Consensus Α

E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) L. pneumophila MDH (Q52T13.1) C. burnetii Cbul241 (NP_820236.1) Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP 417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AAI42007.1) L. casei LDH (2ZQY_A)

Consensus

E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) L. pneumophila MDH (Q5ZT13.1) C. burnetii Cbul241 (NP_820236.1) C. DATHELTI CULT241 (HP_020236.1, Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP_417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AAI42007.1) L. casei LDH (2ZQY_A)

Consensus

Consensus E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) L. pneumophila MDH (Q5ZT13.1) C. burnetii Cbul241 (NP_820236.1) Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP_417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AAI42007.1) L. casei LDH (220Y A) L. casei LDH (2ZQY_A)

Consensus

Consensus E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) L. pneumophila MDH (Q5ZT13.1) L. pneumophila MDH (QSZTI3.1) C. burnetii Cbul241 (NP_820236.1) Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP_417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AAI42007.1) L. casei LDH (2ZQY_A)

Consensus

E. coli L-LDH (P33232) E. coli L-LDH (P33232)
Pig heart cytop. MDH (P11708)
T. thermophilus MDH (AFH39418.1)
L. pneumophila MDH (Q5ZT13.1)
C. burnetii Cbul241 (NP_820236.1)
Pig heart mitoch. MDH (P00346.2)
E. coli MDH (NP_417703.1)
B. melitensis LDH/MDH (3GVH_B)
Cow heart LDH (AAT42007.1)
L. casei LDH (Z20Y A) L. casei LDH (2ZQY A)

Consensus

E. coli L-LDH (P33232) E. COIL L-LDE (P3322)
Pig heart cytop. MDH (P11708)
T. thermophilus MDH (AFH39418.1)
L. pneumophila MDH (Q52T13.1)
C. burnetii Cbul241 (NP_820236.1)
Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP_417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AA142007.1) L. casei LDH (2ZQY_A)

Consensus E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) T. thermophilus MDH (AFH39418.1) L. pneumophila MDH (Q5ZT13.1) C. burnetii Cbul241 (NF_820236.1) Pig heart mitoch. MDH (P00346.2) E. coli MDH (NP_417703.1) B. melitensis LDH/MDH (3GVH_B) Cow heart LDH (AAI42007.1) L. casei LDH (2ZQY_A)

Consensus

E. coli L-LDH (P33232) Pig heart cytop. MDH (P11708) T. thermophilus MDH (AFH39418.1) L. Intermophilus MDH (Q5ZT13.1)
L. pneumophila MDH (Q5ZT13.1)
C. burnetii Cbul241 (NP_820236.1)
Pig heart mitoch. MDH (P00346.2)
E. coli MDH (NP_417703.1)
B. melitensis LDH/MDH (3GVH_B)
C. burneti VDP (02420201) Cow heart LDH (AAI42007.1) L. casei LDH (2ZQY_A)

MXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	60 60
L-SAAARPAGAAL	13
-M-ATUKEKLIAPV	12
ETTLFNEKLSMPVALAPUCLCGMYARRGEVQAAKAADAHGIPFTLSTVSVCPIEEVAPAI MSEPIRVLVTQAACGIAYSLL YSIGNGSVFGKDQPIILVILDIPPMM MKAPVRVAVTGAACGICYSLL FRIAAGEMLGKDQPVILGLEIPQAM MTNNRVRVATGAACGICYALV FRIASGQMFGPNEVELN LELEPAL MKHVKVAVTGAACGICYALL FRLASGQAFGLDTVDLH LEIEPAL -RRSFSTSMONAKVAVIGASGICQPLS LLKN-SPLVSRLTYUIA MKVAVUTGASGICQLS LLKN-SPLVSRLTYUIA GPGSMARNIALIG-SCMIGTLA LLLKTQLPSGSELSYDIAP GPGSMARNIALIG-SCMIGTLA HLAGL-KELDELAVDUFDIAE 	115 120 47 47 48 47 59 37 41 56 44
KRPMWFQLYVLRDRGFMRNALERAKAAGCSTLVFTVDW TPGARY DAHSGMSG GVLDCVLMEI QDCALPL-LKDVIATDKEEIAFKDLDVAILVGSM FRDGME KDILKA- KALE GVMBI DDCAFPL-LAGLEATDDPRVAFKDADVALLVGSA FRKAGMER DILEM- PSLECVAMEI DDCAFPL-LKRIVCTADLNKAMDGVNWALLVGSA FRKAGMER SDILQI- PALKCVMMEI EDCAFPL-LKRIVCTADLNKAMDGVNWALLVGSA FRKAGMER SDILQI- HT-PCVAADI SHIETRATVKGYLGPEQLPDCLKGCDVVVIPAGV FRKAGMER SDILQI- VT-PCVAVDI SHIETRATVKGYLGPEQLPDCLKGCDVVVIPAGV FRKAGMER SDIFNT- GTPQCKGLDIAESSPVDGFDAKFTGANDYAAIEGADVVIVTAGV FRKAGMER DDIGI- DLKKGEMMD QHGSLFLQ-TPKIVADKDYSVTANSKIVVVTAGVRQQE ESILNIVQF- DKTKGDAID SNALPF-T-SPKKIYSAEYSDAKDADLVVITAGA QKRGET IDIVNK-	173 174 104 105 104 116 93 99 113 100
NAMMRYL-QAVTH-PQWAWDVGLNGRIHDL	229 204 159 159 160 159 173 150 153 167 154
-GNISAYLGKPTGLEDYIGWLGNNFDPS ISWKDLEWIR-DFWD HN AKAQIALKLGVTSDDVKNVIIWGNHSSTYM DVNHAKVKLQAKEVGVYEAVKDDSWL HN AKAQIALKLGVPVDRIRRMTVWGNHSSTMP DLFHAEVDGR PALELV-DMEWY DIRARTQLAKKAGVDITAVTQMTIWGNHSSTQY DFYNAKINGT SAQVINDETWL QNRAIGQLALKAGVDVPSVKNMIIWGNHSSTQY DFYHATIDGK PATEVIRDKNWL IW ANAFVAELKGLDPARVSVPVIGHAGKTIILISQCT-PKV DF SAFRYFLSEEFNVSVEDVTVFVLGHGDSVTILLLSQV-PGV SF	285 245 219 214 216 215 218 194 207 221 208
GPMVIKGILDPEDARDAVRFGADGIVVSNH GGRQLDGVLSSARAL	332 290 261 256 258 257 266 242 254 254 254
XXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	368 345 297 291 293 292 300 276 287 302 287
NLLNLIEKEM-KVAMTLTGAKSISEITQDSLVQGLGKELPAALA NLLNLIEKEM-KVAMTLTGAKSISEITQDSLVQGLGKELPAALA MIVEGLPINDFSREKMDLTAKEIAEKET AFEFLSSA	418 396 334 327 330 328 338 312 324 324 324 326

Consensus L. pneumophila NAD-ME (Q5ZXTO) MLDXXXXXXXXXXXXXJXXXXXXJLXXPXLNKGXAFXXXERXXXXLXGXLPXXVZXX B Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) -----MKKGYEV RD OLNT -----MKYTPEQIIND 0. oeni MLE (Q48796.1) FIN AFTEA EEL L. pneumophila NAD-ME (Q5ZW08) C. burnetii Cbu0823(NP_819843. L. pneumophila NAD-ME (Q5ZRB1) MLDFSLNRDPQT-GELYIETSLCGKPL MLEITFKTD-KN-NKPYLETGITGKAL -----MAIKVTKRGMDI .1) -----MEPKTKKQRSLYIPYAGPVL E. coli NAD-ME (NP 415996.2) Consensus L. pneumophila NAD-ME (Q5ZXTO) Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) L. Casel MLE (CAQ5929.1) O. ceni MLE (Q48796.1) L. pneumophila NAD-ME (Q52W08) C. burnetii Cbu0823(NP_819843.1) L. pneumophila NAD-ME (Q52RB1) E. coli NAD-ME (NP_415996.2) OVIEHRLVKNHVOEMLET: Consensus XXXXXXXXPXG XXJXXXXXXXJXXXJXXXXXXXXXJ L. pneumophila NAD-ME (Q5ZXTO) AIAEA---PEN-AY-----RF--TSKGNLVA HYGLAFRRPRG-LFITIHDRGHIATMLQSWPE-SVIKAI MTNCTA' D. PREUMOPHIA NAD-ME (QSZAIO)
 Pigeon liver NADP-ME (P40927.1)
 L. casei MLE (CAQ65929.1)
 O. ceni MLE (Q48796.1)
 L. pneumophila NAD-ME (Q5ZN08)
 C. burnetii Cbu0823(NP_819843.1)
 L. pneumophila NAD-ME (Q5ZRB1)
 E. coli NDD ME (ND A15006.2) HYGLAFKRING DETTIHDIGHIATMUQSWEE-SVIKAI NYSALFVNGONATYLSIDOPDHIESALKHSANGROIRLI NYSELFVEGGAAFLDINHPENIQSTLKNAANGROIKLL RFSHEYRQIRG LVIAHSDKNQLEEIINNRSN-PDIDLV AFNKRFMHRG-LVISVEDRNQIKKILNNRSH-PIIDLI MFSHIYRQERG-VVFLSYPERKLDSIIQNIASTRSTKVI E. coli NAD-ME (NP 415996.2) RESEIYERS G-VFISYONRHNMDDILONVPN-HNKV IXXGKLXXYTXXXGIXPXXXLPXXL XGTNNZXLLXDPXYJGXRXXRXXXXXXXXXXXXXX Consensus L. pneumophila NAD-ME (05ZXT0) KAVLFKRFADL Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) MLI VLI LALYTACGC AAA D YGPI MVYTVAAC MVYSLCGC MVYTAIGC 0. oeni MLE (048796.1) /RGD C. ochi MLE (Q43790.1) L. pneumophila NAD-ME (Q5ZW08) C. burnetii Cbu0823(NP_819843.1) L. pneumophila NAD-ME (Q5ZRB1) E. coli NAD-ME (NP_415996.2) SGN SI Consensus XXXXXXXX -XXXI.XXF YYYNAYY.TLYYY XBXJX pneumophila NAD-ME (Q5ZXTO) IATAKRIAPTFGGINI ΕĦ DQH IEQLNIP Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) MEAVTSRYGMNCLIQH FANANAFRLI ΗKΥ RNKYC VTTAEKLEP-NLYLH GRSNZ GRSNZ (DOIT: L. ADT 0. oeni MLE (Q48796.1) VNHAESLF SNI OKIA C. beni MLE (Q43790.1)
L. pneumophila NAD-ME (Q5ZW08)
C. burnetii Cbu0823(NP_819843.1)
L. pneumophila NAD-ME (Q5ZRB1)
E. coli NAD-ME (NP_415996.2) VNEIHKOF NAI GRG RRI DELC IEAVOATE RTN ITC VQSIKRHM IQAVKQRW Consensus XXXXXLXXXXXXX KGIXXXJXXXXXXGLSXXXAXXXX AG TASMRLLV------ALGAPKSNMI DALIGTANLIVMAMOKE WSKEDI I KRIMM TACAG I TSRVYEAFIED I SPEDAKKHFYI TACAG I VKQLHEEMVEQ GI SPEDAKKHFYI SATGI SDQI VDAWVKSI SIJIDA VDRFWI SATGI SDQI VDAWVKSI SIJIDA VDRFWI L. pneumophila NAD-ME (Q5ZXT0) SDIKIVC ALGAPKSNMLII Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) ITKNR SDHTVLFC ISKQK FDQVYLSI O. oeni MLE (Q48796.1) ISGO DOTYMSF L. pneumophila NAD-ME (Q5ZW08) C. burnetii Cbu0823(NP_819843.1) L. pneumophila NAD-ME (Q5ZRB1) LTD EKE VTGL HEHRIVVE PEQRIAV DTLFRALSON ITRS VINTP KEHRVAL EOLVHAMMN EEE RSRFY GIAEMIISQTQRE E. coli NAD-ME (NP_415996.2) AAGGQLSEKKIVFLO E T Consensus XXXXXEXZXIXXXXXX . pneumophila NAD-ME (Q5ZXT0) /KFAFARNTSCRT-------EDAL-EDIVK VAR-PI VAAIGO L. pneumophila NAD-ME (Q52X10) Pigeon liver NADP-ME (P40927.1) L. casei MLE (CA065929.1) O. ceni MLE (Q48796.1) L. pneumophila NAD-ME (Q52W08) VI VI II II TI ECKPTARKRSEFANAD----ALTNIEAVVKANHPYV TI ECKPFARKRSEFANAD----QLTNIQAAVEAVHPTII TI BOKPFAAKRSDFKNAN----QLTNIQAAVEAVHPTII TI DOKPYARNPIDIOSWEINNKQHPSFTDTIRWKPII VTSAQPYLRKKEEIASWKIKNPQISILEVIEN KPTII LI BOKFVRSSTSLQNWKLEKKGEITITDVINNAQPII LI BOTKLVQKRENLSDWDTDS-DVLSLDVVRVKKBDI ISTVPG C. burnetii Chu0823(NP_819843.1) L. pneumophila NAD-ME (Q5ZRB1) E. coli NAD-ME (NP_415996.2) OSHA Consensus TXXXEAXXXDJXXWXXGXXLXATGXPXXXXXXX-XXXXXX XXXRI Consensus L. pneumophila NAD-ME (Q52XTO) Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) O. ceni MLE (Q48796.1) L. pneumophila NAD-ME (Q52W08) NPV: RKDLVMAT FDPVTL FNI PAEQLY RGI KAI RAI HT: KT.A KAD**D**I VIKW VIKW IAI ICI P P ANVDY SYAI PVDDIEYE AFAPIEYÇ TSI SNAYQI SCERP: NRMVQI DEK C. burnetii Chou823(NP 819843.1)
L. pneumophila NAD-ME (Q52RB1)
E. coli NAD-ME (NP_415996.2) HVEK E NOIFPV hR! EDITE HC Consensus L. pneumophila NAD-ME (Q5ZXT0) LDVRATCINQAMQIAA VEAIRQLVHEPVPQVVKDN VNWDFGPDYII D. Dimensionality in the (p40927.1) L. casei MLE (CAQ65929.1) O. oeni MLE (Q48796.1) AEVIAÕEVSEENLÕEGR KHIGDDVFI GLGLG GLGFG IAS IA7 TAKLLTDSM: ISAAAHSI ISAAAHSI GIVDPDQPGA-A GIVDTTKVGA-A SKLLTPE Sasrltki Cent MLE (Q48/90.1)
 L. pneumophila NAD-ME (Q5ZW08)
 C. burnetii Cbu0823 (NP_819843.1)
 L. pneumophila NAD-ME (Q5ZRB1)
 E. coli NAD-ME (NP_415996.2) ILAAAQTISKFAPSKKDSFLF LWSASQAISRYANESTHR---MMAAAVAISELAPAIRTGEGR LMSASETLAQYSPLVLNGEGM SRITDE LK ---XXXXSXXXAXA ***** Consensus L. pneumophila NAD-ME (Q5ZXTO) Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) O. oeni MLE (Q48796.1) IQQVSLKIAV LDQFSQTVAI LADFSRTVAV L. pneumophila NAD-ME (Q5ZW08) C. burnetii Cbu0823(NP_819843.1) L. pneumophila NAD-ME (Q5ZRB1) AQIVAKEI/ QEASRQVA IREV QHI/ IOKV E coli NAD-ME (NP_415996.2) Consensus AMKVKL pneumophila NAD-ME (Q5ZXT0) L. pneumophila NAD-ME (Q52XTO) Pigeon liver NADP-ME (P40927.1) L. casei MLE (CAQ65929.1) O. oeni MLE (Q48796.1) L. pneumophila NAD-ME (Q52X08) C. burnetii Cbu0823(NP 819843.1) L. pneumophila NAD-ME (Q52RB1) AMKVKL E. coli NAD-ME (NP 415996.2)

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355 232

335 337

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353 352

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347

415 275 385

400

474

321 445

452

451 472

459

465

523 381

494

500 499

579

440

551 554

577

564

570

585 411

565

LR 275 277

MN

LК 292

XXXXXX

VIHSGRED

TVKGRAS

DDMSD

DDDPD

ATDOE

HDEMTD

DKMPN

AΑ 393 392 413

٩ĸ 412

AL

ΥL 471

FEEIIREM HК 406

FLGO

AL

et the 59 58

IADTIE

TADTIE

AAAK 119 118

NAVR OACE 105 113 AACE

YDI YDI

S1 Fig. Protein sequence alignments of representative (A) MDHs and LDHs including CBU1241, and

(B) MEs and MLEs including CBU0823.

The pertinent accession numbers are provided in parentheses. Residues in sequences sharing identity with consensus are highlighted.