fearing that the spectrum of daylight might become superposed on the cometary spectrum.

It would seem that these photographs strengthen the hypothesis of the presence of carbon in comets, but a series of comparisons will be necessary, and it is not improbable that a part of the spectrum may be due to other elements.

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