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Utility of molecular phylogenetic methods: a critique of immuno-taxonomy

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In a seminal paper that recognized informational macromolecules such as DNA as the preferred source of molecular phylogenetic data, Zuckerkandl and Pauling (1965) laid the foundation of molecular phylogenetics. Guiding principles of phylogenetic systematics have been widely recognized (Hennig 1966; Wiley 1981; Patterson 1987) and, more recently, facile methods for phylogenetic applications of DNA sequencing have been developed (Hillis & Moritz 1990).

Zuckerkandl and Pauling (1965) also described a class of 'episemantic' molecules (exemplified by ATP and a polysaccharide) that should *not* be used for phylogenetics. These '... cannot furnish the basis for a universal phylogeny for ... if universal, [such episemantides] are not variable ... and if variable, are not universal ... wrong inferences about phylogenetic relationships may be drawn from the presence of identical or similar episemantic molecules in different organisms'. Nevertheless, a recently-proposed molecular immuno-taxonomy of living and fossil brachiopods (Collins *et al.* 1988; Collins *et al.* 1991b; Curry *et al.* 1991) appears to be based on episemantides:

closeness of phylogenetic relationship is measured by 'immunological distance' determined with antibodies raised against glycoproteins whose antigenic determinants are apparently 'predominantly ... carbohydrate' (Collins *et al.* 1991a).

Unfortunately, the phylogenetic utility of this immuno-taxonomy (given as '... less precise ... than sequencing' - Curry *et al.* 1991) only loosely describes the true value of the determinants in question, presumably because their status as episemantic molecules was not taken fully into account. Moreover, although it was recognized that immuno-taxonomy is a phenetic, not a phylogenetic method (Collins *et al.* 1988), discussion of the results (Collins *et al.* 1988; Curry *et al.* 1991) may be thought paradoxically to imply phylogenetic systematics.

The purpose of this note is to draw attention to the limited value of immuno-taxonomy (especially of episemantides) and to caution against according to it attributes of phylogenetic power and utility associated with sequences of genetic informational macromolecules that are true 'documents of evolutionary history' (Zuckerkandl & Pauling 1965).

Among the defects of phylogenetic utility from which immuno-taxonomy based on epismantic molecules suffers are:

(a) Antigens similar enough to react with a given antibody are not necessarily homologous antigens, i.e. antigens controlled by homologous genes and serving homologous cellular functions. Differences (or similarities) expressed as immuno-distance could be due to mixed and/or mimic, phylogenetically independent epitopes or even to differences in antigen concentration (shell weight, not antigen quantity was standardized per reaction in Collins *et al.* 1988, 1991a, b). Thus, there is no strong basis for a test of character homology and, since homology is in doubt, phylogenetic interpretation is inappropriate.

(b) Whilst immuno-distances based on *polypeptide* antigens of knowable sequence divergence can be calibrated against genetic (hence evolutionary) divergence, calibration is essentially impossible with polysaccharide epismantides because the underlying genetic variation occurs in the unanalysed genes coding for either the enzymes which attach the sugars, or the protein moiety of the glycoprotein, or both. For such epismantic antigens, immuno-distances correspond to no definable measure of genetic or evolutionary divergence: the analysis can provide only a qualitative, phenetic classification. Moreover, even with divergence-calibrated polypeptide epitopes, the 'power' of immuno-distance analyses (the underlying number of phylogenetically informative nucleotide sites in genes controlling the variation) is as much as two orders of magnitude lower than the power of specific gene sequencing.

(c) Maximum immunological distance (no cross-reaction) is indistinguishable from absence of antigen, i.e. the character is not universally present. Thus, as Zuckerkandl and Pauling (1965) recognized, epismantic molecular characters may at most define parts of a phylogenetic tree.

In passing, we may note that the difficulty of obtaining brachiopod DNAs has been overstated (Curry *et al.* 1991). In fact, phylogenetically informative DNA sequences can be recovered from dried and alcohol-preserved brachiopods and a survey of genomic and mitochondrial gene sequences from most of the collectable brachiopod family-level taxa is in progress (B.L.C. unpublished work). For these studies, certain additional samples from museum or personal collections will be welcomed; for information write to the author.

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