explosions to explosively amplify the perturbed mass scale up to galactic dimensions, as discussed by J. Ostriker & L. Cowie (*Astrophys. J. Lett.* **243**, 127; 1981) and S. Ikeuchi (*Publ. astr. Soc. Japan* **33**, 211; 1981).

The one source of solace is that the large-scale bulk motion does seem to be a likely consequence of the existence of the Hubble bubbles. These apparent voids, on scales up to 50 h^{-1} Mpc, could have been generated by the large-scale flows which would evidently be present in a hot dark matter-dominated universe. Of course, these flows must have maintained considerable coherence to preserve the well-defined bubble surfaces on which the galaxies are found. If this were the case, the bubble interiors should be genuinely devoid of matter.

There is an alternative, needless to say, offered by advocates of cold dark matter — namely that the voids are illusory, simply reflecting the large-scale inhomogeneity of the luminous matter, concentrated into great clusters and into ridges of galaxies, from the relatively smooth dark matter distribution. Such a situation could arise if only the highest peaks in the primordial fluctuation spectrum managed to form galaxies. But however this biasing arose, one consequence is inevitable: the large-scale flows must turn out to be an artefact of observational error. Astronomers are now rushing to verify the reality of the large-scale flows: their confirmation promises to mark a turning point in cosmology. □

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Biochemistry

New role for transfer RNA

from Robert Haselkorn

BIOCHEMISTRY is conservative, and as a rule the same biochemical step is carried out in pretty much the same way throughout the kingdoms, microbes and man alike. It is unusual, therefore, that this rule is broken by a basic step in the biosynthesis of haem and chlorophyll. These molecules are both modified forms of a conjugated ring molecule called a tetra pyrrole nucleus, made by the condensation of several molecules of the amino acid δ-amino-levulinic acid. But it turns out that δ-amino-levulinic acid is made in very different ways in the cells of animals and plants. As Schön *et al.* report in this issue (*Nature* **322**, 281; 1986), a glutamyl transfer RNA molecule participates in this pathway in chloroplasts.

Labelled acetate and glycine were shown 40 years ago (Shemin, D. & Rittenberg, D. *J. biol. Chem.* **166**, 621; 1946) to be the exclusive precursors of the carbon atoms of haem in mammals and, later, in photosynthetic bacteria. Subsequent work showed that acetate entered the tricarboxylic acid cycle and the key step in the synthesis of haem is the condensation of the cycle intermediate succinyl CoA, with glycine, to make δ-amino-levulinic acid. This is then transported from the mitochondria to the cytoplasm where subsequent steps in porphyrin biosynthesis occur. When the radioactive tracer experiments were eventually repeated using plant extracts (Beale, S.I., Gough, S.P.& Granick, S. *Proc. natn. Acad. Sci. U.S.A.* **72**, 2719; 1975), it was found that the carbon atoms of δ-amino-levulinic acid were not derived from acetate and glycine but from α-ketoglutarate via glutamate.

During the past decade it was shown that glutamate is reduced to glutamic semialdehyde and the latter transaminated to produce δ-amino-levulinic acid in chloroplast extracts. Various mechanisms were proposed for the glutamate reduction, some involving phosphorylated intermediates. Participation of RNA in the conversion of glutamate to δ-amino-levulinic acid was first indicated by work at the Carlsberg Laboratory in Copenhagen and at the University of Iowa (Huang, D.-D. *et al. Science* **225**, 1482; 1984). Evidence that the RNA is a glutamyl-tRNA was obtained independently by W.-Y. Wang in Iowa, S.I. Beale at Brown University and the group of D. Söll at Yale University. In this issue, Söll's group reports that the intermediate in barley chloroplasts is one of three isoaccepting glutamyl-tRNAs. This tRNA, which has the unusual modified base 5-methylaminomethyl-2-thiouridine in the first anticodon position, is the only one that functions as a substrate for the reduction to glutamic-semialdehyde. Whether this glutamyl-tRNA also functions in protein synthesis is not yet known. The tRNA is encoded in chloroplast DNA.

The two alternative paths to δ-amino-levulinic acid arose, I believe, separately in the heterotrophic and photosynthetic bacteria on the one hand and in cyanobacteria on the other. Heterotrophic bacteria are the evolutionary precursors of mammalian mitochondria while cyanobacteria are the ancestors of chloroplasts. Succinyl CoA and glycine are available raw materials in heterotrophic bacteria, but succinyl CoA is in short supply in most cyanobacteria, which lack the complete tricarboxylic acid cycle. Reduction of an organic acid to an aldehyde proceeds nicely via an ester intermediate; what better source of glutamate ester than glutamyl-tRNA, already on hand for protein synthesis? To avoid competition for the same intermediate, the glutamyl-tRNA used to make δ-amino-levulinic acid should be modified to prevent its use in protein synthesis, but whether that is actually the case remains to be determined, as noted above.

The failure to observe incorporation of glycine into porphyrins in plants and most green algae suggests that the chloroplast pathway provides δ-amino-levulinic acid for all biosynthesis in plants. What is wrong with plant mitochondria? Where did they come from? Plant mitochondrial DNA is much larger than its mammalian counterpart, replete with direct and inverted repeats that recombine frequently to generate an array of circular molecules. Some plant mitochondrial DNA sequences are homologous to chloroplast DNA; at least one such sequence originated in the chloroplast because it encodes a major chloroplast enzyme. Other plant mitochondrial DNA sequences have nuclear homologues, suggesting a history of rather promiscuous exchange of genetic material between organelles in the evolution of plants. With δ-amino-levulinic acid supplied by chloroplasts, selection for the mitochondrial pathway in plants would be relaxed and the relevant genes could have been lost in the shuffle.

An exception to the general proposal that plants lack the glycine-succinyl CoA condensation pathway is known. The alga *Euglena*, evolutionarily bizarre in other respects, has been shown to contain both pathways (Weinstein, J. & Belae, S.I. *J. biol. Chem.* **258**, 6799; 1983). However, so far the green algae *Chorella* and *Chlamydomonas*, as well as cyanobacteria, are believed to contain only the plant pathway to δ-amino-levulinic acid. A number of the outstanding questions raised by Schön *et al.* could be approached conveniently by the isolation and characterization of mutants, for which *Chlamydomonas* and *Anacystis* appear to be the organisms of choice. Useful in this connection could be a compound called gabaculine (5-amino-1,3-cyclohexadienyl acid) that probably inhibits the transaminase that converts glutamic semialdehyde to δ-amino-levulinic acid (Gardner, G. & Gorton, H.L. *Plant Physiol.* **77**, 540; 1985). A collection of mutants resistant to gabaculine ought to include a few that affect the tRNA and the tRNA ligase as well as the transaminase. Examination of the δ-amino-levulinic acid pathway in fungi would also be rewarding from an evolutionary viewpoint. □

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