gymnosperms, monocots and dicots all appeared within the first 100 Myr of land plant evolution, or these fossils do not represent the common ancestor of all the preceding lineages. In conclusion, our estimate is more compatible with the fossil record and fits well with Cleal's view.

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MARTIN, GIERL AND SAEDLER REPLY— Molecular phylogenies[13] and estimates of angiosperm age[14] were derived many years ago through protein sequencing of plant mitochondrial cytochrome *c* in the laboratory of Don Boulter. The ages suggested in these pioneering studies vastly exceeded the lower Cretaceous and were interpreted by Van Valen[15] as evidence for a higher rate of substitution within angiosperms. Implicit therein is the assumption that the angiosperm fossil record would permit calculation of rate for comparison. This, is the salient issue in our contribution[1]; *Sanmiguelia* is a case in point.

Crane *et al.* are quite critical of our arguments concerning angiosperm age. Is the fossil record of angiosperm history sufficiently complete to preclude the search for further specimens? We agree that fossil pollen represents an excellent monitor of total angiosperm diversity through time, although we do not recognize a compelling rebuttal of Axelrod's arguments. Seeds, required to conquer drier habitats, clearly evolved very early in land-plant evolution[16,17]. Regarding equality of rate, we note that relative rate tests performed both with yeast and bryophyte GAPDH strongly support our arguments. Are relative rate tests applicable to phenotypic evolution? Parsimony cladistics[3] indicate Triassic angiosperm origins, yet accept 33 changes of character state (including 10 reversals) to derive *Gnetum* from a putative progenitor which required only three changes to fulfil angiospermous criteria for the characters examined; is *Gnetum* thus presumed to have evolved 10 times faster? The polyphyly debate for carpel closure can only be resolved with molecular methods if representatives from the distinct gymnospermous progenitor clades in question persist in extant floras.

We concede that Wolfe *et al.*'s careful estimate[12] for the time of monocot–dicot divergence is based on a 20-fold-greater number of total nucleotide sites than our own[1]. Yet maximizing the number of sites for comparison reduces the number of species from which these have been sequenced. In the absence of suitable outgroups and for clades represented by a single species, constancy of rate within the clade was, by necessity[12], assumed.

A true consensus has yet to be reached with regard to the nature of putative angiosperm ancestors[18]. Until crucial 'missing links'[16] for angiosperms are found, reconstruction of flowering plant phylogeny could prove a difficult problem for some time to come.

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Cysteine or serine proteinase?

SIR—We have noticed an apparent discrepancy in the sequence alignment published in a recent scientific correspondence by Higgins *et al.*[1] in reporting the possible identification of a new cysteine proteinase in *Plasmodium falciparum*. The cysteine at amino-acid position 22 of papain was incorrectly labelled as the active site cysteine. This cysteine has been shown to form an essential disulphide bridge in papain, whereas Cys 25 of papain has been shown by crystallographic and chemical studies to be the catalytic cysteine[2,3]. Cys 25 forms an ion pair with the imidizole of His 159, with Asn 175 completing the essential catalytic triad of papain. These residues are conserved in cysteine proteinases of highly divergent organisms.

It is interesting that the amino-acid residue which is in the correct catalytic site of the *P. falciparum* protein is a serine. All known serine proteinases contain a catalytic triad (composed of histidine, aspartic acid and the catalytic serine) that has convergent active-site geometry with the cysteine proteinases. The presence of a serine at the catalytic site of the *P. falciparum* antigen indicates that this protein is actually a serine proteinase with a cysteine proteinase conformation, a structure that is similar to a class of cysteine trypsin-like proteinases found in viruses[4].

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SIR—Higgins *et al.*[1] showed that the 111K antigen of *Plasmodium falciparum* has significant similarity to cysteine proteinases. We wish to point out that the cysteine labelled as the putative active-site residue is in fact involved in a disulphide bridge in papain, actinidin and probably other cysteine proteinases[5]. The gene sequence for the 111K antigen predicts a serine at the active-site position (residue 588; see refs 6 and 7). Although it has yet to be confirmed that the protein itself contains an active-site serine, as post-transcriptional modification could result in the generation of a cysteine[8], the presence of a serine would have functional and evolutionary implications. The serine could have arisen from a cysteine by a single base mutation (TGC → TCC), with a subsequent change to the present serine codon, TCA. This would support the suggestion that proteinases with serine at the active site may have evolved from cysteine proteinases[9]. Could this malarial protein represent an intermediate between these two classes of proteinase?

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