−3 (relative to the A of ATG) A is better than G which is much better than Y, and at position +4, G is better than T. These are the two most important positions. She has also shown that some initiation can occur at a 'better' sequence downstream from the first initiation codon. The nucleotide sequence surrounding methionine 596 is AAGATGG. Thus there is an A at −3 and a G at +4, which by Kozak's hypothesis makes the sequence a good initiation region. At the start codon predicted by Kang *et al.* the sequence GCGATGC has a G at −3 and a C at +4.

Of the 19 other methionine residues in the sequence only that at amino acid 141 is close to the optimal Kozak sequence. Indeed, less than 5 per cent of eukaryotic mRNAs have the ideal sequence suggesting that correct initiation is regulated by other factors. Thus it is conceivable that failure of regulation leads to inappropriate initiation at methionine 596 in Alzheimer's disease. The peptide formed would not necessarily be inserted into the cell membrane, overcoming the difficulty of intramembrane cleavage raised by Kang *et al.*, as that region of the peptide would be exposed in the cytoplasm.

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Chloranthoid angiosperms

SIR—The report by Friis *et al.*[1] providing new evidence for chloranthoid angiosperms based on fossil androecia with pollen *in situ* from the Lower and Upper Cretaceous, is a very stimulating addition to previous palaeopalynological knowledge, particularly that due to Muller[2] who succeeded in reconstituting the continuous history of the *Clavatipollenites–Ascarina* complex (Chloranthaceae) from the Aptian onwards. The palaeobotanical record shows that some chloranthoid angiosperms with small, simple, anemophilous or entomophilous, unisexual or bisexual flowers must have played a dominant part in the earliest phases of angiosperm evolution. Friis *et al.* agree that these results contrast with those of most neobotanists who consider the chloranthaceae flower derived, compared to the large Magnoliales chlamydous flowers. Only a few botanists[3,4] have rejected this last view.

I would like to point out that as early as 1981 I published a paper[5] entitled "An ancestral dicotyledon with a strobiloid flower, *Hedyosmum*, is living today". The male flower of this genus of Chloranthaceae, generally considered as highly advanced, was conceived as a primitive, primarily anemophilous, polystaminate strobilous (comparable to the male cone in conifers), and derived from a spike of small and naked flowers not fundamentally unlike those of the extant *Ascarina*[6-8]. I think the *Hedyosmum* female flower might be derived in the same way from a spike of inconspicuous flowers. Thus I emphasize in a subsequent paper[6] that the new interpretation of the *Hedyosmum* flower leads me "to think very seriously that some (many?) angiosperm trends must have had a chloranthoid origin". The discoveries of Friis *et al.* are a strong new argument in favour of my views.

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Bacterial sex timely

SIR—In a Commentary[1] entitled "Postmature scientific discovery?", Zuckerman and Lederberg suggest that the discovery of sexuality in bacteria by Lederberg and Tatum in 1946 was postmature. Among the criteria they use to characterize such discoveries are that they could have been made earlier with then available methods, and that they answer previously unrecognized problems.

Could bacterial sex have been discovered earlier? The reminisence and the historical record say no. Lederberg states that he had to develop doubly auxotrophic mutants of *Escherichia coli* specifically to search for sex once he discovered that the spontaneous reversion rate of *Neurospora* was too high to detect recombination. At least two approximately contemporaneous papers report searches for bacterial sex [2,3]. The results were negative, because only single auxotrophs were used and insufficient numbers of bacteria were screened.

Was bacterial sex a legitimate research problem and, if not, why did Lederberg decide to search for it? In both ref. 1 and the accompanying reminisence[4], Lederberg states that the identification of DNA as the substance responsible for the transformation of *Pneumococcus* by Avery *et al.* was critical in triggering his investigations. "Questions about the biology of transformation would remain inaccessible to conventional genetic analysis if bacteria lacked a sexual stage" (ref. 4). Thus the work of Avery *et al.* made the question of bacterial sex "newly consequential." (ref. 2). The link between the discovery of change in genotype caused by a molecule isolated from cells and the postulation of a bacterial sexual cycle needs to be clarified. How would sex illuminate the mechanism of transformation? The discovery of transformation gave Lederberg the hope that "the chemistry of the gene" could be understood. One could postulate that as the transforming principle was isolated from bacteria, they were appropriate organisms in which to study genes. By all precedents, the study of genetics required a sexual stage and therefore one had to establish sexuality in bacteria before advancing to the chemistry. Was this in fact Lederberg's reasoning?

Although the authors present a convincing account of the conventional wisdom's working against the study of sex in bacteria, there are indications that it was a legitimate research problem in the 1930s and 1940s.

The presence of bacterial sex was a problem which other investigators deemed important[2,3]. The reaction of at least some of the scientific community to the data presented by Lederberg and Tatum, proposing ways to eliminate a possible alternative explanation for the result, also suggests that sex in bacteria was a legitimate problem which they wanted solved.

The unique contribution of Lederberg was his experimental design, the use of different triple auxotrophs in the input strains, so that the presence of cells prototrophic for all markers or combinations of markers in the absence of recombination would be the multiple of the reversion rate for each of the auxotrophic genes. This design is critically dependent on the work of Luria and Delbruck[5], which was not published until 1943. There is therefore a very small window of time for which the Lederberg–Tatum experiments could be considered postmature."

Finally, if the authors wish to convince us that this observation could have made earlier, I believe they are obligated to identify the investigators who had the tools, both methodological and intellectual, to do so.

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