Supplement Figure 1 Carius et al.

			βA	αΒ	βΒ	αC	βC	
		•			\longrightarrow		\rightarrow	
		1 10	20	30	40	50	60	_
GatDH	1	MDYRTVFRLDGA	CAAVTGAGS	GIGLEICRAFAAS	GARLIL.IDR	EAAALDRAAQELG	AAVAARIVA.	<mark>D</mark>
1VL8 2IR/D	5	FDLRGR	VALVIGGSR	GLGFGIAQGLAEA	GCSVVV.ASRI	ILEEASEAAQKLT	EKYGVETMAF	RCD
2CFC	1		VAIVIGASS	GNGLAIATRFLAR	GDRVAA.LDL	SAETLEETARTHW	HAYADKVLRV	RAD
		αD		βD	0.4	α Ε1	αΕ2	~ ~
					100			
	C 7							130
GatDH 1VT.8	68	VID. AEAMIAAA VSNYEEVKKLLE	AEAEAVAPV	TVVNAAGINBRH	DALETDDA PA EEFPIJ	ATWROVMAVNVDG DEFROVIEVNLFG	MFWASRAFGR TYYVCREAFS	А т.
2UVD	63	VANAEDVTNMVK	QTVDVFGQV	DILVNNAGVIKDN	LLMRMKE	EWDTVINTNLKG	V.FLCTKAVS	RFM
2CFC	61	VADEGDVNAAIA	ATMEQFGAI	D <mark>VLVNNAGIT</mark> GNS	EAGVLHTTPVI	EQFDK <mark>VMAVN</mark> VRG	IFLGC <mark>RA</mark> VLP	н
						*		
		ßF			~ F	8 F		~FC1
		2222 <mark>βε</mark>		20000000	αF <u>0000000000</u>	β F	→	α FG1 QQQ
		<u>βE</u> 140	150	<u>00000000</u> 160	αF 2000000000 170	<u>βF</u> 180	190	αFG1 LLL 200
GatDH	131	βE 140 MVARGAGAIVNL	150 G <mark>SM</mark> SGT <mark>IV</mark> NI	<u>0000000</u> 160 REQFASSYMASKG	αF 000000000000000000000000000000000000	βF 180 LEWAGRGVRVNAL	190 APGYVATEMT	αFG1 200 200 LKM
GatDH 1VL8	131 133	βE 140 MVARGAGAIVNL LRESDNPSIINI	150 G <mark>SM</mark> SGTIVNI G <mark>SLTVEEV</mark> TI	<u>20200000</u> 160 RPQFASSYMASKG MPN . ISAYAASKG	αF 000000000 170 AVHQLTRALA GVASLTKALA	βF 180 EWAGRGVRVNAL CEWGRYGIRVNVI	190 APGYVATEMT APGWYRTKMT	αFG1 ۵۵۵ 200 LKM EAV
GatDH 1VL8 2UVD 2CFC	131 133 129	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MILOCOCUUNI	150 GSMSGTIVNI GSLTVEVTI ASV.VGVTGI	00000000 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.OANYVAAKA	αF 00000000000 170 AVHQLTRALAA GVIGLTKTSA GVIGLTKTSA	βF 180 AEWAGRGVRVNAL KEWGRYGIRVNVI KELASRNITVNAI KELASRNITVNAI	190 APGYVATEMT APGWYRTKMT APGFIATDMT	αFG1 200 LKM EAV D.V
GatDH 1VL8 2UVD 2CFC	131 133 129 129	βE 140 MVARGAGAIVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVAI	00000000 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.OANYVAAKA FPG.RSAYTTSKG	αF 00000000000 170 AVHQLTRALAF GVASLTKALAF GVIGLTKTSAF AVLQLTKSVA	βF 180 AEWAGRGVRVNAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV	190 A PGYVATEMT A PGWYRTKMT A PGFIATDMT C PGMIETPMT	αFG1 <u>200</u> LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC	131 133 129 129	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA:	00000000 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTTSKG * *	αF 00000000000 170 AVHQLTRALAF GVASLTKALAF GVIGLTKTSAF AVLQLTKSVA	βF 180 AEWAGRGVRVNAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV	190 APGYVATEMT APGWYRTKMT APGFIATDMT CPGMIETPMT	αFG1 200 LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC	131 133 129 129	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI αFG2	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA:	<u>00000000</u> 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.OANYVAAKA PG.RSAYTTSKG * *	αF 170 170 AVHQLTRALAF GVASLTKALAF GVIGLTKTSAF AVLQLTKSVA	βF 180 AEWAGRGVRVNAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV 3G	190 APGYVATEMT APGWYRTKMT APGFIATDMT CPGMIETPMT	αFG1 200 LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC	131 133 129 129	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI αFG2 0	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA: *	00000000 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTTSKG * * 000000000000000000000000000000000	αF 170 170 AVHQLTRALAF GVASLTKALAF GVIGLTKTSAF AVLQLTKSVA	βF 180 AEWAGRGVVVAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV	190 APGYVATEMT APGWYRTKMT APGFIATDMT CPGMIETPMT	αFG1 <u>200</u> LKM EAV D.V QWR
GatDH 1vL8 2UVD 2CFC	131 133 129 129	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI αFG2 000000000 2100000000	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA *	00000000 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTTSKG * * 000000000000000000000000000000000	αF 00000000000 170 AVHQLTRALAF GVASLTKALAF GVIGLTKTSAF AVLQLTKSVA 240	βF 180 180 AEWAGRGVVVAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV 3G 250	190 APGYVATEMT APGWYRTKMT APGFIATDMT CPGMIETPMT	αFG1 200 LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC GatDH	131 133 129 129 201	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MLLQGAGVIVNI αFG2 000000000000000000000000000000000000	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA *	<u>00000000</u> 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTTSKG * * αG 000000000000 230 PSEIAAAALSLAS	αF 0000000000 170 AVHQLTRALA GVASLTKALA GVIGLTKTSA AVLQLTKSVA 240 PAASYVTGAII	βF 180 180 AEWAGRGVVNAL CEWGRYGIRVNVI CELASRNITVNAI DYAGSGIRCNAV 3G 250 AVDGGYTVW	190 APGYVATEMT APGWYRTKMT APGFIATDMT CPGMIETPMT	αFG1 200 200 LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC GatDH 1VL8 2UVD	131 133 129 129 201 202 195	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MILQGAGVIVNI αFG2 00000000 210 RERPELFETWLD FSDPEKLDYMLK	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA * 220 MTPMGRCGE RIPLGRTGV	<u>00000000</u> 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTTSKG * * αG 0000000000000 230 PSEIAAALTSLAS PEDLKGVAVBLAS 0001ANVT2FAS	αF 00000000000 170 AVHQLTRALAF GVIGLTKTSAF AVLQLTKSVA 240 PAASYVTGAII EEAKYVTGQII DOSKVTGQII	βF 180 AEWAGRGVVVNAL KEWGRYGIRVNVI KELASRNITVNAI DYAGSGIRCNAV 250 250 AVDGGYTVW FVDGGWTAN NYDGGWTAN	190 A PGYVATEMT A PGWYRTKMT A PGFIATDMT C PGMIETPMT	αFG1 200 200 LKM EAV D.V QWR
GatDH 1VL8 2UVD 2CFC GatDH 1VL8 2UVD 2CFC	131 133 129 129 201 202 195 197	βE 140 MVARGAGATVNL LRESDNPSIINI MRQR.HGRIVNI MILQGAGVIVNI αFG2 00000000 210 RERPELFETWLD FSDPEKLDYMLK LDENIKAE.MLK LDENIKAE.MLK	150 GSMSGTIVNI GSLTVEEVTI ASV.VGVTGI ASVA.SLVA * * * MTPMGRCGE RIPLGRTGV LIPAAQFGE RIPQE	<u>00000000</u> 160 RPOFASSYMASKG MPN.ISAYAASKG NPG.QANYVAAKA PG.RSAYTSKG * * αG 00000000000 PSEIAAAILFLAS PEDLKGVAVELAS AQUADAVMELAS	αF 170 170 AVHQITRALAF GVASITKALAF GVIGLTKTSAF AVLQITKSVA 240 PAASYVTGAII EEAKYVTGQII DQSKYITGQTI EDATYVNGAAI	βF 180 AEWAGRGVVVNAL CEWGRYGIRVNVI CELASRNITVNAI DYAGSGIRCNAV 3G 250 AVDGGYTVW EVDGGWTAN NVDGGMVM. VMDGAYTAI	190 A PGYVATEMT A PGWYRTKMT A PGFIATDMT C PGMIETPMT	αFG1 200 LKM EAV D.V QWR

Supplement Figure 1.

Structure-based sequence alignment of GatDH with the structurally closest SDR relatives as identified by the *DALI* server (1). The DALI server identified 2-(*R*)-hydroxypropyl-COM-dehydrogenase (PDB-entry 2CFC (2) from *Xantho-bacter autotrophicus* and 3-oxoacylreductase (PDB-entry 2UVD (3) from *Bacillus anthracis* as the closest structural homologues of GatDH. The structure of gluconate 5-dehydrogenase (PDB-entry 1VL8) from *Thermotoga maritima* was used as the template for homology modeling with *SwissModel* (4). The four conserved catalytic key residues and further GatDH positions discussed in the text are labeled by blue asterisks and the main binding motifs for the NAD(H) cofactor are underlined in green. The alignment was prepared with *SuperPose* (5) and *ESPript* (6). The secondary structure elements of GatDH as determined by *DSSP* (7) are shown above its sequence and are labeled according to (8).

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