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Endopeptidase-24.5 is not a metallo-endopeptidase

We would like to comment on the paper by Zolfaghari *et al.* (1987). In the title, abstract and text the enzyme is referred to as neutral endopeptidase-24.5. The numbers derive from the EC number for the enzyme (3.4.24.5), which would indicate that the enzyme is a metallo-endopeptidase. In fact, the authors show (Table 2 of their paper) that this high- M_r peptidase is not a metallo-endopeptidase since it is not inhibited by EDTA or 1,10-phenanthroline. Several other investigators have found this high- M_r multicatalytic proteinase in other tissues and have also demonstrated that it is not a metallo-endopeptidase (e.g. Dahlmann *et al.*, 1983; Wilk & Orłowski, 1983; Ray & Harris, 1985; Rivett, 1985; Bond & Butler, 1987). It is clear that the enzyme was erroneously catalogued (Webb, 1984); the continued use of the enzyme number should therefore be avoided. There is a category in the peptide hydrolase nomenclature scheme for enzymes of unknown catalytic mechanism

(EC 3.4.99), and, until the enzyme is properly classified as to catalytic residues, it should be placed in this subclass.

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Nomenclature of esterases: another proposal

In a recent BJ Letter, Pen & Beintema (1986) yet again draw attention to the fact that the IUB nomenclature regarding some categories of carboxylic ester hydrolases, EC 3.1.1, 'has no practical value for workers in the field'. The authors propose to combine the various categories of so-called non-specific esterases into one single group of general esterases. Following this suggestion, only those esterases for which the natural substrate *in vivo* is known, and hence for which the physiological reaction that is catalysed is sufficiently defined, are to be classified as separate entities according to the customary four-digit EC scheme. In addition, separate EC numbers would have to be attributed to those esterases, too, for which sufficient information about structural and physico-chemical properties is available.

Supporting the authors' view in principle, we would like to draw different conclusions, taking into account mainly genetic aspects. Putting together a great number of entries into one general class counteracts the objectives of a classification system and depreciates its utilities, which, at the worst, might be lost altogether. Hence, in contrast with Pen & Beintema (1986), we propose to extend the number of esterase categories in two directions, for reasons as follows.

(1) Regarding non-specific mammalian esterases, a sizeable number of them in fact are discernible and can be identified in various species as being homologous by

using classical biochemical criteria such as subunit structure, substrate preference, activators and inhibitors, but which cannot be placed into one of the existing categories appropriately.

This is true, for example, for the dimeric 'D-esterase' which has been identified in man, mouse, chinese hamster, cat, dog, and mink (Lalley & McKusick, 1985). Another example is the tetrameric 'butyryl esterase' of erythrocytes, which has been identified in many mammalian species too (von Deimling & de Looze, 1983). Certainly, there are many other examples.

In these cases the number of categories of the EC classification system should be extended. A common EC number for each of these esterases would stress the close relationship of these homologous enzymes, even if the physiological role is still unknown.

(2) Mammalian non-specific esterases are an extreme example of a 'multilocus enzyme system', a term derived from and reflecting both biochemical and genetic reasoning (Harris, 1979). It is the complexity of the esterase multilocus system which makes for the major part of classification problems as far as the EC scheme is concerned. The aforementioned 'general principles' of IUB enzyme nomenclature do not cover the particular and inter-related biochemical and genetic features of complex multilocus enzyme systems. Concerning the members of such a system, the classification according to the four-digit system is too coarse to be of utility.

This is true, for example, for the serum pre-albuminesterase which has been identified in the rat,