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Evolution toward small molecule inhibitor resistance affects native enzyme function and stability, generating acarbose-insensitive cyclodextrin glucanotransferase variants

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SUPPLEMENTAL DATA

Supplementary Table S1. Alignment of region around residues (1. H140, 2. A230, 3. K232, 4. F283) responsible for acarbose (in)sensitivity in *Bacillus circulans* 251 CGTase, with other inhibitor susceptible and resistant GH13 members.

Enzymes	Sequence	Accession no.
<u>Cyclodextrin glucanotransferase</u>		
	1. * 2. 3. 4.	
<i>Bacillus circulans</i> 251	DFAPNH . . . GIRMD AVKH . . . LLDF - - RFA	P43379
<i>Tabium</i> ^a	DFAPNH . . . GIRLD AVKH . . . LLDF - - RFS	P26827
<i>Bacillus macerans</i>	DFAPNH . . . GIRFD AVKH . . . LLDF - - RFA	P04830
<i>Klebsiella pneumonia</i>	DYAPNH . . . AIRID AIKH . . . LLDF - - GFR	P08704
<i>Anaerobranca gottschalkii</i>	DFAPNH . . . GIRVD AVKH . . . LLDF - - EFA	Q5ZEQ7
<u>Acarviosyl transferase</u>		
<i>Actinoplanes sp.</i> ^b	DWTPNG . . . GIRVD AVKH . . . AMDF - - YTN	Q9K5L5
<u>α-amylase</u>		
Human pancreas	DAVINH . . . GFRLD ASKH . . . VTEF - - KYG	P04746
<i>Aspergillus oryzae</i>	DVVANH . . . GLRID TVKH . . . YPIY - - YPL	P10529
<i>Actinoplanes sp. (AcbZ)</i> ^b	DIIVNH . . . GYRMD TVKH . . . DFS FQSAAR	Q27GS8
<i>Aspergillus niger</i>	DVVPDH . . . GLRID SVLE . . . YPIY - - WQL	P56271
<i>Actinoplanes sp. (AcbE)</i> ^b	DIVVNH . . . GYRLD TLKA . . . DFP FQGAQ	Q27GR6
<u>Maltogenic amylase</u>		
<i>Thermus sp.</i> ^b	DAVFNH . . . GWRLD VANE . . . LRF F - - AKE	O69007
<i>Bacillus stearothermophilus</i> ^b	DAVFNH . . . GWRLD VANE . . . LRF F - - AQH	Q45490
<i>Novamyl</i>	DFVPNH . . . GLRID AVKH . . . VLDF - - DLN	P19531
<i>B.licheniformis</i>	DWTPNG . . . GIRVD AVKH . . . AMDF - - YTN	Q04977

^a *Thermoanaerobacterium thermosulfurigenes* strain EM1

^b Members of GH13 displaying increased or complete resistance to acarbose.

* Catalytic nucleophile