Carrier screening in CF

SIR—P.N. Goodfellow (*Nature* **341**, 102–103; 1989) disagrees with Kerem *et al.*, who suggest (*Science* **245**, 1073–1080; 1989) the postponement of carrier testing for cystic fibrosis (CF) until all the mutations have been identified. Goodfellow states that carrier testing is worthwhile now. A serious problem associated with immediate screening, however, is that it will reveal many couples in which one member carries the CF mutation, whereas for the other carriership cannot be excluded. Such couples are at significantly increased risk of having a child with cystic fibrosis, without the option of prenatal diagnosis or artificial insemination by donor. For a population in which 1 person in 25 is a carrier and assuming that two-thirds of the mutations are detectable (*Science* **245**, 1066–1073; 1989), 5.2 per cent of couples would have to be told that their risk has changed from 1 in 2,500 to 1 in 300. It is questionable whether this would be counterbalanced by the advantage of detecting 4 out of 9 couples with a 1 in 4 risk.

In general, if a is the proportion of mutations detectable, and q the prevalence of carriers in the population, the prevalences of different mating types and their risk of having an affected child are shown in the table.

The larger the proportion of detectable mutations, the less is the increase in risk for m × n couples. Only when the proportion of undetectable mutations (1–a) is less than the carrier frequency (q), will the after-screening risk for m × n couples of having an affected child become less than the before-screening risk. This means that with CF at a carrier frequency of 1 in 25, screening should be postponed until 96 per cent of the mutations can be detected.

Type of mating*	Prevalence in population	Risk of having affected child	Options available
m × m	a^2q^2	1/4	yes
m × n	$2aq\ (1-aq)$	$(1/4)(1-a)q$	no
n × n	$(1-aq)^2$	$(1/4)(1-a)^2q^2$	no

*m, person in which the mutation is demonstrated; n, person in which the mutation is not demonstrated

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Angiosperm origins

SIR—Martin *et al.*[1] attempt to date the origin of angiosperms by analysing sequences of the glycolytic enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDH) in nine angiosperm species, assuming an approximately constant (clock-like) rate of nucleotide substitution calibrated largely by estimated divergence times in other eukaryotes. They conclude that angiosperms first split into monocotyledons and dicotyledons in the Carboniferous, then into Magnoliidae and four 'higher' dicot subclasses in the Permian. They use these results to argue that angiosperms diversified much earlier than the first generally accepted angiosperm fossils in the Early Cretaceous. But they underestimate the strength of the relevant fossil evidence and neglect crucial methodological issues.

Cladistic analyses indicate that angiosperms are related to Bennettitales and Gnetales, implying that the angiosperm line was distinct by the Late Triassic[2,3]. But despite equivocal evidence of Triassic angiosperms[4,5], fossil data clearly indicate that their main radiation did not occur until the Cretaceous. This view is not based solely on the absence of angiosperms in earlier rocks. The earliest unequivocal angiosperm pollen grains (Hauterivian-Barremian) are of the monosulcate type restricted to magnoliids and monocots — they are not 'highly diversified'[1]. Similar monosulcate angiosperm pollen may have escaped recognition before the Cretaceous. But the four higher dicot subclasses all have multiaperturate pollen ultimately derived from the distinctive tricolpate type, which appears near the Barremian-Aptian boundary and soon becomes ubiquitous. This appearance is difficult to ascribe to independent origin of tricolpate pollen in several long-distinct lines because the higher dicots appear to form a monophyletic group[6]. Subsequently, angiosperm pollen and macrofossils (which now include many reproductive structures) become steadily more abundant and diverse, but even by the early Cenomanian only magnoliids and relatively primitive hamamelids and rosids have been recognized. We submit that this orderly sequence, which is based on rich pollen floras from both hemispheres and agrees with relationships derived from cladistic analyses, casts serious doubt on the molecular clock assumption[1].

The study[1] is also weakened by failure to include other seed plant groups ('gymnosperms'). The implication that monocots and dicots are sister groups[1,7] is based on midpoint rooting, which is invalid if rates of evolution are unequal, unlike rooting with outgroups[8]. It should be noted that their result is consistent with trees with angiosperms rooted among Nymphaeales, Piperales and monocots[9], which are almost as parsimonious morphologically as trees with angiosperms rooted near Magnoliales[6]. Martin *et al.* also suggest that their data may favour a polyphyletic origin of angiosperms. But besides ignoring strong evidence that angiosperms are monophyletic[2,3,9], this view is unwarranted without inclusion of gymnosperm groups. Addition of gymnosperms could also shed light on age estimates. If angiosperms are separated from gymnosperms by a branch two-thirds as long as branches within angiosperms, as they are with ribosomal RNA data (ref. 9; E. A. Zimmer, personal communication), the inferred differentiation of seed plants would predate the first evidence of land plants (Ordovician). We hope such a result would be taken as further evidence against a molecular clock[10,11].

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SIR—Our recent analysis[12] of extensive chloroplast and nuclear DNA sequence data firmly supports Martin *et al.*'s evidence for a pre-Cretaceous origin of angiosperms. But our estimate of the monocot–dicot divergence at 200 million years (Myr) ago (with an uncertainty of about 40 Myr) is much younger than their estimate of 319 ± 33 Myr. (Note that the monocot–dicot divergence date represents a minimum age for the angiosperms, if one assumes that angiosperms are monophyletic.) Our estimate appears to be more reliable as it is based on much more sequence data.

The origin of angiosperms at 200 Myr ago seems to be more reasonable. As pointed out by Cleal[7], Martin *et al.*'s estimate is ~150 Myr before the appearance of indisputable angiosperms in the fossil record. Although angiosperms probably did arise in 'upland' areas, it seems unlikely that they took so long to occupy the lowlands. Another difficulty is that because the earliest land plant fossils are only about 420 Myr old, Martin *et al.*'s estimate would imply that the lineages leading to bryophytes, pteridophytes,