

1 **Unexpected insights into antibacterial activity of zinc oxide nanoparticles**  
2 **against methicillin resistant**  
3 ***Staphylococcus aureus* (MRSA)**  
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5 **Supplemental Information**  
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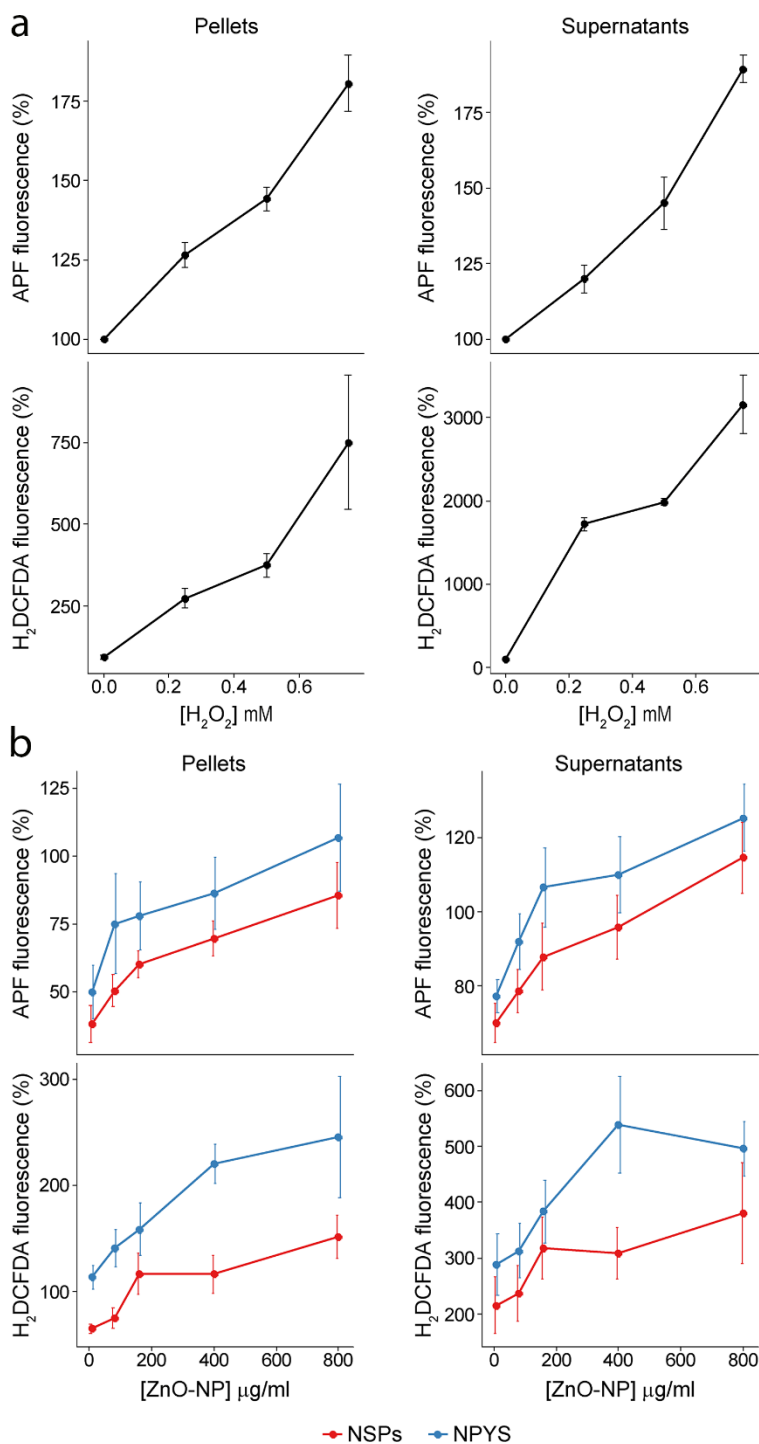
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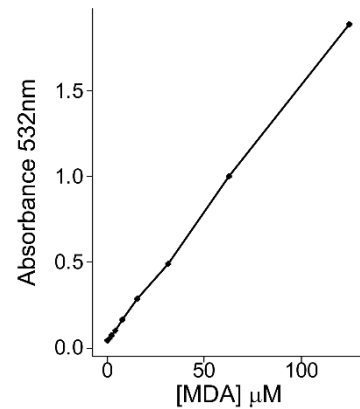
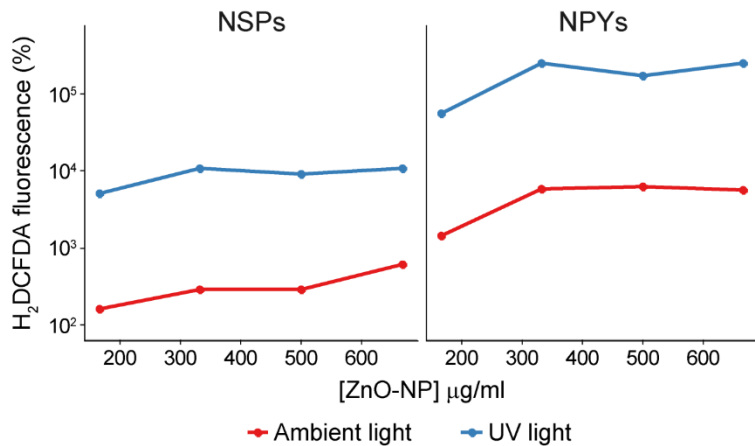
25 The authors have no competing conflicts of interest related to this work.  
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27 **Figures:**



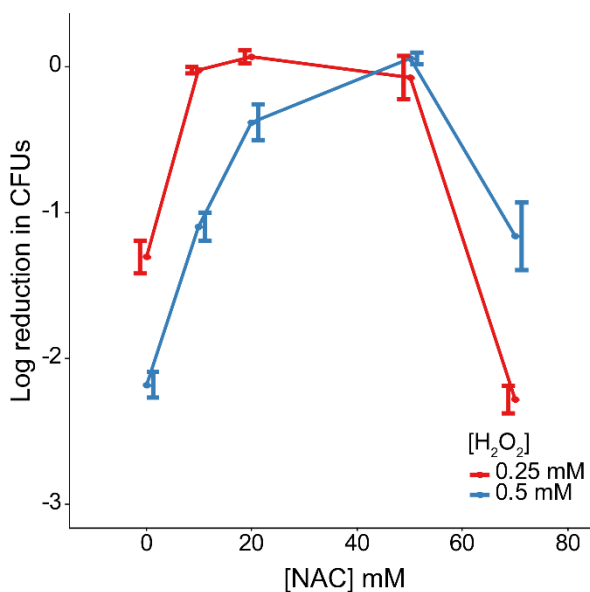
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29 **Supplemental Figure 1:** ROS detection in bacterial pellets and supernatants by APF and  
 30 H<sub>2</sub>DCFDA fluorescence after 30-minute exposure to increasing concentrations of (a) H<sub>2</sub>O<sub>2</sub> or (b)  
 31 ZnO-NSPs and -NPYS. Error bars represent standard error of five independent experiments run  
 32 on different days. Note that the trends for the supernatants and pellets are identical.

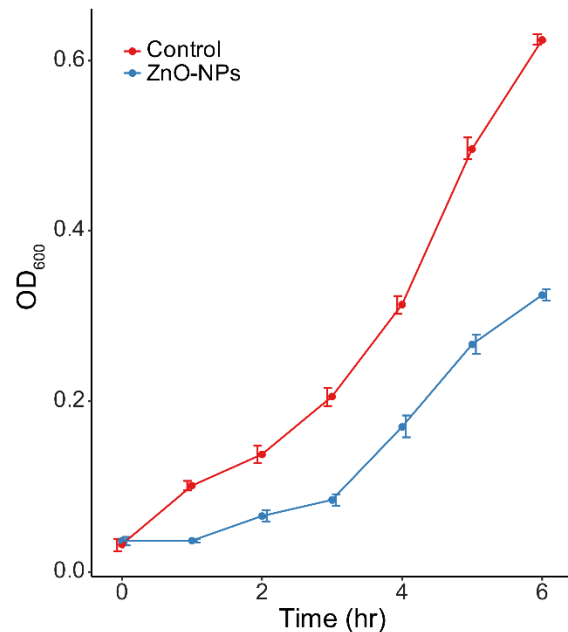


**Supplemental Figure 3:** MDA standard curve for TBARS

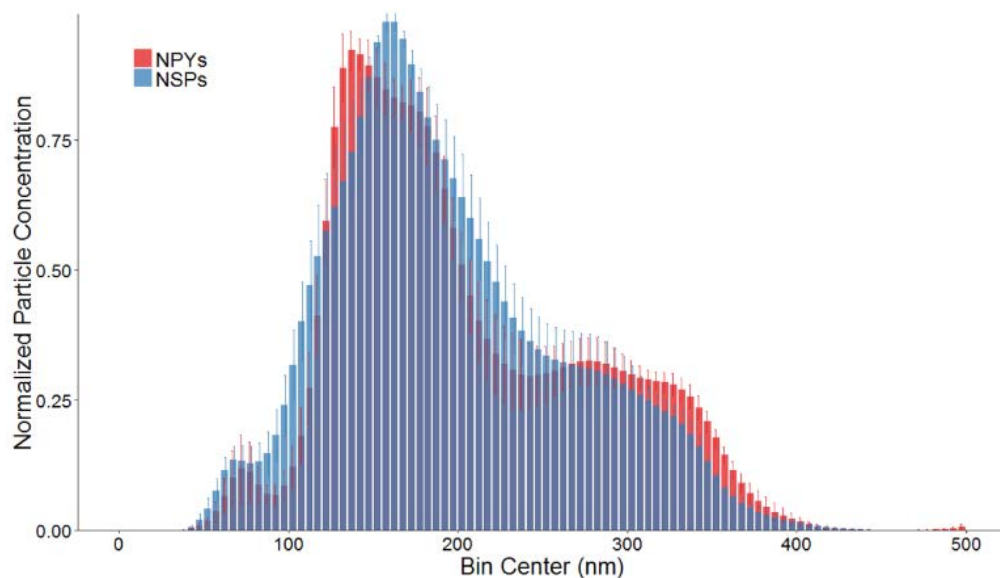
**Supplemental Figure 2:** Two minutes of UV light exposure resulted in significant increase in ROS production by ZnO-NPs as measured by H<sub>2</sub>DCFDA fluorescence. However, the general dose dependence trend is unchanged.



**Supplemental Figure 4:** Dose response of bacterial recovery after exposure to 0.25 and 0.5mM H<sub>2</sub>O<sub>2</sub> in the presence of increasing doses of N-acetylcysteine (NAC). The initial inoculum was 5x10<sup>7</sup> CFU. 50mM NAC leads to complete recovery from a >2 log reduction in colonies caused by 0.5mM H<sub>2</sub>O<sub>2</sub>. Increased doses of NAC beyond 50mM however, lead to toxicity and cell death.



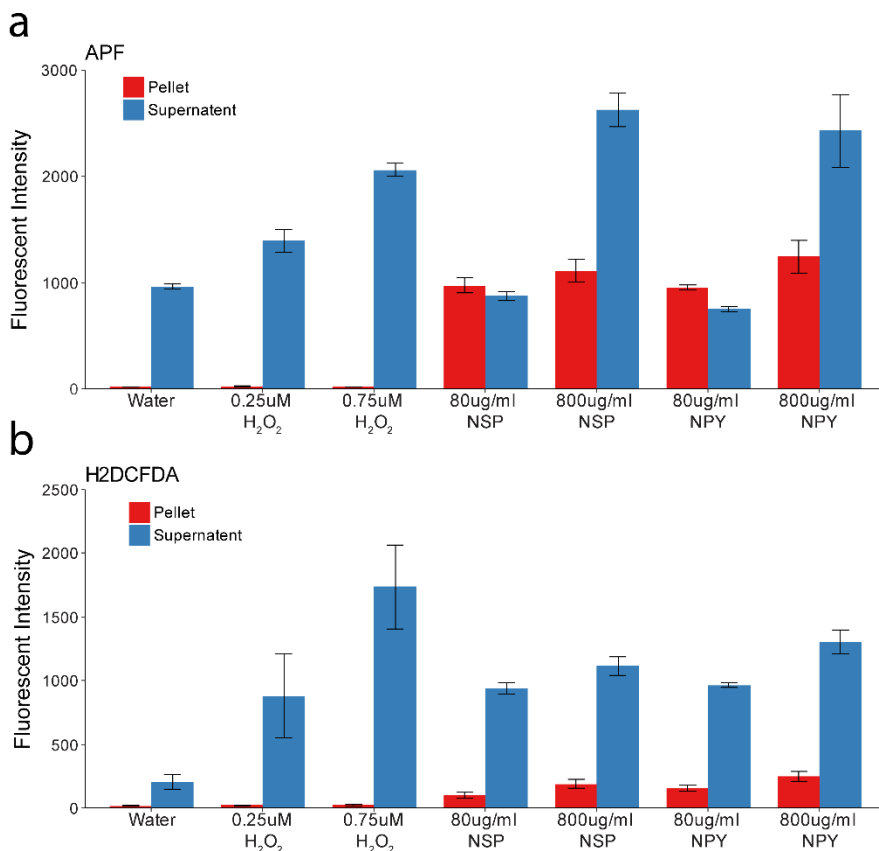
**Supplemental Figure 5:** Growth curves of *S. aureus* with and without 160µg/ml ZnO-NPs used for the gene expression microarray analysis. Each measurement was made in triplicate. Error bars represent standard error.



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44 **Supplemental Figure 6:** Size distribution of nanoparticle aggregates in aqueous dispersion. Error  
 45 bars represent standard deviation from 5 independent samples.

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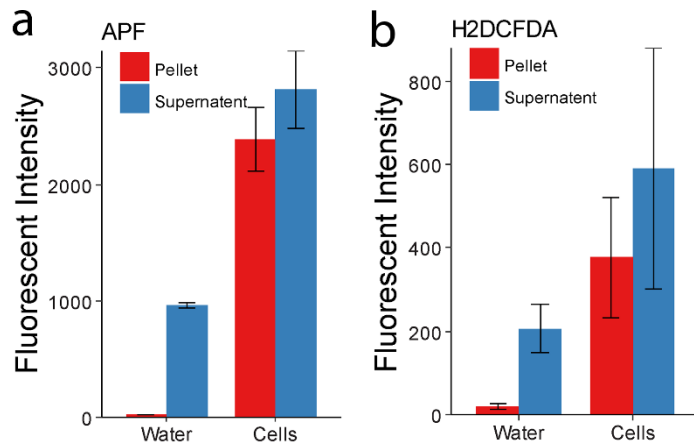


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48 **Supplemental Figure 7:** Fluorescence of (a) APF and (b) H<sub>2</sub>DCFDA in water, H<sub>2</sub>O<sub>2</sub>, and ZnO-  
 49 NPs. Each measurement was made in triplicate. Error bars represent standard error of three  
 50 independent experiments run on different days.

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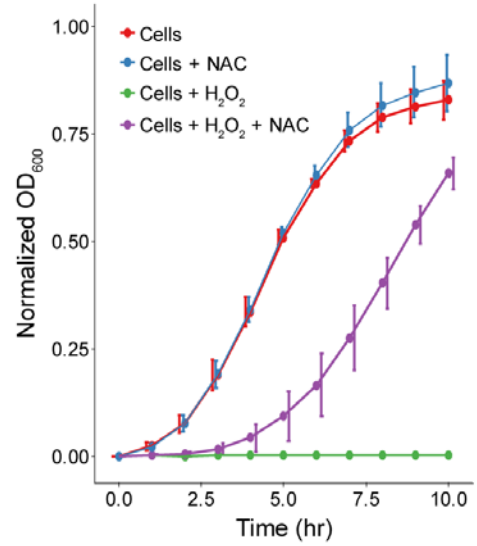
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**Supplemental Figure 8:** Fluorescence of (a) APF and (b) H<sub>2</sub>DCFDA due to baseline cellular respiration. Each measurement was made in triplicate. Error bars represent standard error of three independent experiments run on different days.



**Supplemental Figure 9:** Growth curves of *S. aureus* with H<sub>2</sub>O<sub>2</sub>, NAC and H<sub>2</sub>O<sub>2</sub> plus NAC. Each measurement was made in triplicate. Error bars represent standard error of five independent experiments run on different days.

**Supplemental Table 1:** Primer pairs for RT-PCR Gene Expression Quantification

<b>Orientation</b>	<b>Gene</b>	<b>Primer Sequence (5'--3')</b>
+	<i>16s rRNA</i>	TCGTGTCGTGAGATGTTGGG
-	<i>16s rRNA</i>	GTTTGTACCCGGCAGTCAAC
+	<i>leuD</i>	GTCGTGAACATGCTGCTTGG
-	<i>leuD</i>	TGGAAACGCTTGTCTGGTGA
+	<i>lycC</i>	ATCCGCCACGTGGAAATGTA
-	<i>lycC</i>	CTGACGTCCCACAAGAAGCA
+	<i>katA</i>	GGAGCGTGACATTCGAGGAT
-	<i>katA</i>	GACCCGTCCAGAAATCCCAG
+	<i>pyrE</i>	GCTGGTATTCCACATGCAGC
-	<i>pyrE</i>	GACTGAAGATCCCCCTGTCTG

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

Accession	Common Name	Fold Change	Gene products	Summary
<i>Downregulated</i>				
SACOL0200	uhpT	31.92	sugar phosphate antiporter	cytoplasmic membrane protein that functions as a monomer; catalyzes the active transport of sugar-phosphates such as glucose-6-phosphate with the obligatory exchange of inorganic phosphate or organophosphate
SACOL1173	hiY	11.68	alpha-hemolysin precursor	identified by similarity to SP:P09616; match to protein family HMM PF01117; match to protein family HMM TIGR01002
SACOL2022	hld	8.13	delta-hemolysin	Lyses erythrocytes and other mammalian cells
SACOL1083	purD	7.45	phosphoribosylamine--glycine ligase	catalyzes the formation of N(1)-(5-phospho-D-ribosyl)glycinamide from 5-phospho-D-ribosylamine and glycine in purine biosynthesis
SACOL1082	purH	6.30	bifunctional phosphoribosylaminoimidazole carboxamide formyltransferase/IMP cyclohydrolase	involved in de novo purine biosynthesis
SACOL2146		5.48	PTS system, mannitol-specific IIBC components	identified by match to protein family HMM PF02302; match to protein family HMM PF02378; match to protein family HMM TIGR00851
SACOL2443		5.22	hypothetical protein	
SACOL1081	purN	4.98	phosphoribosylglycinamide formyltransferase	identified by similarity to EGAD:16303; match to protein family HMM PF00551; match to protein family HMM TIGR00639
SACOL0095	spa	4.31	immunoglobulin G binding protein A precursor	identified by similarity to SP:P02976; match to protein family HMM PF00746; match to protein family HMM PF01476; match to protein family HMM PF02216; match to protein family HMM PF03373; match to protein family HMM PF04650; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL1080	purM	4.22	phosphoribosylaminoimidazole synthetase	catalyzes the formation of 1-(5-phosphoribosyl)-5-aminoimidazole from 2-(formamido)-N1-(5-phosphoribosyl)acetamide and ATP in purine biosynthesis
SACOL0008	hutH	4.11	histidine ammonia-lyase	catalyzes the degradation of histidine to urocanate and ammonia
SACOL0882		4.02	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL2422	hlgB	4.01	gamma hemolysin, component B	identified by similarity to SP:P31715; match to protein family HMM PF01117; match to protein family HMM TIGR01002
SACOL2395	narG	3.97	respiratory nitrate reductase subunit alpha	identified by similarity to EGAD:30702; match to protein family HMM PF00384; match to protein family HMM PF01568; match to protein family HMM TIGR01580
SACOL2421	hlgC	3.82	gamma hemolysin, component C	identified by similarity to SP:P31716; match to protein family HMM PF01117; match to protein family HMM TIGR01002
SACOL1477	ilvA1	3.71	threonine dehydratase	catalyzes the formation of 2-oxobutanoate from L-threonine; catabolic
SACOL2396		3.67	uroporphyrinogen III methylase SirB	identified by similarity to GP:4433641; match to protein family HMM PF00590; match to protein family HMM TIGR01469
SACOL0704		3.55	iron compound ABC transporter ATP-binding protein	identified by similarity to EGAD:37683; match to protein family HMM PF00005
SACOL0883		3.55	ABC transporter permease	identified by match to protein family HMM PF00528
SACOL2044		3.48	acetolactate synthase 1 regulatory subunit	with lvi1 catalyzes the formation of 2-acetolactate from pyruvate, this subunit is required for full activity and valine sensitivity; also known as acetolactate synthase small
SACOL1658		3.29	hypothetical protein	
SACOL1478	ald1	3.22	alanine dehydrogenase	identified by match to protein family HMM PF01262; match to protein family HMM PF05222; match to protein family HMM TIGR00518
SACOL0690		3.13	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL0874		3.13	nitroreductase	identified by match to protein family HMM PF00881
SACOL2554		3.12	hypothetical protein	identified by match to protein family HMM PF04172
SACOL2024	agrD	3.08	accessory gene regulator protein D	identified by similarity to EGAD:18902; match to protein family HMM PF05931
SACOL2043	ilvB	3.04	acetolactate synthase large subunit	identified by match to protein family HMM PF00205; match to protein family HMM PF02776; match to protein family HMM TIGR00118
SACOL0768		3.04	hypothetical protein	identified by similarity to GB:AAO04078.1
SACOL0413		3.04	ribosomal-protein-serine acetyltransferase	identified by match to protein family HMM PF00583
SACOL1923		3.03	hypothetical protein	identified by match to protein family HMM PF06081
SACOL0404		3.02	MarR family transcriptional regulator	identified by match to protein family HMM PF01047
SACOL2716		3.02	hypothetical protein	identified by match to protein family HMM PF03551
SACOL1114		3.01	manganese transport protein MntH	identified by match to protein family HMM PF01566; match to protein family HMM TIGR01197
SACOL0994	oppF	3.00	oligopeptide ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL2258	sarV	2.95	hypothetical protein	identified by similarity to OMNI:SA2258; match to protein family HMM TIGR01889
SACOL2394	narH	2.95	respiratory nitrate reductase subunit beta	identified by similarity to EGAD:16236; similarity to EGAD:30703; match to protein family HMM TIGR01660
SACOL1428	lysC	2.91	aspartate kinase	catalyzes the formation of 4-phospho-L-aspartate from L-aspartate and ATP, in Bacillus, lysine sensitive; regulated by response to starvation.
SACOL2006		2.89	Aerolysin/leukocidin family protein	identified by match to protein family HMM PF01117

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL2734		2.89	hypothetical protein	identified by similarity to GB:AAO06055.1
SACOL1476		2.87	amino acid permease	identified by match to protein family HMM PF00324
SACOL2630		2.86	hypothetical protein	identified by similarity to GP:4574119
SACOL1475		2.86	drug transporter	identified by match to protein family HMM PF07690
SACOL0445		2.84	hypothetical protein	identified by similarity to GB:AAO06012.1
SACOL1741	icd	2.84	isocitrate dehydrogenase	Converts isocitrate to alpha ketoglutarate
SACOL2020		2.83	hypothetical protein	identified by match to protein family HMM PF00881
SACOL1429	asd	2.83	aspartate semialdehyde dehydrogenase	identified by similarity to EGAD:15165; match to protein family HMM PF01118; match to protein family HMM PF02774; match to protein family HMM TIGR01296
SACOL2042	ilvD	2.81	dihydroxy-acid dehydratase	catalyzes the dehydration of 2,3-dihydroxy-3-methylbutanoate to 3-methyl-2-oxobutanoate in valine and isoleucine biosynthesis
SACOL0884		2.75	ABC transporter substrate-binding protein	identified by match to protein family HMM PF03180
SACOL2023	agrB	2.73	accessory gene regulator protein B	identified by match to protein family HMM PF04647
SACOL2398	nirB	2.73	nitrite reductase [NAD(P)H], large subunit	identified by similarity to EGAD:30822; match to protein family HMM PF00070; match to protein family HMM PF01077; match to protein family HMM PF03460; match to protein family HMM PF04324
SACOL0152		2.71	heme-degrading monooxygenase IsdI	iron regulated; catalyzes the release of heme from hemoglobin allowing bacterial pathogens to use the host heme as an iron source
SACOL1846		2.71	hypothetical protein	
SACOL0119		2.71	cell wall surface anchor family protein	identified by match to protein family HMM PF00746; match to protein family HMM TIGR01167
SACOL1784	acuA	2.70	acetoin utilization protein AcuA	identified by similarity to EGAD:23882
SACOL2025	argC2	2.69	accessory gene regulator protein C	identified by match to protein family HMM PF02518
SACOL2393	narJ	2.68	respiratory nitrate reductase subunit delta	identified by match to protein family HMM PF02613; match to protein family HMM TIGR00684
SACOL2694	geh	2.66	lipase	identified by similarity to SP:Q02510; similarity to EGAD:17843; match to protein family HMM PF04650; match to protein family HMM TIGR01168
SACOL0707		2.63	dihydroxyacetone kinase subunit DhaK	with DhaL and DhaM forms dihydroxyacetone kinase, which is responsible for phosphorylating dihydroxyacetone; DhaK is the dihydroxyacetone binding subunit of the dihydroxyacetone kinase
SACOL1546	proC	2.63	pyrroline-5-carboxylate reductase	identified by similarity to EGAD:45894; match to protein family HMM PF01089; match to protein family HMM TIGR00112
SACOL0907	seb	2.62	enterotoxin B	identified by similarity to GP:3212819; match to protein family HMM PF01123; match to protein family HMM PF02876
SACOL0153		2.62	hypothetical protein	identified by match to protein family HMM PF04304
SACOL2386		2.59	nitrite extrusion protein	identified by similarity to EGAD:30454; match to protein family HMM PF07690
SACOL0995		2.58	oligopeptide ABC transporter oligopeptide-binding protein	identified by match to protein family HMM PF00496
SACOL1182	arcC1	2.58	carbamate kinase	catalyzes the reversible synthesis of carbamate and ATP from carbamoyl phosphate and ADP
SACOL0991	oppB	2.57	oligopeptide ABC transporter permease	identified by match to protein family HMM PF00528
SACOL2392	narI	2.56	respiratory nitrate reductase subunit gamma	identified by similarity to EGAD:30704; match to protein family HMM PF02665; match to protein family HMM TIGR00351
SACOL2628	betB	2.56	betaine aldehyde dehydrogenase	identified by similarity to EGAD:97843; match to protein family HMM PF00171; match to protein family HMM TIGR01804
SACOL2147		2.55	BglG family transcriptional antiterminator	identified by match to protein family HMM PF00874
SACOL2399	nirR	2.53	transcriptional regulator NirR	identified by similarity to GP:4433637
SACOL2145	glmS	2.52	glucosamine-fructose-6-phosphate aminotransferase	Catalyzes the first step in hexosamine metabolism, converting fructose-6P into glucosamine-6P using glutamine as a nitrogen source
SACOL1847		2.52	hypothetical protein	identified by similarity to EGAD:108623
SACOL2391		2.51	hypothetical protein	identified by similarity to GB:AAO05612.1
SACOL2531		2.51	MarR family transcriptional regulator	identified by match to protein family HMM PF01047
SACOL1711		2.50	DNA-3-methyladenine glycosylase	identified by similarity to EGAD:6433; match to protein family HMM PF03352
SACOL2521		2.49	transporter	identified by match to protein family HMM PF07690
SACOL2045	ilvC	2.49	ketol-acid reductoisomerase	catalyzes the formation of (R)-2,3-dihydroxy-3-methylbutanoate from (S)-2-hydroxy-2-methyl-3-oxobutanoate in valine and isoleucine biosynthesis
SACOL2397	nirD	2.48	nitrite reductase [NAD(P)H], small subunit	identified by similarity to EGAD:30823; match to protein family HMM PF00355
SACOL0993	oppD	2.47	oligopeptide ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005; match to protein family HMM TIGR01727
SACOL2026	agrA	2.46	accessory gene regulator protein A	identified by similarity to EGAD:16137; match to protein family HMM PF00072; match to protein family HMM PF04397
SACOL0402		2.46	PTS system, IIA component	identified by match to protein family HMM PF00359
SACOL0205	pflA	2.45	pyruvate formate-lyase-activating enzyme	identified by similarity to SP:O68575; match to protein family HMM PF04055
SACOL2651		2.45	tributyryn esterase EstA	identified by similarity to GP:7453516; similarity to OMNI:NTL01LL1811; match to protein family HMM PF00756
SACOL2661		2.43	hypothetical protein	identified by similarity to GB:AAO05863.1



**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL1432	dapD	2.43	2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-succinyltransferase	identified by similarity to EGAD:165602; match to protein family HMM PF00132
SACOL2046	leuA	2.42	2-isopropylmalate synthase	catalyzes the formation of 2-isopropylmalate from acetyl-CoA and 2-oxoisovalerate in leucine biosynthesis
SACOL1431	dapB	2.42	dihydrodipicolinate reductase	catalyzes the reduction of 2,3-dihydrodipicolinate to 2,3,4,5-tetrahydrodipicolinate in lysine and diaminopimelate biosynthesis
SACOL2199	budB	2.42	acetolactate synthase	catalyzes the formation of 2-acetolactate from pyruvate in stationary phase
SACOL0718		2.42	ABC transporter ATP-binding protein	identified by similarity to EGAD:108398; match to protein family HMM PF00005
SACOL1596	aroK	2.42	shikimate kinase	identified by similarity to EGAD:29699; match to protein family HMM PF01202
SACOL1430	dapA	2.41	dihydrodipicolinate synthase	catalyzes the formation of dihydrodipicolinate from L-aspartate 4-semialdehyde and pyruvate in lysine and diaminopimelate biosynthesis
SACOL2047	leuB	2.41	3-isopropylmalate dehydrogenase	catalyzes the oxidation of 3-isopropylmalate to 3-carboxy-4-methyl-2-oxopentanoate in leucine biosynthesis
SACOL0821		2.39	HD domain-containing protein	
SACOL2632	cudT	2.38	BCCT family osmoprotectant transporter	identified by similarity to EGAD:45763; match to protein family HMM PF02028; match to protein family HMM TIGR00842
SACOL2389		2.37	transcriptional regulatory protein DegU	identified by match to protein family HMM PF00072; match to protein family HMM PF00196
SACOL0516		2.37	PTS system, IIBC components	identified by match to protein family HMM PF00367; match to protein family HMM PF02378; match to protein family HMM TIGR00826; match to protein family HMM TIGR01992
SACOL2333		2.34	hypothetical protein	identified by match to protein family HMM PF02694
SACOL1350		2.34	hypothetical protein	identified by similarity to GB:AAO04593.1
SACOL1043		2.33	glycosyl transferase, group 1 family protein	identified by match to protein family HMM PF00534
SACOL2627	betA	2.33	choline dehydrogenase	catalyzes the oxidation of choline to betaine aldehyde and betain aldehyde to glycine betaine
SACOL2049	leuD	2.32	isopropylmalate isomerase small subunit	catalyzes the isomerization between 2-isopropylmalate and 3-isopropylmalate in leucine biosynthesis; forms a heterodimer of LeuC/D
SACOL2050	ilvA2	2.31	threonine dehydratase	catalyzes the formation of 2-oxobutanoate from L-threonine; biosynthetic
SACOL2390		2.30	sensory box histidine kinase	identified by match to protein family HMM PF02518
SACOL2458		2.30	amino acid permease	identified by match to protein family HMM PF00324
SACOL2167		2.28	iron compound ABC transporter iron compound-binding protein	identified by match to protein family HMM PF01497
SACOL1397	msrA	2.28	methionine sulfoxide reductase A	this stereospecific enzymes reduces the S isomer of methionine sulfoxide while MsrB reduces the R form; provides protection against oxidative stress
SACOL2535		2.27	D-lactate dehydrogenase	catalyzes the formation of pyruvate from lactate
SACOL2676		2.27	LPXTG cell wall surface anchor family protein	identified by match to protein family HMM PF00746; match to protein family HMM PF05345; match to protein family HMM TIGR01167
SACOL2565		2.26	FeoA domain-containing protein	identified by match to protein family HMM PF04023
SACOL2519		2.25	hypothetical protein	
SACOL2322		2.23	M20/M25/M40 family peptidase	identified by match to protein family HMM PF01546; match to protein family HMM PF07687; match to protein family HMM TIGR01891
SACOL0204	pflB	2.22	formate acetyltransferase	identified by similarity to SP:P09373; match to protein family HMM PF01228; match to protein family HMM PF02901; match to protein family HMM TIGR01255
SACOL0992	oppC	2.22	oligopeptide ABC transporter permease	identified by match to protein family HMM PF00528
SACOL2660	isaB	2.22	immunodominant antigen B	
SACOL1362	hom	2.21	homoserine dehydrogenase	catalyzes the formation of L-aspartate 4-semialdehyde from L-homoserine
SACOL1060		2.19	MarR family transcriptional regulator	identified by match to protein family HMM PF01047
SACOL1171		2.19	hypothetical protein	
SACOL0796		2.18	iron compound ABC transporter permease	identified by similarity to EGAD:37681; match to protein family HMM PF01032
SACOL0708		2.17	DAK2 domain-containing protein	identified by similarity to OMNI:NTL01BH3400; match to protein family HMM PF02734; match to protein family HMM TIGR02365
SACOL1816	putA	2.17	proline dehydrogenase	identified by match to protein family HMM PF01619
SACOL0007		2.17	hypothetical protein	identified by similarity to EGAD:21908; match to protein family HMM PF01256
SACOL2550		2.16	hypothetical protein	
SACOL1363	thrC	2.16	threonine synthase	catalyzes the formation of L-threonine from O-phospho-L-homoserine
SACOL0871		2.15	hypothetical protein	
SACOL0458	xpt	2.15	xanthine phosphoribosyltransferase	Catalyzes the transfer of the phosphoribosyl moiety from 5-phospho--D-ribose-1-pyrophosphate (PRib-PP) to the 6-oxo-guanine and -xanthine
SACOL2618	ldh2	2.13	L-lactate dehydrogenase	identified by similarity to EGAD:16887; match to protein family HMM PF00056; match to protein family HMM PF02866; match to protein family HMM TIGR01771
SACOL0176		2.13	hypothetical protein	identified by match to protein family HMM PF05913
SACOL2304		2.13	hypothetical protein	
SACOL2451		2.13	amino acid ABC transporter amino acid-binding protein	identified by match to protein family HMM PF04069
SACOL2048	leuC	2.13	isopropylmalate isomerase large subunit	dehydratase component, catalyzes the isomerization between 2-isopropylmalate and 3-isopropylmalate

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SACOL1556		2.12	hypothetical protein	
SACOL1659		2.12	hypothetical protein	identified by similarity to GP:10174438; similarity to OMNI:NTL01BH1823
SACOL2569		2.12	1-pyrroline-5-carboxylate dehydrogenase	catalyzes the conversion of 1-proline-5-carboxylate dehydrogenase to L-glutamate
SACOL0660	adhP	2.11	alcohol dehydrogenase	similar to zinc-dependent eukaryotic ADH enzymes and distinct from fermentative ADHs
SACOL0009	serS	2.11	seryl-tRNA synthetase	catalyzes a two-step reaction, first charging a serine molecule by linking its carboxyl group to the alpha-phosphate of ATP, followed by transfer of the aminoacyl-adenylate to its tRNA
SACOL2453		2.10	amino acid ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005; match to protein family HMM PF00571; match to protein family HMM TIGR01186
SACOL0599		2.09	hypothetical protein	identified by similarity to OMNI:NT01TA1215
SACOL2125		2.08	M20/M25/M40 family peptidase	identified by match to protein family HMM PF01546; match to protein family HMM PF07687; match to protein family HMM TIGR01891
SACOL1783	acs	2.07	acetyl-CoA synthetase	Acs; catalyzes the conversion of acetate and CoA to acetyl-CoA
SACOL1742	gltA	2.07	citrate synthase	catalyzes the formation of citrate from acetyl-CoA and oxaloacetate
SACOL0703		2.07	hypothetical protein	identified by similarity to EGAD:108622; match to protein family HMM PF02588
SACOL0111		2.06	acetoin reductase	identified by match to protein family HMM PF00106
SACOL1175		2.06	hypothetical protein	
SACOL1020		2.05	hypothetical protein	similar to 2'-5' RNA ligase
SACOL2324	hutU	2.04	urocanate hydratase	catalyzes the formation of 4-imidazolone-5-propanoate from urocanate during histidine metabolism
SACOL0689		2.04	ABC transporter permease	identified by match to protein family HMM PF00950
SACOL2319		2.03	Na <sup>+</sup> /H <sup>+</sup> antiporter family protein	identified by similarity to OMNI:VCA0193; match to protein family HMM PF03553
SACOL1366		2.03	hypothetical protein	identified by similarity to GB:AAO04611.1
SACOL0934		2.03	hypothetical protein	identified by similarity to GB:AAO04220.1
SACOL0700	abcA	2.02	ABC transporter ATP-binding protein/permease	identified by match to protein family HMM PF00005; match to protein family HMM PF00664
SACOL2011		2.01	sodium transport family protein	identified by match to protein family HMM PF02386
SACOL2516	gntR	2.01	gluconate operon transcriptional repressor	identified by similarity to EGAD:17516; match to protein family HMM PF00392
SACOL2620		2.00	4-aminobutyrate aminotransferase	catalyzes the formation of succinate semialdehyde and glutamate from 4-aminobutanoate and 2-oxoglutarate
SACOL0688		1.98	ABC transporter substrate-binding protein	identified by match to protein family HMM PF01297
SACOL2448		1.98	2-dehydropantoate 2-reductase	ketopantoate reductase; catalyzes the NADPH reduction of ketopantoate to pantoate; functions in pantothenate (vitamin B5) biosynthesis
SACOL2718		1.97	anion transporter family protein	identified by match to protein family HMM PF00939; match to protein family HMM TIGR00785
SACOL2059		1.97	hypothetical protein	
SACOL0314		1.96	hypothetical protein	identified by similarity to EGAD:15022; match to protein family HMM PF01380
SACOL0494	nuoF	1.95	NADH dehydrogenase subunit 5	Catalyzes the transfer of electrons from NADH to ubiquinone
SACOL1151		1.95	hypothetical protein	identified by similarity to EGAD:107725; match to protein family HMM PF05164
SACOL0609	sdrD	1.95	sdrD protein	identified by similarity to GP:3550594; match to protein family HMM PF00746; match to protein family HMM PF02412; match to protein family HMM PF04650; match to protein family HMM PF05738; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL1981		1.95	isochorismatase	identified by match to protein family HMM PF00857
SACOL0245	lytS	1.94	sensor histidine kinase LytS	identified by similarity to EGAD:42940; match to protein family HMM PF02518; match to protein family HMM PF06580; match to protein family HMM PF07694
SACOL0709		1.94	phosphotransferase mannose-specific family component IIA	identified by similarity to OMNI:NTL01LL0257; match to protein family HMM PF03610; match to protein family HMM TIGR02364
SACOL2407		1.93	lipoprotein	identified by similarity to EGAD:109043; match to protein family HMM PF01323
SACOL0027		1.93	hypothetical protein	
SACOL1181	arcB1	1.92	ornithine carbamoyltransferase	catalyzes the formation of L-citrulline from carbamoyl phosphate and L-ornithine in arginine biosynthesis and degradation
SACOL1660		1.91	LamB/YcsF family protein	identified by match to protein family HMM PF03746
SACOL2552		1.91	PTS system, IIABC components	identified by match to protein family HMM PF00358; match to protein family HMM PF00367; match to protein family HMM PF02378; match to protein family HMM TIGR00826; match to protein family HMM TIGR00830; match to protein family HMM TIGR02002
SACOL0961	gluD	1.91	glutamate dehydrogenase	identified by match to protein family HMM PF00208; match to protein family HMM PF02812
SACOL0546	pth	1.91	peptidyl-tRNA hydrolase	Enables the recycling of peptidyl-tRNAs produced at termination of translation
SACOL0960	rocD	1.91	ornithine--oxo-acid transaminase	identified by similarity to EGAD:21835; match to protein family HMM PF00202; match to protein family HMM TIGR01885
SACOL0208		1.90	hypothetical protein	
SACOL1033		1.90	hypothetical protein	
SACOL0766	saeR	1.90	DNA-binding response regulator SaeR	identified by similarity to GP:5726300; match to protein family HMM PF00072; match to protein family HMM PF00486
SACOL2021		1.90	carbon-nitrogen family hydrolase	identified by match to protein family HMM PF00795

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL1451	arlR	1.90	DNA-binding response regulator ArlR	identified by similarity to GP:9230552; similarity to OMNI:SA1451; match to protein family HMM PF00072; match to protein family HMM PF00486
SACOL0459	pbuX	1.89	xanthine permease	identified by similarity to EGAD:30678; match to protein family HMM PF00860; match to protein family HMM TIGR00801
SACOL1908	fumC	1.89	fumarate hydratase	class II family (does not require metal); tetrameric enzyme; fumarase C; reversibly converts (S)-malate to fumarate and water; functions in the TCA cycle
SACOL0403		1.89	BglG family transcriptional antiterminator	identified by match to protein family HMM PF00359; match to protein family HMM PF00874
SACOL0730		1.87	hypothetical protein	identified by similarity to EGAD:173390; match to protein family HMM PF04167
SACOL1113		1.86	hypothetical protein	
SACOL2154	rocF	1.86	arginase	identified by similarity to EGAD:14086; match to protein family HMM PF00491; match to protein family HMM TIGR01229
SACOL0012		1.85	homoserine O-acetyltransferase	identified by match to protein family HMM PF00561
SACOL2198	budA1	1.84	alpha-acetolactate decarboxylase	identified by similarity to EGAD:17067; match to protein family HMM PF03306; match to protein family HMM TIGR01252
SACOL1351	cls1	1.84	cardiolipin synthetase	identified by similarity to SP:O66043; match to protein family HMM PF00614
SACOL2331		1.84	hypothetical protein	
SACOL1988		1.84	hypothetical protein	identified by match to protein family HMM PF03417
SACOL0456		1.84	hypothetical protein	identified by similarity to GB:AAO05995.1
SACOL1349		1.83	hypothetical protein	identified by similarity to OMNI:PG0474
SACOL0460	guaB	1.83	inosine-5'-monophosphate dehydrogenase	identified by similarity to SP:P21879; match to protein family HMM PF00478; match to protein family HMM PF00571; match to protein family HMM TIGR01302
SACOL2188	lacR	1.83	lactose phosphotransferase system repressor	identified by similarity to SP:P16644; match to protein family HMM PF00455
SACOL1147		1.83	RNA methyltransferase	identified by match to protein family HMM PF00588
SACOL0301		1.82	formate/nitrite transporter family protein	identified by match to protein family HMM PF01226
SACOL0096	sarS	1.82	accessory regulator S	identified by similarity to OMNI:SA0096; match to protein family HMM TIGR01889
SACOL0750		1.82	anion transporter family protein	identified by match to protein family HMM PF00939; match to protein family HMM TIGR00785
SACOL0215		1.82	propionate CoA-transferase	identified by match to protein family HMM PF01144
SACOL0320		1.82	hypothetical protein	
SACOL1324		1.81	hfq protein	identified by similarity to EGAD:12661; match to protein family HMM PF01423
SACOL2615	panB	1.81	3-methyl-2-oxobutanoate hydroxymethyltransferase	catalyzes the formation of tetrahydrofolate and 2-dehydropantoate from 5,10-methylenetetrahydrofolate and 3-methyl-2-oxobutanoate
SACOL2086		1.81	TenA family transcription regulator	identified by similarity to EGAD:24145; match to protein family HMM PF03070
SACOL1450	arlS	1.81	sensor histidine kinase ArlS	identified by similarity to GP:9230553; similarity to OMNI:SA1450; match to protein family HMM PF00512; match to protein family HMM PF00672; match to protein family HMM PF02518
SACOL1308		1.81	pyruvate ferredoxin oxidoreductase subunit alpha	identified by match to protein family HMM PF01558; match to protein family HMM PF01855
SACOL2070	kdpD	1.80	sensor histidine kinase KdpD	identified by similarity to EGAD:149594; match to protein family HMM PF00512; match to protein family HMM PF02518; match to protein family HMM PF02702
SACOL2272	modA	1.80	molybdenum ABC transporter molybdenum-binding protein ModA	identified by similarity to EGAD:13554; match to protein family HMM PF01547; match to protein family HMM TIGR01256
SACOL2505		1.80	cell wall surface anchor family protein	identified by match to protein family HMM PF00746; match to protein family HMM PF04650; match to protein family HMM PF07501; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL0190	acpD	1.80	azoreductase	FMN-dependent; requires NADH; catalyzes the cleavage of azo bond in aromatic azo compounds
SACOL2514	gntP	1.79	gluconate transporter, permease	identified by similarity to EGAD:19179; match to protein family HMM PF02447; match to protein family HMM TIGR00791
SACOL0466		1.79	hypothetical protein	identified by match to protein family HMM PF06993
SACOL2452		1.79	amino acid ABC transporter permease	identified by match to protein family HMM PF00528
SACOL1434		1.79	alanine racemase	identified by match to protein family HMM PF00842; match to protein family HMM PF01168
SACOL2437	bcr	1.78	bicyclomycin resistance protein	identified by similarity to SP:P28246; match to protein family HMM PF00083; match to protein family HMM PF07690; match to protein family HMM TIGR00710
SACOL2585		1.77	hypothetical protein	
SACOL1338		1.77	hypothetical protein	
SACOL1661		1.76	acetyl-CoA carboxylase, biotin carboxylase	identified by similarity to SP:P49787; match to protein family HMM PF00289; match to protein family HMM PF02785; match to protein family HMM PF02786
SACOL0244	scdA	1.76	cell wall biosynthesis protein ScdA	involved in peptidoglycan cross-linking
SACOL1323	miaA	1.75	tRNA delta(2)-isopentenylpyrophosphate transferase	IPP transferase; isopentenyltransferase; involved in tRNA modification; in Escherichia coli this enzyme catalyzes the addition of a delta2-isopentenyl group from dimethylallyl diphosphate to the N6-nitrogen of adenosine adjacent to the anticodon of tRNA species that read codons starting with uracil; further tRNA modifications may occur; mutations in miaA result in defects in translation efficiency and fidelity
SACOL1165		1.75	hypothetical protein	
SACOL1321	glpD	1.75	aerobic glycerol-3-phosphate dehydrogenase	identified by similarity to EGAD:18115; match to protein family HMM PF01266

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL1850		1.75	hypothetical protein	
SACOL2449		1.75	drug transporter	identified by match to protein family HMM PF00083; match to protein family HMM PF07690
SACOL1010	relA1	1.74	GTP pyrophosphokinase	identified by match to protein family HMM PF04607
SACOL2587		1.74	hypothetical protein	
SACOL0724		1.74	hypothetical protein	identified by similarity to GB:AAO04031.1
SACOL1159	sdhA	1.74	succinate dehydrogenase flavoprotein subunit	part of four member succinate dehydrogenase enzyme complex that forms a trimeric complex (trimer of tetramers); SdhA/B are the catalytic subcomplex and can exhibit succinate dehydrogenase activity in the absence of SdhC/D which are the membrane components and form cytochrome b556; SdhC binds ubiquinone; oxidizes succinate to fumarate while reducing ubiquinone to ubiquinol
SACOL1072	folD	1.74	bifunctional 5,10-methylene-tetrahydrofolate dehydrogenase/ 5,10-methylene-tetrahydrofolate cyclohydrolase	catalyzes the formation of 5,10-methenyltetrahydrofolate from 5,10-methylenetetrahydrofolate and subsequent formation of 10-formyltetrahydrofolate from 5,10-methenyltetrahydrofolate
SACOL0506		1.74	ABC transporter substrate-binding protein	identified by match to protein family HMM PF03180
SACOL2294		1.73	hypothetical protein	
SACOL0959		1.72	Oye family NADH-dependent flavin oxidoreductase	identified by match to protein family HMM PF00724
SACOL2345		1.72	esterase	identified by similarity to EGAD:16024
SACOL1368	kataA	1.72	catalase	identified by similarity to EGAD:29401; match to protein family HMM PF00199
SACOL2133		1.71	hypothetical protein	identified by similarity to GB:AAO05339.1
SACOL1001	trpS	1.71	tryptophanyl-tRNA synthetase	catalyzes a two-step reaction, first charging a tryptophan molecule by linking its carboxyl group to the alpha-phosphate of ATP, followed by transfer of the aminoacyl-adenylate to its tRNA
SACOL1776		1.71	1-acyl-sn-glycerol-3-phosphate acyltransferase	identified by match to protein family HMM PF01553; match to protein family HMM TIGR00530
SACOL2019		1.70	sdrH protein	identified by similarity to GP:8101009
SACOL0667		1.70	HAD superfamily hydrolase	identified by match to protein family HMM PF00702; match to protein family HMM TIGR01509; match to protein family HMM TIGR01549
SACOL2323	hutI	1.70	imidazolonepropionase	catalyzing the hydrolysis of 4-imidazolone-5-propionate to N-formimidoyl-L-glutamate, the third step in the histidine degradation pathway
SACOL1812	rot	1.70	repressor of toxins	identified by similarity to GP:6651452; match to protein family HMM TIGR01889
SACOL2483		1.70	transporter	identified by match to protein family HMM PF03806
SACOL2534	frp	1.69	NAD(P)H-flavin oxidoreductase	identified by match to protein family HMM PF00881
SACOL0920		1.69	hypothetical protein	
SACOL0135		1.69	bifunctional acetaldehyde-CoA/alcohol dehydrogenase	identified by similarity to SP:P17547; match to protein family HMM PF00465
SACOL0271		1.69	hypothetical protein	identified by match to protein family HMM PF06013
SACOL1009		1.69	hypothetical protein	identified by similarity to OMNI:NTL01BH2853
SACOL2441		1.69	amino acid permease	identified by match to protein family HMM PF00324
SACOL1785	acuC	1.69	acetoin utilization protein AcuC	identified by similarity to EGAD:19784; match to protein family HMM PF00850
SACOL2332	galM	1.68	aldose 1-epimerase	identified by match to protein family HMM PF01263
SACOL0312	nanA	1.68	N-acetylneuraminase lyase	catalyzes the formation of pyruvate and N-acetylmannosamine from N-acetylneuraminic acid
SACOL1222	rpoZ	1.68	DNA-directed RNA polymerase subunit omega	Promotes RNA polymerase assembly; latches the N- and C-terminal regions of the beta' subunit thereby facilitating its interaction with the beta and alpha subunits
SACOL1167		1.68	hypothetical protein	
SACOL1158	sdhC	1.68	succinate dehydrogenase, cytochrome b558 subunit	identified by similarity to EGAD:20778; match to protein family HMM TIGR02046
SACOL0797		1.68	iron compound ABC transporter permease	identified by similarity to EGAD:37682; match to protein family HMM PF01032
SACOL2715		1.68	hypothetical protein	
SACOL0643		1.67	hypothetical protein	identified by similarity to GP:11230708
SACOL1935		1.67	hypothetical protein	identified by similarity to GP:10173504; match to protein family HMM PF04055
SACOL2607		1.67	hypothetical protein	
SACOL2644		1.66	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL1393		1.66	transcription antiterminator	identified by similarity to SP:P39805; match to protein family HMM PF00874; match to protein family HMM PF03123
SACOL2619		1.66	amino acid permease	identified by match to protein family HMM PF00324
SACOL2363		1.65	L-lactate permease	identified by similarity to EGAD:8633; match to protein family HMM PF02652; match to protein family HMM TIGR00795
SACOL2439		1.64	hypothetical protein	identified by similarity to GB:AAO05643.1
SACOL1848		1.64	hypothetical protein	
SACOL0179		1.64	RpiR family phosphosugar-binding transcriptional regulator	identified by match to protein family HMM PF01380; match to protein family HMM PF01418
SACOL2143		1.64	hypothetical protein	identified by similarity to GP:10174364; match to protein family HMM PF00702; match to protein family HMM TIGR00099; match to protein family HMM TIGR01484

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL1436		1.64	hypothetical protein	
SACOL0505		1.64	ABC transporter permease	identified by match to protein family HMM PF00528
SACOL0307	pfoR	1.64	perfringolysin O regulator protein	identified by similarity to EGAD:33437
SACOL2124		1.64	hypothetical protein	identified by similarity to GB:AAO05329.1
SACOL1322		1.63	alpha/beta fold family hydrolase	identified by match to protein family HMM PF00561
SACOL1041		1.63	hypothetical protein	
SACOL1891		1.63	RNAIII-activating protein TRAP	identified by similarity to OMNI:SA1891
SACOL0818	prfB	1.63	peptide chain release factor 2	recognizes the termination signals UGA and UAA during protein translation a specificity which is dependent on amino acid residues residing in loops of the L-shaped tRNA-like molecule of RF2; in some organisms control of PrfB protein levels is maintained through a +1 ribosomal frameshifting mechanism; this protein is similar to release factor 1
SACOL1804		1.63	polysaccharide biosynthesis protein	identified by match to protein family HMM PF01943
SACOL1367		1.63	amino acid permease	identified by match to protein family HMM PF00324
SACOL0788		1.63	proton-dependent oligopeptide transporter family protein	identified by match to protein family HMM PF00854; match to protein family HMM PF07690; match to protein family HMM TIGR00924
SACOL1591		1.63	lipoate-protein ligase A family protein	identified by match to protein family HMM PF03099
SACOL2058		1.63	PemK family protein	identified by similarity to GP:10834755; match to protein family HMM PF02452
SACOL1161	murl	1.63	glutamate racemase	converts L-glutamate to D-glutamate, a component of peptidoglycan
SACOL0394		1.62	hypothetical protein	identified by match to protein family HMM PF00296
SACOL0600	ilvE	1.62	branched-chain amino acid aminotransferase	catalyzes the transamination of the branched-chain amino acids to their respective alpha-keto acids
SACOL2408		1.62	lipoprotein	identified by similarity to GB:AAO05629.1
SACOL2567		1.62	hypothetical protein	
SACOL1734	gapA2	1.62	glyceraldehyde 3-phosphate dehydrogenase 2	identified by similarity to EGAD:107759; match to protein family HMM PF00044; match to protein family HMM PF02800; match to protein family HMM TIGR01534
SACOL0720		1.62	ABC transporter permease	
SACOL0418		1.61	mttA/Hcf106 family protein	identified by match to protein family HMM PF02416; match to protein family HMM TIGR01411
SACOL1031		1.61	5' nucleotidase	identified by match to protein family HMM PF02872
SACOL1826		1.61	hypothetical protein	identified by similarity to GB:AAN32737.1
SACOL1396	fmtC	1.61	fmtC protein	identified by match to protein family HMM PF04329; match to protein family HMM PF04330; match to protein family HMM PF04331
SACOL0616	nagB	1.61	glucosamine-6-phosphate isomerase	identified by similarity to EGAD:107403; match to protein family HMM PF01182
SACOL0608	sdrC	1.61	sdrC protein	identified by similarity to GP:3550592; match to protein family HMM PF00746; match to protein family HMM PF04650; match to protein family HMM PF05738; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL0668		1.61	alpha/beta fold family hydrolase	identified by match to protein family HMM PF00561
SACOL1878	epiA	1.61	lantibiotic epidermin precursor EpiA	identified by similarity to EGAD:6281; match to protein family HMM PF02052
SACOL0281		1.61	hypothetical protein	
SACOL1412		1.61	hydrolase-like protein	identified by match to protein family HMM TIGR00099; match to protein family HMM TIGR01484
SACOL1772		1.61	class V aminotransferase	identified by match to protein family HMM PF00266
SACOL0513	gltC	1.60	transcriptional regulatory protein GltC	identified by similarity to EGAD:6257; match to protein family HMM PF00126
SACOL2064		1.60	hypothetical protein	
SACOL2338		1.60	hypothetical protein	
SACOL0319		1.60	hypothetical protein	
SACOL1539		1.60	hypothetical protein	identified by similarity to EGAD:12647; match to protein family HMM PF03745
SACOL0658		1.59	HD domain-containing protein	identified by match to protein family HMM PF01966
SACOL1662		1.59	acetyl-CoA carboxylase, biotin carboxyl carrier protein	identified by similarity to SP:P49786; match to protein family HMM PF00364
SACOL0171	brnQ1	1.59	branched-chain amino acid transport system II carrier protein	identified by match to protein family HMM PF05525; match to protein family HMM TIGR00796
SACOL2369		1.59	pyridine nucleotide-disulfide oxidoreductase	identified by match to protein family HMM PF00070
SACOL0072		1.59	hypothetical protein	identified by match to protein family HMM PF00126; match to protein family HMM PF03466
SACOL0632		1.59	hypothetical protein	identified by match to protein family HMM PF06738
SACOL1221	gmk	1.59	guanylate kinase	Essential for recycling GMP and indirectly, cGMP
SACOL0166		1.59	hypothetical protein	identified by match to protein family HMM PF07274
SACOL2541		1.59	acetyltransferase	identified by match to protein family HMM PF00583
SACOL2078		1.58	hypothetical protein	identified by match to protein family HMM PF02583
SACOL0161		1.58	hypothetical protein	
SACOL1842		1.58	hypothetical protein	identified by similarity to OMNI:NTL01BH2832; match to protein family HMM PF01809; match to protein family HMM TIGR00278

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SACOL1797		1.58	metallo-beta-lactamase	identified by match to protein family HMM PF00753
SACOL2193		1.58	MerR family transcriptional regulator	identified by match to protein family HMM PF00376
SACOL2502		1.58	hypothetical protein	
SACOL1992		1.57	hypothetical protein	identified by similarity to GB:BAC14289.1
SACOL1304	recA	1.57	recombinase A	catalyzes the hydrolysis of ATP in the presence of single-stranded DNA, the ATP-dependent uptake of single-stranded DNA by duplex DNA, and the ATP-dependent hybridization of homologous single-stranded DNAs
SACOL0566	nupC	1.57	nucleoside permease NupC	identified by similarity to EGAD:6216; match to protein family HMM PF01773; match to protein family HMM PF07662; match to protein family HMM PF07670
SACOL1042		1.57	hypothetical protein	
SACOL2527		1.57	fructose-1,6-bisphosphatase	identified by similarity to EGAD:37656; match to protein family HMM PF06874
SACOL1364	thrB	1.57	homoserine kinase	catalyzes the formation of O-phospho-L-homoserine from L-homoserine in threonine biosynthesis from aspartate
SACOL0514	gltB	1.57	glutamate synthase	identified by similarity to EGAD:109137; match to protein family HMM PF01493; match to protein family HMM PF01645; match to protein family HMM PF04897; match to protein family HMM PF04898
SACOL2442		1.57	Na <sup>+</sup> /H <sup>+</sup> antiporter	identified by match to protein family HMM PF00999
SACOL1037		1.56	hypothetical protein	
SACOL1435	lysA	1.56	diaminopimelate decarboxylase	identified by similarity to SP:P23630; match to protein family HMM PF00278; match to protein family HMM PF02784; match to protein family HMM TIGR01048
SACOL0870		1.56	LysE/YggA family protein	identified by match to protein family HMM PF01810
SACOL2551		1.56	hypothetical protein	identified by similarity to OMNI:VC1938
SACOL2672		1.56	hypothetical protein	identified by similarity to GB:AAK17000.1
SACOL1374	lexA	1.56	LexA repressor	Represses a number of genes involved in the response to DNA damage
SACOL1164		1.56	fibrinogen binding-like protein	identified by similarity to EGAD:16905
SACOL2673		1.55	hypothetical protein	identified by similarity to GB:AAK16999.1
SACOL2142		1.55	SAP domain-containing protein	
SACOL2296		1.55	glycerate dehydrogenase	Catalyzes the reduction of hydroxypyruvate to form D-glycerate, using NADH as an electron donor
SACOL1689	relA2	1.55	GTP pyrophosphokinase	identified by similarity to EGAD:107375; match to protein family HMM PF01842; match to protein family HMM PF01966; match to protein family HMM PF02824; match to protein family HMM PF04607; match to protein family HMM TIGR00691
SACOL0611		1.55	glycosyl transferase, group 1 family protein	identified by match to protein family HMM PF00534
SACOL0317		1.55	lipase precursor, interruption-N	identified by similarity to EGAD:17843; match to protein family HMM PF04650; match to protein family HMM TIGR01168
SACOL2733		1.55	hypothetical protein	identified by similarity to GB:AAO06054.1
SACOL0455		1.54	hypothetical protein	identified by similarity to SP:Q8CQQ7
SACOL2549		1.54	hypothetical protein	identified by similarity to EGAD:16024
SACOL1645		1.54	comE operon protein 2	identified by similarity to EGAD:23914; match to protein family HMM PF00383
SACOL0756		1.54	ebsC protein	identified by similarity to SP:P36922; match to protein family HMM PF04073; match to protein family HMM TIGR00011
SACOL1058		1.54	aminotransferase, class I	identified by match to protein family HMM PF00155
SACOL2450		1.54	amino acid ABC transporter permease	identified by match to protein family HMM PF00528
SACOL1758	ald2	1.54	alanine dehydrogenase	identified by similarity to EGAD:15508; match to protein family HMM PF01262; match to protein family HMM PF05222; match to protein family HMM TIGR00518
SACOL0715		1.53	hypothetical protein	identified by similarity to GB:AAO04023.1
SACOL2639	cysJ	1.53	sulfite reductase (NADPH) flavoprotein alpha-component	identified by similarity to SP:P38038; match to protein family HMM PF00175; match to protein family HMM PF00258; match to protein family HMM PF00667; match to protein family HMM TIGR01931
SACOL2144		1.53	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL0747		1.53	cobalamin synthesis protein/P47K family protein	identified by match to protein family HMM PF02492; match to protein family HMM PF07683
SACOL0666		1.53	iron compound ABC transporter permease	identified by match to protein family HMM PF01032
SACOL2658		1.53	ArgR family transcriptional regulator	identified by similarity to EGAD:18464; match to protein family HMM PF02863
SACOL2522		1.53	DedA family protein	identified by match to protein family HMM PF00597
SACOL1549	zwf	1.52	glucose-6-phosphate 1-dehydrogenase	catalyzes the formation of D-glucono-1,5-lactone 6-phosphate from D-glucose 6-phosphate
SACOL1448	sucB	1.52	dihydroliipoamide succinyltransferase	component of 2-oxoglutarate dehydrogenase complex; catalyzes the transfer of succinyl coenzyme A to form succinyl CoA as part of the conversion of 2-oxoglutarate to succinyl-CoA
SACOL2459	pnbA	1.52	para-nitrobenzyl esterase	identified by similarity to SP:P37967; match to protein family HMM PF00135
SACOL0180		1.52	type I restriction-modification enzyme, R subunit	identified by match to protein family HMM PF00270; match to protein family HMM PF04313; match to protein family HMM PF04851; match to protein family HMM TIGR00348
SACOL1339		1.52	hypothetical protein	
SACOL2491		1.51	hypothetical protein	identified by similarity to GB:AAO05679.1

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL2562	ogt	1.51	methylated-DNA--protein-cysteine methyltransferase	identified by similarity to EGAD:29038; match to protein family HMM PF01035; match to protein family HMM PF02870; match to protein family HMM TIGR00589
SACOL2400		1.51	acetyltransferase	identified by match to protein family HMM PF00583
SACOL1775		1.51	PTS system, IIBC components	identified by match to protein family HMM PF00367; match to protein family HMM PF02378; match to protein family HMM TIGR01998
SACOL2077		1.51	hypothetical protein	identified by similarity to GB:AAO05284.1; match to protein family HMM PF00403
SACOL1307		1.51	hypothetical protein	identified by similarity to EGAD:108574; match to protein family HMM PF00149; match to protein family HMM TIGR00282
SACOL0512		1.51	hypothetical protein	
SACOL0120		1.51	GntR family transcriptional regulator	identified by similarity to EGAD:37606; match to protein family HMM PF00392
SACOL2278		1.51	acyl-CoA dehydrogenase-like protein	identified by match to protein family HMM PF00441; match to protein family HMM PF02770
SACOL0612		1.51	glycosyl transferase, group 1 family protein	identified by match to protein family HMM PF00534
SACOL1883		1.51	hypothetical protein	
SACOL0751		1.50	deoxyribodipyrimidine photolyase	identified by match to protein family HMM PF03441
SACOL2063		1.50	hypothetical protein	identified by match to protein family HMM PF03703

**Upregulated**

SACOL2186		16.75	galactose-6-phosphate isomerase subunit LacA	catalyzes the interconversion of galactose 6-phosphate to tagatose 6-phosphate; tagatose pathway for galactose utilization
SACOL1217	pyrE	16.44	orotate phosphoribosyltransferase	involved in fifth step of pyrimidine biosynthesis; converts orotidine 5'-phosphate and diphosphate to orotate and 5-phospho-alpha-D-ribose 1-diphosphate
SACOL1215	carB	15.86	carbamoyl phosphate synthase large subunit	four CarB-CarA dimers form the carbamoyl phosphate synthetase holoenzyme that catalyzes the production of carbamoyl phosphate; CarB is responsible for the amidotransferase activity
SACOL1216	pyrF	12.07	orotidine 5'-phosphate decarboxylase	type 1 subfamily; involved in last step of pyrimidine biosynthesis; converts orotidine 5'-phosphate to UMP and carbon dioxide; OMP decarboxylase; OMPDCase; OMPdecase
SACOL1212	pyrB	10.95	aspartate carbamoyltransferase catalytic subunit	catalyzes the transfer of the carbamoyl moiety from carbamoyl phosphate to L-aspartate in pyrimidine biosynthesis
SACOL1214	carA	10.26	carbamoyl phosphate synthase small subunit	catalyzes production of carbamoyl phosphate from bicarbonate and glutamine in pyrimidine and arginine biosynthesis pathways; forms an octamer composed of four CarAB dimers
SACOL1213	pyrC	9.21	dihydroorotase	catalyzes the formation of N-carbamoyl-L-aspartate from (S)-dihydroorotate in pyrimidine biosynthesis
SACOL1211	uraA	4.76	uracil permease	identified by similarity to EGAD:20988; match to protein family HMM PF00860; match to protein family HMM TIGR00801
SACOL2185	lacB	4.75	galactose-6-phosphate isomerase subunit LacB	catalyzes the interconversion of galactose 6-phosphate to tagatose 6-phosphate
SACOL2572		3.61	copper-translocating P-type ATPase	identified by match to protein family HMM PF00122; match to protein family HMM PF00403; match to protein family HMM PF00702; match to protein family HMM TIGR01494; match to protein family HMM TIGR01511; match to protein family HMM TIGR01525
SACOL2184	lacC	3.59	tagatose-6-phosphate kinase	catalyzes the formation of tagatose 1,6-bisphosphate from tagatose 6-phosphate and ATP
SACOL1218		3.54	hypothetical protein	identified by similarity to GB:AAO04479.1
SACOL0263	lytM	3.46	peptidoglycan hydrolase	identified by similarity to GP:2239274; match to protein family HMM PF01551
SACOL2573		3.16	copper ion binding protein	identified by match to protein family HMM PF00403; match to protein family HMM TIGR00003
SACOL0439	rpsR	3.07	30S ribosomal protein S18	binds as a heterodimer with protein S6 to the central domain of the 16S rRNA; helps stabilize the platform of the 30S subunit
SACOL0584	rplA	2.94	50S ribosomal protein L1	in Escherichia coli and Methanococcus, this protein autoregulates expression; the binding site in the mRNA mimics the binding site in the 23S rRNA
SACOL2138		2.87	cation efflux family protein	identified by match to protein family HMM PF01545; match to protein family HMM TIGR01297
SACOL1306		2.83	hypothetical protein	identified by similarity to GB:AAO04562.1
SACOL0625		2.61	hypothetical protein	
SACOL1994		2.56	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL2246		2.55	sugar transporter	identified by match to protein family HMM PF06800
SACOL2524		2.55	MarR family transcriptional regulator	identified by match to protein family HMM PF01047
SACOL0678		2.53	phage integrase integrase/recombinase	identified by similarity to EGAD:9824; match to protein family HMM PF00589
SACOL0545	rplY	2.50	50S ribosomal protein L25/general stress protein Ctc	the Ctc family of proteins consists of two types, one that contains the N-terminal ribosomal protein L25 domain only which in Escherichia coli binds the 5S rRNA while a subset of proteins contain a C-terminal extension that is involved in the stress response
SACOL2088		2.46	sceD protein	identified by match to protein family HMM PF06737
SACOL2247		2.39	hypothetical protein	
SACOL1257	rplS	2.37	50S ribosomal protein L19	this protein is located at the 30S-50S ribosomal subunit interface and may play a role in the structure and function of the aminoacyl-tRNA binding site

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL0583	rplK	2.34	50S ribosomal protein L11	binds directly to 23S ribosomal RNA
SACOL2731		2.33	CSD family cold shock protein	identified by match to protein family HMM PF00313
SACOL2295		2.33	staphyloxanthin biosynthesis protein	identified by match to protein family HMM PF05257
SACOL0586	rplL	2.19	50S ribosomal protein L7/L12	present in two forms; L12 is normal, while L7 is aminoacylated at the N-terminal serine; the only multicopy ribosomal protein; 4:1 ratio of L7/L12 per ribosome; two L12 dimers bind L10; critically important for translation efficiency and fidelity; stimulates GTPase activity of translation factors
SACOL2137	czrA	2.18	transcriptional regulator CzrA	identified by similarity to GP:4126673; similarity to OMNI:SA2137; match to protein family HMM PF01022
SACOL2112	rpmE2	2.16	50S ribosomal protein L31	RpmE2; there appears to be two types of ribosomal proteins L31 in bacterial genomes; some contain a CxxC motif while others do not; Bacillus subtilis has both types; the proteins in this cluster do not have the CXXC motif; RpmE is found in exponentially growing Bacilli while YtiA was found after exponential growth; expression of ytiA is controlled by a zinc-specific transcriptional repressor; RpmE contains one zinc ion and a CxxC motif is responsible for this binding; forms an RNP particle along with proteins L5, L18, and L25 and 5S rRNA; found crosslinked to L2 and L25 and EF-G; may be near the peptidyltransferase site of the 50S ribosome
SACOL2093		2.15	hypothetical protein	identified by match to protein family HMM PF06612; match to protein family HMM TIGR02327
SACOL1095	cydB	2.13	cytochrome d ubiquinol oxidase subunit II	identified by similarity to GP:4514629
SACOL1996		2.12	ABC transporter ATP-binding protein	identified by match to protein family HMM PF00005
SACOL2621		2.12	hypothetical protein	
SACOL0799		2.12	transferrin receptor	identified by similarity to EGAD:22102; match to protein family HMM PF01497
SACOL1995		2.10	hypothetical protein	identified by similarity to GB:AAO05222.1
SACOL2291		2.08	staphyloxanthin biosynthesis protein	identified by match to protein family HMM PF05257
SACOL0144	cap5I	2.03	capsular polysaccharide biosynthesis protein Cap5I	
SACOL1997		2.02	GntR family transcriptional regulator	identified by match to protein family HMM PF00392
SACOL1254	rpsP	2.02	30S ribosomal protein S16	binds to lower part of 30S body where it stabilizes two domains; required for efficient assembly of 30S; in Escherichia coli this protein has nuclease activity
SACOL0537		2.01	hypothetical protein	identified by similarity to EGAD:13222; match to protein family HMM PF06257
SACOL1247	acpP	2.01	acyl carrier protein	carries the fatty acid chain in fatty acid biosynthesis
SACOL0142	cap5G	2.00	UDP-N-acetylglucosamine 2-epimerase Cap5G	identified by match to protein family HMM PF02350; match to protein family HMM TIGR00236
SACOL1094	cydA	2.00	cytochrome d ubiquinol oxidase subunit I	identified by match to protein family HMM PF01654
SACOL2290		1.97	AraC family transcriptional regulator	identified by match to protein family HMM PF00165
SACOL2511	fnbA	1.95	fibronectin-binding protein A	identified by similarity to SP:P14738; match to protein family HMM PF00746; match to protein family HMM PF02986; match to protein family HMM PF04650; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL1035		1.95	hypothetical protein	identified by similarity to EGAD:107617
SACOL1993		1.93	hypothetical protein	identified by similarity to GB:AAO05220.1
SACOL0585	rplJ	1.91	50S ribosomal protein L10	binds the two ribosomal protein L7/L12 dimers and anchors them to the large ribosomal subunit
SACOL2581		1.89	staphyloxanthin biosynthesis protein	identified by match to protein family HMM PF05257
SACOL1769	rpsD	1.89	30S ribosomal protein S4	primary rRNA binding protein; nucleates 30S assembly; involved in translational accuracy with proteins S5 and S12; interacts with protein S5; involved in autogeneously regulating ribosomal proteins by binding to pseudoknot structures in the polycistronic mRNA; interacts with transcription complex and functions similar to protein NusA in antitermination
SACOL2740	rpmH	1.89	50S ribosomal protein L34	in Escherichia coli transcription of this gene is enhanced by polyamines
SACOL1036		1.88	protease	identified by match to protein family HMM PF02517
SACOL1292	rpsO	1.88	30S ribosomal protein S15	primary rRNA binding protein; helps nucleate assembly of 30S; binds directly to the 16S rRNA and an intersubunit bridge to the 23S rRNA; autoregulates translation through interactions with the mRNA leader sequence
SACOL2532		1.87	acetyltransferase	
SACOL1274	rpsB	1.87	30S ribosomal protein S2	truncated; one of the last subunits in the assembly of the 30S subunit; absence of S2 does not inhibit assembly but results in an inactive subunit
SACOL1960	gatB	1.86	aspartyl/glutamyl-tRNA amidotransferase subunit B	allows the formation of correctly charged Asn-tRNA(Asn) or Gln-tRNA(Gln) through the transamidation of misacylated Asp-tRNA(Asn) or Glu-tRNA(Gln) in organisms which lack either or both of asparaginyl-tRNA or glutaminyl-tRNA synthetases; reaction takes place in the presence of glutamine and ATP through an activated phospho-Asp-tRNA(Asn) or phospho-Glu-tRNA



**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL2226	rpsN	1.85	30S ribosomal protein S14	located in the peptidyl transferase center and involved in assembly of 30S ribosome subunit; similar to what is observed with proteins L31 and L33, some proteins in this family contain CXXC motifs that are involved in zinc binding; if two copies are present in a genome, then the duplicated copy appears to have lost the zinc-binding motif and is instead regulated by zinc; the proteins in this group appear to contain the zinc-binding motif
SACOL2481		1.85	hypothetical protein	
SACOL1053		1.84	alpha/beta fold family hydrolase	identified by match to protein family HMM PF00561
SACOL2227	rplE	1.83	50S ribosomal protein L5	part of 50S and 5S/L5/L18/L25 subcomplex; contacts 5S rRNA and P site tRNA; forms a bridge to the 30S subunit in the ribosome by binding to S13
SACOL1650	nadD	1.83	nicotinate (nicotinamide) nucleotide adenyltransferase	identified by similarity to OMNI:NTL01SPL0234; match to protein family HMM PF01467; match to protein family HMM TIGR00125; match to protein family HMM TIGR00482
SACOL1649		1.83	hypothetical protein	identified by similarity to OMNI:NTL01BH1330; match to protein family HMM PF01966; match to protein family HMM TIGR00488
SACOL0146	cap5K	1.82	capsular polysaccharide biosynthesis protein Cap5K	
SACOL2251		1.82	hypothetical protein	identified by similarity to GB:AAO05474.1
SACOL0437	rpsF	1.82	30S ribosomal protein S6	binds cooperatively with S18 to the S15-16S complex, allowing platform assembly to continue with S11 and S21
SACOL2250		1.79	hypothetical protein	
SACOL2229	rplN	1.79	50S ribosomal protein L14	binds to the 23S rRNA between the centers for peptidyl transferase and GTPase
SACOL2711		1.79	hypothetical protein	identified by match to protein family HMM PF04264
SACOL1256	trmD	1.79	tRNA (guanine-N(1)-)-methyltransferase	methylates guanosine-37 in various tRNAs; uses S-adenosyl-L-methionine to transfer methyl group to tRNA
SACOL0680		1.79	monovalent cation/H+ antiporter subunit B	subunit B of antiporter complex involved in resistance to high concentrations of Na+, K+, Li+ and/or alkali
SACOL1481		1.78	hypothetical protein	identified by similarity to OMNI:NTL01BH1857; match to protein family HMM PF03413; match to protein family HMM PF03929
SACOL0356		1.77	hypothetical protein	identified by similarity to GP:8918447; match to protein family HMM PF06260
SACOL2509	fnbB	1.77	fibronectin binding protein B	identified by match to protein family HMM PF00746; match to protein family HMM PF02986; match to protein family HMM PF04650; match to protein family HMM TIGR01167; match to protein family HMM TIGR01168
SACOL1642	rpsT	1.77	30S ribosomal protein S20	binds directly to the 16S rRNA and is involved in post-translational inhibition of arginine and ornithine decarboxylase
SACOL2289	sarY	1.76	hypothetical protein	identified by match to protein family HMM TIGR01889
SACOL1666	udk	1.74	uridine kinase	functions in pyrimidine salvage; pyrimidine ribonucleoside kinase; phosphorylates nucleosides or dinucleosides to make UMP or CMP using ATP or GTP as the donor
SACOL2213	rpoA	1.73	DNA-directed RNA polymerase subunit alpha	catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. Dimerization of the alpha subunit is the first step in the sequential assembly of subunits to form the holoenzyme
SACOL2230	rpsQ	1.73	30S ribosomal protein S17	primary binding protein; helps mediate assembly; involved in translation fidelity
SACOL0939		1.72	NifU domain-containing protein	identified by match to protein family HMM PF01106
SACOL0684		1.72	monovalent cation/H+ antiporter subunit E	subunit E of antiporter complex involved in resistance to high concentrations of Na+, K+, Li+ and/or alkali; in <i>S. meliloti</i> it is known to be involved specifically with K+ transport
SACOL2225	rpsH	1.72	30S ribosomal protein S8	binds directly to 16S rRNA central domain where it helps coordinate assembly of the platform of the 30S subunit
SACOL1384	opuD1	1.72	BCCT family osmoprotectant transporter	identified by similarity to EGAD:45763; match to protein family HMM PF02028; match to protein family HMM TIGR00842
SACOL0141	cap5F	1.71	capsular polysaccharide biosynthesis protein Cap5F	
SACOL2520		1.71	hypothetical protein	identified by match to protein family HMM PF05976
SACOL2212	rplQ	1.71	50S ribosomal protein L17	is a component of the macrolide binding site in the peptidyl transferase center
SACOL1443	brnQ3	1.71	branched-chain amino acid transport system II carrier protein	identified by match to protein family HMM PF05525; match to protein family HMM TIGR00796
SACOL0143	cap5H	1.70	capsular polysaccharide biosynthesis protein Cap5H	identified by match to protein family HMM PF00132
SACOL0685		1.70	monovalent cation/H+ antiporter subunit F	subunit F of antiporter complex involved in resistance to high concentrations of Na+, K+, Li+ and/or alkali
SACOL2183	lacD	1.69	tagatose 1,6-diphosphate aldolase	catalyzes the reversible reaction of dihydroxyacetone phosphate with glyceraldehyde 3-phosphate to produce tagatose 1,6-bisphosphate; in <i>Streptococcus pyogenes</i> there are two paralogs of tagatose-bisphosphate aldolase, encoded by lacD1 and lacD2; expression of lacD1 is highly regulated by environmental conditions while lacD2 specializes in an efficient utilization of carbohydrate sources
SACOL2224	rplF	1.69	50S ribosomal protein L6	ribosomal protein L6 appears to have arisen as a result of an ancient gene duplication as based on structural comparison of the <i>Bacillus stearothermophilus</i> protein; RNA-binding appears to be in the C-terminal domain; mutations in the L6 gene confer resistance to aminoglycoside antibiotics such as gentamicin and these occur in truncations of the C-terminal domain; it has been localized to a region between the base of the L7/L12 stalk and the central protuberance
SACOL1761		1.69	hypothetical protein	identified by similarity to EGAD:11836

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL2214	rpsK	1.69	30S ribosomal protein S11	located on the platform of the 30S subunit, it bridges several disparate RNA helices of the 16S rRNA; forms part of the Shine-Dalgarno cleft in the 70S ribosome; interacts with S7 and S18 and IF-3
SACOL1685	aspS	1.68	aspartyl-tRNA synthetase	catalyzes a two-step reaction, first charging an aspartate molecule by linking its carboxyl group to the alpha-phosphate of ATP, followed by transfer of the aminoacyl-adenylate to its tRNA; contains discriminating and non-discriminating subtypes
SACOL2215	rpsM	1.67	30S ribosomal protein S13	located at the top of the head of the 30S subunit, it contacts several helices of the 16S rRNA; makes contact with the large subunit via RNA-protein interactions and via protein-protein interactions with L5; contacts P-site tRNA
SACOL0630		1.67	amino acid permease	identified by match to protein family HMM PF00324
SACOL1482		1.67	hypothetical protein	
SACOL1286		1.67	hypothetical protein	identified by similarity to OMNI:NTL01BH2418; match to protein family HMM PF04296
SACOL1298		1.66	M16 family peptidase	identified by match to protein family HMM PF00675; match to protein family HMM PF05193
SACOL1378		1.66	hypothetical protein	identified by similarity to SP:Q8CSP3; match to protein family HMM PF03672
SACOL2580		1.66	hypothetical protein	
SACOL2222	rpsE	1.66	30S ribosomal protein S5	located at the back of the 30S subunit body where it stabilizes the conformation of the head with respect to the body; contacts S4 and S8; with S4 and S12 plays a role in translational accuracy; mutations in this gene result in spectinomycin resistance
SACOL1287		1.66	50S ribosomal protein L7	identified by similarity to EGAD:9717; match to protein family HMM PF01248
SACOL0438	ssb2	1.66	single-stranded DNA-binding protein	identified by similarity to EGAD:17778; match to protein family HMM PF00436; match to protein family HMM TIGR00621
SACOL2737	gidA	1.65	tRNA uridine 5-carboxymethylaminomethyl modification enzyme GidA	GidA; glucose-inhibited cell division protein A; involved in the 5-carboxymethylaminomethyl modification (mnm(5)s(2)U) of the wobble uridine base in some tRNAs
SACOL0360		1.65	hypothetical protein	
SACOL0679		1.65	monovalent cation/H <sup>+</sup> antiporter subunit A	subunit A of antiporter complex involved in resistance to high concentrations of Na <sup>+</sup> , K <sup>+</sup> , Li <sup>+</sup> and/or alkali
SACOL0686		1.65	monovalent cation/H <sup>+</sup> antiporter subunit G	subunit G of antiporter complex involved in resistance to high concentrations of Na <sup>+</sup> , K <sup>+</sup> , Li <sup>+</sup> and/or alkali
SACOL2231	rpmC	1.65	50S ribosomal protein L29	one of the stabilizing components for the large ribosomal subunit
SACOL2221	rpmD	1.64	50S ribosomal protein L30	L30 binds domain II of the 23S rRNA and the 5S rRNA; similar to eukaryotic protein L7
SACOL1118	typA	1.64	GTP-binding protein TypA	identified by match to protein family HMM PF00009; match to protein family HMM PF00679; match to protein family HMM PF03144; match to protein family HMM TIGR00231; match to protein family HMM TIGR01394
SACOL2220	rplO	1.64	50S ribosomal protein L15	late assembly protein
SACOL2082		1.64	hypothetical protein	identified by match to protein family HMM PF02096
SACOL0946		1.64	Na <sup>+</sup> /H <sup>+</sup> antiporter family protein	identified by similarity to GP:10175982; match to protein family HMM PF03553
SACOL1299		1.64	acetoacetyl-CoA reductase	identified by similarity to GP:10175011; match to protein family HMM PF00106
SACOL0468		1.63	superantigen-like protein	these proteins share structural homology to known superantigen proteins but do not exhibit any of the properties expected such as histocompatibility complex class II binding or broad T-cell activation
SACOL1651		1.63	hypothetical protein	identified by similarity to EGAD:45796; match to protein family HMM PF01985; match to protein family HMM TIGR00253
SACOL2134		1.63	hypothetical protein	identified by similarity to GB:AAO5341.1
SACOL2107		1.62	phosphotyrosine protein phosphatase	identified by similarity to EGAD:30369; match to protein family HMM PF01451
SACOL0590		1.62	ribosomal protein L7Ae-like	in <i>Bacillus subtilis</i> this non-essential protein associates with the ribosome
SACOL1238	rpmB	1.61	50S ribosomal protein L28	required for 70S ribosome assembly
SACOL1288	infB	1.61	translation initiation factor IF-2	Protects formylmethionyl-tRNA from spontaneous hydrolysis and promotes its binding to the 30S ribosomal subunits during initiation of protein synthesis. Also involved in the hydrolysis of GTP during the formation of the 70S ribosomal complex
SACOL2306		1.61	hypothetical protein	identified by similarity to GP:10173173; match to protein family HMM PF02517
SACOL2482	fabG2	1.61	3-oxoacyl-(acyl carrier protein) reductase	3-oxoacyl-(acyl carrier protein) reductase, authentic point mutation; this gene contains a premature stop which is not the result of sequencing error; identified by similarity to EGAD:108288
SACOL1255	rimM	1.61	16S rRNA-processing protein RimM	Essential for efficient processing of 16S rRNA
SACOL2232	rplP	1.60	50S ribosomal protein L16	located in the peptidyl transferase center and may be involved in peptidyl transferase activity; similar to archaeal L10e
SACOL1567	xseB	1.60	exodeoxyribonuclease VII small subunit	catalyzes the bidirectional exonucleolytic cleavage of DNA
SACOL0763		1.60	aldo/keto reductase oxidoreductase	identified by match to protein family HMM PF00248
SACOL2136		1.60	hypothetical protein	
SACOL1317	glpP	1.60	glycerol uptake operon antiterminator regulatory protein	identified by similarity to EGAD:18158; match to protein family HMM PF04309
SACOL1587	efp	1.60	elongation factor P	Involved in peptide bond synthesis; alters the affinity of the ribosome for aminoacyl-tRNA

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL2052		1.59	hypothetical protein	identified by match to protein family HMM PF03926
SACOL0357	dut	1.58	prophage L54a, deoxyuridine 5'-triphosphate nucleotidohydrolase	identified by similarity to SP:P33316; match to protein family HMM PF00692
SACOL1647		1.58	hypothetical protein	identified by similarity to OMNI:NTL01BH1333
SACOL2223	rplR	1.58	50S ribosomal protein L18	binds 5S rRNA along with protein L5 and L25
SACOL2233	rpsC	1.58	30S ribosomal protein S3	forms a complex with S10 and S14; binds the lower part of the 30S subunit head and the mRNA in the complete ribosome to position it for translation
SACOL2182	lacF	1.58	PTS system, lactose-specific IIA component	identified by similarity to EGAD:18801; match to protein family HMM PF02255; match to protein family HMM TIGR00823
SACOL1208	lspA	1.57	lipoprotein signal peptidase	lipoprotein signal peptidase; integral membrane protein that removes signal peptides from prolipoproteins during lipoprotein biosynthesis
SACOL1788		1.57	hypothetical protein	
SACOL0859		1.57	hypothetical protein	
SACOL1653		1.57	GTP-binding protein YqeH	in <i>Bacillus subtilis</i> this enzyme appears to be involved in 30S ribosomal RNA subunit biogenesis
SACOL1652	aroE	1.57	shikimate 5-dehydrogenase	identified by similarity to EGAD:45757; match to protein family HMM PF01488; match to protein family HMM TIGR00507
SACOL1665	greA	1.57	transcription elongation factor GreA	necessary for efficient RNA polymerase transcription elongation past template-encoded arresting sites; arresting sites in DNA have the property of trapping a certain fraction of elongating RNA polymerases that pass through, resulting in locked ternary complexes. Cleavage of the nascent transcript by cleavage factors such as GreA or GreB allows the resumption of elongation from the new 3'terminus
SACOL1722	tig	1.56	trigger factor	Tig; RopA; peptidyl-prolyl cis/trans isomerase; promotes folding of newly synthesized proteins; binds ribosomal 50S subunit; forms a homodimer
SACOL1635	prmA	1.56	50S ribosomal protein L11 methyltransferase	methylates ribosomal protein L11 at multiple amino acid positions; mutations of these genes in <i>Escherichia coli</i> or <i>Thermus thermophilus</i> has no apparent phenotype
SACOL0746	norR	1.56	MarR family transcriptional regulator	identified by match to protein family HMM PF01047
SACOL2228	rplX	1.55	50S ribosomal protein L24	assembly initiator protein; binds to 5' end of 23S rRNA and nucleates assembly of the 50S; surrounds polypeptide exit tunnel
SACOL1693	yajC	1.55	preprotein translocase, YajC subunit	identified by match to protein family HMM PF02699; match to protein family HMM TIGR00739
SACOL0589	rpoC	1.55	DNA-directed RNA polymerase subunit beta'	DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. Subunit beta' binds to sigma factor allowing it to bind to the -10 region of the promoter
SACOL0987	fabH	1.54	3-oxoacyl-ACP synthase	FabH; beta-ketoacyl-acyl carrier protein synthase III; catalyzes the condensation of acetyl-CoA with malonyl-ACP to initiate cycles of fatty acid elongation; differs from 3-oxoacyl-(acyl carrier protein) synthase I and II in that it utilizes CoA thioesters as primers rather than acyl-ACPs
SACOL0145	cap5J	1.54	capsular polysaccharide biosynthesis protein Cap5J	identified by match to protein family HMM PF04932
SACOL1965	ligA	1.54	DNA ligase, NAD-dependent	identified by similarity to SP:O87703; match to protein family HMM PF00533; match to protein family HMM PF01653; match to protein family HMM PF03119; match to protein family HMM PF03120; match to protein family HMM TIGR00575
SACOL2736	gidB	1.54	16S rRNA methyltransferase GidB	glucose-inhibited division protein B; SAM-dependent methyltransferase; methylates the N7 position of guanosine in position 527 of 16S rRNA
SACOL2216	rpmJ	1.54	50S ribosomal protein L36	smallest protein in the large subunit; similar to what is found with protein L31 and L33 several bacterial genomes contain paralogs which may be regulated by zinc; the protein from <i>Thermus thermophilus</i> has a zinc-binding motif and contains a bound zinc ion; the proteins in this group have the motif
SACOL1489	recU	1.54	Holliday junction-specific endonuclease	functions in homologous recombination, DNA repair, and chromosome segregation; binds preferentially to three- and four-stranded DNA intermediates; introduces specific nick sites in four-stranded DNA substrates; functions similarly to <i>Escherichia coli</i> RuvC
SACOL2680		1.54	hypothetical protein	
SACOL1290	truB	1.53	tRNA pseudouridine synthase B	catalyzes isomerization of specific uridines in RNA to pseudouridine; responsible for residues in T loops of many tRNAs
SACOL1067	qoxD	1.53	quinol oxidase subunit IV	identified by match to protein family HMM PF03626
SACOL1716	hemD	1.53	uroporphyrinogen III synthase	identified by match to protein family HMM PF02602
SACOL1953		1.52	hypothetical protein	
SACOL1646	comEA	1.52	comE operon protein 1-like protein	identified by similarity to OMNI:NTL01SA1471; match to protein family HMM PF00633; match to protein family HMM TIGR00426
SACOL1632	rpsU	1.52	30S ribosomal protein S21	a small basic protein that is one of the last in the subunit assembly; omission does not prevent assembly but the subunit is inactive; binds central domain of 16S rRNA
SACOL1282	proS	1.52	prolyl-tRNA synthetase	catalyzes the formation of prolyl-tRNA(Pro) from proline and tRNA(Pro)
SACOL1297		1.52	hypothetical protein	identified by similarity to OMNI:NTL01BH2396; match to protein family HMM PF05193
SACOL1316	mutL	1.52	DNA mismatch repair protein	This protein is involved in the repair of mismatches in DNA. It is required for dam-dependent methyl-directed DNA mismatch repair. Promotes the formation of a stable complex between two or more DNA-binding proteins in an ATP-dependent manner without itself being part of a final effector complex
SACOL1700	rpmA	1.52	50S ribosomal protein L27	involved in the peptidyltransferase reaction during translation

**Supplemental Table 2: Genes with significantly altered expression in response to ZnO-NPs**

SACOL1968	1.51	hypothetical protein	identified by match to protein family HMM PF01371
SACOL1242	1.51	fatty acid biosynthesis transcriptional regulator	negative regulator of genes involved in fatty acid and phospholipid biosynthesis for gram positive bacteria
SACOL2375	1.51	CorA family protein	identified by match to protein family HMM PF01544
SACOL2720	1.51	hypothetical protein	
SACOL1791	1.51	FtsK/SpoIIIE family protein	identified by match to protein family HMM PF01580
SACOL1667	1.50	U32 family peptidase	identified by match to protein family HMM PF01136
SACOL0682	1.50	monovalent cation/H <sup>+</sup> antiporter subunit D	subunit D of antiporter complex involved in resistance to high concentrations of Na <sup>+</sup> , K <sup>+</sup> , Li <sup>+</sup> and/or alkali; contains an oxidoreductase domain; catalyzes the transfer of electrons from NADH to ubiquinone; in <i>S. meliloti</i> it is known to be involved specifically with K <sup>+</sup> transport
SACOL1154	1.50	recombination and DNA strand exchange inhibitor protein	MutS2; MutS-II; involved in blocking homologous and homeologous recombination; has ATPase activity stimulated by recombination intermediates; inhibits DNA strand exchange

**Supplemental Table 3:** Pathways with genes significantly enriched (up or downregulated) by ZnO-NPs

Pathways	p-values	Genes	Sub-Pathways
<b>Downregulated</b>			
Amino acids biosynthesis	0.0169459	aroK ilvH ilvE rocF rocD proC rocA ilvB budB ilvC ilvD pth lysC asd dapA dapD lysA leuC leuD leuA leuB gltB arcB1 ilvA1 ilvA2 hom metX thrC thrB acsA	This class contains the pathways of biosynthesis of each of the 21 amino acids present normally in proteins.
<b>Upregulated</b>			
Superpathway of pyrimidine <i>de novo</i> biosynthesis	0.002223	pyrF pyrE pyrC pyrB carB carA dut	UTP and CTP <i>de novo</i> biosynthesis; UMP biosynthesis; Superpathway of pyrimidine ribonucleotides <i>de novo</i> biosynthesis; Pyrimidine deoxyribonucleotides <i>de novo</i> biosynthesis
Lactose and galactose degradation	0.02163352	lacD lacB lacA lacC	

**Supplemental Table 4:** Oxidation/reduction gene expression altered by ZnO-NPs

<b>Gene</b>	<b>ID</b>	<b>Fold change</b>
<b><i>Down-regulated</i></b>		
Nitrate reductase gamma chain (narL)	SACOL2392	-2.56
Thioredoxin	SACOL2550	-2.16
NAD dehydrogenase	SACOL0941	-2.11
Acyl carrier protein phosphodiesterase (acpD)	SACOL0190	-1.80
Succinate dehydrogenase (sdhA)	SACOL1159	-1.74
Catalase (katA)	SACOL1368	-1.72
NADP flavin oxidoreductase (frpP)	SACOL2534	-1.69
Luciferase	SACOL0394	-1.62
Thioredoxin reductase	SACOL2369	-1.59
<b><i>Up-regulated</i></b>		
Oxidoreductase	SACOL0763	1.60
Cytochrome d ubiquinol oxidase subunit I (cydA)	SACOL1094	2.00
Cytochrome d ubiquinol oxidase subunit II (cydB)	SACOL1095	2.13