FEBS Letters 353 (1994) 119–123

FEBS 14632

Minireview

Parallel β/α-barrels of α-amylase, cyclodextrin glycosyltransferase and oligo-1,6-glucosidase versus the barrel of β-amylase: evolutionary distance is a reflection of unrelated sequences

Štefan Janeček*

Institute of Ecobiology, Slovak Academy of Sciences, Štefánikova 3, SK-81434 Bratislava, Slovakia

Received 17 July 1994; revised version received 30 August 1994

Abstract The structures of functionally related β/α-barrel starch hydrolases, α-amylase, β-amylase, cyclodextrin glycosyltransferase and oligo-1,6-glucosidase, are discussed, their mutual sequence similarities being emphasized. Since these enzymes (except for β-amylase) along with the predicted set of more than ten β/α-barrels from the α-amylase enzyme superfamily fulfil the criteria characteristic of the products of divergent evolution, their unrooted distance tree is presented.

Key words: Parallel β/α-barrel fold; α-Amylase enzyme superfamily; β-Amylase; Sequence similarities; Structure comparison; Evolutionary relationships

1. Introduction

Parallel β/α-barrel structural fold formed by eight parallel β-strands surrounded by eight α-helices has been firstly recognized in the structure of chicken muscle triosephosphate isomerase (TIM) [1]. Therefore the enzymes with this folding motif are frequently named as TIM-barrel enzymes [2]. Nowadays this family comprises more than 20 enzymes (for reviews, see [2–5]). Only one protein without known catalytic function, narbonin, adopts the structure of β/α-barrel [6]. The fact, that all the members of β/α-barrel protein family were enzymes, served as an argument for their divergent evolution from a common ancestor [3]. As for the narbonin, Farber [4] has pointed out that it may be either an enzyme waiting to be discovered as such, or a storage protein that was recruited from a β/α-barrel enzyme.

Generally, the problem of evolution of these enzymes has not yet been solved unambiguously. In fact, three different ways are possible: (i) divergent evolution from a common ancestor [3], (ii) convergent evolution to a stable fold [7], and (iii) exon combination [8]. The present trend is to accept the most probable opinion that many of these enzymes certainly descended from a common ancestor. On the other hand, their great functional diversity could reflect a general convergency to the same structure, either as a result of the intrinsic stability of the barrels or their ease of formation [9].

In this review, the attention is paid to the functionally related crystallographically determined β/α-barrel enzymes, α-amylase (AMY), β-amylase (BMY), cyclodextrin glycosyltransferase (CGT) and oligo-1,6-glucosidase (OGL) as well as to the group of predicted β/α-barrels from the AMY enzyme superfamily. Structure comparisons document that, despite the closely related functions, from an evolutionary point of view, BMY is far removed from the rest of these β/α-barrels as also supported by a complete lack of sequential homology in the catalytic β/α-barrel domains.

2. Sequence-structural similarities and differences between AMY superfamily enzymes and BMY

The X-ray structures of these enzymes from several sources are known: AMY from *Aspergillus oryzae* [10,11], *Aspergillus niger* [12], barley [13] and pig pancreas [14,15]; BMY from soybean [16]; CGT from *Bacillus circulans* strain 8 [17], *Bacillus circulans* strain 251 [18] and *Bacillus stearothermophilus* [19]; and OGL from *Bacillus cereus* [20]. The predicted group of β/α-barrels from AMY superfamily comprises more than ten different enzymes (Table 1) [21]. The three-dimensional structure of *Saccharomycopsis fibuligera* AMY was recently modeled with the AMY from *A. oryzae* as the reference protein [27].

Secondary structure elements of AMY, CGT, OGL and BMY are shown in Table 2. The ordering of segments especiallly for AMY, CGT and OGL is quite similar. Their β/α-barrels are discontinued by a small domain protruding out from the barrels between strand $\beta 3$ and helix $\alpha 3$. The overall structure of BMY, however, less ressembles the structures of the other three enzymes since this domain of BMY in contrast with the equivalent domains of AMY, CGT and OGL is not well-separated from the barrel. Moreover, this BMY can be compared with the single-domain structure of TIM rather than with the multidomain structures of AMY, CGT and OGL [16]. As for the function of the small protruding domain, for instance, in barley AMY it determines several functional and stability properties that distinguish the individual barley isozymes [28]. The structures of AMY, CGT and OGL contain further behind their β/α-barrels even one domain consisting of either ten (AMY) or eight (CGT, OGL) antiparallel β-strands with a

*Corresponding author.
Fax: (42) (7) 334 967; E-mail: sjanecek@ue.savba.sk

Abbreviations: AMY, α-amylase; BMY, β-amylase; CGT, cyclodextrin glycosyltransferase; GMY, gluco-amylase; OGL, oligo-1,6-glucosidase; TIM, triosephosphate isomerase.

SSDI 0014-5793(94)01019-6

Greek key topology [14,17]. In AMY and OGL they usually form the C-terminal domains [14,20], whereas in CGT this domain is followed by two other small domains (each less than 100 amino acid residues; cf. Table 2) [17].

The higher degree of mutual similarity among the structures of AMY, CGT and OGL (when compared with BMY) is certainly a reflection of the similarity throughout their amino acid sequences. They are alignable over their entire length [23,26]. BMY on the one side and AMY, CGT and OGL on the other side constitute in the classification of all glycosylases two sequentially unrelated families [29,30]. AMY contains five highly conserved sequence regions [31,32]. Interestingly, all these regions can be found in the sequences of CGT and OGL as well as of predicted β/α-barrels from Table 1. The regions comprise the proposed catalytic residues of all these β/α-barrel enzymes which are essentially the same: Asp^{206}, Glu^{230} and Asp^{297} (*A. oryzae* AMY numbering) [10]. The active sites of AMY, CGT, OGL and BMY are located at the C-terminal ends of their barrels, a feature characteristic of all β/α-barrel enzymes [2–5]. The differences in the active sites of AMY-type β/α-barrel and the barrel of BMY are shown in Fig. 1. Close evolutionary homology of structures from the AMY enzyme superfamily is manifested by overlapping the three catalytic residues of AMY and CGT (Fig. 1b).

Based on the analysis of available AMY amino acid sequences, four sequence similarities additional to the above mentioned conserved regions have been identified recently [33]. Also these stretches can be traced in the sequences of CGT, OGL and predicted β/α-barrel AMY-related enzymes (Fig. 2). They enable one to construct a phylogenetic tree common for the whole AMY enzyme superfamily (see next section).

Paradoxically, the only sequence similarity joining the two sequentially unrelated amylase families from the evolutionary point of view (Fig. 3) is structurally located outside the catalytic β/α-barrel domains. This similarity reported originally by Svensson et al. [34] comprises so-called putative raw-starch binding domains from AMY, BMY, CGT and glucoamylase (GMY). This domain corresponds to the C-terminal, fifth domain of *B. circulans* CGT (domain E, cf. Table 2) [17] composed of eight mostly antiparallel β-strands. It should be pointed out that the presence of this domain strongly depends on the origin of AMY and BMY, i.e. the enzymes of bacterial origin predominantly possess it. For example, the structure of soybean BMY does not contain this domain [16] but it will almost certainly be determined in the structure of *Clostridium thermosulfurogenes* BMY (cf. Fig. 3). The presence of this domain also is of special interest in GMY owing to the fact that the structure of *Aspergillus awamori* GMY does not contain a catalytic β/α-barrel. There is only some helical copy of it called α/α-barrel [35], i.e. in contrast with AMY and BMY, the GMY is not a β/α-barrel enzyme.

Table 1
Predicted β/α-barrel enzymes from the AMY superfamily[a]

Name	EC
Branching enzyme	2.4.1.18
Glycogen debranching enzyme	2.4.1.25, 3.2.1.33
α-Glucosidase	3.2.1.20
Pullulanase	3.2.1.41
α-Amylase-pullulanase	3.2.1.1/41
Cyclomaltodextrinase	3.2.1.54
Maltotetraohydrolase	3.2.1.60
Isoamylase	3.2.1.68
Dextran glucosidase	3.2.1.70
Maltohexaohydrolase	3.2.1.98
Maltopentaohydrolase	3.2.1.
Neopullulanase	3.2.1.–

[a] The predictions were made in [22–26] using the template structure of AMY β/α-barrel.

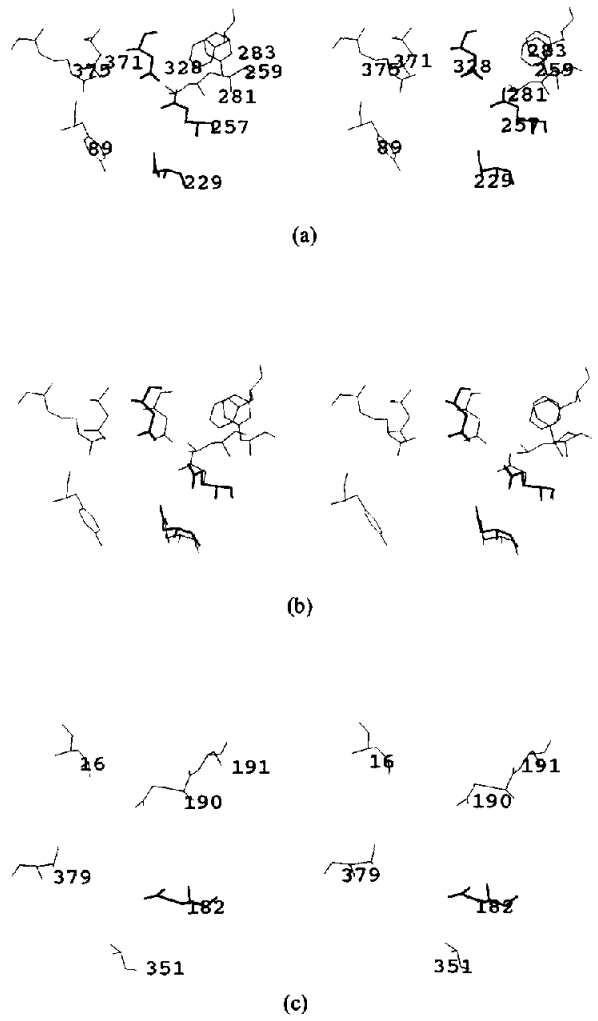

Fig. 1. Differences between AMY-type and BMY active sites. (a) Proposed catalytic residues Asp^{229}, Glu^{257} and Asp^{328} (thick lines) of CGT from *Bacillus circulans* strain 251 (Protein Data Bank entry: 1CDG). Glu^{257} is surrounded by mostly hydrophobic residues (Phe^{259}, Leu^{281}, Phe^{283}), whereas Asp^{229} and Asp^{328} are in a more polar environment (Tyr^{89}, Asp^{371}, Arg^{375}). (b) The same picture (thin lines) with overlapped catalytic residues of AMY from *Aspergillus oryzae* (Protein Data Bank entry: 6TAA): Asp^{206}, Glu^{230} and Asp^{297} (thick lines). (c) Active site cavity of soybean BMY (Protein Data Bank entry: 1BTC). The length of the cavity is indicated from Leu^{16} to Ala^{351}, the width from Gln^{190} to Leu^{379} and the depth from the catalytic Glu^{182} (thick lines) to Ser^{191}.

3. Evolution of the AMY enzyme superfamily

As mentioned above, the amino acid sequences of AMY, CGT, OGL and of the enzymes listed in Table 1 are mutually homologous. The β/α-barrels of all of them are discontinued by the long loop between the strand $\beta 3$ and helix $\alpha 3$ (cf. Table 2), as reported in a recent prediction study by Jespersen et al. [26]. More importantly, all these enzymes exhibit common con-

served sequence stretches (Fig. 2), first pointed out for AMY [31–33]. These regions can be found with slight modifications in the alignment given by Jespersen et al. [26] or in earlier studies [22–25].

Several important facts can be extracted from Fig. 2: (i) there are invariant residues in positions equivalent to Asp^{197}, Glu^{233} and Asp^{300} (pig pancreatic AMY numbering; stretches V, VI, VII, respectively) involved in the catalysis of AMY, CGT and OGL [14,17,20]; this is probably true for the rest of presented enzymes as well; (ii) the Asp^{167} (AMY numbering; stretch IV) that was identified to bind a calcium ion in AMY [14,36] and CGT [17] is not conserved in all the enzymes; the strict conservation of this aspartate pointed out firstly in AMY [32] could be closely related to the eventual binding of a calcium by an enzyme from this group, such as amylopullulanase (cf. [37]); and (iii) the stretches I and II provide two clear 'fingerprints' of a CGT amino acid sequence [23,26,38] (Š. Janeček, E.A. MacGregor and B. Svensson, submitted for publication), i.e. nine residues from Gly to Pro (that is preceded by Gln, Fig. 4) around the strand β2 in stretch I along with the sequence Phe-Ala-Pro around the strand β3 in stretch II.

Table 2
Secondary structure elements of AMY, CGT, OGL and BMY[a]

AMY	CGT	OGL	BMY
Aβ1[b]	Aβ1	Aβ1	Aβ1
Aα1	Aα1	Aα1	Aα1
Aβ2	Aβ2	Aβ2	Aβ2
α	$\beta 1_A$	Aα2	Bα1[c]
Aα2	$\beta 2_A$	Aβ3	Aα2
Aβ3	Aα2	Bα	Aβ3
$B\beta 1_A$	Aβ3	$B\beta 1_A$	$B\beta 1_A$
$B\beta 2_B$	$B\beta 1_B$	$B\beta 2_A$	$B\beta 2_A$
$B\beta 3_B$	$B\beta 2_C$	$B\beta 3_A$	Bα2
$B\beta 4_B$	$B\beta 3_C$	Aα3	$B\beta 3_B$
$B\beta 5_B$	Bα	Aβ4	$B\beta 4_B$
Bα	$B\beta 4_B$	Aα4	Aα3
$B\beta 6_A$	Aα3	Aβ5	α
Aα3	Aβ4	Aα5	Aβ4
Aβ4	Aα4	Aβ6	Bα3
Aα4	Aβ5	α	Aα4
Aβ5	Aα5	Aα6	Aβ5
Aα5	Aβ6	Aβ7	Bα4
Aβ6	α	α	Aα5
α	Aα6	Aα7	Aβ6
Aα6	Aβ7	Aβ8	Aα6
α	Aα7	α	Aβ7
Aβ7	Aβ8	α	Aα7
α	Aα8	α	Aβ8
Aα7	α	Aα8	Aα8
Aβ8	$C\beta 1_D$	$C\beta 1_B$	α
$\beta 1_C$	$C\beta 2_D$	$C\beta 2_B$	
$\beta 2_C$	$C\beta 3_D$	$C\beta 3_B$	
Aα8	$C\beta 4_E$	$C\beta 4_C$	
$C\beta 1_D$	$C\beta 5_F$	$C\beta 5_B$	
$C\beta 2_D$	$C\beta 6_F$	Cβ6	
$C\beta 3_D$	$C\beta 7_E$	$C\beta 7_C$	
$C\beta 4_E$	$C\beta 8_D$	$C\beta 8_B$	
$C\beta 5_E$	$D\beta 1_G$		
$C\beta 6_F$	$D\beta 2_H$		
$C\beta 7_F$	$D\beta 3_G$		
$C\beta 8_E$	$D\beta 4_H$		
$C\beta 9_E$	$D\beta 5_H$		
$C\beta 10_D$	$D\beta 6_G$		
	$D\beta 7_G$		
	$D\beta 8_H$		
	$D\beta 9_H$		
	$E\beta 1_I$		
	$E\beta 2_J$		
	$E\beta 3_J$		
	$E\beta 4_I$		
	$E\beta 5_J$		
	$E\beta 6_J$		
	$E\beta 7_J$		
	$E\beta 8_I$		

[a] Data extracted from [14–17,20].
[b] Domains are specified by capital letters: A, parallel β/α-barrel; B, small domain protruding out of the barrel; C, Greek key behind the barrel; D, immunoglobulin-like fold; E, putative starch-binding domain. β-Sheets are indicated by subscript italicised capitals.
[c] The segments designated here as belonging to domain B in BMY form in fact a small lobe extending from the C-terminal end of the barrel core.

Having equivalent sequence stretches, one may calculate an evolutionary tree. An unrooted distance tree, first one for various α-1,4-along with α-1,6-D-glucan cleaving enzymes, has been constructed [26] on the extraction of the most conserved β-strands (β3, β4, β5 and β7) in the sequences of these enzymes that correspond to the four well-accepted conserved sequence regions of AMY [31] (the regions II, V, VI, VII in Fig. 2). The tree satisfactorily reflected the differences in the enzyme specificity. Similar tree calculated on all the sequence stretches of Fig. 2 by the neighbour-joining method [39] is shown in Fig. 5. As in the tree of Jespersen et al. [26], the glycogen debranching enzyme along with branching enzyme are on the two longest branches of this tree. This indicates that these enzymes the least resemble the others. The insertions in their sequences around the strand β7 (stretch VII in Fig. 2) seem to be responsible for their positions in the tree. The clustering of the rest of enzymes follows their α-1,4-, α-1,6- or dual bond specificity (Fig. 5). It is worth noting that the similar evolutionary conclusions resulting from both the trees ([26] and Fig. 5) indicate comparable evolutionary importance of the four well-accepted conserved regions [31], the fifth conserved region (stretch IV in Fig. 2) [32] and the rest of sequence similarities (stretches I, III, VIII in Fig. 2) [33].

4. Conclusions

The β/α-barrel enzymes from the AMY superfamily are good example of a homologous group that almost certainly has evolved divergently. All they have similar amino acid sequences, three-dimensional structures, functions and active sites. BMY containing similar fold of a β/α-barrel is probably not closely related to them. The evolutionary distance is in direct relation to the lack of homology between their β/α-barrel domains. As for evolution of the whole present-day family of β/α-barrel proteins (22 enzymes and 1 protein narbonin [4–6,40]), the draft of its divergency given by Farber and Petsko [3] represents the most compact view of the problem despite the general lack of sequence homology. Perhaps, a lack of obvious sequence similarity among the amino acid sequences of β/α-barrel enzymes is partly caused by an effort to get their sequence alignments always structurally satisfactory. For example, based on the multiple alignment of five β/α-barrel enzymes (among them AMY and TIM), Pickett et al. [41] have derived sequence motifs for discrimination of the β/α-barrel fold but their templates have not been sufficient in themselves to define categorically a protein as a β/α-barrel. Detailed analysis of the amino acid sequences of different β/α-barrel enzymes around their β-strands forming the inner barrel may indicate so-called 'hidden homologies' (Š. Janeček, unpublished results). For

		I		II		III		IV		V		VI		VII		VIII	
		β2		β3		loop3		loop3		β4		β5		β7		β8	
AMY	1-35	GFGGVQVS-P	51	DAVINH	48	SYND	11	LLDLA	23	GFRLDASKH	31	EVID	58	FVD--NHD	33	GFTRVMSSY	343-496
OGL	1-43	GIDVIWLS-P	45	DLVVNH	46	QYDE	13	QPDLN	23	GFRMDVINP	51	EMPG	65	YWN--NHD	30	GTPYIYQGE	369-558
AGL	1-51	GVDAIWVC-P	45	DLVINH	52	TFDE	13	QVDLN	24	GFRIDTAGL	57	EVAH	64	YIE--NHD	31	GTLYVYQGQ	390-586
PUL	1-209	GVTHVELL-P	62	DVVYNH	21	AYGN	7	GNDIA	24	GFRFDLMGI	24	EGWD	79	YVE--SHD	35	GIPFLHSGQ	514-658
APU	1-434	GISVIYLN-P	44	DGVFNH	33	PYGD	34	WADFI	23	GWRLDVANE	24	ELWG	68	LLG--SHD	41	GMPSIYYGD	754-1450
CMD	1-186	GVNALYFN-P	44	DAVFNH	38	TYDT	6	MPKLN	24	GWRLDVANE	24	EIMH	58	LLG--SHD	26	GTPCIYYGD	457-591
MTF	1-49	GFSAIWMPVP	52	DVVPNH	27	NYPN	11	ESDLN	24	GFRFDFVRG	21	ELWK	66	FVD--NHD	32	GTPVVYWSH	336-530
ISA	1-216	GVTAVEFL-P	65	DVVYNH	31	TSGN	9	GANFN	24	GFRFDLASV	37	EFTV	83	FID--VHD	61	GTPLMQGGD	579-745
DGL	1-43	GVMAIWLS-P	45	DLVVNH	41	QYDD	13	QPDLN	23	GFRMDVIDM	37	ETWG	68	FWN--NHD	30	GTPYI-QGE	352-445
MHF	1-37	GITAVWIP-P	55	DVVMNH	58	DWDQ	33	YADID	24	GFRIDAVKH	25	EFWK	58	FVD--NHD	28	GYPSVFYGD	371-485
MPF	1-30	GFAAVQIS-P	55	DAVINH	37	NYGD	11	LQDLN	23	GLRVDAAKH	26	EVIG	60	FVD--NHD	32	GYPALMSAT	327-588
NPU	1-187	GINGIYLT-P	44	DAVFNH	37	NYDT	6	MPKLN	24	GWRLDVANE	24	EVWH	58	LLG--SHD	26	GTPCIYYGD	459-583
BRE	1-278	GFTHLELL-P	46	DWVPGH	15	LYEH	7	HQDWN	29	ALRVDAVAS	48	EEST	57	FVLPLSHD	28	GWMWAFPGK	563-727
CGT	1-69	GVTALWISQP	54	DFAPNH	44	SLEN	8	LADFN	23	GIRVDAVKH	23	EWFL	62	FID--NHD	25	GVPAIYYGT	363-684
GDE	1-136	GYNMIHFT-P	52	DVVYNH	44	KYKE	199	LRNFA	49	GVRLDNCHS	24	ELFT	62	FMD-ITHD	31	GYDELVPHQ	651-1515
		*								* *		*		**		*	
con		G a	P	D v nH		y		dln		gfR D		E	f	nHD		G p	g

Fig. 2. Conserved sequence stretches in the AMY enzyme superfamily. Enzymes sources: AMY, α-amylase; OGL, oligo-1,6-glucosidase; AGL, α-glucosidase; PUL, pullulanase; APU, amylopullulanase; CMD, cyclomaltodextrinase; MTF, maltotetraohydrolase; ISA, isoamylase; DGL, dextran glucosidase; MHF, maltohexaohydrolase; MPF, maltopentaohydrolase; NPU, neopullulanase; BRE, branching enzyme; CGT, cyclodextrin glycosyltransferase; GDE, glycogen debranching enzyme. The second line denotes the elements of secondary structure, as determined for AMY [14]. The enzymes are numbered from the N-terminal end. The numbers represent the length of sequence between the regions as well as at the start and the end of the sequence. The asterisks signify invariable amino acid residues. A residue is written in the consensus (*con*) sequence if it is present in more than half of the enzymes. Similar stretches (with minor modifications in several positions) can be found in the alignment of a related set of enzymes published in [26].

AMY	442	---QTSASFHVN-ATTAWGENIYVTGDQAALGNWDPAR-ALKLDPAAY----PVW	487
BMY	422	----IPVTFTINNATTYYGQNVYIVGSTSDLGNWNT-TYARGPA---SCPNYPTW	468
GMY	514	---AVAVTFDLT-ATTTYGENIYLVGSISQLGDWETSD-GIALSADKYTSSDPLW	563
CGT	581	TGDQVTVRFVVNNASTTLGQNLYLTGNVAELGNWSTGSTAIGPAFNQVIHQYPTW	635

AMY	488	KLDVPLAAGTPFQYKYLRKDAAGKAVWESGANRTATVG---TTGALTLNDTWRG*	538
BMY	469	TITLNLLPGEQIQFKAVKIDSSGNVTWEGGSNHTYTVP---TSGTGSVTITWQN*	519
GMY	564	YVTVTLPAGESFEYKFIRIESDDSVEWESDPNREYTVPQACGTSTATVTDTWR*	616
CGT	636	YYDVSVPAGKQLEFRFFKKNGST-ITWESGSNHTFTTP---ASGTATVTVNWQ*	684

Fig. 3. Starch-binding domain motif in amylases and cyclodextrin glycosyltransferase. Sources of enzymes: AMY, α-amylase from *Streptomyces limosus*; BMY, β-amylase from *Clostridium thermosulfurogenes*; GMY, glucoamylase from *Aspergillus niger*; CGT, cyclodextrin glycosyltransferase from *Bacillus circulans*. Gaps are indicated by dashes. Asterisks signify the C-terminal amino acid residues of the enzymes. Invariant residues are in bold print. The residues identified as consensus in [34] are italicised.

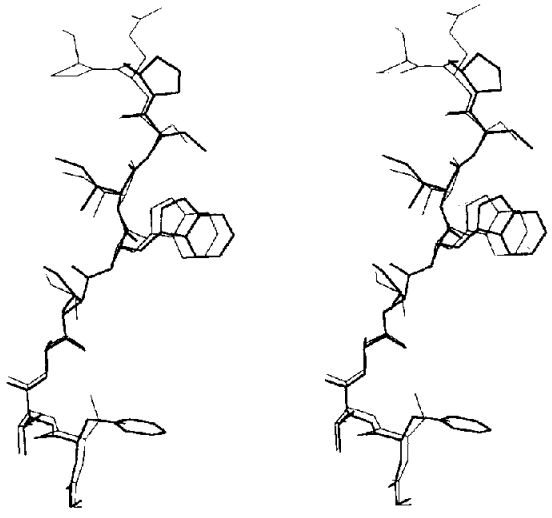

Fig. 4. Strands β2 from the β/α-barrel of AMY (thick lines) and CGT (thin lines) are shown overlapped. Corresponding sequences: AMY (*Aspergillus oryzae*), 56-GFTAIWITP; CGT (*Bacillus circulans* strain 251), 70-GVTAIWISQP. Protein Data Bank files used were 6TAA and 1CDG for AMY and CGT, respectively. Gln residue (Gln^{78} in CGT) preceding proline which is invariant in all enzymes from AMY superfamily, is a feature characteristic of only CGT (cf. Fig. 2).

instance, around the strand β2, several β/α-barrel enzymes, such as cellobiohydrolase II [42], *N*-(5′-phosphoribosyl)-anthranilate isomerase [43], ribulose-1,5-bisphosphate carboxylase/oxygenase [44], tryptophane synthase (α-subunit) [45], have glycines and prolines alike the enzymes from the AMY superfamily (see Figs. 2 and 4). Since these 'homologous' residues adopted different structural roles during evolution, they will be 'hidden' in every structurally derived alignment.

To summarize, for the present, the only conclusion that can be drawn is: some of the β/α-barrel enzymes *may be the products* of convergent evolution to a symmetric and stable fold but several others *have been almost certainly diverged* from a common ancestor(s). If the ancestors were still available, they could be made, for instance, by a process of exon combination. In the light of the present knowledge no one of the three possibilities (convergent evolution, divergent evolution, exon combination) can be excluded. Perhaps, all of them were used during evolution.

Acknowledgements: The author thanks Dr. Štefan Baláž for providing facilities necessary for visualising and overlapping protein structures. The skilful assistance of Katka Piršelová during first contacts with the program HYPERCHEM is gratefully acknowledged. Dr. Dezider Tóth is thanked for carefully reading the manuscript.

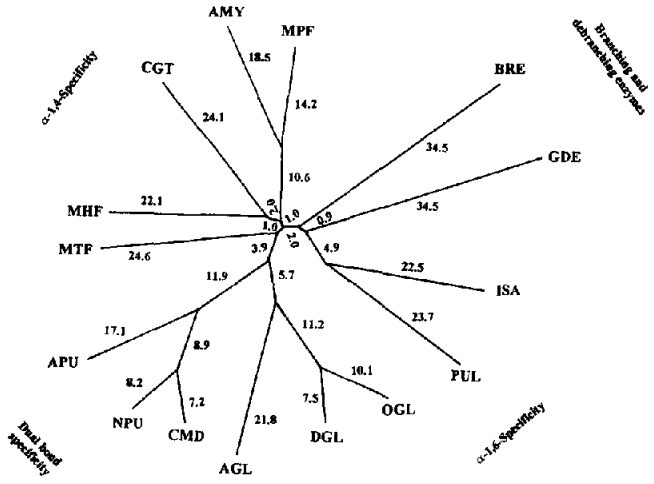

Fig. 5. Evolutionary tree of the AMY enzyme superfamily. The abbreviations of enzyme sources are given in the legend to Fig. 2. The branch lengths are indicated by numbers and are proportional to the sequence divergency. The sum length of the branches linking any pair of enzymes is a measure of the evolutionary distance among them. A similar tree (based on the stretches II, V, VI, VII of Fig. 2) can be found in [26].

References

[1] Banner, D.W., Bloomer, A.C., Petsko, G.A., Phillips, D.C., Pogson, C.I., Wilson, I.A., Corran, P.H., Furth, A.J., Milman, J.D., Offord, R.E., Priddle, J.D. and Waley, S.G. (1975) Nature 255, 609–614.
[2] Brändén, C.-I. (1991) Curr. Opin. Struct. Biol. 1, 978–983.
[3] Farber, G.K. and Petsko, G.A. (1990) Trends Biochem. Sci. 15, 228–234.
[4] Farber, G.K. (1993) Curr. Opin. Struct. Biol. 3, 409–412.
[5] Janeček, Š. and Baláž, Š. (1993) J. Protein Chem. 12, 509–514.
[6] Hennig, M., Schlesier, B., Dauter, Z., Pfeffer, S., Betzel, C., Höhne, W.E. and Wilson, K.S. (1992) FEBS Lett. 306, 80–84.
[7] Lesk, A.M., Brändén, C.-I. and Chothia, C. (1989) Proteins: Struct., Funct., Genet. 5, 139–148.
[8] Gilbert, W. and Glynias, M. (1993) Gene 135, 137–144.
[9] Doolittle, R.F. (1994) Trends Biochem. Sci. 19, 15–18.
[10] Matsuura, Y., Kusunoki, M., Harada, W. and Kakudo, M. (1984) J. Biochem. 95, 697–702.
[11] Swift, H.J., Brady, L., Derewenda, Z.S., Dodson, E.J., Dodson, G.G., Turkenburg, J.P. and Wilkinson, A.J. (1991) Acta Crystallogr. B47, 535–544.
[12] Brady, R.L., Brzozowski, A.M., Derewenda, Z.S., Dodson, E.J. and Dodson, G.G. (1991) Acta Crystallogr. B47, 527–535.
[13] Kadziola, A., Abe, J., Svensson, B. and Haser, R. (1994) J. Mol. Biol. 239, 104–121.
[14] Qian, M., Haser, R. and Payan, F. (1993) J. Mol. Biol. 231, 785–799.
[15] Larson, S.B., Greenwood, A., Cascio, D., Day, J. and McPherson, A. (1994) J. Mol. Biol. 235, 1560–1584.
[16] Mikami, B., Hehre, E.J., Sato, M., Katsube, Y., Hirose, M., Morita, Y. and Sacchettini, J.C. (1993) Biochemistry 32, 6836–6845.
[17] Klein, C. and Schulz, G.E. (1991) J. Mol. Biol. 217, 737–750.
[18] Lawson, C.L., van Montfort, R., Strokopytov, B., Rozeboom, H.J., Kalk, K.H., de Vries, G.E., Penninga, D., Dijkhuizen, L. and Dijkstra, B.W. (1994) J. Mol. Biol. 236, 590–600.
[19] Kubota, M., Matsuura, Y., Sakai, S. and Katsube, Y. (1991) Denpun Kagaku 38, 141–146.
[20] Kizaki, H., Hata, Y., Watanabe, K., Katsube, Y. and Suzuki, Y. (1993) J. Biochem. 113, 646–649.
[21] MacGregor, E.A. (1993) Starch 45, 232–237.
[22] Svensson, B. (1988) FEBS Lett. 230, 72–76.
[23] MacGregor, E.A. and Svensson, B. (1989) Biochem. J. 259, 145–152.
[24] Watanabe, K., Kitamura, K., Iha, H. and Suzuki, Y. (1990) Eur. J. Biochem. 192, 609–620.
[25] Jespersen, H.M., MacGregor, E.A., Sierks, M.R. and Svensson, B. (1991) Biochem. J. 280, 51–55.
[26] Jespersen, H.M., MacGregor, E.A., Henrissat, B., Sierks, M.R. and Svensson, B. (1993) J. Protein Chem. 12, 791–805.
[27] Matsui, I., Yoneda, S., Ishikawa, K., Miyairi, S., Fukui, S., Umeyama, H. and Honda, K. (1994) Biochemistry 33, 451–458.
[28] Rodenburg, K.W., Juge, N., Guo, X-J., Søgaard, M., Chaix, J.-C. and Svensson, B. (1994) Eur. J. Biochem. 221, 277–284.
[29] Henrissat, B. (1991) Biochem. J. 280, 309–316.
[30] Henrissat, B. and Bairoch, A. (1993) Biochem. J. 293, 781–788.
[31] Nakajima, R., Imanaka, T. and Aiba, S. (1986) Appl. Microbiol. Biotechnol. 23, 355–360.
[32] Janeček, Š. (1992) Biochem. J. 288, 1069–1070.
[33] Janeček, Š. (1994) Eur. J. Biochem. 224, 519–524.
[34] Svensson, B., Jespersen, H., Sierks, M.R. and MacGregor, E.A. (1989) Biochem. J. 264, 309–311.
[35] Aleshin, A., Golubev, A., Firsov, L.M. and Honzatko, R.B. (1992) J. Biol. Chem. 267, 19291–19298.
[36] Boel, E., Brady, L., Brzozowski, A.M., Derewenda, Z., Dodson, G.G., Jensen, V.J., Petersen, S.B., Swift, H., Thim, L. and Woldike, H.F. (1990) Biochemistry 29, 6244–6249.
[37] Mathupala, S.P., Lowe, S.E., Podkovyrov, S.M. and Zeikus, J.G. (1993) J. Biol. Chem. 268, 16332–16344.
[38] Janeček, Š. and Tóth, D. (1994) Biologia 49, 301–306.
[39] Saitou, N. and Nei, M. (1987) Mol. Biol. Evol. 4, 406–425.
[40] Izard, T., Lawrence, M.C., Malby, R.L., Lilley, G.G. and Colman, P.M. (1994) Structure 2, 361–369.
[41] Pickett, S.D., Saqi, M.A.S. and Sternberg, M.J.E. (1992) J. Mol. Biol. 228, 170–187.
[42] Rouvinen, J., Bergfors, T., Teeri, T., Knowles, J.K.C and Jones, T.A. (1990) Science 249, 380–386.
[43] Wilmanns, M., Priestle, J.P., Niermann, T. and Jansonius, J.N. (1992) J. Mol. Biol. 223, 477–507.
[44] Schneider, G., Lindqvist, Y. and Lundqvist, T. (1990) J. Mol. Biol. 211, 989–1008.
[45] Hyde, C.C., Ahmed, S.A., Padlan, E.A., Miles, E.W. and Davies, D.R. (1988) J. Biol. Chem. 263, 17857–17871.