

that reacts with DNA, and instead provide suggestive, though not conclusive evidence that a non-K-region diol-9,10-epoxide is primarily implicated in the metabolic activation of benzo[a]pyrene. Support for this has also come from the similar studies of Weinstein *et al.* (*Biochem. biophys. Res. Commun.*, **70**, 1172; 1976). Weinstein, Harvey and their collaborators have now succeeded in isolating and identifying the adducts from RNA degradation after *in vivo* incubation of benzo[a]pyrene in bovine bronchial explants. The intermediate is the (1) 7 β ,8 α -dihydroxy-9 α ,10 α -epoxy-7,8,9,10-tetrahydro derivative, that is a non-K-region diol epoxide, with subsequent attachment of the 10 position to the 2-amino guanine group (*Science*, **193**, 592; 1976). This compound has also been shown by Newbold and Brookes (*Nature*, **261**, 53; 1976) and Sachs *et al.* (*Proc. natn. Acad. Sci. U.S.A.*, **73**, 607; 1976) to be by far the most active mutagen (and therefore carcinogen) of a range of possible benzo[a]pyrene metabolites, including the K-epoxide.

There still remain however, several unanswered questions concerning the ultimate carcinogenic intermediates arising from benzo[a]pyrene, and indeed from polycyclic aromatic hydrocarbons in general. Certainly the diol epoxide is by no means the only reactive intermediate; others remain to be isolated and defined. One should perhaps add that although there is now some evidence that the benzo[a]pyrene diol epoxide is an intermediate in other tissues and species during hydrocarbon binding to DNA, it is not really known whether the same is true for binding to other cellular macromolecules. □

Nucleic acid modification at Erlangen

from Ernest Borek

An international conference on post-transcriptional modification of nucleic acids, organised by Drs Helga and Walter Kersten, was held at the University of Erlangen on July 19–24, 1976.

THE field of nucleic acid modification is burgeoning, making this a most timely meeting. In eukaryotes every species of nucleic acid is modified and the number of known modifications is increasing—six new modifications were reported at this meeting.

W. Kersten (University of Erlangen)

led a round table discussion on the status of tRNA methyltransferases and isoaccepting tRNAs in tumour tissue. In all tumours, except benign ones, the tRNA methyltransferases are altered both qualitatively and quantitatively compared with their counterparts in normal tissue. All tumours examined contain novel isoaccepting tRNAs some of which are also found in embryonic tissue. There is no evidence for extensive hypermethylation of bulk tRNA isolated from tumour tissue, however, but since there are only a few tumour-specific isoaccepting tRNAs in each tumour, each of these purified tRNAs will have to be analysed. The extraordinarily high turnover of tRNAs in tumour tissue has been established recently by reliable analyses of urinary excretion products stemming from the breakdown of tRNA, determined at the US National Cancer Institute. A normal adult may be excreting about 2 mg of dimethylguanosine in his urine per day whereas some patients with Burkitt's lymphoma and cancer of the breast may be excreting as much as 20 mg. If we assume a tumour burden of 1–2 pounds per 100-pound patient, then 1–2% of his metabolising machinery may be producing the breakdown product at a rate 500% higher than a corresponding

amount of normal tissue. Some unknown effect of the tumour on the metabolism of the rest of the body cannot be excluded. Such a high turnover of tRNA has also been demonstrated recently in an animal model.

The significance of these aberrations in tumour metabolism is, of course, obscure. They may be part of the oncogenic process or they may contribute to the maintenance of the morbid condition. In view of the many functions and activities of tRNA the problem presents an interesting challenge.

Nothing is yet known about methylation of DNA in tumour tissue. The technology of eukaryotic DNA methyltransferase is still lagging behind the rest of the field, because of the impossibility until recently of preparing soluble enzymes, and there are still conflicting reports of cofactor requirements.

Large strides have been made, however, in the understanding of rRNA modification and processing. J. Dahlberg (University of Wisconsin) identified some of the "spacer" polynucleotides between 16S and 23S rRNA genes as tRNA genes, two of which have been identified as tRNA^{Glu}₂ and tRNA^{Ile}₁. This distribution can account for the coordinate control of the transcription of tRNA and rRNA. R. J. Planta (University of Amsterdam) reported on the species specificity of rRNA modification. The ψ (pseudouridine) content of bacteria, yeast and human rRNA, per thousand nucleotides, is 2.5, 8 and 12 respectively. New modified nucleosides are still turning up. Planta has identified a ψ methylated at N₁ and hypermodified at N₃ by an α -amino- α -carboxyl-propyl moiety. (The latter stems from methionine by the elimination of the thiomethyl group.) Nishimura had reported earlier on the modification of U in tRNA by the same fragment of methionine. The versatility of S-adenosylmethionine as the progenitor of modifications is astonishing.

Nishimura (National Cancer Institute, Tokyo) reported his latest studies on the fascinating hypermodified Q base which is present, adjacent to the anticodon, in several tRNAs of many species. What had been thought to be an isomer, Q*, is actually a still more modified form of it. In Q*, position 4 of the cyclopentene ring can be condensed with either mannose or galactose. The method of achieving modification of tRNA by the Q base is fascinatingly complex. In 1972, Farkas (University of Tennessee) discovered an enzyme which inserts guanine into tRNA^{His} of reticulocytes. Nishimura has now found a function for this "guanine insertase"—it introduces a guanine to replace the Q base

Curious atom

from W. T. Toner

A HYDROGEN-like atom in which short-lived elementary particles substitute for both the nucleus and the orbital electron has been detected as the direct product of the decay of a third unstable elementary particle. Professor Schwartz and his colleagues (Coombes *et al.*, *Phys. Rev. Lett.*, **37**, 249; 1976) hope that a study of this most intriguing scientific curiosity will yield new information on the properties of π and μ mesons.

The parent is the longer lived of the two neutral K-mesons, the K_L⁰ which frequently decays into a π meson, a μ meson and a neutrino. In a minute fraction ($\sim 10^{-7}$) of these decays, the oppositely charged mesons are emitted travelling by chance in the same direction with such similar velocities that they remain together long enough to be bound by their mutual electrical attraction. The bound systems are observed after they have passed down a long straight channel swept clear of charged particles by a magnetic field, in an apparatus which detects their charged components when the " π - μ atoms" are dissociated in an aluminium foil.