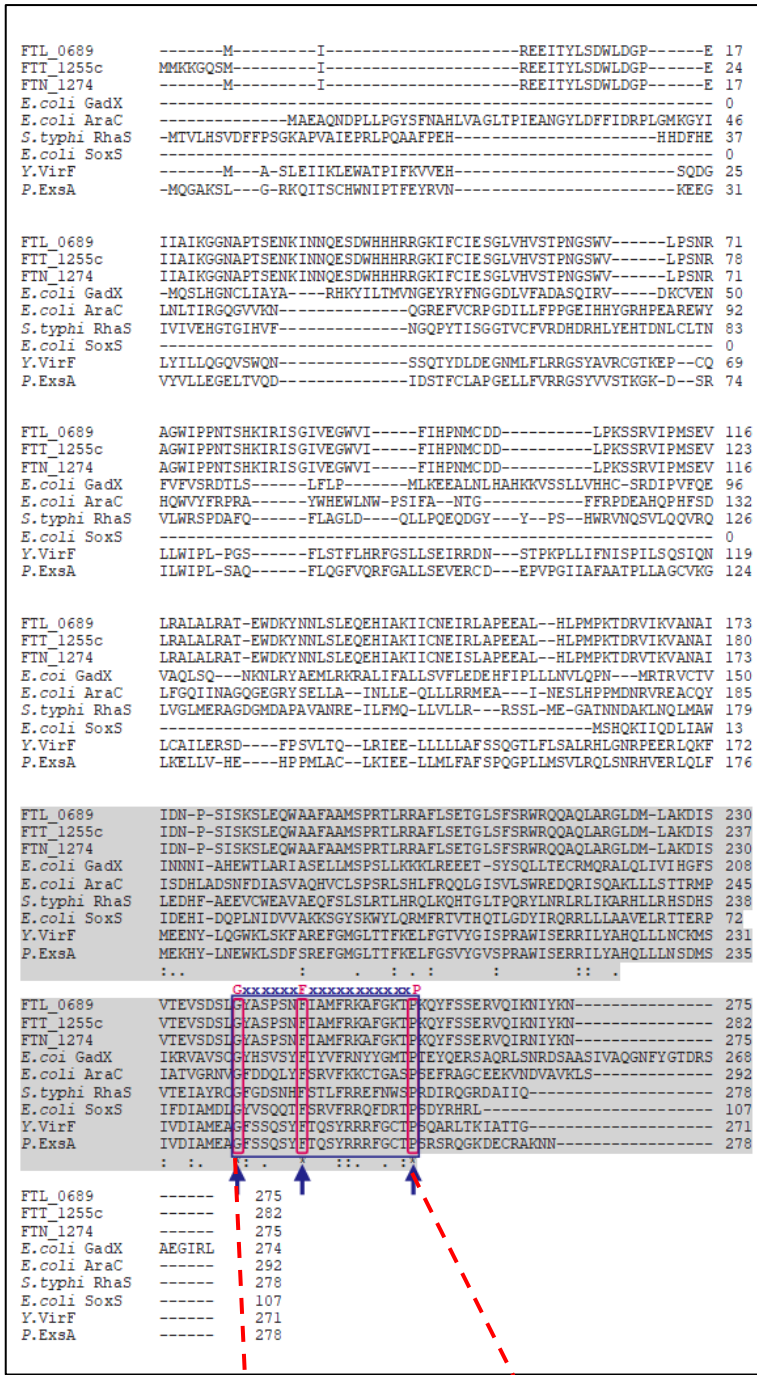


**Figure S1**

**A**



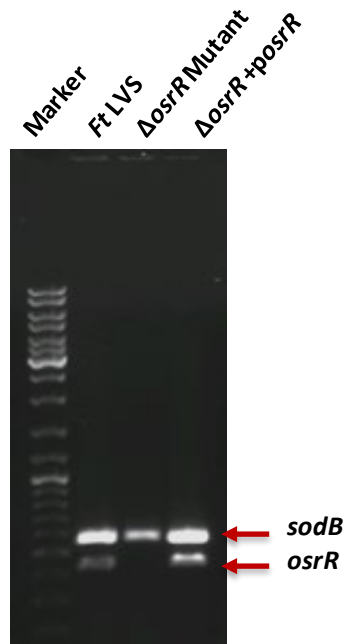
**C**



**B**

Pathogen	Locus tag	Product	% Identity
<i>F. tularensis</i> subsp. <i>tularensis</i> SchuS4	FTT_1255c	AraC family transcriptional regulator <i>osrR</i>	99.65%
<i>F. novicida</i> U112	FTN_1274	AraC family Transcriptional regulator <i>osrR</i>	98.91%
<i>E. coli</i> K-12	U069_c0078	AraC family putative transcriptional regulator protein	33.33%
<i>E. coli</i>	N/A	DNA-binding transcriptional regulator SoxS	27.27%
<i>S. enterica</i> subsp. <i>enterica</i> serovar Typhi	CJP42_0176	HTH-type transcriptional activator RhaS	26%
<i>Y. enterocolitica</i>	RLY99535	Virulence regulon transcriptional activator VirF	28%
<i>P. aeruginosa</i> PAO1	PA1713	transcriptional regulator ExsA	20.46%

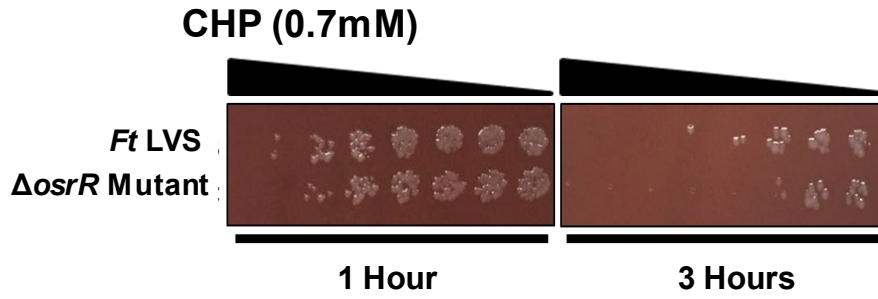
**D**



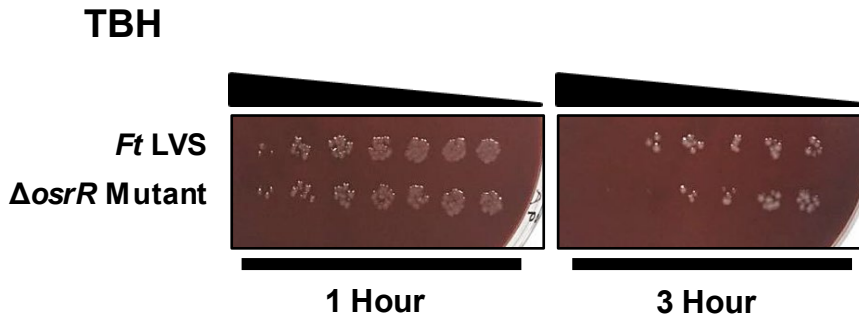
**Figure S1:** (A) Amino acid sequence alignment of the *osrR* (*FTL\_0689*) of *F. tularensis* (*Ft*) LVS and XylS/AraC family proteins from indicated bacterial pathogens. Multiple alignments were generated using Clustal W software. The C-terminal region (highlighted in grey) shows a conserved DNA binding motif GxxxxxxFxxxxxxxxxxxP. (B) Amino acid sequence homology of the AraC of indicated bacterial strains as compared to the OsrR of *Ft* LVS. (C) OsrR C-terminal region showing the conserved DNA binding motif (GxxxxxxFxxxxxxxxGxxP). (D) Confirmation of *osrR* gene deletion and transcomplementation by PCR. The wild type *Ft* LVS and *sodB* gene primers were used as positive and internal controls, respectively.

Figure S2

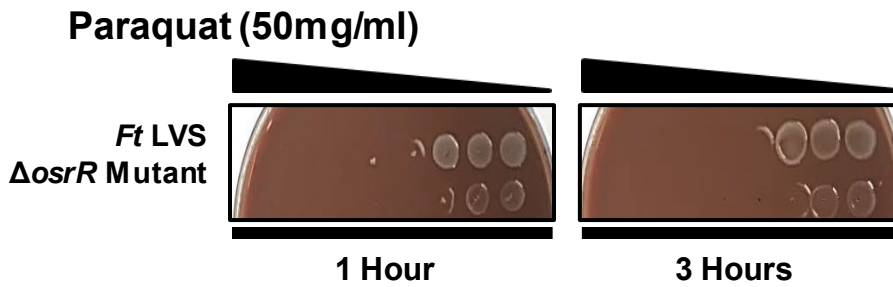
A



B

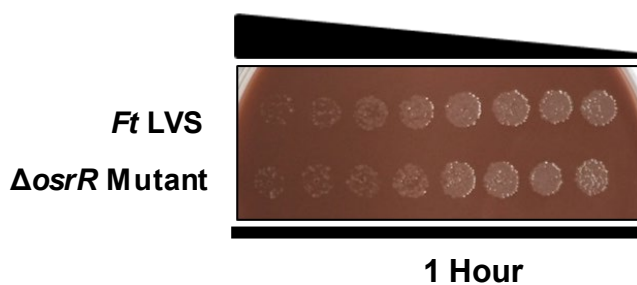


C



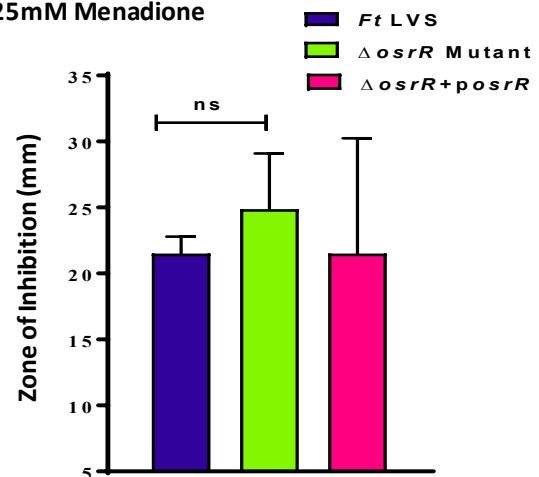
D

Menadione (1.25mM)



E

1.25mM Menadione



**Figure S2:** Wild type *F. tularensis* LVS (*Ft* LVS) and the  $\Delta osrR$  mutant were exposed to **(A)** Cumene hydroperoxide (CHP); **(B)** Tert-butyl hydroperoxide (TBH); **(C)** Paraquat; and **(D)** Menadione diluted two-fold with a starting indicated concentrations for one hour and three hours in a spot assay. **(E)** The sensitivities of the wild type *F. tularensis* LVS (*Ft* LVS), the  $\Delta osrR$  mutant and the transcomplemented strain ( $\Delta osrR+posrR$ ) to menadione was determined by disc diffusion assay and the zone of inhibition around the discs impregnated with the indicated concentration of menadione was measured. The results shown in A, B, C and D are representative of two independent experiments. The data shown in E are representative of two independent experiments, each conducted with three technical replicates.

# Figure S3

## A

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	Old locus	Product	Pathway
FTL_RS03610	14.29	-0.67	0.15	-4.42	9.76E-06	1.95E-02	FTL_0689	AraC family transcriptional regulator	Transcription
FTL_RS00320	33.74	-0.41	0.17	-2.47	1.35E-02	9.99E-01	FTL_0061	FUSC family protein	Transport
FTL_RS00345	131.18	-0.34	0.16	-2.09	3.64E-02	9.99E-01	FTL_0069	outer membrane protein assembly factor BamE	Transport
FTL_RS00390	58.87	-0.33	0.16	-2.05	4.03E-02	9.99E-01	FTL_0078	Bifunctional diaminohydroxyphosphoribosylaminopyrimidine deaminase/5-amino-(5-phosphoribosylamino)uracil reductase RibD	Metabolism
FTL_RS00520	8.44	-0.3	0.13	-2.25	2.45E-02	9.99E-01	FTL_0106	nicotinamide ribonucleoside (NR) uptake permease (PnuC) family protein	Transport
FTL_RS01090	10.05	-0.31	0.14	-2.2	2.78E-02	9.99E-01	FTL_0205	tetratricopeptide repeat protein	Stress response
FTL_RS01120	56.94	-0.38	0.17	-2.27	2.34E-02	9.99E-01	FTL_0211	hypothetical protein	Hypothetical Protein
FTL_RS01880	37.29	-0.4	0.17	-2.41	1.58E-02	9.99E-01	N/A	hypothetical protein	Hypothetical Protein
FTL_RS02295	54.81	-0.48	0.17	-2.87	4.07E-03	9.99E-01	FTL_0443	MFS transporter	Transport
FTL_RS02905	99.44	-0.35	0.16	-2.12	3.37E-02	9.99E-01	FTL_0555	tRNA pseudouridine(55) synthase TruB	Translation
FTL_RS02910	444.76	-0.34	0.15	-2.18	2.96E-02	9.99E-01	FTL_0556	ribonuclease R	Transcription
FTL_RS05040	931.64	-0.28	0.13	-2.19	2.88E-02	9.99E-01	FTL_0986	ribonucleotide-diphosphate reductase subunit alpha	Replication
FTL_RS05695	17.35	-0.33	0.16	-2.1	3.57E-02	9.99E-01	FTL_1121	hypothetical protein	Hypothetical Protein
FTL_RS06425	55.15	-0.35	0.17	-2.13	3.28E-02	9.99E-01	N/A	carbon-nitrogen hydrolase	Metabolism
FTL_RS06605	283	-0.33	0.16	-2.03	4.20E-02	9.99E-01	FTL_1294	short-chain dehydrogenase/reductase	Metabolism
FTL_RS07875	39.87	-0.33	0.17	-1.98	4.77E-02	9.99E-01	FTL_1540	cell division protein FtsL	Replication
FTL_RS07980	10.97	-0.32	0.14	-2.27	2.32E-02	9.99E-01	N/A	asparaginase	Metabolism
FTL_RS08090	25.08	-0.43	0.16	-2.61	9.01E-03	9.99E-01	FTL_1587	EF-P lysine aminoacylase GenX	Translation
FTL_RS08465	27.14	-0.42	0.17	-2.52	1.17E-02	9.99E-01	FTL_1661	nucleoside permease	Transport

## B

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	Old locus	Product	Pathway
FTL_RS00470	2930.62	0.27	0.13	1.98	4.72E-02	9.99E-01	FTL_0094	ATP-dependent chaperone ClpB	Stress response
FTL_RS01035	83.16	0.36	0.16	2.25	2.46E-02	9.99E-01	FTL_0194	cytochrome o ubiquinol oxidase subunit IV	Metabolism
FTL_RS01485	1105.61	0.3	0.13	2.34	1.95E-02	9.99E-01	FTL_0281	molecular chaperone DnaJ	Stress response
FTL_RS10075	617.39	0.4	0.13	3	2.73E-03	9.99E-01	N/A	bacterial RNase P	Translation
FTL_RS10065	6619.12	0.37	0.14	2.72	6.58E-03	9.99E-01	N/A	RNA component of RNaseP	Translation
FTL_RS01505	2724.23	0.39	0.15	2.6	9.25E-03	9.99E-01	FTL_0285	Bifunctional (p)ppGpp synthetase/guanosine-3',5'-bis(diphosphate) 3'-pyrophosphohydrolase	Stress response
FTL_RS02050	242.13	0.32	0.14	2.19	2.85E-02	9.99E-01	FTL_0396	phosphoribosylamine--glycine ligase	Metabolism
FTL_RS03180	79.79	0.32	0.16	2.02	4.32E-02	9.99E-01	FTL_0609	phosphomannomutase	Metabolism
FTL_RS04205	20.62	0.35	0.16	2.14	3.23E-02	9.99E-01	N/A	KR domain-containing protein	Metabolism
FTL_RS05345	55.93	0.34	0.17	2.06	3.99E-02	9.99E-01	FTL_1047	30S ribosomal protein S21	Translation
FTL_RS07065	30.58	0.47	0.17	2.81	4.92E-03	9.99E-01	N/A	hypothetical protein	Hypothetical Protein
FTL_RS06915	46.03	0.33	0.17	1.96	5.00E-02	9.99E-01	FTL_1357	UTP--glucose-1-phosphate uridylyltransferase	Metabolism
FTL_RS08085	15.25	0.33	0.16	2.09	3.65E-02	9.99E-01	FTL_1586	biotin--[acetyl-CoA-carboxylase] ligase	Metabolism
FTL_RS08730	7562.92	0.27	0.12	2.19	2.85E-02	9.99E-01	FTL_1714	molecular chaperone GroEL	Stress response
FTL_RS08735	1597.28	0.29	0.13	2.22	2.65E-02	9.99E-01	FTL_1715	molecular chaperone GroES	Stress response
FTL_RS09410	67.12	0.34	0.16	2.08	3.77E-02	9.99E-01	FTL_1840	hypothetical protein	Hypothetical Protein
FTL_RS09725	72.44	0.33	0.16	2.04	4.10E-02	9.99E-01	FTL_1911	nucleoside deaminase	Translation
FTL_RS09945	1524.81	0.3	0.13	2.4	1.62E-02	9.99E-01	FTL_1957	Hsp20/alpha crystallin family protein	Stress response
FTL_RS09950	806.88	0.3	0.14	2.16	3.07E-02	9.99E-01	FTL_1958	bifunctional indole-3-glycerol-phosphate synthase TrpC/phosphoribosylanthranilate isomerase TrpF	Translation

**Figure S3:** Expression profile of  $\Delta osrR$  mutant as compared to the wild type *F. tularensis* in the absence of oxidative stress. (A) The expression profile of down regulated and (B) up regulated genes in the  $\Delta osrR$  mutant.

**Figure S4**

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	Old locus	Product	Function
FTL_RS01645	205.1	-0.53	0.18	-3	2.70E-03	1.18E-01	FTL_0310	pyruvate dehydrogenase complex dihydrolipoyllysine-residue acetyltransferase	Metabolism
FTL_RS01650	228.55	-0.88	0.18	-4.86	1.19E-06	6.03E-04	FTL_0311	dihydrolipoyl dehydrogenase	Metabolism
FTL_RS03505	168.4	-0.85	0.18	-4.61	3.96E-06	7.46E-04	FTL_0671	pantothenate kinase	Metabolism
FTL_RS03510	52.61	-0.61	0.21	-2.9	3.78E-03	NA	FTL_0672	aspartate 1-decarboxylase	Metabolism
FTL_RS03515	486.39	-0.77	0.16	-4.74	2.13E-06	6.03E-04	FTL_0673	pantothenate synthetase	Metabolism
FTL_RS03520	384.19	-0.49	0.17	-2.84	4.46E-03	1.46E-01	FTL_0674	3-methyl-2-oxobutanoate hydroxymethyltransferase	Metabolism
FTL_RS01350	298.56	-0.66	0.17	-4.01	5.99E-05	7.93E-03	FTL_0256	preprotein translocase subunit SecY	Transport
FTL_RS01335	411.81	-0.5	0.16	-3.11	1.87E-03	9.62E-02	FTL_0253	30S ribosomal protein S5	Translation
FTL_RS09120	254.01	-0.46	0.17	-2.67	7.53E-03	1.85E-01	FTL_1783	dihydrolipoyllysine-residue succinyltransferase	Transcription
FTL_RS09125	353.5	-0.65	0.16	-3.98	7.02E-05	7.93E-03	FTL_1784	2-oxoglutarate dehydrogenase E1 component	Metabolism
FTL_RS05840	284.77	-0.33	0.17	-2.01	4.47E-02	4.73E-01	FTL_1147	phosphoglycerate kinase	Metabolism
FTL_RS05845	248.88	-0.47	0.18	-2.63	8.47E-03	1.91E-01	FTL_1148	pyruvate kinase	Metabolism
FTL_RS05850	115.76	-0.75	0.2	-3.86	1.11E-04	1.05E-02	FTL_1149	fructose-bisphosphate aldolase class II	Metabolism
FTL_RS09330	50.37	-0.61	0.22	-2.85	4.32E-03	NA	FTL_1823	NADH-quinone oxidoreductase subunit H	Metabolism
FTL_RS09335	191.8	-0.4	0.18	-2.16	3.05E-02	3.83E-01	FTL_1824	NADH-quinone oxidoreductase subunit G	Metabolism
FTL_RS09340	219.1	-0.61	0.17	-3.49	4.82E-04	3.89E-02	FTL_1825	NADH-quinone oxidoreductase subunit F	Metabolism
FTL_RS03460	158.86	-0.64	0.2	-3.17	1.51E-03	9.08E-02	FTL_0662	helix-turn-helix domain-containing protein	Transcription
FTL_RS06610	228.05	-0.64	0.2	-3.15	1.61E-03	9.08E-02		amino acid transporter	Transport
FTL_RS08895	366.42	-0.51	0.17	-3.03	2.41E-03	1.14E-01	FTL_1743	DNA-directed RNA polymerase subunit beta'	Transcription
FTL_RS08900	704.89	-0.34	0.17	-1.99	4.64E-02	4.73E-01	FTL_1744	DNA-directed RNA polymerase subunit beta	Transcription
FTL_RS01275	160	-0.45	0.18	-2.59	9.60E-03	1.96E-01	FTL_0241	50S ribosomal protein L22	Translation
FTL_RS01280	197.66	-0.51	0.18	-2.89	3.88E-03	1.38E-01	FTL_0242	30S ribosomal protein S3	Translation
FTL_RS01285	147.97	-0.49	0.17	-2.83	4.65E-03	1.46E-01	FTL_0243	50S ribosomal protein L16	Translation
FTL_RS01290	70.44	-0.45	0.2	-2.31	2.11E-02	NA	FTL_0244	50S ribosomal protein L29	Translation
FTL_RS01255	238.45	-0.46	0.18	-2.58	1.00E-02	1.96E-01	FTL_0237	50S ribosomal protein L4	Translation
FTL_RS01260	86.86	-0.41	0.2	-2.07	3.84E-02	NA	FTL_0238	50S ribosomal protein L23	Translation
FTL_RS01270	115.52	-0.39	0.18	-2.16	3.04E-02	3.83E-01	FTL_0240	30S ribosomal protein S19	Translation
FTL_RS02205	163.94	-0.51	0.17	-2.9	3.73E-03	1.38E-01	FTL_0426	type I DNA topoisomerase	Replication
FTL_RS09190	100.84	-0.55	0.19	-2.88	3.92E-03	1.38E-01	FTL_1796	ATP synthase subunit gamma	Metabolism
FTL_RS09185	174.03	-0.48	0.17	-2.81	4.98E-03	1.48E-01	FTL_1795	ATP synthase subunit beta	Metabolism
FTL_RS04390	852.67	-0.55	0.2	-2.74	6.23E-03	1.60E-01	FTL_0852	3-phosphoshikimate 1-carboxyvinyltransferase	Metabolism
FTL_RS04395	199.42	-0.52	0.2	-2.53	1.15E-02	2.03E-01	FTL_0853	hypothetical protein	Hypothetical protein
FTL_RS04400	216.32	-0.48	0.2	-2.41	1.61E-02	2.40E-01	FTL_0854	ribonuclease HI	Replication
FTL_RS00575	269.73	-0.49	0.19	-2.57	1.03E-02	1.96E-01	FTL_0116	hypothetical protein	Hypothetical protein
FTL_RS00580	22.68	-0.57	0.22	-2.57	1.01E-02	NA	FTL_0117	hypothetical protein	Hypothetical protein
FTL_RS05915	269.73	-0.49	0.19	-2.57	1.03E-02	1.96E-01	FTL_1162	hypothetical protein	Hypothetical protein
FTL_RS05920	22.68	-0.57	0.22	-2.57	1.01E-02	NA	FTL_1163	hypothetical protein	Hypothetical protein
FTL_RS06055	203.72	-0.51	0.21	-2.49	1.28E-02	2.12E-01	FTL_1183	sodium:solute symporter	Transport
FTL_RS02520	187.98	-0.42	0.17	-2.47	1.35E-02	2.18E-01	FTL_0480	glycine dehydrogenase (aminomethyl-transferring)	Metabolism
FTL_RS04690	174.23	-0.43	0.18	-2.43	1.51E-02	2.30E-01	FTL_0916	ketol-acid reductoisomerase	Metabolism
FTL_RS01170	109.9	-0.39	0.19	-2.07	3.81E-02	4.44E-01	FTL_0221	APC family permease	Metabolism
FTL_RS06605	245.75	-0.4	0.2	-2.01	4.48E-02	4.73E-01	FTL_1294	short-chain dehydrogenase/reductase	Metabolism
FTL_RS03560	69.37	-0.51	0.2	-2.48	1.32E-02	NA	FTL_0681	polyamine ABC transporter ATP-binding protein	Transport
FTL_RS03610	9.94	-1.08	0.21	-5.17	2.29E-07	NA	FTL_0689	AraC family transcriptional regulator	Transcription
FTL_RS03730	40.05	-0.69	0.22	-3.21	1.32E-03	NA	FTL_0714	phosphoglycerate dehydrogenase	Metabolism
FTL_RS04310	66.19	-0.57	0.2	-2.8	5.15E-03	NA	FTL_0837	MetQ/NlpA family lipoprotein	Transport
FTL_RS04845	3.83	-0.36	0.16	-2.17	2.98E-02	NA	FTL_0947	MFS transporter	Transport
FTL_RS06245	21.98	-0.47	0.22	-2.13	3.32E-02	NA	FTL_1221	hypothetical protein	Hypothetical protein
FTL_RS06305	12.04	-0.53	0.22	-2.47	1.37E-02	NA	FTL_1234	hypothetical protein	Hypothetical protein
FTL_RS06435	17.74	-0.51	0.22	-2.31	2.07E-02	NA		MFS transporter	Transport
FTL_RS06440	13.13	-0.45	0.22	-2.08	3.72E-02	NA		hypothetical protein	Hypothetical protein
FTL_RS06615	19.92	-0.56	0.22	-2.54	1.12E-02	NA	FTL_1297	hypothetical protein	Hypothetical protein
FTL_RS10045	67.36	-0.48	0.21	-2.23	2.57E-02	NA	FTL_1368	hypothetical protein	Hypothetical protein
FTL_RS08465	15.13	-0.55	0.22	-2.51	1.22E-02	NA	FTL_1661	nucleoside permease	Transport

**Figure S4:** The expression profile of down regulated genes in the  $\Delta osrR$  mutant as compared to the wild type *F. tularensis* in the presence of oxidative stress induced by menadione.



# Figure S5

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	Old locus	Product	Pathway
FTL_RS05365	316.56	0.56	0.16	3.39	7.04E-04	4.97E-02	FTL_1051	NAD(P)/FAD-dependent oxidoreductase	Metabolism
FTL_RS09215	124.12	0.39	0.19	2.06	3.95E-02	4.46E-01	FTL_1801	FOF1 ATP synthase subunit A	Metabolism
FTL_RS00130	1120.2	0.53	0.19	2.78	5.43E-03	1.49E-01	FTL_0024	serine/threonine transporter	Transport
FTL_RS04110	132.05	0.52	0.19	2.77	5.56E-03	1.49E-01		hypothetical protein	Hypothetical protein
FTL_RS04920	416.96	0.41	0.16	2.66	7.89E-03	1.86E-01	FTL_0964	HslU--HslV peptidase ATPase subunit	Stress Response
FTL_RS01485	563.33	0.39	0.15	2.56	1.04E-02	1.96E-01	FTL_0281	molecular chaperone DnaJ	Stress Response
FTL_RS05820	302.53	0.41	0.16	2.53	1.15E-02	2.03E-01	FTL_1143	SOS ribosomal protein L32	Translation
FTL_RS01505	2259.55	0.37	0.15	2.5	1.25E-02	2.12E-01	FTL_0285	bifunctional (p)ppGpp synthetase/guanosine-3',5'-bis(diphosphate)3'-pyrophosphohydrolase	Stress Response
FTL_RS02360	254.92	0.45	0.19	2.44	1.46E-02	2.30E-01	FTL_0449	hypothetical protein	Hypothetical protein
FTL_RS06090	211.11	0.44	0.18	2.39	1.69E-02	2.45E-01	FTL_1190	nucleotide exchange factor GrpE	Stress Response
FTL_RS06100	553.37	0.31	0.15	2.09	3.68E-02	4.42E-01	FTL_1192	molecular chaperone DnaJ	Stress Response
FTL_RS04450	102.64	0.42	0.18	2.3	2.17E-02	3.06E-01	FTL_0864	SIS domain-containing protein	Transport
FTL_RS01410	2338.4	0.37	0.17	2.22	2.61E-02	3.52E-01	FTL_0267	molecular chaperone HtpG	Stress Response
FTL_RS09265	411.73	0.36	0.16	2.22	2.62E-02	3.52E-01	FTL_1811	ribosome maturation factor	Translation
FTL_RS10065	5687.52	0.34	0.15	2.18	2.90E-02	3.81E-01		RNA component of RNaseP	Translation
FTL_RS08735	1054.01	0.36	0.17	2.16	3.12E-02	3.83E-01	FTL_1715	molecular chaperone GroES	Stress Response
FTL_RS00140	110.82	0.38	0.18	2.07	3.85E-02	4.44E-01		3-hydroxyisobutyrate dehydrogenase	Metabolism
FTL_RS03780	117.59	0.36	0.18	1.98	4.71E-02	4.73E-01	FTL_0724	S-formyltetrahydrofolate cyclo-ligase	Metabolism
FTL_RS03820	206.83	0.36	0.18	1.97	4.84E-02	4.73E-01	FTL_0732	lactoylglutathione lyase	Metabolism
FTL_RS04585	1102.72	0.29	0.15	1.99	4.65E-02	4.73E-01	FTL_0891	trigger factor	Stress Response
FTL_RS04590	243.44	0.33	0.17	1.98	4.75E-02	4.73E-01	FTL_0892	ATP-dependent Clp protease proteolytic subunit	Stress Response
FTL_RS08215	118.52	0.37	0.19	1.97	4.87E-02	4.73E-01	FTL_1611	glycosyltransferase	Metabolism
FTL_RS02740	81.17	0.48	0.2	2.36	1.81E-02	NA	FTL_0523	hypothetical protein	Hypothetical protein
FTL_RS03255	29.61	0.45	0.22	2.06	3.95E-02	NA	FTL_0623	ABC transporter ATP-binding protein	Transport
FTL_RS03715	9.93	0.42	0.21	2	4.56E-02	NA	FTL_0710	choloylglycine hydrolase	Metabolism
FTL_RS04215	45.86	0.44	0.21	2.07	3.80E-02	NA	FTL_0814	photosystem reaction center subunit H	Transport
FTL_RS04430	23.1	0.45	0.22	2.05	4.06E-02	NA	FTL_0860	hypothetical protein	Hypothetical protein
FTL_RS04660	11.84	0.45	0.22	2.06	3.91E-02	NA		threonine synthase	Metabolism
FTL_RS05685	6.82	0.55	0.19	2.84	4.46E-03	NA	FTL_1120	hypothetical protein	Hypothetical protein
FTL_RS08415	2.16	0.27	0.13	2.13	3.35E-02	NA	FTL_1643	peptide ABC transporter permease	Transport
FTL_RS09825	64.32	0.44	0.2	2.18	2.91E-02	NA	FTL_1931	hypoxanthine phosphoribosyltransferase	Metabolism

**Figure S5:** Expression profile of up regulated genes in the  $\Delta osrR$  mutant as compared to the wild type *F. tularensis* LVS in the presence of oxidative stress induced by menadione.