The $E.\ coli$ molecular phenotype under different growth conditions

Supplementary materials

Mehmet U. Caglar*, John R. Houser, Craig S. Barnhart, Daniel R. Boutz, Sean M. Carroll, Aurko Dasgupta, Walter F. Lenoir, Bartram L. Smith, Viswanadham Sridhara, Dariya K. Sydykova, Drew Vander Wood, Christopher J. Marx, Edward M. Marcotte*, Jeffrey E. Barrick*, Claus O. Wilke*

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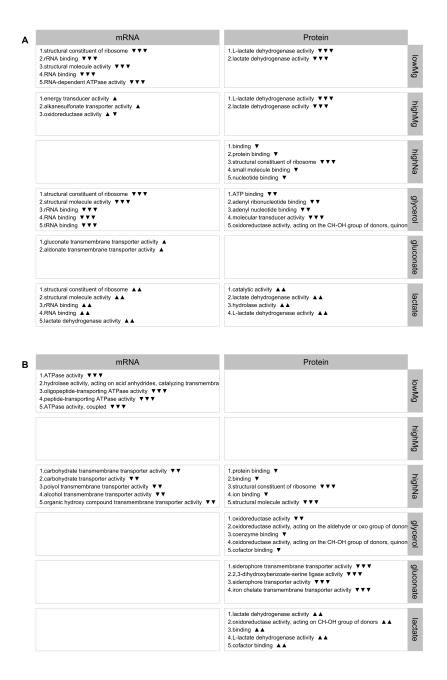


Figure S1: Significantly differentially expressed molecular functions, as determined by GO annotations. For each condition, we show the top-5 differentially expressed molecular functions according to either mRNA or protein abundances. Empty boxes indicate that no differentially expressed pathways were found. The arrows next to pathway names indicate the proportion of up- and down-regulated genes among the significantly differentially expressed genes in this pathway. One up arrow indicates that 60% or more of the genes are up-regulated, two arrows correspond to 80% or more genes, and three arrows correspond to 95% or more genes being up-regulated. Similarly, down arrows indicate the proportion of down-regulated genes. (A) Exponential phase. (B) Stationary phase.

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Figure S2: Significantly differentially expressed KEGG pathways and associated genes with glycerol as carbon source, as determined by mRNA abundances in exponential phase. The top 2 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway we show up to 15 of the most significantly changing genes.

Log2 Fold Change

-3

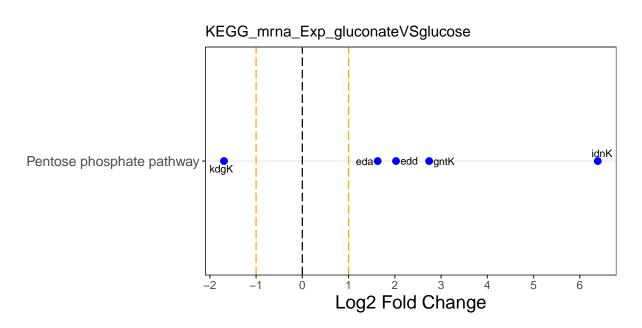


Figure S3: Significantly differentially expressed KEGG pathway and associated genes with gluconate as carbon source, as determined by mRNA abundances in exponential phase. The top differentially expressed KEGG pathway is shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway we show up to 15 of the most significantly changing genes.

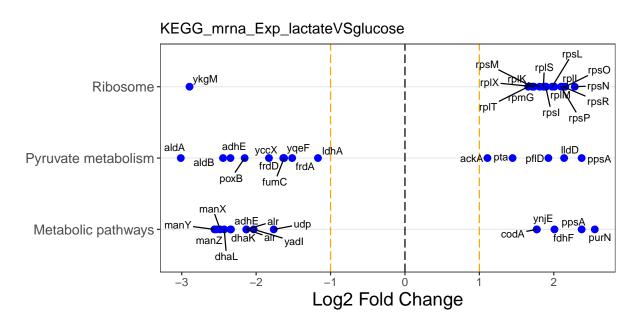


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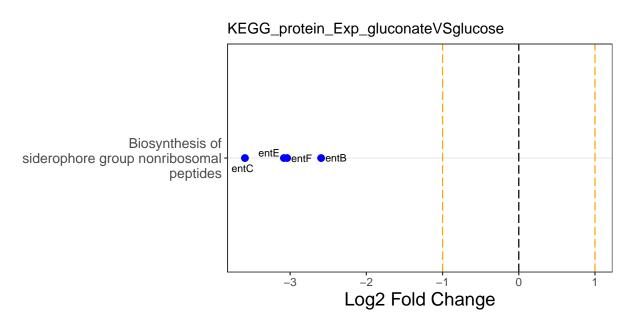


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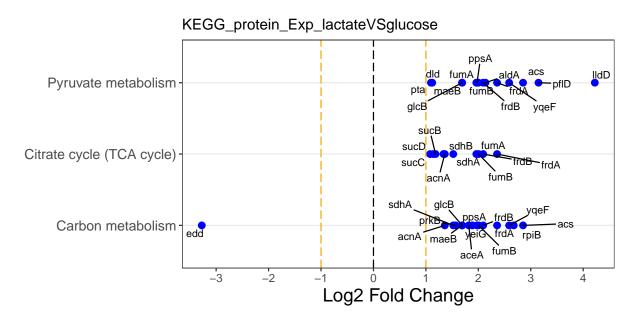


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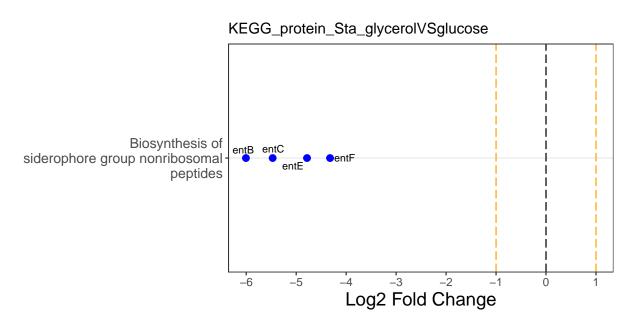


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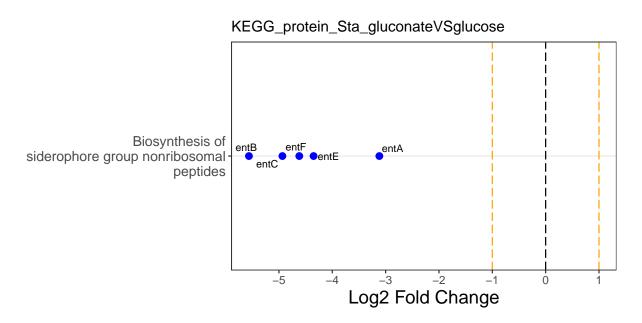


Figure S8: Significantly differentially expressed KEGG pathway and associated genes with gluconate as carbon source, as determined by protein abundances in stationary phase. The top differentially expressed KEGG pathway is shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

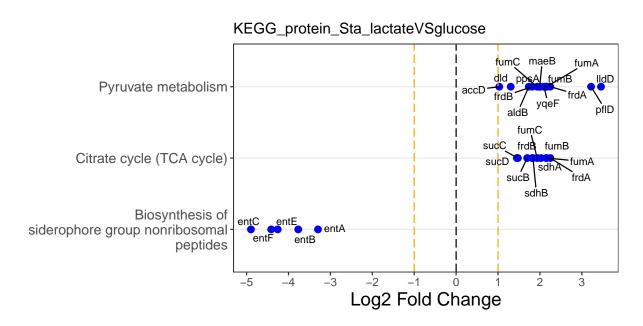


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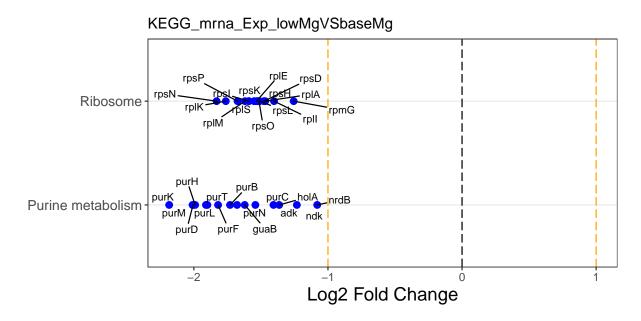


Figure S10: Significantly differentially expressed KEGG pathways and associated genes with low  $\mathrm{Mg^{2+}}$  levels, as determined by mRNA abundances in exponential phase. The top 2 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

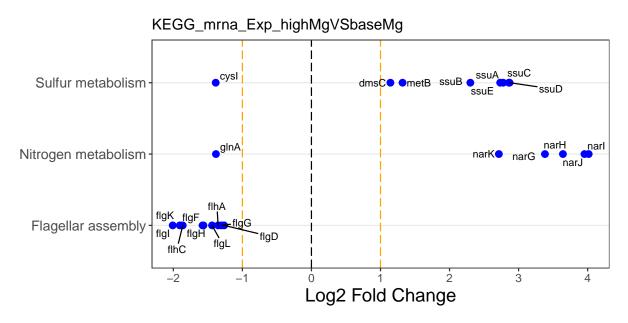


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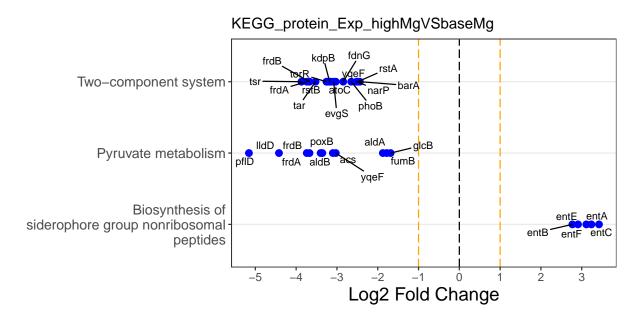


Figure S12: Significantly differentially expressed KEGG pathways and associated genes with high  $\mathrm{Mg^{2+}}$  levels, as determined by protein abundances in exponential phase. The top 3 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

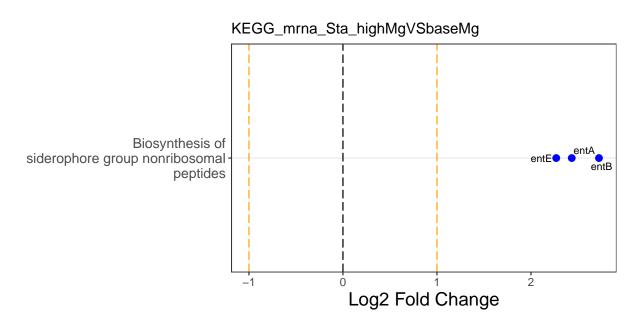


Figure S13: Significantly differentially expressed KEGG pathway and associated genes with high  $\mathrm{Mg^{2+}}$  levels, as determined by mRNA abundances in stationary phase. The top differentially expressed KEGG pathway is shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

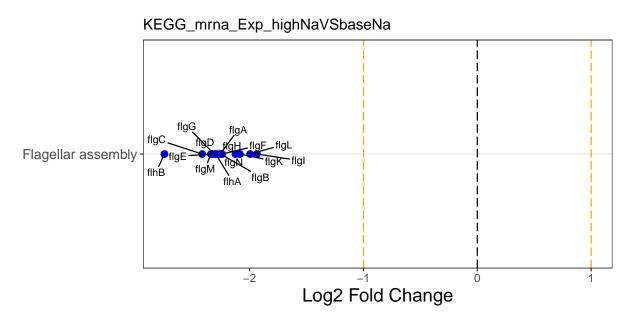


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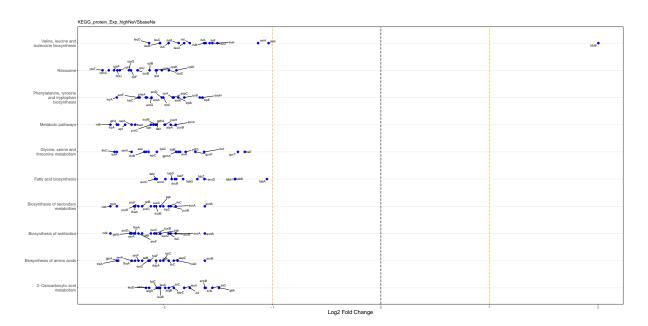


Figure S15: Significantly differentially expressed KEGG pathways and associated genes with high  $\mathrm{Na^+}$  levels, as determined by protein abundances in exponential phase. The top 10 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

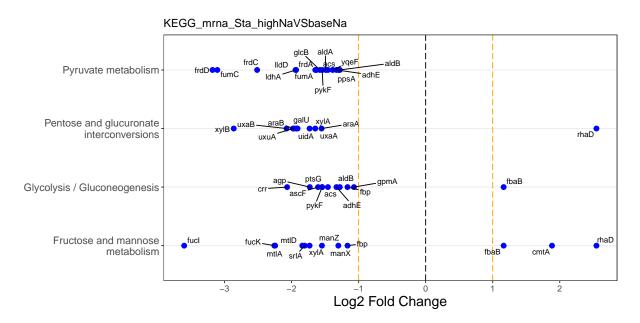


Figure S16: Significantly differentially expressed KEGG pathways and associated genes with high  $\mathrm{Na^+}$  levels, as determined by mRNA abundances in stationary phase. The top 4 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

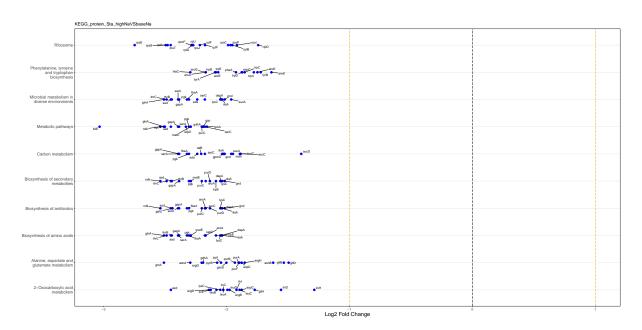


Figure S17: Significantly differentially expressed KEGG pathways and associated genes with high  $\mathrm{Na^+}$  levels, as determined by protein abundances in stationary phase. The top 10 differentially expressed KEGG pathways are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed pathways and for each pathway, we show up to 15 of the most significantly changing genes.

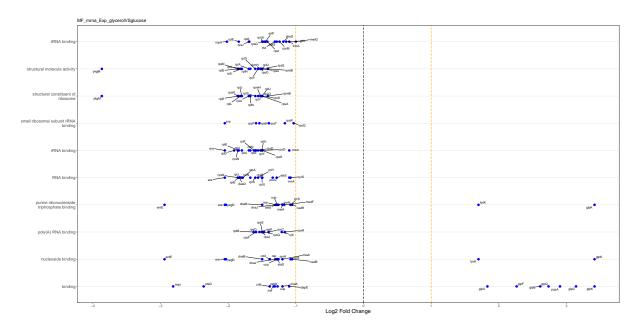


Figure S18: Significantly differentially expressed GO annotations related with molecular functions and associated genes with glycerol as carbon source, as determined by mRNA abundances in exponential phase. The top 10 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

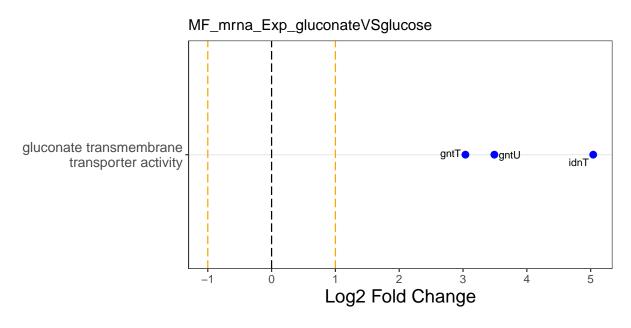


Figure S19: Significantly differentially expressed GO annotations related with molecular functions and associated genes with gluconate as carbon source, as determined by mRNA abundances in exponential phase. The top 2 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

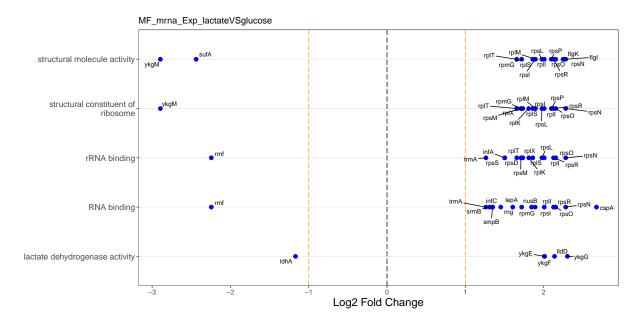


Figure S20: Significantly differentially expressed GO annotations related with molecular functions and associated genes with lactate as carbon source, as determined by mRNA abundances in exponential phase. The top 5 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

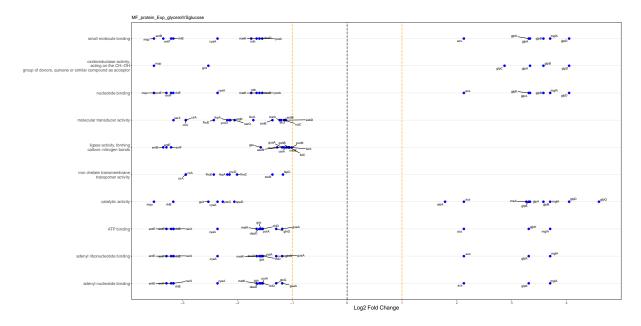


Figure S21: Significantly differentially expressed GO annotations related with molecular functions and associated genes with glycerol as carbon source, as determined by protein abundances in exponential phase. The top 10 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

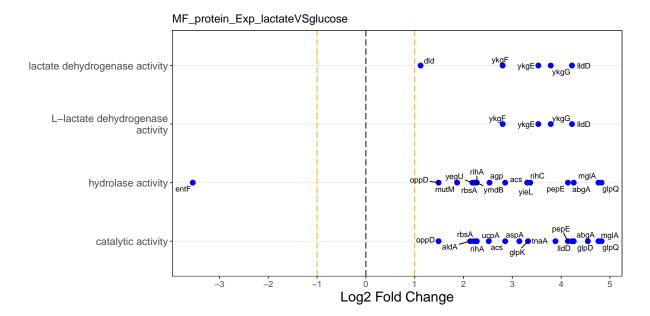


Figure S22: Significantly differentially expressed GO annotations related with molecular functions and associated genes with lactate as carbon source, as determined by protein abundances in exponential phase. The top 4 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

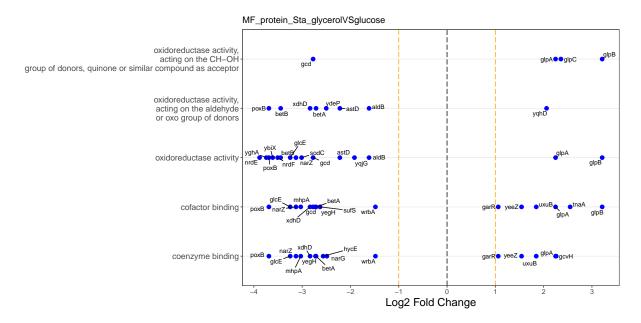


Figure S23: Significantly differentially expressed GO annotations related with molecular functions and associated genes with glycerol as carbon source, as determined by protein abundances in stationary phase. The top 5 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

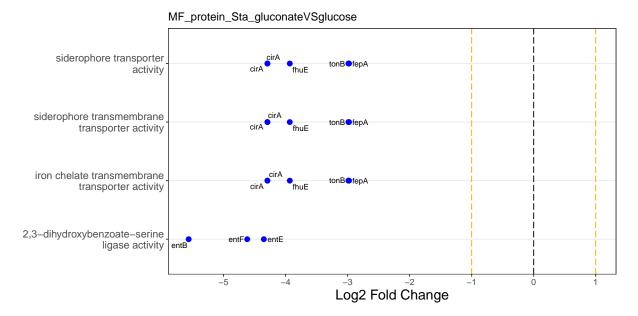


Figure S24: Significantly differentially expressed GO annotations related with molecular functions and associated genes with gluconate as carbon source, as determined by protein abundances in stationary phase. The top 4 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

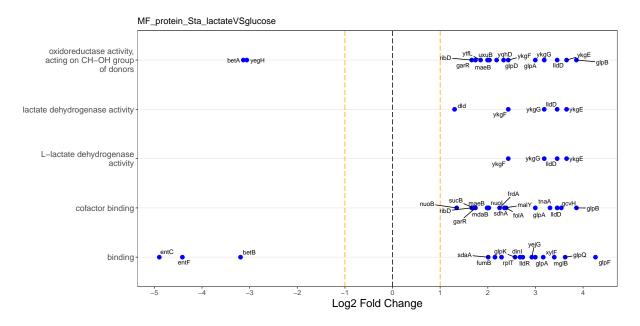


Figure S25: Significantly differentially expressed GO annotations related with molecular functions and associated genes with lactate as carbon source, as determined by protein abundances in stationary phase. The top 5 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

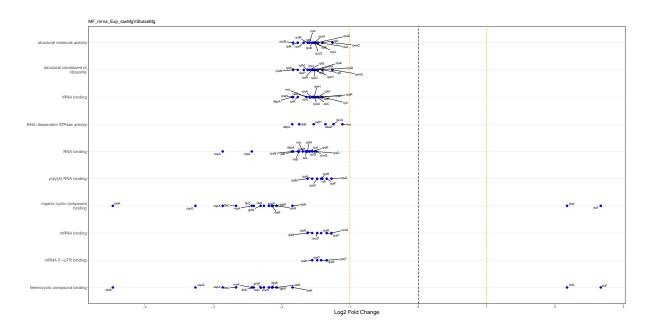


Figure S26: Significantly differentially expressed GO annotations related with molecular functions and associated genes with low  $Mg^{2+}$  levels, as determined by mRNA abundances in exponential phase. The top 10 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

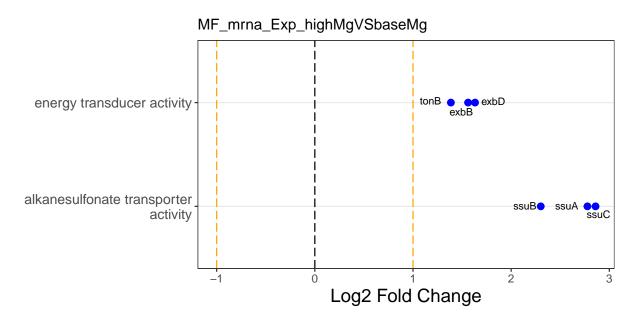


Figure S27: Significantly differentially expressed GO annotations related with molecular functions and associated genes with high  $\mathrm{Mg^{2+}}$  levels, as determined by mRNA abundances in exponential phase. The top 3 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

# lactate dehydrogenase activity L-lactate dehydrogenase activity

Figure S28: Significantly differentially expressed GO annotations related with molecular functions and associated genes with low  $Mg^{2+}$  levels, as determined by protein abundances in exponential phase. The top 2 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

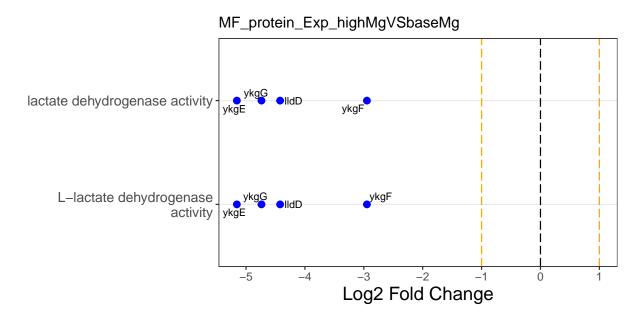


Figure S29: Significantly differentially expressed GO annotations related with molecular functions and associated genes with high  $Mg^{2+}$  levels, as determined by protein abundances in exponential phase. The top 2 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

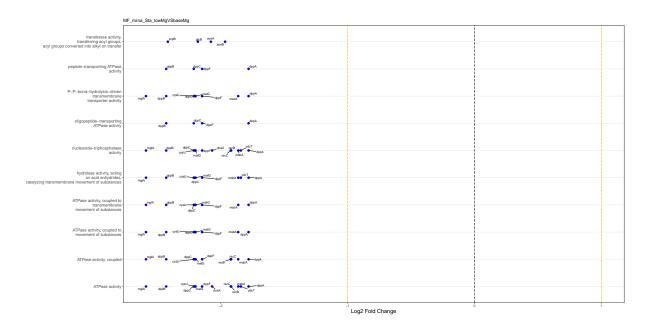


Figure S30: Significantly differentially expressed GO annotations related with molecular functions and associated genes with low  $Mg^{2+}$  levels, as determined by mRNA abundances in stationary phase. The top 10 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

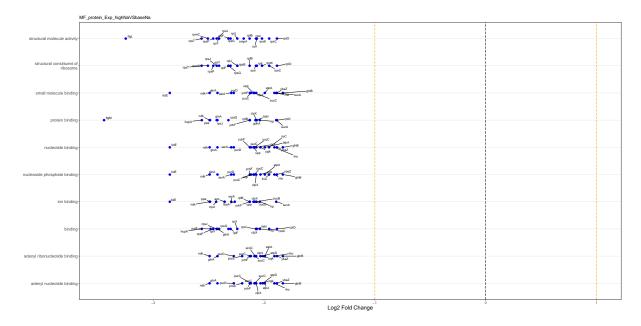


Figure S31: Significantly differentially expressed GO annotations related with molecular functions and associated genes with high  $Na^+$  levels, as determined by protein abundances in exponential phase. The top differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

# mrna_Sta_highNaVSbaseNa polyol transmembrane transporter activity carbohydrate transmembrane transporter activity alcohol transmembrane transporter activity

Figure S32: Significantly differentially expressed GO annotations related with molecular functions and associated genes with high  $Na^+$  levels, as determined by mRNA abundances in stationary phase. The top 5 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

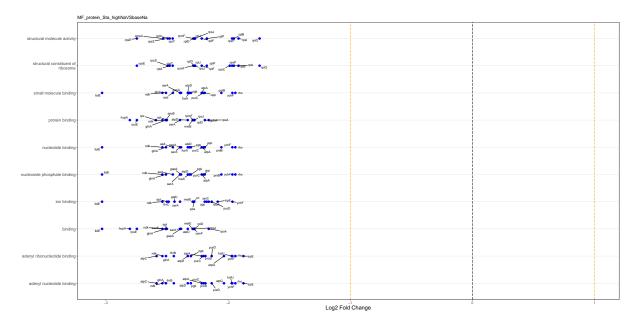


Figure S33: Significantly differentially expressed GO annotations related with molecular functions and associated genes with high  $Na^+$  levels, as determined by protein abundances in stationary phase. The top 10 differentially expressed molecular functions are shown along the y axis, and the relative fold change of the corresponding genes is shown along the x axis. We show up to 10 of the most significantly changed molecular functions and for each molecular function, we show up to 15 of the most significantly changing genes.

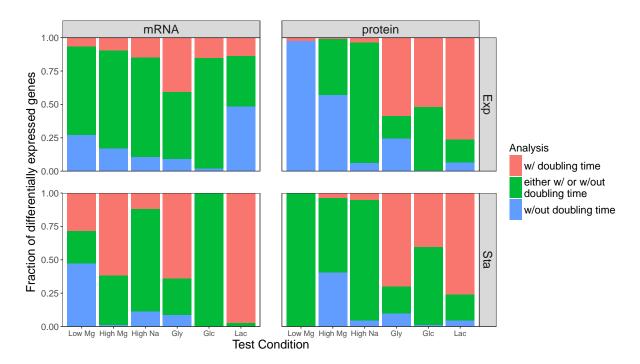


Figure S34: Fraction of differentially expressed genes that are found in analyses with or without controlling for doubling time. Shown are the fractions of genes identified as differentially expressed only when controlling for doubling time (red), only when not controlling for doubling time (blue), or in both cases (green). Combined with the absolute numbers of differentially expressed genes in the various conditions (Figure 5), we can see that the main differences in analyses with or without doubling time arise for protein abundances analyzed with respect to different carbon sources.

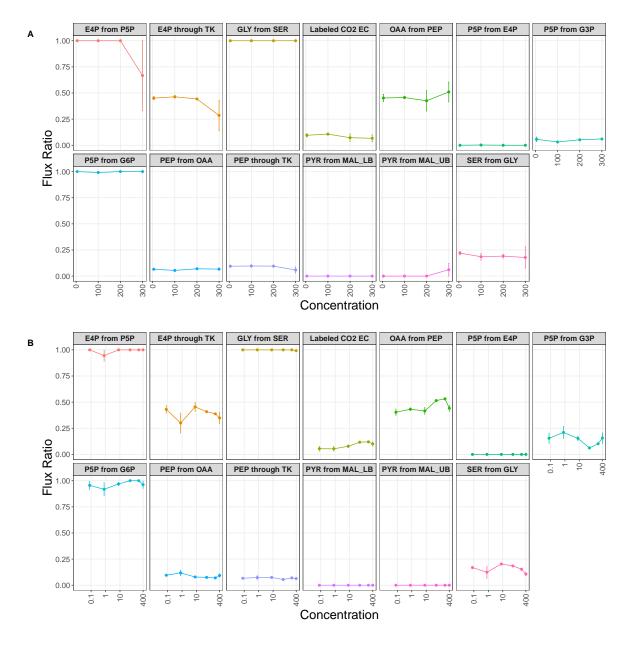


Figure S35: Flux ratios versus ion concentrations. 13 different flux ratios were measured with respect to four different  $\mathrm{Na^+}$  and five different  $\mathrm{Mg^{2+}}$  concentrations. (A) Concentrations with respect to changing  $\mathrm{Na+}$  concentrations. (B) Concentrations with respect to changing  $\mathrm{Mg^{2+}}$  concentrations. There was no significant trend of increase or decrease in flux ratios with respect to either  $\mathrm{Na^+}$  or  $\mathrm{Mg^{2+}}$  concentrations (Supplementary Table 12).