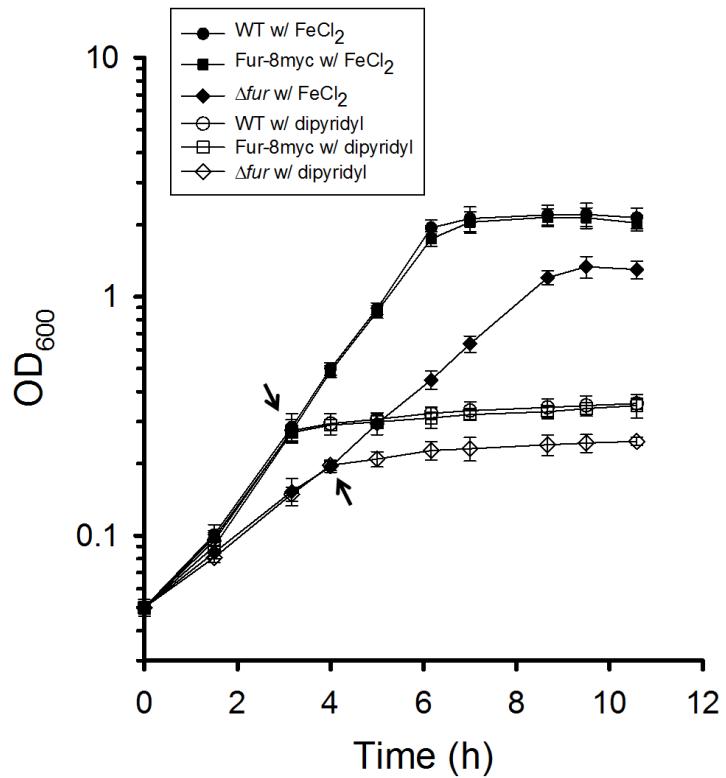
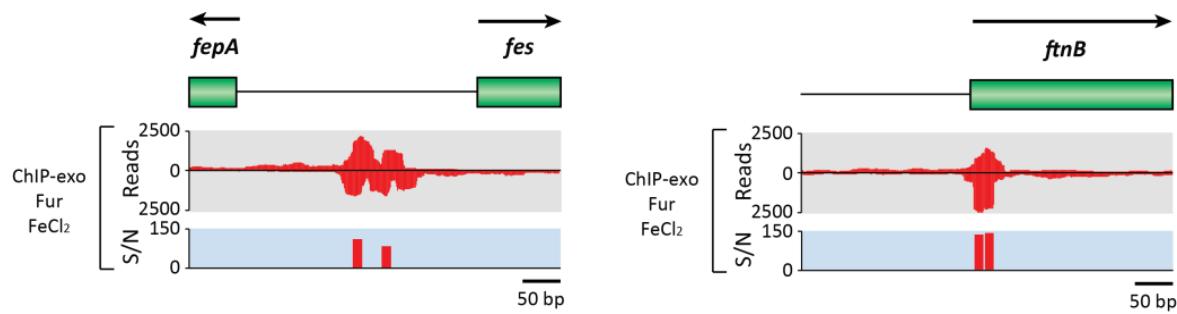


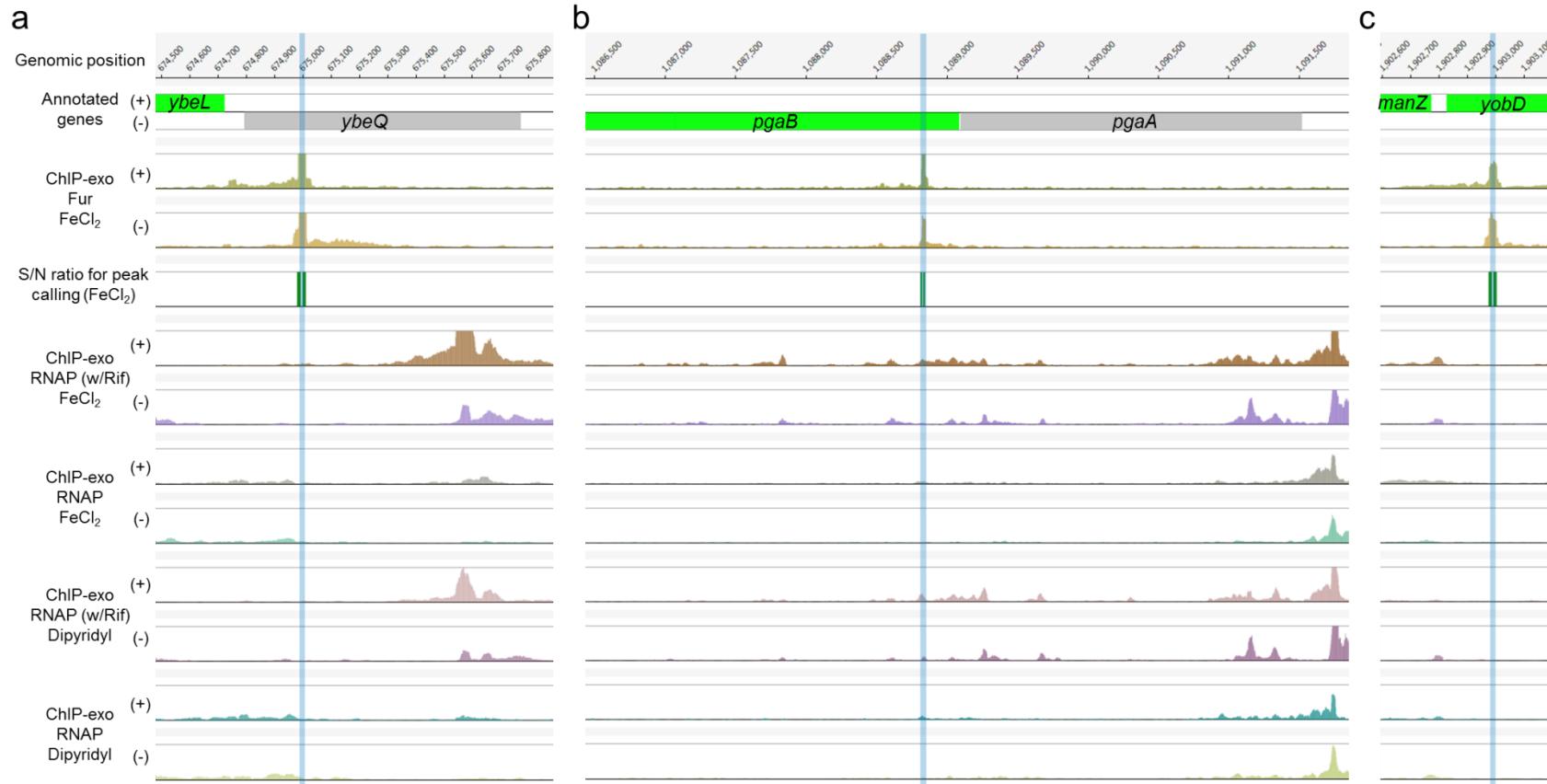
Supplementary Figures



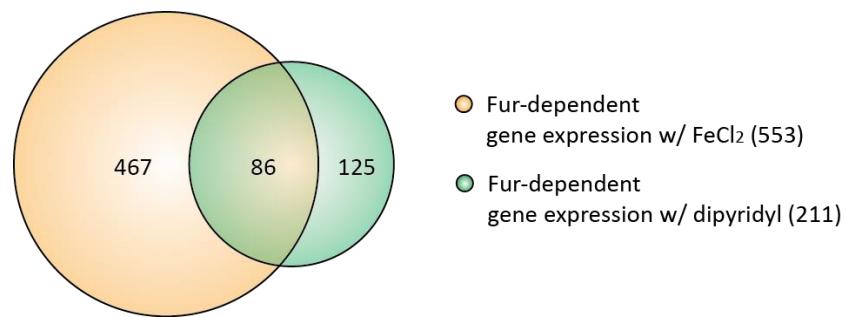
Supplementary Figure 1. Growth profiles of *E. coli* strains used in this study in response to iron availability. Doubling times of WT (K-12 MG1655), Fur-8myc, and Δfur strains were 66.01 min^{-1} , 67.29 min^{-1} , and 113.63 min^{-1} , respectively. The arrows indicate the time when dipyridyl was added into the media. The error bar indicates standard deviation of triplicate experiments.



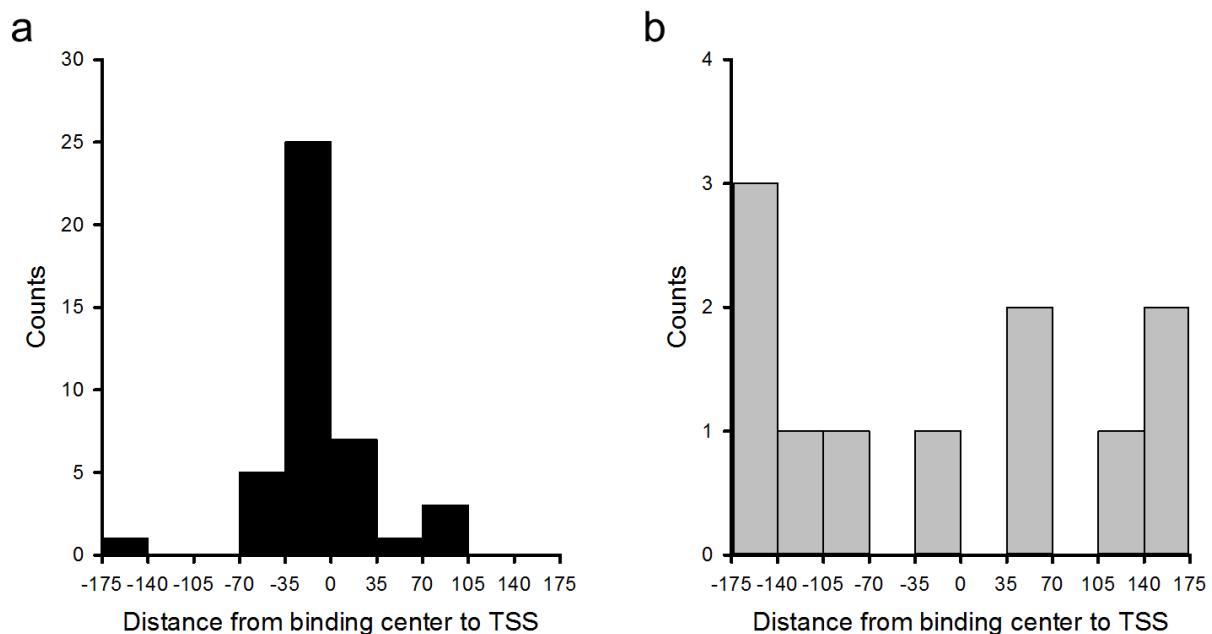
Supplementary Figure 2. Zoom-in examples of Fur bindings identified by ChIP-exo. The high-resolution of ChIP-exo method enabled us to separate binding peaks in divergent promoter regions between *fepA* and *fes* as well as identify multiple bidding peaks for *ftnB*. Arrows indicate the direction of transcription of each gene.



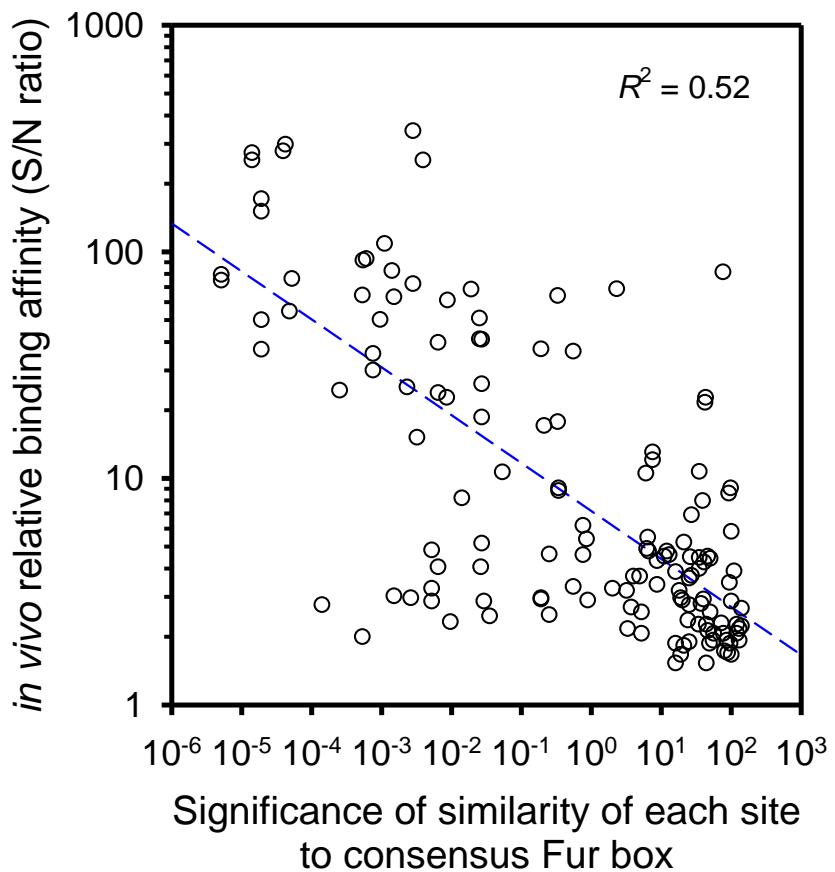
Supplementary Figure 3. Zoom-in examples of RNAP-binding profiles where Fur binds to non-regulatory regions. From ChIP-exo analysis of RNAP under both static (with rifampicin that blocks transcription elongation) and dynamic (without rifampicin) conditions, we could confirm that bindings of Fur on the annotated non-regulatory regions were not related with active transcription events under both iron-replete (FeCl₂) and starvation (dipyridyl) conditions. The shaded blue lines indicate where Fur binds. The data were visualized by using MetaScope (<http://systemsbiology.ucsd.edu/Downloads/MetaScope>).



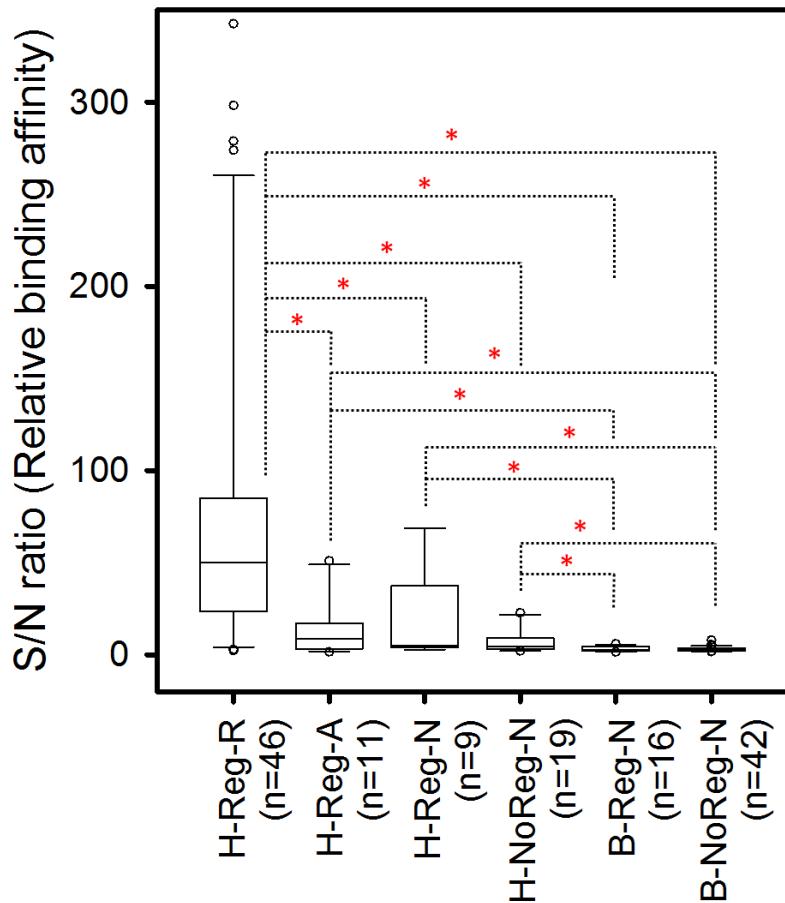
Supplementary Figure 4. Fur-dependent transcriptome in response to iron availability.
Transcription level was compared between wild-type and Δfur mutant under both iron-replete (FeCl₂) and starvation (dipyridyl) conditions.



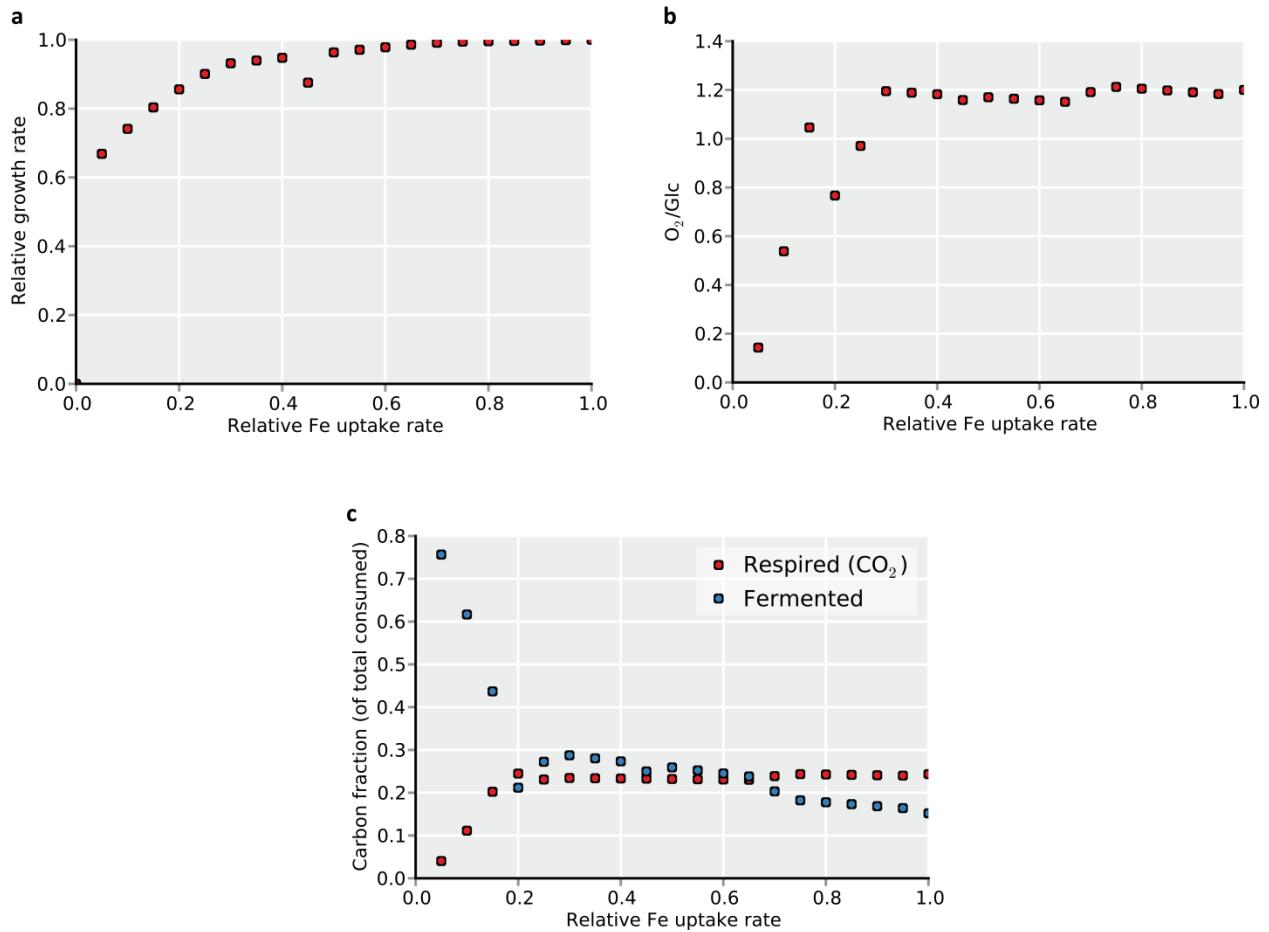
Supplementary Figure 5. Relative distance of Fur binding center to transcription start site (TSS). We calculated distance of Fur binding center to TSS of each gene in case of (a) repression and (b) activation.



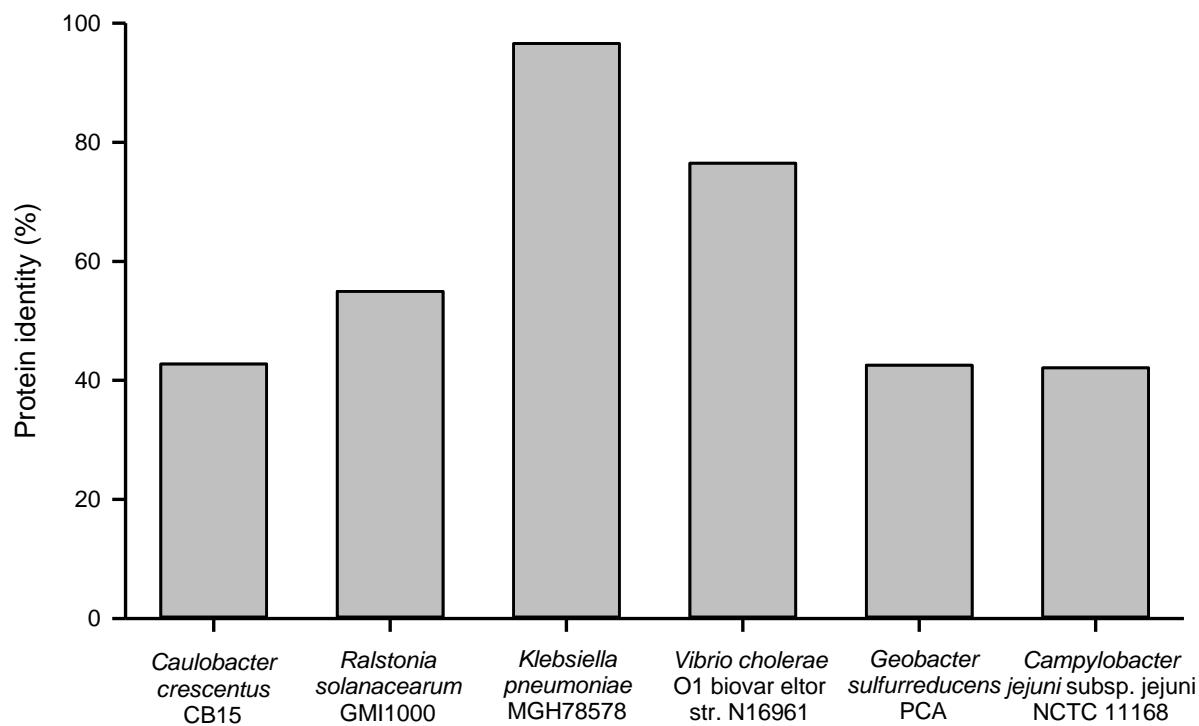
Supplementary Figure 6. Relationship between sequence similarity to consensus Fur box and *in vivo* relative binding affinity. The signal-to-noise (S/N) ratio of each Fur-binding peak was assigned to *in vivo* relative binding affinity of each site. The significance of similarity of each site to consensus Fur box was represented by statistical significance (*P*-value) computed from the match score of the site with the position specific scoring matrix for the motif. The more different the binding sequence was from the consensus Fur box, the lower the *in vivo* relative binding affinity was.



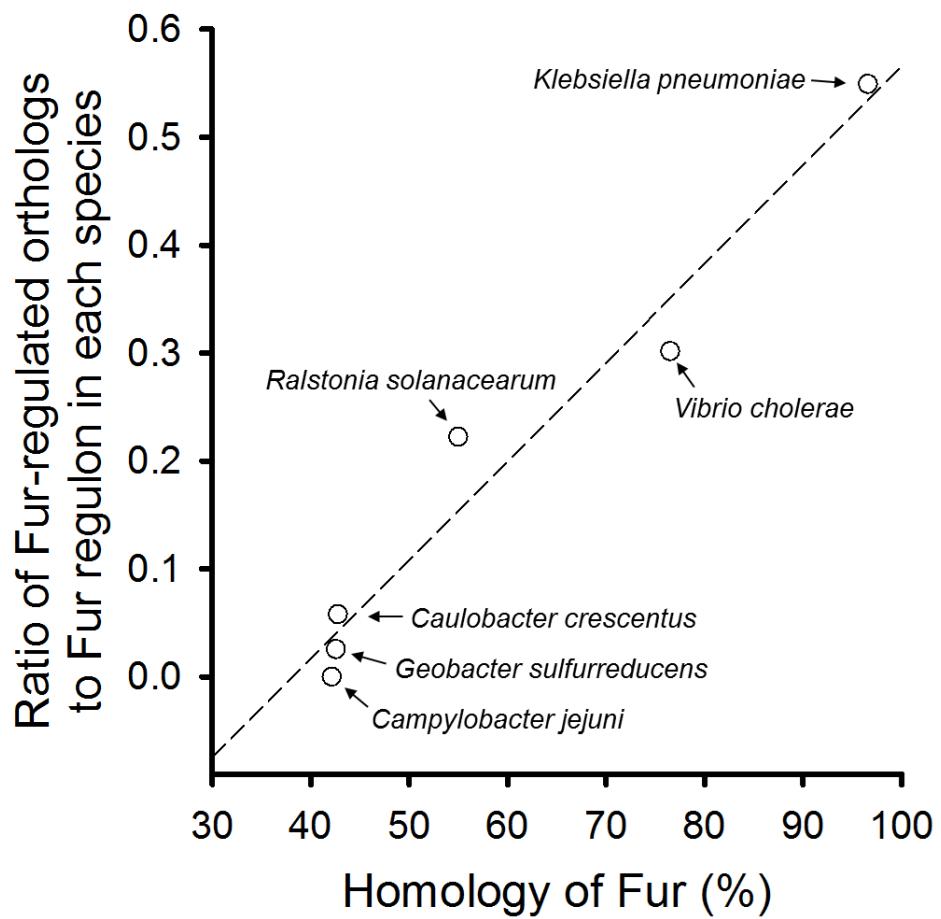
Supplementary Figure 7. Fur occupancy level of depending on Fur binding modes (with or without iron), binding location (regulatory or non-regulatory region), and change of transcript level (repression, activation, or no change in transcript). Each category has 46 binding peaks in *holo*-Fur repression (H-Reg-R), 11 binding peaks in *holo*-Fur activation (H-Reg-A), 9 holo-Fur binding peaks in regulatory regions but no change in transcript level (H-Reg-N), 19 holo-Fur binding peaks in non-regulatory regions (H-NoReg-N), 16 binding peaks regardless of iron availability in regulatory regions but no change in transcript (B-Reg-N), and 42 binding peaks regardless of iron availability in non-regulatory regions (B-NoReg-N). Signal-to-noise (S/N) ratio of each Fur-binding peak in ChIP-exo data was used to indicate a relative binding affinity. Red asterisk (*) indicates $P\text{-value} < 0.01$. The plot is median-quartile boxplots with decile error bars.



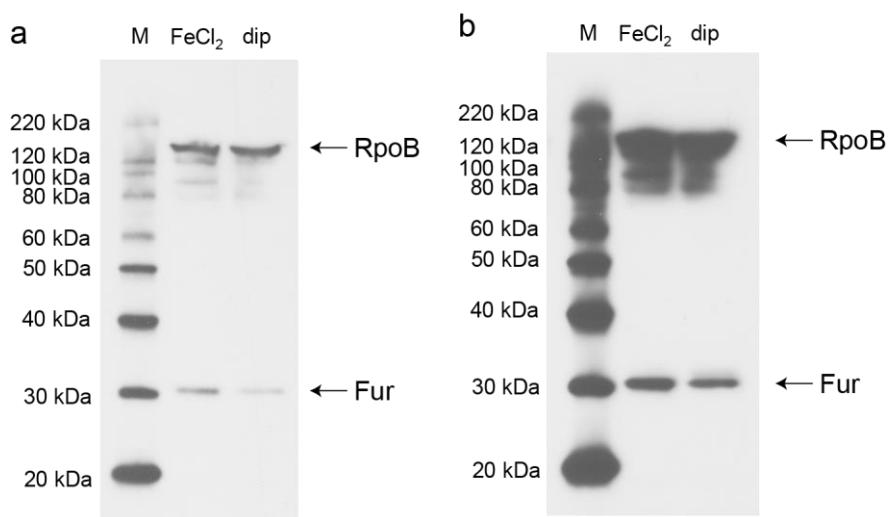
Supplementary Figure 8. ME-model simulation results as a function of the iron uptake rate. From ME-model simulation, we predicted (a) relative growth rate, (b) O₂ uptake rate relative to glucose uptake, and (c) fraction of carbon secretion in response to different iron uptake rate. As iron is scarce, both growth rate and O₂ uptake rate are decreased. However, the fraction of fermented carbon dramatically increases while that of respiration decreases, indicating metabolism shifts towards fermentative pathways.



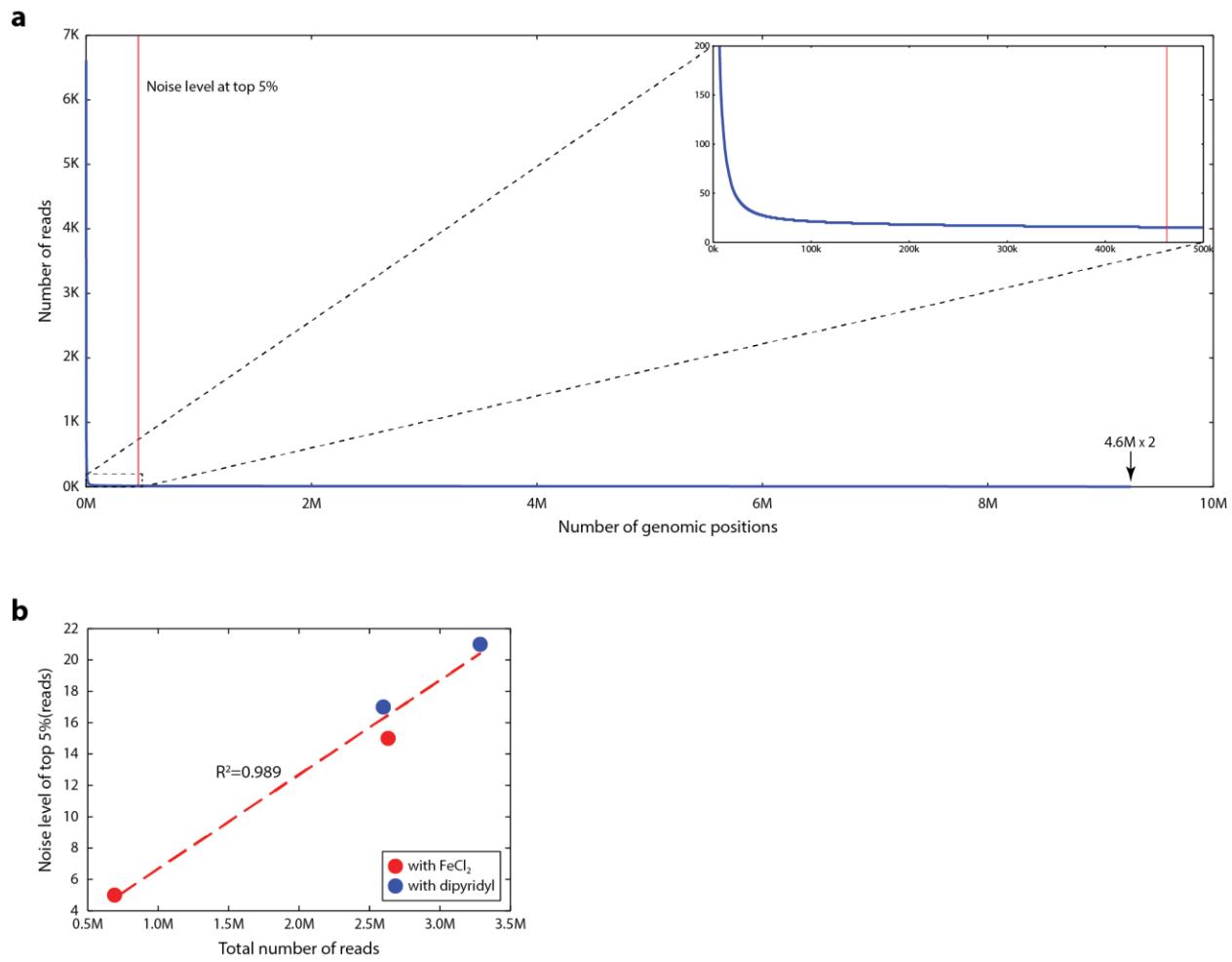
Supplementary Figure 9. Homology of Fur in each species compared to that in *E. coli* K-12 MG1655. *Caulobacter crescentus* (α -proteobacteria), *Ralstonia solanacearum* (β -proteobacteria), *Klebsiella pneumonia* (γ -proteobacteria), *Vibrio cholerae* (γ -proteobacteria), *Geobacter sulfurreducens* (δ -proteobacteria), and *Campylobacter jejuni* (ϵ -proteobacteria) were analyzed.



Supplementary Figure 10. The relationship between conservation of Fur and Fur-regulated orthologs. The ratio of Fur-regulated orthologs to the known Fur regulon in each species was linearly correlated with the degree of conservation of Fur ($R^2 = 0.95$).



Supplementary Figure 11. Western blot analysis. The *E. coli* strain harboring Fur-8myc was grown under iron-replete (FeCl₂) and iron starvation (Dipyridyl, dip) conditions. Antibodies that specifically recognize RpoB subunit of RNAP and myc-tag for Fur were used after separating membranes into two pieces. They were exposed together to generate blot image. The exposure time is (a) 1 sec and (b) 5 sec. The M lane indicates molecular marker (MagicMark™ XP Standard, Life Technologies).



Supplementary Figure 12. Noise level setting for ChIP-exo analysis. (a) Noise level (reads) at top 5% (red line) resembles background level in plateau. (b) Noise level of top 5% (reads) from each ChIP-exo replicates across conditions was correlated with the total number of reads.

Supplementary Tables

Supplementary Table 1. Confirmation of previously characterized Fur-binding sites

| Number | Transcription Unit | Decision |
|--------|---------------------------|-------------|
| 1 | <i>fhuACDB</i> | Yes |
| 2 | <i>fepA-entD</i> | Yes |
| 3 | <i>fes-ybdZ-entF-fepE</i> | Yes |
| 4 | <i>fepD-fepG-fepC</i> | Yes |
| 5 | <i>entS</i> | Yes |
| 6 | <i>fepB</i> | Yes |
| 7 | <i>entCEBAH</i> | Yes |
| 8 | <i>fur</i> | No |
| 9 | <i>gpmA</i> | Yes |
| 10 | <i>pyrC</i> | No |
| 11 | <i>oppABCDF</i> | No |
| 12 | <i>tonB</i> | Yes |
| 13 | <i>nohA-ydfN</i> | No |
| 14 | <i>sufABCDSE</i> | Yes |
| 15 | <i>ftnA</i> | Yes |
| 16 | <i>cirA</i> | Yes |
| 17 | <i>mntH</i> | Yes |
| 18 | <i>hmp</i> | No |
| 19 | <i>exbBD</i> | Yes |
| 20 | <i>garPLRK</i> | No |
| 21 | <i>gspCDEFGHIJKLMNOP</i> | No |
| 22 | <i>ryhB</i> | Yes |
| 23 | <i>sodA</i> | Yes |
| 24 | <i>fecABCDE</i> | Yes |
| 25 | <i>fecIR</i> | Yes |
| 26 | <i>fhuF</i> | Yes |
| 27 | <i>yjjZ</i> | Yes |
| Total | | 20/27 (74%) |

Supplementary Table 2. Genes directly regulated by Fur in response to iron availability.

| Number | bnum | Gene | Regulatory Mode | Cog ^a | Description |
|--------|-------|-------------|-----------------|------------------|---|
| 1 | b0150 | <i>fhuA</i> | HR | P | ferrichrome outer membrane transporter |
| 2 | b0151 | <i>fhuC</i> | HR | H,P | iron-hydroxamate transporter subunit |
| 3 | b0152 | <i>fhuD</i> | HR | P | iron-hydroxamate transporter subunit |
| 4 | b0153 | <i>fhuB</i> | HR | P | fused iron-hydroxamate transporter subunits of ABC superfamily |
| 5 | b0273 | <i>argF</i> | HA | E | ornithine carbamoyltransferase 2 |
| 6 | b0272 | <i>yagI</i> | HA | K | predicted DNA-binding transcriptional regulator |
| 7 | b0468 | <i>ybaN</i> | HR | S | inner membrane protein |
| 8 | b0474 | <i>adk</i> | HA | F | adenylate kinase |
| 9 | b0584 | <i>fepA</i> | HR | P | iron-enterobactin outer membrane transporter |
| 10 | b0583 | <i>entD</i> | HR | Q | phosphopantetheinyltransferase component of enterobactin synthase multienzyme complex |
| 11 | b0585 | <i>fes</i> | HR | P | Enterochelin esterase |
| 12 | b4511 | <i>ybdZ</i> | HR | S | stimulator of EntF adenylation activity, MbtH-like |
| 13 | b0586 | <i>entF</i> | HR | Q | Enterobactin synthase component F |
| 14 | b0587 | <i>fepE</i> | HR | M | Ferric enterobactin transport protein |
| 15 | b0590 | <i>fepD</i> | HR | P | iron-enterobactin transporter subunit |
| 16 | b0589 | <i>fepG</i> | HR | P | iron-enterobactin transporter subunit |
| 17 | b0588 | <i>fepC</i> | HR | H,P | iron-enterobactin transporter subunit |
| 18 | b0591 | <i>entS</i> | HR | - | enterobactin exporter |
| 19 | b0592 | <i>fepB</i> | HR | P | iron-enterobactin transporter subunit |
| 20 | b0593 | <i>entC</i> | HR | H,Q | isochorismate synthase 1 |
| 21 | b0594 | <i>entE</i> | HR | Q | 2,3-dihydroxybenzoate-AMP ligase component of enterobactin synthase multienzyme complex |
| 22 | b0595 | <i>entB</i> | HR | Q | isochorismatase |
| 23 | b0596 | <i>entA</i> | HR | I,Q,R | 2,3-dihydro-2,3-dihydroxybenzoate dehydrogenase |
| 24 | b0597 | <i>entH</i> | HR | Q | thioesterase required for efficient enterobactin production |
| 25 | b0755 | <i>gpmA</i> | HR | G | phosphoglyceromutase 1 |
| 26 | b0805 | <i>fiu</i> | HR | P | catecholate siderophore receptor Fiu |

| | | | | | |
|----|-------|---------------|----|-----|--|
| 27 | b0804 | <i>ybiX</i> | HR | S | conserved protein, Fe(II)-dependent oxygenase superfamily |
| 28 | b1017 | <i>efeU_2</i> | HR | - | pseudogene |
| 29 | b1018 | <i>efeO</i> | HR | P | Iron uptake system component EfeO |
| 30 | b1019 | <i>efeB</i> | HR | P | Deferrochelatase/peroxidase EfeB |
| 31 | b1102 | <i>fhuE</i> | HR | P | ferric-rhodotorulic acid outer membrane transporter |
| 32 | b1164 | <i>ycgZ</i> | AA | - | RcsB connector protein for regulation of biofilm and acid-resistance |
| 33 | b1165 | <i>ymgA</i> | AA | - | RcsB connector protein for regulation of biofilm |
| 34 | b1166 | <i>ariR</i> | AA | - | RcsB connector protein for regulation of biofilm and acid-resistance |
| 35 | b1167 | <i>ymgC</i> | AA | - | predicted protein |
| 36 | b1252 | <i>tonB</i> | HR | M | membrane spanning protein in TonB-ExbB-ExbD transport complex |
| 37 | b1267 | <i>acnA</i> | HA | C | aconitate hydratase 1 |
| 38 | b1452 | <i>yncE</i> | HR | S | ATP-binding protein |
| 39 | b1478 | <i>adhP</i> | HR | R | ethanol-active dehydrogenase/acetaldehyde-active reductase |
| 40 | b1496 | <i>yddA</i> | HR | R | Inner membrane ABC transporter ATP-binding protein |
| 41 | b1495 | <i>yddB</i> | HR | P | putative porin protein |
| 42 | b1586 | <i>ynfD</i> | HR | - | lipoprotein |
| 43 | b1684 | <i>sufA</i> | HR | S | Fe-S cluster assembly protein |
| 44 | b1683 | <i>sufB</i> | HR | O | component of SufBCD Fe-S cluster assembly scaffold |
| 45 | b1682 | <i>sufC</i> | HR | O | SufBCD Fe-S cluster assembly scaffold protein |
| 46 | b1681 | <i>sufD</i> | HR | O | component of SufBCD Fe-S cluster assembly scaffold |
| 47 | b1680 | <i>sufS</i> | HR | E | cysteine desulfurase |
| 48 | b1679 | <i>sufE</i> | HR | R | sulfur acceptor protein |
| 49 | b1705 | <i>ydiE</i> | HR | P | hemin uptake protein HemP homolog |
| 50 | b1902 | <i>ftnB</i> | HA | P | ferritin B |
| 51 | b1905 | <i>ftnA</i> | HA | P | ferritin iron storage protein |
| 52 | b1995 | <i>yoeA</i> | HR | - | pseudogene |
| 53 | b2155 | <i>cirA</i> | HR | P | catecholate siderophore receptor CirA |
| 54 | b2211 | <i>yojI</i> | HR | P,Q | fused ABC transporter permease and ATP-binding components |
| 55 | b2392 | <i>mntH</i> | HR | P | manganese/divalent cation transporter |
| 56 | b2673 | <i>nrdH</i> | HR | O | hydrogen donor for NrdEF electron transport system |
| 57 | b2674 | <i>nrdI</i> | HR | F | flavodoxin required for NrdEF cluster assembly |

| | | | | | |
|----|-------|-------------|----|-----|---|
| 58 | b2675 | <i>nrdE</i> | HR | F | ribonucleoside-diphosphate reductase 2, alpha subunit |
| 59 | b2676 | <i>nrdF</i> | HR | F | ribonucleoside-diphosphate reductase 2, beta subunit |
| 60 | b2997 | <i>hybO</i> | HA | C | hydrogenase 2, small subunit |
| 61 | b2996 | <i>hybA</i> | HA | C | hydrogenase 2 4Fe-4S ferredoxin-type component |
| 62 | b3006 | <i>exbB</i> | HR | U | membrane spanning protein in TonB-ExbB-ExbD complex |
| 63 | b3005 | <i>exbD</i> | HR | U | membrane spanning protein in TonB-ExbB-ExbD complex |
| 64 | b3070 | <i>yqjH</i> | HR | P | predicted siderophore interacting protein |
| 65 | b3408 | <i>feoA</i> | HR | P | ferrous iron transporter |
| 66 | b3409 | <i>feoB</i> | HR | P | fused ferrous iron transporter |
| 67 | b3410 | <i>feoC</i> | HR | K | predicted DNA-binding transcriptional regulator |
| 68 | b4451 | <i>ryhB</i> | HR | - | sRNA antisense regulator mediating positive Fur regulon response, Hfq-dependent |
| 69 | b3928 | <i>zapB</i> | HA | S | FtsZ stabilizer |
| 70 | b4291 | <i>fecA</i> | HR | P | ferric citrate outer membrane transporter |
| 71 | b4290 | <i>fecB</i> | HR | P | iron-dicitrate transporter subunit |
| 72 | b4289 | <i>fecC</i> | HR | P | iron-dicitrate transporter subunit |
| 73 | b4288 | <i>fecD</i> | HR | P | iron-dicitrate transporter subunit |
| 74 | b4287 | <i>fecE</i> | HR | H,P | iron-dicitrate transporter subunit |
| 75 | b4293 | <i>fecI</i> | HR | K | RNA polymerase, sigma 19 factor |
| 76 | b4292 | <i>fecR</i> | HR | T,P | transmembrane signal transducer for ferric citrate transport |
| 77 | b4322 | <i>uxuA</i> | HA | G | mannonate hydrolase |
| 78 | b4323 | <i>uxuB</i> | HA | G | D-mannonate oxidoreductase |
| 79 | b4342 | <i>yjiT</i> | HA | - | pseudogene |
| 80 | b4367 | <i>fhuF</i> | HR | R | ferric iron reductase involved in ferric hydroximate transport |
| 81 | b4567 | <i>yjjZ</i> | HR | - | predicted protein |

^a “-” indicates genes that are not classified in Cog.

Supplementary Table 3. Other transcription factors known to regulate direct Fur regulon (81 genes).

| TF | # of bindings | Target genes |
|-------------|------------------|---|
| <i>crp</i> | 16 | <i>fepA/entD/entC/entE/entB/entA/fiu/acnA/cirA/fecA/fecB/fecC/fecD/fecE/uxuA/uxuB</i> |
| <i>oxyR</i> | 10 | <i>sufA/sufB/sufC/sufD/sufS/sufE/mntH/uxuA/uxuB/fhuF</i> |
| <i>nsrR</i> | 6 | <i>sufA/sufB/sufC/sufD/sufS/sufE</i> |
| <i>iscR</i> | 6 | <i>sufA/sufB/sufC/sufD/sufS/sufE</i> |
| <i>ihfB</i> | 6 | <i>sufA/sufB/sufC/sufD/sufS/sufE</i> |
| <i>ihfA</i> | 6 | <i>sufA/sufB/sufC/sufD/sufS/sufE</i> |
| <i>pdhR</i> | 5 | <i>fecA/fecB/fecC/fecD/fecE</i> |
| <i>fnr</i> | 4 | <i>fes/entF/acnA/feoB</i> |
| <i>arcA</i> | 3 | <i>acnA/hybO/hybA</i> |
| <i>uxuR</i> | 2 | <i>uxuA/uxuB</i> |
| <i>nrdR</i> | 2 | <i>nrdE/nrdF</i> |
| <i>narL</i> | 2 | <i>hybO/hybA</i> |
| <i>hns</i> | 2 | <i>fes/entF</i> |
| <i>fnrS</i> | 2 | <i>gpmA/adhP</i> |
| <i>exuR</i> | 2 | <i>uxuA/uxuB</i> |
| <i>soxS</i> | 1 | <i>acnA</i> |
| <i>rutR</i> | 1 | <i>fepB</i> |
| <i>rob</i> | 1 | <i>acnA</i> |
| <i>nagC</i> | 1 | <i>feoB</i> |
| <i>mntR</i> | 1 | <i>mntH</i> |
| <i>marA</i> | 1 | <i>acnA</i> |
| <i>fruR</i> | 1 | <i>acnA</i> |
| <i>argR</i> | 1 | <i>argF</i> |

Supplementary Table 4. Sequence bound by *apo*-Fur for the activation of *ycgZ-ymgA-ariR-ymgC* operon.

| Peak | ChIP-exo Start | ChIP-exo End | Sequence |
|---------------------------------------|-------------------|-----------------|--------------|
| P38 (<i>ycgZ-ymgA-ariR-ymgC</i>) | 1214895 | 1214907 | TATATGCATTAG |

Supplementary Table 5. The transporter and utilization genes regulated by Fur without iron in other pathogenic species.

| Strains | Name | Regulatory Mode | Description | Ref |
|------------------|------------------------------------|-----------------|--|-----|
| <i>C. jejuni</i> | <i>Cj1364</i> | AR | fumarate hydratase | (6) |
| <i>C. jejuni</i> | <i>Cj1345c</i> | AA | putative periplasmic protein | (6) |
| <i>H. pylori</i> | <i>pfr</i> | AR | prokaryotic ferritin | (1) |
| <i>H. pylori</i> | <i>sodB</i> | AR | Fe-containing superoxide dismutase | (1) |
| <i>H. pylori</i> | cytochrome <i>c</i> ₅₅₃ | AR | transferring electrons from cytochrome reductase to a cbb3-type terminal oxidase | (5) |
| <i>H. pylori</i> | <i>hydA</i> | AR | quinone-reactive Ni/Fe hydrogenase | (5) |
| <i>S. aureus</i> | <i>norA</i> | AA | efflux transporter | (7) |

Supplementary Table 6. The lists of functional groups that significantly overlap with DEGs due to *fur* deletion under iron-replete condition.

| Group ^a | p-value ^b | # of target genes in group | # of total genes in group |
|----------------------------|----------------------|----------------------------|---------------------------|
| Fur_REPRESSION_regulon_db | 4.21E-35 | 68 | 114 |
| ArcA_REPRESSION_regulon_db | 3.04E-22 | 56 | 118 |
| Fur_ACTIVATION_regulon_db | 1.87E-14 | 18 | 21 |
| FNR_REPRESSION_regulon_db | 2.63E-10 | 39 | 114 |
| IscR_ACTIVATION_regulon_db | 5.55E-09 | 10 | 11 |
| IHF_REPRESSION_regulon_db | 1.08E-07 | 29 | 87 |
| NarL_ACTIVATION_regulon_db | 4.31E-07 | 18 | 42 |
| FNR_ACTIVATION_regulon_db | 9.15E-07 | 47 | 194 |
| CusR_ACTIVATION_regulon_db | 2.88E-06 | 6 | 6 |
| Zur_REPRESSION_regulon_db | 2.88E-06 | 6 | 6 |
| ArgR_REPRESSION_regulon_db | 4.02E-06 | 14 | 31 |
| Fis_ACTIVATION_regulon_db | 6.69E-06 | 22 | 68 |
| BirA_REPRESSION_regulon_db | 2.43E-05 | 5 | 5 |
| CueR_REPRESSION_regulon_db | 2.43E-05 | 5 | 5 |
| PdhR_ACTIVATION_regulon_db | 2.43E-05 | 5 | 5 |
| YjiE_REPRESSION_regulon_db | 2.43E-05 | 5 | 5 |
| GadW_REPRESSION_regulon_db | 2.96E-05 | 7 | 10 |
| IHF_ACTIVATION_regulon_db | 4.22E-05 | 37 | 160 |
| OxyR_ACTIVATION_regulon_db | 5.76E-05 | 10 | 21 |
| GadX_ACTIVATION_regulon_db | 6.05E-05 | 11 | 25 |
| AdiY_ACTIVATION_regulon_db | 6.52E-05 | 6 | 8 |
| GlcC_ACTIVATION_regulon_db | 0.000131 | 5 | 6 |
| IscR_REPRESSION_regulon_db | 0.000235 | 9 | 20 |
| OxyR_REPRESSION_regulon_db | 0.000395 | 6 | 10 |
| GadE_ACTIVATION_regulon_db | 0.000475 | 12 | 35 |
| MarA_ACTIVATION_regulon_db | 0.00134 | 10 | 29 |
| Lrp_REPRESSION_regulon_db | 0.001413 | 11 | 34 |
| SoxS_ACTIVATION_regulon_db | 0.001413 | 11 | 34 |
| CRP_ACTIVATION_regulon_db | 0.001464 | 68 | 403 |
| HdfR_ACTIVATION_regulon_db | 0.001712 | 3 | 3 |
| DcuR_ACTIVATION_regulon_db | 0.00202 | 5 | 9 |
| Nac_REPRESSION_regulon_db | 0.00202 | 5 | 9 |
| NrdR_REPRESSION_regulon_db | 0.00202 | 5 | 9 |
| ModE_ACTIVATION_regulon_db | 0.002376 | 10 | 31 |
| GatR_REPRESSION_regulon_db | 0.002507 | 4 | 6 |
| GadW_ACTIVATION_regulon_db | 0.003645 | 5 | 10 |
| LexA_REPRESSION_regulon_db | 0.004285 | 14 | 55 |
| ModE_REPRESSION_regulon_db | 0.005553 | 6 | 15 |

| | | | |
|----------------------------|----------|---|---|
| MqsA_REPRESSION_regulon_db | 0.006234 | 3 | 4 |
| OmpR_REPRESSION_regulon_db | 0.009598 | 4 | 8 |

^a The functional groups were assigned based on the regulonDB¹⁰ database.

^b The hypergeometric *p*-value cutoff was < 0.01.

Supplementary Table 7. The lists of functional groups that significantly overlap with DEGs due to *fur* deletion under iron starvation condition.

| Group ^a | p-value ^b | # of target genes in group | # of total genes in group |
|----------------------------|----------------------|----------------------------|---------------------------|
| MetJ_REPRESSION_regulon_db | 2.45E-12 | 11 | 15 |
| GadE_ACTIVATION_regulon_db | 1.18E-11 | 15 | 35 |
| GadW_REPRESSION_regulon_db | 9.35E-10 | 8 | 10 |
| Lrp_REPRESSION_regulon_db | 1.63E-09 | 13 | 34 |
| GatR_REPRESSION_regulon_db | 1.07E-08 | 6 | 6 |
| Fur_REPRESSION_regulon_db | 5.03E-08 | 21 | 114 |
| GadW_ACTIVATION_regulon_db | 5.22E-08 | 7 | 10 |
| ArgR_REPRESSION_regulon_db | 7.73E-08 | 11 | 31 |
| GadX_ACTIVATION_regulon_db | 8.16E-08 | 10 | 25 |
| H-NS_REPRESSION_regulon_db | 1.68E-06 | 18 | 106 |
| ArcA_REPRESSION_regulon_db | 1.98E-06 | 19 | 118 |
| YjiE_ACTIVATION_regulon_db | 1.14E-05 | 5 | 8 |
| ArgR_ACTIVATION_regulon_db | 2.38E-05 | 4 | 5 |
| PurR_REPRESSION_regulon_db | 6.88E-05 | 8 | 31 |
| FNR_REPRESSION_regulon_db | 7.63E-05 | 16 | 114 |
| GcvA_ACTIVATION_regulon_db | 0.000105434 | 3 | 3 |
| AdiY_ACTIVATION_regulon_db | 0.000296818 | 4 | 8 |
| GcvA_REPRESSION_regulon_db | 0.000406934 | 3 | 4 |
| ModE_REPRESSION_regulon_db | 0.000466248 | 5 | 15 |
| NrdR_REPRESSION_regulon_db | 0.00051448 | 4 | 9 |
| IscR_ACTIVATION_regulon_db | 0.001249676 | 4 | 11 |
| FliZ_REPRESSION_regulon_db | 0.001545033 | 5 | 19 |
| RutR_ACTIVATION_regulon_db | 0.002242304 | 2 | 2 |
| SoxR_ACTIVATION_regulon_db | 0.002242304 | 2 | 2 |
| Fur_ACTIVATION_regulon_db | 0.002501929 | 5 | 21 |
| MarA_REPRESSION_regulon_db | 0.003200328 | 3 | 7 |
| NsrR_REPRESSION_regulon_db | 0.004987506 | 10 | 82 |
| PepA_REPRESSION_regulon_db | 0.006516043 | 2 | 3 |
| TorR_REPRESSION_regulon_db | 0.006516043 | 2 | 3 |
| YdeO_ACTIVATION_regulon_db | 0.006516043 | 2 | 3 |
| IHF_REPRESSION_regulon_db | 0.007591188 | 10 | 87 |
| LeuO_ACTIVATION_regulon_db | 0.008919028 | 4 | 18 |

^a The functional groups were assigned based on the regulonDB¹⁰ database.

^b The hypergeometric p-value cutoff was < 0.01.

Supplementary Table 8. The lists of orthologs for direct Fur regulon in *E. coli* K-12 MG1655.

| <i>E.coli</i> K-12 MG1655 Fur regulon | <i>Caulobacter</i> <i>crescentus</i> CB15 | <i>Ralstonia</i> <i>solanacearum</i> GMI1000 | <i>Klebsiella</i> <i>pneumoniae</i> MGH78578 | <i>Vibrio</i> <i>cholerae</i> O1 biovar eltor str. N16961 | <i>Geobacter</i> <i>sulfurreducens</i> PCA | <i>Campylobacter</i> <i>jejuni</i> subsp. <i>jejuni</i> NCTC 11168 |
|---|---|--|--|--|--|---|
| <i>fhuA</i> | CC1778 | RS00173 | KPN_00165 | VC0200 | | |
| <i>fhuC</i> | | | KPN_00166 | VC0201 | | Cj1354 |
| <i>fhuD</i> | | | KPN_00167 | VC0202 | | |
| <i>fhuB</i> | | | KPN_00168 | VC0203 | | |
| <i>argF</i> | | | KPN_04659 | | | |
| <i>yagI</i> | | RS03973 | | | | GSU0514 |
| <i>ybaN</i> | | | KPN_00450 | VC1052 | | GSU0917 |
| <i>adk</i> | CC1269 | RSc2533 | KPN_00456 | VC0986 | | GSU2836 |
| <i>fepA</i> | | | KPN_01244 | | | |
| <i>entD</i> | | | KPN_00601 | VC0780 | | |
| <i>fes</i> | | | KPN_00603 | | | |
| <i>ybdZ</i> | | RS05513 | KPN_00604 | | | |
| <i>entF</i> | | RS05860 | KPN_00605 | VC2209 | | Cj1307 |
| <i>fepE</i> | | | | | | |
| <i>fepD</i> | | | KPN_00608 | VC0777 | | |
| <i>fepG</i> | | | KPN_00607 | VC0778 | | |
| <i>fepC</i> | | RS02720 | KPN_00606 | VC0779 | | |
| <i>entS</i> | CC0403 | RS05067 | KPN_00609 | | GSU0752 | |
| <i>fepB</i> | | | KPN_00610 | VC0776 | | |
| <i>entC</i> | | | KPN_00611 | VC0773 | | |
| <i>entE</i> | | | KPN_00612 | VC0772 | | |
| <i>entB</i> | | | KPN_00613 | VC0771 | | |
| <i>entA</i> | | | KPN_00614 | VC0774 | | |
| <i>entH</i> | | | KPN_00615 | | | GSU1128 |
| <i>gpmA</i> | CC2261 | RSc0353 | KPN_00768 | | | GSU1612 |
| <i>fiu</i> | CC0028 | RS02469 | KPN_01250 | | | |
| <i>ybiX</i> | CC0027 | | KPN_01249 | | | |
| <i>efeU_2</i> | | | | | | |
| <i>efeO</i> | | | KPN_01046 | | | |
| <i>efeB</i> | | | KPN_01047 | | | |
| <i>fhuE</i> | | | | | | |
| <i>ycgZ</i> | | | | | | |
| <i>yngA</i> | | | | | | |
| <i>ariR</i> | | | | | | |
| <i>yngC</i> | | | | | | |
| <i>tonB</i> | | | KPN_02186 | VC1544 | | |
| <i>acnA</i> | CC3667 | RSc2003 | KPN_01272 | VC1338 | | GSU0846 |
| <i>yncE</i> | | | KPN_01908 | | | |
| <i>adhP</i> | | RSc3130 | KPN_01853 | | | GSU0573 |
| <i>yddA</i> | | RS04444 | | | | |
| <i>yddB</i> | | | | | | |
| <i>ynfD</i> | | | KPN_01581 | | | |
| <i>sufA</i> | | | KPN_02141 | | | |
| <i>sufB</i> | CC1864 | | KPN_02140 | | | |
| <i>sufC</i> | CC1862 | | KPN_02139 | | | |
| <i>sufD</i> | CC1861 | | KPN_02138 | | | |
| <i>sufS</i> | CC1860 | | KPN_02137 | VC2309 | | GSU1868 |

| | | | | | |
|-------------|---------------|----------------|------------------|----------------|----------------|
| <i>sufE</i> | CC1061 | | KPN_02136 | | |
| <i>ydiE</i> | | | KPN_02163 | | |
| <i>ftnB</i> | | | KPN_02397 | | |
| <i>ftnA</i> | | | KPN_02402 | VC0078 | GSU1307 |
| <i>yoeA</i> | | | | | |
| <i>cirA</i> | | RS03722 | KPN_02593 | VC0475 | GSU1445 |
| <i>yojL</i> | | RS03729 | KPN_02632 | | Cj0755 |
| <i>mntH</i> | | RS00399 | KPN_02743 | | |
| <i>nrdH</i> | | | KPN_03004 | | |
| <i>nrdI</i> | | | KPN_03005 | | |
| <i>nrdE</i> | CC3492 | | KPN_03006 | | GSU1871 |
| <i>nrdF</i> | | | KPN_03007 | | |
| <i>hybO</i> | | | | | GSU0782 |
| <i>hybA</i> | | | | | GSU0783 |
| <i>exbB</i> | CC2336 | | KPN_03426 | | Cj0179 |
| <i>exbD</i> | CC2335 | RSc1965 | KPN_03425 | | GSU0027 |
| <i>yqjH</i> | | RS03709 | KPN_03499 | VC2210 | Cj0180 |
| <i>feoA</i> | | | KPN_03778 | VC2078 | |
| <i>feoB</i> | CC0712 | RSp0251 | KPN_03779 | VC2077 | GSU3268 |
| <i>feoC</i> | | | KPN_03780 | | Cj1398 |
| <i>ryhB</i> | | | | | |
| <i>zapB</i> | | | KPN_04009 | VC2686 | |
| <i>fecA</i> | CC0139 | | | VCA0064 | |
| <i>fecB</i> | | | | VCA0227 | Cj1355 |
| <i>fecC</i> | | | | | |
| <i>fecD</i> | | | KPN_02102 | | |
| <i>fecE</i> | | | | | |
| <i>fecI</i> | CC2707 | RSp0849 | | | GSU0721 |
| <i>fecR</i> | CC2708 | RS00175 | | | |
| <i>uxuA</i> | | | KPN_02604 | | |
| <i>uxuB</i> | CC1487 | | | | |
| <i>yjiT</i> | | | | | |
| <i>fhuF</i> | | | KPN_04821 | | |
| <i>yjjZ</i> | | | KPN_04823 | | |

Bold text indicates orthologous genes that have been identified as Fur regulon in each species.