

Supplementary Table S4. Essential proteins involved in lice, acarine specific pathway, their KO list, and their pathways.

Pathways	Assigned KO list	Protein	Pathogen
Two-component system	K02313	chromosomal replication initiator protein DnaA	<i>Borrelia recurrentis</i>
	K03413	response regulator	<i>Borrelia recurrentis</i>
	K03412	chemotaxis protein CheB	<i>Borrelia recurrentis</i>
	K07659	PETR protein (ompR)	<i>Rickettsia prowazekii</i> Madrid E
	K07638	osmolarity sensor protein ENVZ (envZ)	<i>Rickettsia prowazekii</i> Madrid E
	K00426	cytochrome D ubiquinol oxidase subunit II (cydB)	<i>Rickettsia prowazekii</i> Madrid E
	K02313	chromosomal replication initiation protein	<i>Rickettsia prowazekii</i> Madrid E
	K02313	chromosomal replication initiator protein DnaA	<i>Orientia tsutsugamushi</i> str. Boryong
	K13584	response regulator transcription factor	<i>Orientia tsutsugamushi</i> str. Boryong

	K02488	PleD family two-component system response regulator	<i>Orientia tsutsugamushi</i> str. Boryong
	K07716	two-component sensor histidine kinase	<i>Orientia tsutsugamushi</i> str. Boryong
	K02313	chromosomal replication initiator protein DnaA	<i>Borrelia mayonii</i>
	K03413	response regulator	<i>Borrelia mayonii</i>
	K03406	methyl-accepting chemotaxis protein	<i>Borrelia mayonii</i>
Peptidoglycan biosynthesis	K00790	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	<i>Borrelia recurrentis</i>
	K01924	UDP-N-acetylmuramate--L-alanine ligase	<i>Rickettsia prowazekii</i> Madrid E
	K01921	D-alanine--D-alanine ligase	<i>Rickettsia prowazekii</i> Madrid E
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Rickettsia prowazekii</i> Madrid E
	K03587	penicillin binding protein (pbpA2)	<i>Rickettsia prowazekii</i> Madrid E
	K00790	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	<i>Rickettsia prowazekii</i> Madrid E

	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Rickettsia prowazekii</i> Madrid E
	K01928	UDP-N-acetylmuramoylalanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Rickettsia prowazekii</i> Madrid E
	K01928	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Borrelia recurrentis</i>
	K06153	undecaprenyl-diphosphate phosphatase	<i>Borrelia recurrentis</i>
	K01925	UDP-N-acetylmuramoyl-L-alanine--D-glutamate ligase	<i>Borrelia recurrentis</i>
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Borrelia recurrentis</i>
	K01929	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase	<i>Borrelia recurrentis</i>
	K05366	BP1A family penicillin-binding protein	<i>Borrelia recurrentis</i>
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Borrelia recurrentis</i>
	K01924	UDP-N-acetylmuramate--L-alanine ligase	<i>Borrelia recurrentis</i>
	K03587	PASTA domain-containing protein	<i>Borrelia recurrentis</i>
	K00075	UDP-N-acetylmuramate dehydrogenase	<i>Borrelia recurrentis</i>

	K00790	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	<i>Orientia tsutsugamushi</i> str. Boryong
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Orientia tsutsugamushi</i> str. Boryong
	K00075	UDP-N-acetylmuramate dehydrogenase	<i>Orientia tsutsugamushi</i> str. Boryong
	K00790	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	<i>Borrelia mayonii</i>
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Borrelia mayonii</i>
	K06153	undecaprenyl-diphosphate phosphatase	<i>Borrelia mayonii</i>
	K01925	UDP-N-acetylmuramoyl-L-alanine--D-glutamate ligase	<i>Borrelia mayonii</i>
	K01928	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Borrelia mayonii</i>
	K00075	UDP-N-acetylmuramate dehydrogenase	<i>Borrelia mayonii</i>
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Borrelia mayonii</i>
	K03587	transpeptidase family protein	<i>Borrelia mayonii</i>
Lysine biosynthesis-	K01928	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Borrelia recurrentis</i>

	K01929	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase	<i>Borrelia recurrentis</i>
	K00215	dihydrodipicolinate reductase	<i>Rickettsia prowazekii</i> Madrid E
	K01928	UDP-N-acetylmuramoylalanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Rickettsia prowazekii</i> Madrid E
	K00928	aspartate kinase	<i>Orientia tsutsugamushi</i> str. Boryong
	K00215	4-hydroxy-tetrahydrodipicolinate reductase	<i>Orientia tsutsugamushi</i> str. Boryong
	K01928	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2,6-diaminopimelate ligase	<i>Borrelia mayonii</i>
Quorum sensing-	K15582	MULTISPECIES: ABC transporter permease	<i>Borrelia recurrentis</i>
	K15580	peptide ABC transporter substrate-binding protein	<i>Borrelia recurrentis</i>
	K03076	preprotein translocase subunit SecY	<i>Rickettsia prowazekii</i> Madrid E
	K03217	membrane protein insertase YidC	<i>Borrelia recurrentis</i>
	K03076	preprotein translocase subunit SecY	<i>Orientia tsutsugamushi</i> str. Boryong

	K03075	preprotein translocase subunit SecG	<i>Borrelia mayonii</i>
	K03076	preprotein translocase subunit SecY	<i>Borrelia mayonii</i>
	K15580	peptide ABC transporter substrate-binding protein	<i>Borrelia mayonii</i>
	K15582	ABC transporter permease	<i>Borrelia mayonii</i>
	K03076	preprotein translocase subunit SecY	<i>Borrelia miyamotoi</i>
	K15580	peptide ABC transporter substrate-binding protein	<i>Borrelia miyamotoi</i>
	K15582	ABC transporter permease	<i>Borrelia miyamotoi</i>
Insect hormone biosynthesis pathway	K10718	conserved hypothetical protein	<i>Ixodes scapularis</i> (black-legged tick)
	K14938	conserved hypothetical protein	<i>Pediculus humanus</i> var. <i>corporis</i> (human body louse)
D-Alanine metabolism	K01775	alanine racemase	<i>Borrelia recurrentis</i>
	K01775	alanine racemase	<i>Rickettsia prowazekii</i> Madrid E
	K01921	D-alanine--D-alanine ligase	<i>Rickettsia prowazekii</i> Madrid E

Bacterial chemotaxis	K03412	chemotaxis protein CheB	<i>Borrelia recurrentis</i>
	K03413	response regulator	<i>Borrelia recurrentis</i>
	K03413	UDP-N-acetylglucosamine 1-carboxyvinyltransferase	<i>Borrelia mayonii</i>
	K03406	methyl-accepting chemotaxis protein	<i>Borrelia mayonii</i>
	K03413	response regulator	<i>Borrelia miyamotoi</i>
Methane metabolism	K01624	class II fructose-bisphosphate aldolase	<i>Borrelia recurrentis</i>
	K01624	class II fructose-bisphosphate aldolase	<i>Borrelia mayonii</i>
	K01624	class II fructose-bisphosphate aldolase	<i>Borrelia miyamotoi</i>
Bacterial secretion system	K03074	protein translocase subunit SecF	<i>Borrelia recurrentis</i>
	K03217	membrane protein insertase YidC	<i>Borrelia recurrentis</i>
	K03074	preprotein translocase subunit SecF	<i>Rickettsia prowazekii</i> Madrid E
	K03076	preprotein translocase subunit SecY	<i>Rickettsia prowazekii</i> Madrid E
	K03076	preprotein translocase subunit SecY	<i>Orientia tsutsugamushi</i> str. Boryong

	K03118	twin-arginine translocase subunit TatC	<i>Orientia tsutsugamushi</i> str. Boryong
	K03199	VirB4 family type IV secretion/conjugal transfer ATPase	<i>Orientia tsutsugamushi</i> str. Boryong
	K03201	type IV secretion system protein	<i>Orientia tsutsugamushi</i> str. Boryong
	K03201	type IV secretion system protein	<i>Orientia tsutsugamushi</i> str. Boryong
	K03075	preprotein translocase subunit SecG	<i>Borrelia mayonii</i>
	K03076	preprotein translocase subunit SecY	<i>Borrelia mayonii</i>
	K03074	protein translocase subunit SecF	<i>Borrelia mayonii</i>
	K03076	preprotein translocase subunit SecY	<i>Borrelia miyamotoi</i>
Monobactam biosynthesis	K00215	dihydrodipicolinate reductase	<i>Rickettsia prowazekii</i> Madrid E
	K00928	aspartate kinase	<i>Orientia tsutsugamushi</i> str. Boryong
	K00215	4-hydroxy-tetrahydrodipicolinate reductase	<i>Orientia tsutsugamushi</i> str. Boryong

Lipopolysaccharide biosynthesis	K02517	lipid A biosynthesis lauroyl acyltransferase	<i>Rickettsia prowazekii</i> Madrid E
	K00677	UDP-N-acetylglucosamine acyltransferase	<i>Rickettsia prowazekii</i> Madrid E
	K02527	3-deoxy-D-manno-octulosonic-acid transferase	<i>Rickettsia prowazekii</i> Madrid E
beta-Lactam resistance	K03587	penicillin binding protein (pbpA2)	<i>Rickettsia prowazekii</i> Madrid E
	K15580	peptide ABC transporter substrate-binding protein	<i>Borrelia recurrentis</i>
	K05366	PBP1A family penicillin-binding protein	<i>Borrelia recurrentis</i>
	K03587	transpeptidase family protein	<i>Borrelia recurrentis</i>
	K15582	MULTISPECIES: ABC transporter permease	<i>Borrelia recurrentis</i>
	K15580	peptide ABC transporter substrate-binding protein	<i>Borrelia mayonii</i>
	K15582	ABC transporter permease	<i>Borrelia mayonii</i>
	K03587	transpeptidase family protein	<i>Borrelia mayonii</i>
	K03587	transpeptidase family protein	<i>Borrelia miyamotoi</i>
	K15582	ABC transporter permease	<i>Borrelia miyamotoi</i>

Vancomycin resistance	K01775	alanine racemase	<i>Rickettsia prowazekii</i> Madrid E
	K01921	D-alanine--D-alanine ligase	<i>Rickettsia prowazekii</i> Madrid E
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Rickettsia prowazekii</i> Madrid E
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Rickettsia prowazekii</i> Madrid E
	K01775	alanine racemase	<i>Borrelia recurrentis</i>
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Borrelia recurrentis</i>
	K01929	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase	<i>Borrelia recurrentis</i>
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Borrelia recurrentis</i>
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Orientia tsutsugamushi</i> str. Boryong
	K01000	phospho-N-acetylmuramoyl-pentapeptide-transferase	<i>Borrelia mayonii</i>
	K02563	undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase	<i>Borrelia mayonii</i>

	K01921	D-alanine--D-alanine ligase	<i>Borrelia miyamotoi</i>
	K01000	phospho-N-acetylmuramoyl- pentapeptide-transferase	<i>Borrelia miyamotoi</i>
	K01775	50S ribosomal protein L11	<i>Borrelia miyamotoi</i>
	K02563	undecaprenyldiphospho- muramoylpentapeptide beta-N- acetylglucosaminyltransferase	<i>Borrelia miyamotoi</i>
Cationic antimicrobial peptide (CAMP) resistance	K00677	UDP-N-acetylglucosamine acyltransferase	<i>Rickettsia prowazekii</i> Madrid E
	K01448	LysM peptidoglycan-binding domain-containing protein	<i>Borrelia recurrentis</i>
Ribosome	K02994	transpeptidase family protein	<i>Borrelia miyamotoi</i>
	K02933	50S ribosomal protein L6	<i>Borrelia miyamotoi</i>
	K02867	50S ribosomal protein L11	<i>Borrelia miyamotoi</i>
	K02931	50S ribosomal protein L5	<i>Borrelia miyamotoi</i>
	K02895	50S ribosomal protein L24	<i>Borrelia miyamotoi</i>
	K02888	50S ribosomal protein L21	<i>Borrelia miyamotoi</i>
	K02982	30S ribosomal protein S3	<i>Borrelia miyamotoi</i>
	K02881	50S ribosomal protein L18	<i>Borrelia miyamotoi</i>

	K02907	50S ribosomal protein L30	<i>Borrelia miyamotoi</i>
	K02884	50S ribosomal protein L19	<i>Borrelia miyamotoi</i>
	K02864	50S ribosomal protein L10	<i>Borrelia miyamotoi</i>
	K02890	50S ribosomal protein L22	<i>Borrelia miyamotoi</i>
	K02990	30S ribosomal protein S6	<i>Borrelia miyamotoi</i>
Phosphotransferase system (PTS)	K00882	1-phosphofructokinase	<i>Borrelia recurrentis</i>
	K02804	PTS transporter subunit EIIC	<i>Borrelia recurrentis</i>
Carbon fixation in photosynthetic organisms	K01624	class II fructose-bisphosphate aldolase	<i>Borrelia mayonii</i>
D-Amino acid metabolism	K01925	UDP-N-acetylmuramoyl-L-alanine-- D-glutamate ligase	<i>Borrelia mayonii</i>
Peroxisome	K00869	mevalonate kinase	<i>Borrelia mayonii</i>
Cell cycle - Caulobacter	K02313	chromosomal replication initiator protein DnaA	<i>Borrelia mayonii</i>
	K02314	replicative DNA helicase	<i>Borrelia mayonii</i>
	K03590	cell division protein FtsA	<i>Borrelia mayonii</i>
	K02563	undecaprenyldiphospho- muramoylpentapeptide beta-N- acetylglucosaminyltransferase	<i>Borrelia mayonii</i>

	K03531	cell division protein FtsZ	<i>Borrelia mayonii</i>
Flagellar assembly	K03086	RNA polymerase sigma factor RpoD	<i>Borrelia mayonii</i>
	K02419	flagellar type III secretion system pore protein FliP	<i>Borrelia miyamotoi</i>
	K03086	RNA polymerase sigma factor RpoD	<i>Borrelia miyamotoi</i>
PPAR signaling pathway	K01641	hydroxymethylglutaryl-CoA synthase	<i>Borrelia miyamotoi</i>