

**Table S5:** Results of single deletion studies. Agreements with experimental data are highlighted in gray. A ‘+’ indicates growth under the given condition, ‘-’ means lethal deletion. Reaction abbreviations used herein can be found in supplemental data, Table S2. The details of the media used can be found in Materials & Methods and Table 1. Abbreviations used for subsystem: A: Amino Acid Metabolism, C: Central Metabolism, O: Others, T: Transport, V: Vitamine and Cofactor Metabolism, W: Cell wall metabolism.

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP0003	KdsA	KDOPS	W	-	-	-	-	-
HP0004, HP1186	IcfA, Cah	HCO3E	O	+	+	+	+	+
HP0005	PyrF	OMPDC	N	-	-	-	-	+
HP0006	PanC	PANTS	V	-	-	-	-	-
HP0026	GltA	CS	C	+	+	+	+	+
HP0027	Icd	ICDHyr	C	+	+	+	+	+
HP0029	BioD	DBTSr	V	-	-	-	-	-
HP0034	PanD	ASP1DC	V	-	-	-	-	-
HP0043	AlgA, ManC	MAN6PI, MAN1PT2r	W	-	-	-	-	-
HP0044	Gmd	GMAND	W	-	-	-	-	-
HP0045	Fcl	GFUCS	W	-	-	-	-	-
HP0055	PutP	PROt4r	T	+	+	+	+	+
HP0056	PutA	4HGLSD, HPROX, P5CD, PHCD, PROD2, PUTA3	C	+	+	+	+	+
HP0067 -HP0070, UreA, UreB, UreE, UreF, UreG, UreH	UREA		C	+	+	+	+	+
HP0072-73								
HP0071	Urel	UREAt	T	+	+	+	+	+
HP0075	GlmM	PGAMT	W	-	-	-	-	-
HP0086	Mqo	MDH4	C	-	-	+	+	+
HP0089	Mtn	AHCYSNS, MTAN	O	-	-	-	-	-
HP0090	FabD	MCOATA	W	-	-	-	-	-
HP0093, HP0094, HP0159, HP0208, RfaC, HP0279, HP0826, GalTb	RfaJ, FutC, LPSSYN-HP		W	-	-	-	-	-
HP1416								
HP0096, HP0397	SerA	PGCD	A	-	-	+	+	+
HP0098	ThrC	THRS	A	-	-	-	+	+
HP0105	LuxS	RHCCE	O	-	-	-	-	+
HP0106	MetB	AHSERL2, METB1r, SHSL1r, SHSL2r, SHSL4r	A	-	-	-	-	+
HP0107	CysK	CYSS	A	-	-	-	-	+
HP0112	FucA	FCLPA	W	+	+	+	+	+
HP0121	PpsA	PPS	C	-	+	+	+	+
HP0132	SdaA	SERD-L, THRD-L	A	+	+	+	+	+
HP0133	SdaC	SERt2r	T	+	+	+	+	+
HP0134	Dhs1	DDPA	A	-	-	-	-	-
HP0140, HP0141	LctP	L-LACt2r	T	+	+	+	+	+
HP0154	Eno	ENO	C	-	+	+	+	+
HP0157	AroK	SHKK	A	-	-	-	-	-
HP0163	HemB	PPBNGS	V	-	-	-	-	+
HP0176	Fba	FBA, FBA2	C	-	+	+	+	+
HP0183	GlyA	GHMT2r	A	-	-	-	-	+
HP0192, HP0191, HP0193	FrdA, FrdB, FrdC	FRD5	C	+	+	+	+	+
HP0194	Tpi	TPI	C	-	-	-	-	-
HP0196	LpxD	U23GAAT-HP	W	-	-	-	-	-
HP0197	MetX	METAT	V	-	-	-	-	-

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP0198	Ndk	NDPK1-8	N	-	-	-	-	-
HP0202	FabH	ACOATA, KAS-HP2	W	+	+	+	+	+
HP0212	DapE	SDPDS	A	-	-	-	-	-
HP0215	CdsA	DASYN-HP	W	-	-	-	-	-
HP0216	Dxr	DXPRIi	V	-	-	-	-	-
HP0228	Sop	SULabc	T	+	+	+	+	+
HP0230	KdsB	KDOCT	W	-	-	-	-	-
HP0237	HemC	HMBS	V	-	-	-	-	+
HP0239	HemA	GLUTRR	V	-	-	-	-	+
HP0240	IspB	OCTDPS	O	-	-	-	-	-
HP0255	PurA	ADSS	N	-	-	+	+	+
HP0266, HP0581	PyrC	DHORTS	N	-	-	-	-	+
HP0279	RfaC	RFAC-HP	W	-	-	-	-	-
HP0283	AroB	DHQS	A	-	-	-	-	-
HP0290	LysA	DAPDC	A	-	-	-	+	+
HP0291	PheA	CHORM	A	-	-	-	+	+
HP0293	PabB	PABB	V	-	-	-	-	-
HP0294	AmiE	AMID2, 4, 5	O	+	+	+	+	+
HP0306	HemL	G1SATi	V	-	-	-	-	+
HP0313	NarK	NARK	T	+	+	+	+	+
HP0321	Gmk	DGK1, GK1	N	-	-	-	-	-
HP0329	NadE	NADS1	V	-	-	-	-	+
HP0330	IlvC	KARA1i, KARA2i	A	+	+	+	+	+
HP0349	PyrG	CTPS1	N	-	-	-	-	-
HP0354	Dxs	DXPS	V	-	-	-	-	-
HP0360	GalE	UDPG4E	W	-	-	-	-	+
HP0364, HP0680	NrdA, NrdB	RNDR1-4	N	-	-	-	-	-
HP0372	Dcd	DCTPD, DCTPD2	N	+	+	+	+	+
HP0376	HemH	FCLT	V	-	-	-	-	+
HP0380	GdhA	GLUDy	A	+	+	+	+	+
HP0381	HemK	PPPGO	V	-	-	-	-	+
HP0389	SodB	SPODM	C	+	+	+	+	+
HP0396	UbiD	OPHBDC	V	+	+	+	+	+
HP0400	IspH	DMPPS, IPDPS	V	-	-	-	-	-
HP0401	AroA	PSCVT	A	-	-	-	-	-
HP0409	GuaA	GMPS2	N	-	-	+	+	+
HP0422	SpeA	ARGDC, GLUDC	V	-	-	-	-	-
HP0476, HP0643	GltX	GLUTRS	V	-	-	-	-	+
HP0493	MraY	PAPPT3	W	-	-	-	-	-
HP0494	MurD	UAMAGS	W	-	-	-	-	-
HP0509	GlcD	GLYCTO1	O	-	-	-	-	-
HP0510	DapB	DHDPRy	A	-	-	-	-	-
HP0512	GlnA	GLNS	A	-	-	+	+	+
HP0549	Glr	GLUR	O	-	-	-	-	-
HP0557, HP0370	AccA, AccC, AccD,	ACCOACr	W	-	-	-	-	-
HP0950, HP0371	FabE	ACCOACr	W	-	-	-	-	-
HP0558	FabF	KAS-HP	W	+	+	+	+	+
HP0558, HP0561	FabF, FabG, FabI	C140SN, C160SN, C180SN, C181SN,	W	-	-	-	-	-
HP0195, HP1376	FabZ	KAS15	W	-	-	-	-	-
HP0558, HP0561	FabF, FabG, FabI	C190cSN	W	-	-	-	-	-
HP0195, HP1376	FabZ, Cfa	C190cSN	W	-	-	-	-	-
HP0416				-	-	-	-	-
HP0566	DapF	DAPE	A	-	-	-	-	-
HP0572	Apt	ADPT	N	+	+	+	+	+
HP0574	Rpi	RPI	C	-	-	+	+	+
HP0577	FoID	FTHFLLi, MTHFC, MTHFD	V	-	-	-	+	+

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP0587	PabC	ADCL	V	-	-	-	-	-
HP0588 - HP0591	OorA, OorB, OorC, OorD	OOR	C	-	-	-	-	-
HP0598	BioF	AOXSr	V	-	-	-	-	-
HP0604	HemE	UPPDC1, UPPDC2	V	-	-	-	-	+
HP0618	Adk	ADK1, DADK	N	-	-	-	-	-
HP0620	Ppa	PPA	O	-	-	-	-	-
HP0623	MurC	UAMAS	W	-	-	-	-	-
HP0624	AspB	SDPTA	A	-	-	-	-	-
HP0625	IspG	MECDPDH	V	-	-	-	-	-
HP0626	DapD	THDPS	A	-	-	-	-	-
HP0630	MdaB	NADPHQR	C	+	+	+	+	+
HP0631 - HP0634	HydA, HydB, HydC, HydD	HYDA1	C	+	+	+	+	+
HP0642, HP1161	Fdo, FldA	FLDO	C	-	-	-	-	+
HP0646	GalU	GALU	W	-	-	-	-	+
HP0648	MurZ	UAGCVT	W	-	-	-	-	-
HP0649	AspA	ASPT	A	+	+	+	+	+
HP0652	SerB	PSP-D, PSP-L	A	-	-	+	+	+
HP0663	AroC	CHORS	A	-	-	-	-	-
HP0665, HP1226	HemN	CPPPGO	V	-	-	-	-	+
HP0672	AspB2	ASPTA, EHGLAT, PHETA1, TYRTA	A	-	-	-	+	+
HP0683	GlmU	G1PACT, UAGDP, UAGDP2	W	-	-	-	-	-
HP0687	FeoB	FE2abc	T	-	-	-	-	+
HP0690	AtoB	ACACT1r	O	+	+	+	+	+
HP0691, HP0692	YxjD, YxjE	OCOAT1	C	+	+	+	+	+
HP0700	DgkA	DAGK-HP	W	+	+	+	+	+
HP0723	AnsB	ASNN, ASNS2	W	-	-	+	+	+
HP0724	DcuA	ASnT2, ASPt2r, MALt2r, SUCCt2, SUCFUMti	T	+	+	+	+	+
HP0735	Gpt	GUAPRT, HXPRT, XPPT	N	+	+	+	+	+
HP0736	SerC	PSERT	A	-	-	+	+	+
HP0737	PgpA	PGPP-HP	W	-	-	-	-	-
HP0738	Dd1A	ALAALAR	W	-	-	-	-	-
HP0740	MurF	UGMDDS	W	-	-	-	-	-
HP0742	PrsA	PRPPS	N	-	-	-	-	-
HP0772	AmiA	AMAA	W	+	+	+	+	+
HP0777	PyrH	UMPK	N	-	-	-	-	-
HP0779	Acnb	ACONT	C	+	+	+	+	+
HP0802	RibA	GTPCII	V	-	-	-	-	-
HP0804	RibB	DB4PS	V	-	-	-	-	-
HP0808	AcpS	ACPS	V	+	+	+	+	+
HP0814	ThiF	THZSN	V	+	+	+	+	+
HP0818, HP0819	ProV, ProWX	PROabc	T	+	+	+	+	+
HP0822	MetL	HSDy	A	-	-	-	+	+
HP0822, HP1229	MetL, LysC	ASPK	A	-	-	-	+	+
HP0824, HP1458,	TrxA, TrxB	TRDR	O	-	-	-	-	-
HP0825, HP1164	AtpA, AtpB, AtpC, AtpD, AtpE, AtpF, ATPS4r, AtpG, AtpH		C	+	+	+	+	+
HP0828, HP1212, HP1137								
HP0829	GuaB	IMPD	N	-	-	+	+	+
HP0831	CoaE	DPCOAK	V	-	-	-	-	-
HP0832	SpeE	SPMS, SPRMS	V	-	-	-	-	-
HP0843	ThiB	TMPPP	V	+	+	+	+	+
HP0844	ThiD	PMPK	V	+	+	+	+	+
HP0845	ThiM	HETZK	V	+	+	+	+	+

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP0854	GuaC	GMPR	N	+	+	+	+	+
HP0857	GmhA	S7PI	W	-	-	-	-	-
HP0858	RfaE	GMHEPAT, GMHEPK	W	-	-	-	-	-
HP0859	RfaD	AGMHE	W	-	-	-	-	-
HP0860	YaeD	GMHEPPA	W	-	-	-	-	-
HP0865	Dut	DUTPDP	N	+	+	+	+	+
HP0867	LpxB	LPADSS-HP	W	-	-	-	-	-
HP0871	Cdh	CDAPPA-HP	W	+	+	+	+	+
HP0875	KatA	CAT	C	+	+	+	+	+
HP0903	AckA	ACKr	O	+	+	+	+	+
HP0905	Pta	PTAr	O	+	+	+	+	+
HP0919, HP1237	PyrAa, PyrAb	CBPS	N	-	-	-	-	+
HP0928	FolE	GTPCI	V	-	-	-	-	-
HP0929	IspA	DMATT, GRTT	O	-	-	-	-	-
HP0930	SurE	ACP1(FMN)	V	+	+	+	+	+
HP0936	ProP	PROt2r	T	+	+	+	+	+
HP0941	Alr	ALAR	A	+	+	+	+	+
HP0942	DagA	ALA <sub>t</sub> 2, ALA <sub>t</sub> 4, DALA <sub>t</sub> 2, DSERt2, GLYt2	T	-	-	-	-	-
HP0943	DadA	DAAD	A	+	+	+	+	+
HP0957	KdtA	MOAT-HP	W	-	-	-	-	-
HP0961	GpsA	G3PD1, G3PD2	W	-	-	-	-	-
HP0974	Pgm	PGM	C	-	+	+	+	+
HP0976	BioA	AMAOTr	V	-	-	-	-	-
HP1011	PyrD	DHORD3	N	-	-	-	-	+
HP1013	DapA	DHDPS	A	-	-	-	-	-
HP1016	PgsA	PGSA-HP	W	-	-	-	-	-
HP1017	RocE	ARGt2r, ORNt2r	T	-	-	-	-	-
HP1020	IspDF	MECDPS, MEPCT	V	-	-	-	-	-
HP1036	FolK	HPPK	V	+	+	+	+	+
HP1038	AroQ	DHQD	A	-	-	-	-	-
HP1045	AcoE	ACS	O	+	+	+	+	+
HP1050	ThrB	HSK	A	-	-	-	+	+
HP1052	EnvA	UHGADA-HP	W	-	-	-	-	-
HP1058	PanB	MOHMT	V	-	-	-	-	-
HP1071	PssA	PSSA-HP	W	-	-	-	-	-
HP1077, HP1576	NixA, AbcC	Nlabc	T	+	+	+	+	+
HP1084	PyrB	ASPCT	N	-	-	-	-	+
HP1087	RibF	FMNAT, RBFK	V	-	-	-	-	-
HP1088	Tkta1	TKT1, TKT2	C	-	-	-	-	-
HP1091	KgtP	AKGt2r	T	+	+	+	+	+
HP1099	Eda	DDPGA, EDA	C	+	+	+	+	+
HP1100	Edd	EDD	C	+	+	+	+	+
HP1101	G6pdh2	G6PDH2	C	+	+	+	+	+
HP1102	DevB	PGL	C	+	+	+	+	+
HP1103	Glk	HEX1	C	+	+	+	+	+
HP1104	Cad	ALCD2y	O	+	+	+	+	+
HP1108 - HP1111	PorA, PorB, PorC, PorD	PDH2	C	-	-	-	-	+
HP1112	PurB	ADSL1r, ADSL2r	N	-	-	+	+	+
HP1118	Ggt	GTMLT	O	+	+	+	+	+
HP1140	BirA	BACCL	V	+	+	+	+	+
HP1155	MurG	UAGPT3	W	-	-	-	-	-
HP1158	ProC	HPROa, P5CR	C	-	-	-	+	+
HP1166	Pgi	PGI	C	-	+	+	+	+

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP1169 - HP1172	GlnH, GlnP, GlnQ	GLNabc	T	+	+	+	+	+
HP1174	GluP	GALt2, GLCt2	T	+	+	+	+	+
HP1178	DeoD	DURIPP, PUNP1-7	N	+	+	+	+	+
HP1179	DeoB	PPM, PPM2	N	+	+	+	+	+
HP1180	NupC	ADNt2, CYTDT2, DADNT2, DCYTt2, DURIt2, THMDt2, URIt2	T	+	+	+	+	+
HP1189	Asd	ASAD	A	-	-	-	+	+
HP1210	CysE	SERAT	A	-	-	-	-	+
HP1218	PurD	PRAGSr	N	-	-	+	+	+
HP1221	UppS	UDCPDPS	O	+	+	+	+	+
HP1222	Dld	LDH-D1	C	+	+	+	+	+
HP1224	HemD	UPP3S	V	-	-	-	-	+
HP1227, HP0144	- C553, CcoQ, FixN, FixO, FixP	CYOO-HP	C	+	+	+	+	+
HP0147								
HP1227, HP1538	- C553, FbcF, FbcH	BC10	C	+	+	+	+	+
HP1540								
HP1228	InvA	DNMPPA, DNTPPA	V	-	-	-	-	-
HP1232	FolP	DHPS, FOLD3	V	-	-	-	-	-
HP1238	AmiF	FORAMD	O	+	+	+	+	+
HP1249	AroE	SHK3Dr	A	-	-	-	-	-
HP1257	PyrE	ORPT	N	-	-	-	-	+
	Nqo10, Nqo11, Nqo12, Nqo13, Nqo14, Nqo3, Nqo4, Nqo5, Nqo6, NDH-1 Nqo7, Nqo8, Nqo9, NuoE, NuoF							
HP1260 - HP1273			C	+	+	+	+	+
HP1275	AlgC	PMANM	W	-	-	-	-	-
HP1277, HP1278	TrpA, TrpB	TRPS1-3	A	-	-	-	-	-
HP1279	TrpC	IGPS, PRAli	A	-	-	-	+	+
HP1280	TrpD	ANPRT	A	-	-	-	+	+
HP1281, HP1282	TrpE	ANS, ASN2	A	+	+	+	+	+
HP1290	PnuC	NMNTP	T	+	+	+	+	+
HP1325	FumC	FUM	C	+	+	+	+	+
HP1337	NadD	NMNAT, NNAT	V	-	-	-	-	+
HP1345	Pgk	PGK	C	-	+	+	+	+
HP1346, HP0921	Gap	GAPD	C	-	+	+	+	+
HP1348	PlsB, PlsC	PASYN-HP	W	-	-	-	-	-
HP1355	NadC	NNDPR	V	-	-	-	-	+
HP1356	NadA	QLNS	V	-	-	-	-	+
HP1357	Psd	PSD-HP	W	-	-	-	-	-
HP1360	UbiA	HBZOPT	V	+	+	+	+	+
HP1375	LpxA	UAGAAT-HP	W	-	-	-	-	-
HP1380	TyrA	PPND	A	-	-	-	+	+
HP1385	Fbp	FBP	C	-	+	+	+	+
HP1386	Rpe	RPE	C	+	+	+	+	+
HP1394	PpnK	NADK	V	-	-	-	-	-
HP1398	Ald	ALAD-L	A	+	+	+	+	+
HP1399	RocF	ARGN	C	-	-	-	+	+
HP1400, HP0686, HP0807, HP0888	HP0889, FecA, FecD, FecE	FEDCabc	T	+	+	+	+	+
HP1406	BioB	BTS2	V	-	-	-	-	-
HP1418	MurB	UAPGR	W	-	-	-	-	-
HP1434, HP1141	PurU, Fmt	FTHFD	V	+	+	+	+	+
HP1443	IspE	CDPMEK	V	-	-	-	-	-
HP1461	Cper	CCP	C	+	+	+	+	+
HP1468	IlvE	ILETA, LEUTA, VALTA	A	-	-	-	-	-
HP1474	Tmk	DTMPK, TMDK1, URIDK2r	N	-	-	-	-	-

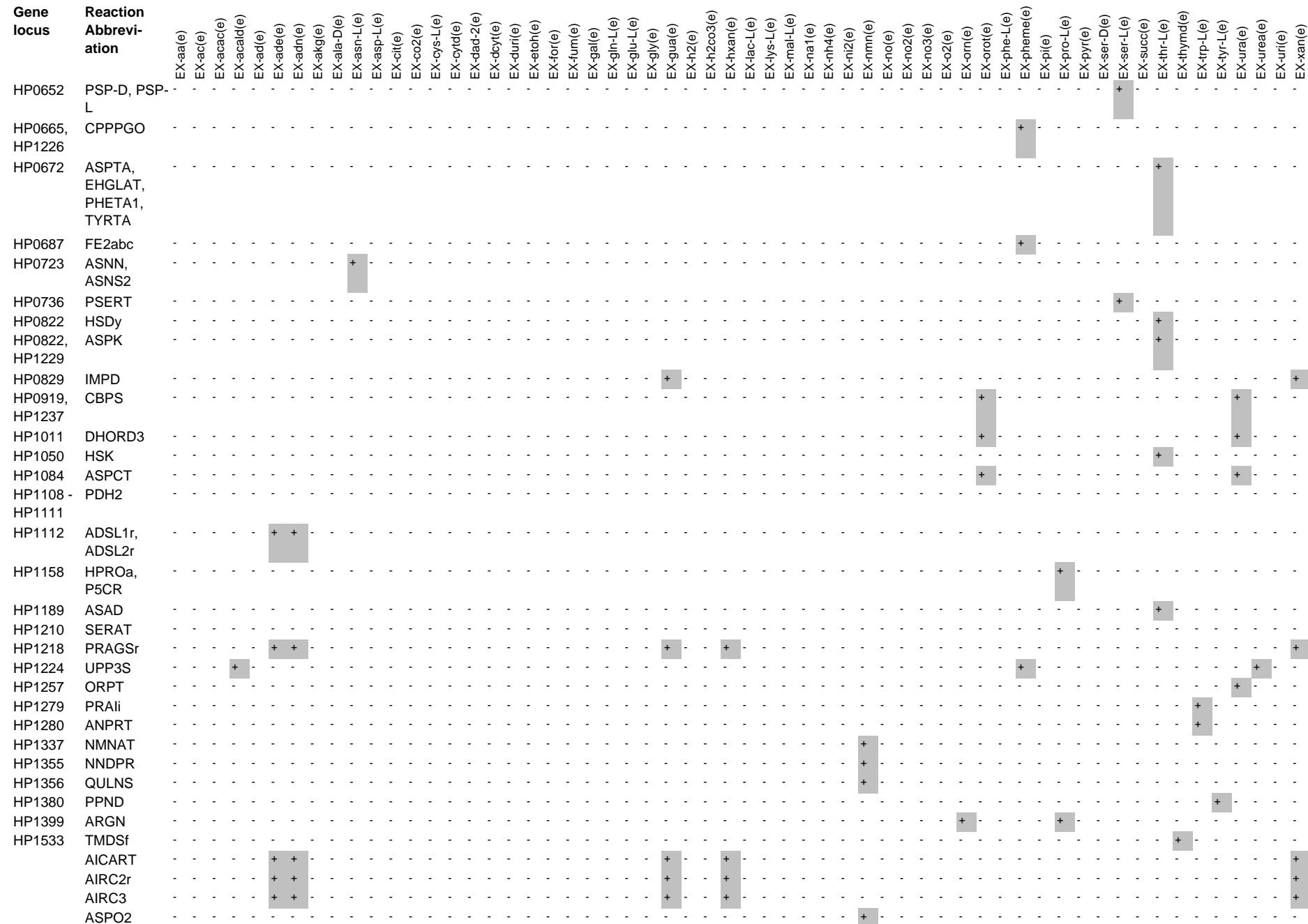
Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
HP1475	KdtB	PTPATi	V	-	-	-	-	-
HP1483	UbiE	AMMQT6, OMBZLM	V	-	-	-	-	-
HP1491	PitB	Plt2r	T	-	-	-	-	-
HP1494	MurE	UAAGDS	W	-	-	-	-	-
HP1495	Tal	TALA	C	+	+	+	+	+
HP1505	RibD	APRAUR, DHPPDA	V	-	-	-	-	-
HP1506	GltS	GLUt2r	T	+	+	+	+	+
HP1510	FolB	DHNPAs	V	-	-	-	-	-
HP1532	GlmS	GF6PTA	W	-	-	-	-	-
HP1533	ThyX	TMDSf	N	-	-	-	-	+
HP1545	FolC	DHFS	V	-	-	-	-	-
HP1552, HP1183	NhaA, NapA	NAT3-1	T	+	+	+	+	+
HP1563	AhpC	NTRARz	O	+	+	+	+	+
HP1574, HP0002	RibC, RibE	RBFSa, RBFSb	V	-	-	-	-	-
		A5PISO	W	-	-	-	-	-
		AAtr	T	+	+	+	+	+
		ACACt2	T	+	+	+	+	+
		ACALDt	T	+	+	+	+	+
		ACt2r	T	+	+	+	+	+
		ADD	N	+	+	+	+	+
		ADEt2	T	+	+	+	+	+
		ADMDCr	V	-	-	-	-	-
		ADNUC	N	+	+	+	+	+
AKO	ADSK	ADSK	O	+	+	+	+	+
		ADtr	T	+	+	+	+	+
		AGMT	V	-	-	-	-	-
		AICART	N	-	-	+	+	+
		AIRC2r	N	-	-	+	+	+
		AIRC3	N	-	-	+	+	+
		AKO	C	+	+	+	+	+
		ARGSL	C	+	+	+	+	+
		ARGSS	C	+	+	+	+	+
		ASNabc	T	+	+	+	+	+
ASPO2	BPNT	ASPO2	V	-	-	-	-	+
		BPNT	V	+	+	+	+	+
		CHCOAL	V	-	-	-	-	-
		CLPNS-HP	W	-	-	-	-	-
		CO2t	T	+	+	+	+	+
		CYSabc	T	+	+	+	+	+
		CYTK1	N	-	-	-	-	-
		DHFRI	V	-	-	-	-	-
		DHNAOT2	V	-	-	-	-	-
		DHPTDC	O	-	-	-	-	+
DKMPPD	DPR	DKMPPD	A	-	-	-	-	-
		DPR	V	-	-	-	-	-
		DURIK1	N	+	+	+	+	+
		ETOHt2r	T	+	+	+	+	+
		FADOX	C	+	+	+	+	+
		FORt	T	+	+	+	+	+
		FRDO	C	-	-	-	-	-
		FUMt3	T	+	+	+	+	+
		G5SADr	A	-	-	-	+	+
		G6PDH1	C	+	+	+	+	+
GALK	GALK	GALK	W	+	+	+	+	+

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
	GALTi	W		+	+	+	+	+
	GARFTi	N		+	+	+	+	+
	GART	N		+	+	+	+	+
	GCALDDr	O		-	-	-	-	-
	GLUN	A		+	+	+	+	+
	GLUPRT	N		-	-	+	+	+
	GLYK	W		-	-	-	-	-
	GND	C		+	+	+	+	+
	GNNUC	N		+	+	+	+	+
	GSNt2	T		+	+	+	+	+
	GUAt	T		+	+	+	+	+
	H2CO3D	O		+	+	+	+	+
	H2CO3D2	O		+	+	+	+	+
	H2CO3TP	T		+	+	+	+	+
	H2Ot	T		+	+	+	+	+
	HEMEti	T		+	+	+	+	+
	HISabc	T		-	-	-	-	-
	HSERTA	A		-	-	-	-	+
	HYXNt	T		+	+	+	+	+
	ICHORSi	V		-	-	-	-	-
	ILEabc	T		-	-	-	-	-
	IMPC	N		-	-	+	+	+
	KAS14	W		-	-	-	-	-
	KDOPP	W		-	-	-	-	-
	LacR	O		+	+	+	+	+
	LEUabc	T		-	-	-	-	-
	LYSt2r	T		+	+	+	+	+
	MALS	C		-	-	-	-	-
	MDRPDr	A		-	-	-	-	-
	ME1-rev	O		+	+	+	+	+
	METabc	T		-	-	-	-	-
	MTHFR2	V		-	-	-	-	-
	MTRI	A		-	-	-	-	-
	MTRK	A		-	-	-	-	-
	NH4t2r	T		+	+	+	+	+
	NO	O		+	+	+	+	+
	NO3t2	T		+	+	+	+	+
	NO3t3	T		+	+	+	+	+
	NOt	T		+	+	+	+	+
	NPHS	V		-	-	-	-	-
	O2t	T		-	-	-	-	-
	OCBTi	C		+	+	+	+	+
	ORNTA	A		-	-	-	+	+
	OROATP	T		+	+	+	+	+
	OXGDC2	V		-	-	-	-	-
	PAPSR	O		+	+	+	+	+
	PEPT-HP	W		+	+	+	+	+
	PGMT	O		-	-	-	-	+
	PHCHGS	C		+	+	+	+	+
	PHEt2r	T		+	+	+	+	+
	PIMEtr	T		-	-	-	-	-
	PMDPHT	V		-	-	-	-	-
	PNTK	V		-	-	-	-	-
	PPCDC	V		-	-	-	-	-

Gene Locus	Gene Name	Reaction abbreviation	Subsystem	min I	min II	min III	min IV	rich
	PPNCL2	V		-	-	-	-	-
	PPNDH	A		-	-	-	+	+
	PPTGS	W		-	-	-	-	-
	PRAIS	N		-	-	+	+	+
	PRASCS	N		-	-	+	+	+
	PRFGS	N		-	-	+	+	+
	PYRDC	O		+	+	+	+	+
	PYRt2r	T		+	+	+	+	+
	RFA-HP	W		-	-	-	-	-
	SADT2	O		+	+	+	+	+
	SHCHCS2	V		-	-	-	-	-
	sink_ahcys	O		-	-	-	-	-
	sink_amob	O		-	-	-	-	-
	SUCBZL	V		-	-	-	-	-
	SUCBZS	V		-	-	-	-	-
	SULR	O		+	+	+	+	+
	THMabc	T		-	-	-	-	-
	THRt2r	T		+	+	+	+	+
	TRPt2r	T		+	+	+	+	+
	TYRt2r	T		+	+	+	+	+
	U2GAAT	W		-	-	-	-	-
	U2GAAT2	W		-	-	-	-	-
	UDCPDP	W		-	-	-	-	-
	UNK2	A		-	-	-	-	-
	UPPRT	N		+	+	+	+	+
	URAt2	T		+	+	+	+	+
	USHD-HP	W		-	-	-	-	-
	VALabc	T		-	-	-	-	-
	XANt2	T		+	+	+	+	+

**Table S6:** Alteration of gene essentiality on dependency of medium composition. Basis is minimum medium plus D-Glucose (min II). Each compound has been added separately to the medium.

Gene locus	Reaction Abbreviation EX-aa(e) EX-ac(e) EX-acad(e) EX-ad(e) EX-ade(e) EX-adn(e) EX-akg(e) EX-ala-D(e) EX-asn-L(e) EX-asp-L(e) EX-cit(e) EX-co2(e) EX-cys-L(e) EX-cyt(d)e EX-dec-2(e) EX-dcyt(e) EX-dur(e) EX-ethoh(e) EX-for(e) EX-fum(e) EX-gal(e) EX-ghn-L(e) EX-ghu-L(e) EX-gly(e) EX-gta(e) EX-h2(e) EX-hco3(e) EX-hxane(e) EX-lac-L(e) EX-lys-L(e) EX-mal-L(e) EX-na1(e) EX-nb4(e) EX-ni2(e) EX-nmn(e) EX-no(e) EX-no2(e) EX-no3(e) EX-o2(e) EX-ornt(e) EX-orot(e) EX-phe-L(e) EX-pheme(e) EX-pile EX-pro-L(e) EX-pyr(e) EX-ser-D(e) EX-ser-L(e) EX-succ(e) EX-thr-L(e) EX-thymd(e) EX-trp-L(e) EX-tyr-L(e) EX-ure(a) EX-unr(e) EX-xan(e)
HP0005	OMPDC
HP0086	MDH4
HP0089	AHCYSNS, MTAN
HP0096, HP0397	PGCD
HP0098	THRS
HP0105	RHCCE
HP0106	AHSERL2, METB1r, SHSL1r, SHSL2r, SHSL4r
HP0107	CYSS
HP0163	PPBNGS
HP0183	GHMT2r
HP0237	HMBS
HP0239	GLUTRR
HP0255	ADSS
HP0266, HP0581	DHORTS
HP0290	DAPDC
HP0291	CHORM
HP0306	G1SATi
HP0329	NADS1
HP0360	UDPG4E
HP0376	FCLT
HP0381	PPPGO
HP0409	GMPS2
HP0476, HP0643	GLUTRS
HP0512	GLNS
HP0574	RPI
HP0577	MTHFC, MTHFD
HP0604	UPPDC1, UPPDC2
HP0642, HP1161	FLDO
HP0646	GALU



Gene locus	Reaction Abbreviation
DHPTDC	- EX-aa(e) EX-ac(e)
G5SADr	- EX-acac(e) EX-acald(e)
GLUPRT	- + + EX-ad(e)
HSERTA	- + + EX-adn(e)
IMPC	- + + EX-ade(e)
ORNTA	- + + EX-ahg(e)
PGMT	- + + EX-ala-D(e)
PPNDH	- + + EX-asn-L(e)
PRAIS	- + + EX-asp-L(e)
PRASCS	- + + EX-cit(e)
PRFGS	- + + EX-co2(e)
	- EX-cys-L(e)
	- EX-cyd(e)
	- EX-dad-2(e)
	- EX-dcyt(e)
	- EX-dun(e)
	- EX-eioh(e)
	- EX-for(e)
	- EX-fum(e)
	- EX-gal(e)
	- EX-gln-L(e)
	- EX-glu-L(e)
	- EX-gly(e)
	- EX-gua(e)
	- EX-h2o2(e)
	- EX-h2co3(e)
	- EX-hxan(e)
	- EX-iac-L(e)
	- EX-lys-L(e)
	- EX-mal-L(e)
	- EX-na1(e)
	- EX-nh4(e)
	- EX-ni2(e)
	- EX-nmn(e)
	- EX-no(e)
	- EX-np2(e)
	- EX-no3(e)
	- EX-o2(e)
	- EX-ornt(e)
	- EX-orot(e)
	- EX-phe-L(e)
	- EX-pheme(e)
	- EX-pl(e)
	+ EX-pro-L(e)
	- EX-pyr(e)
	- EX-ser-D(e)
	- EX-ser-L(e)
	- EX-succ(e)
	- EX-thr-L(e)
	- EX-thymd(e)
	- EX-trp-L(e)
	- EX-urea(e)
	- EX-unl(e)
	- EX-xan(e)