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Does sequence similarity of human choline esterase, *Torpedo* acetylcholine esterase and *Geotrichum candidum* lipase reveal the active site serine residue?

In a recent paper Shimada *et al.* (1989) reported on the complete amino acid sequence, deduced from a cDNA clone, of *Geotrichum candidum* ATCC 34614 lipase. The authors could find no overall sequence similarity between this lipase and other lipases. The amino acid sequence does however show remarkable

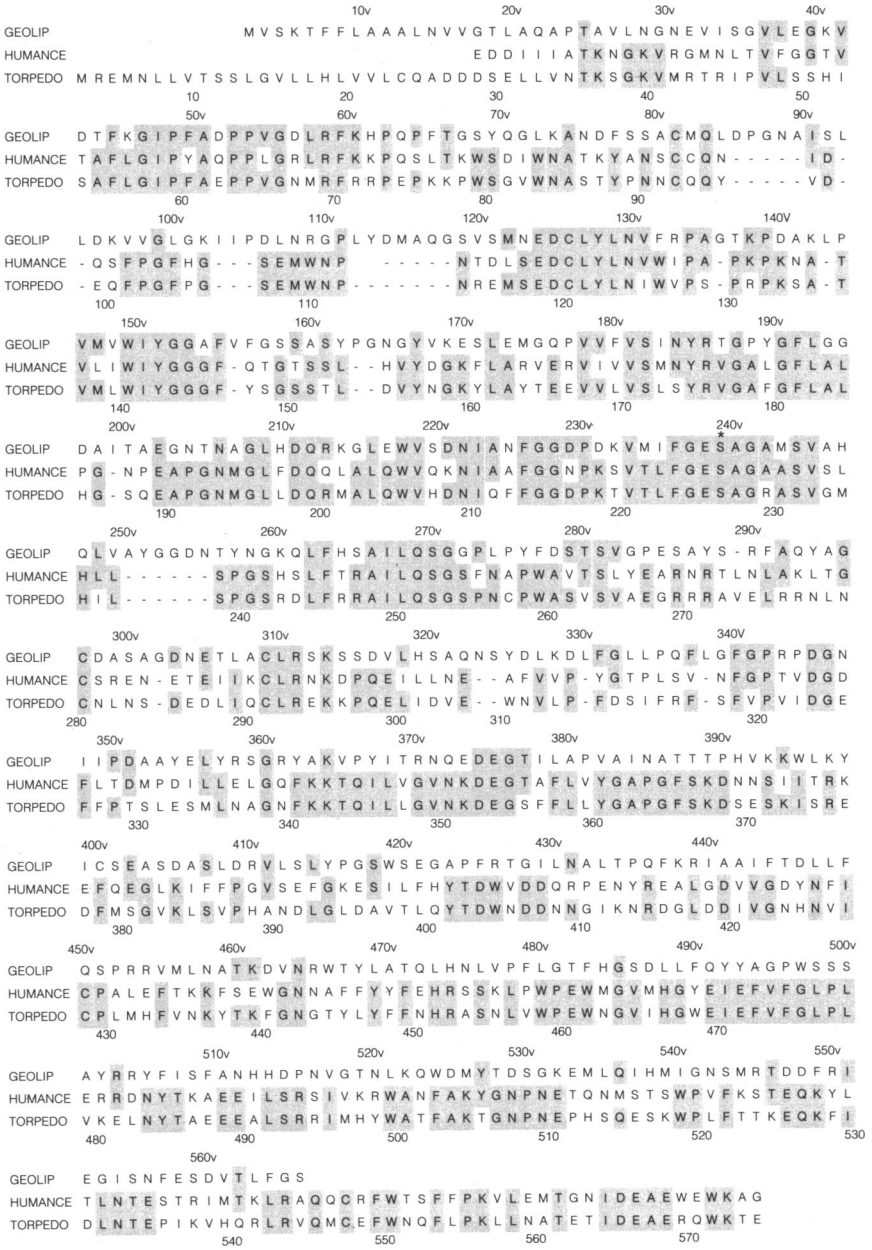

Fig. 1. Amino acid sequence comparison between *Geotrichum candidum* lipase (GEOLIP), human choline esterase (HUMANCE) and *Torpedo* acetylcholine esterase (TORPEDO)

Residues with identity are boxed in. The data are from Shimada *et al.* (1989), Lockridge *et al.* (1987) and Sikarov *et al.* (1987) respectively. The active site serine at residue 236 on GEOLIP has a star above it.

sequence similarity to two other proteins, *Torpedo* acetylcholine esterase (Sikarov *et al.*, 1987) and human choline esterase (Lockridge *et al.*, 1987), which we show in Fig. 1 below. The sequence similarity is highest in the front half of the molecule, there being 32% and 33.4% identity respectively in a 344-amino-acid overlap. Several segments of the proteins are identical, but perhaps the most interesting region is that at amino acid residues 233–238 in the *Geotrichum* sequence. This contains the sequence FGESAG and the serine residue is known to be at the active site, as determined by direct labelling studies, of acetylcholine esterase (MacPhee-Quigley *et al.*, 1985).

Maraganore & Heinrikson (1986) in a recent review article pointed out that there were two classes of serines involved in lipase mechanism; one involved in micellar substrate binding, and the other in the active site. These two sites have led to complications in ascribing assignment of function to these serine residues in lipases. Acetylcholine esterase and choline esterase on the other hand do not appear to require a micellar substrate, the substrate being fully soluble in water; hence the active site can be positively identified. In their paper Shimada *et al.* (1989) have proposed this peptide in *Geotrichum*, by somewhat loose homology with other enzymes, to be a component of the interfacial lipid recognition site, the conserved sequence being -GXSXG-. However, the absolute sequence conservation with acetylcholine esterase, choline esterase and other carboxylesterases (Krisch, 1971) is strongly indicative that this serine is at the active site of the enzyme.

The crystallization of both acetylcholine esterase (Schrag *et al.*, 1988) and *Geotrichum candidum* lipase (Hata *et al.*, 1979) has been achieved and it will be interesting in time to see how the highly conserved regions in the enzymes are related to the three-dimensional structure.

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