

**Supplementary Table 5.** Pathway enrichments for signature genes for different comparisons between strains that contain the RM.EcoGIII system and strains that do not contain this system.

<b>Up Regulated Pathways</b>	<b>C227-11 vs. C227<math>\Delta</math>RM Pathway Fold Enrichment (p value<sup>†</sup>)</b>	<b>C227-11 vs. 55989 Pathway Fold Enrichment (p value<sup>†</sup>)</b>	<b>K12 vs. K12+ <math>\phi</math>Stx104 Pathway Fold Enrichment (p value<sup>†</sup>)</b>
<b>Cation transport</b>	2.4 (8.4x10e-10)	2.0 (1.2x10e-7)	8.5 (9.1x10e-16)
<b>Iron ion transport</b>	4.5 (4.0x10e-16)	3.8 (3.1x10e-16)	116.9 (1.0x10e-40)
<b>di-, tri-valent inorganic cation transport</b>	4.2 (3.0x10e-15)	3.5 (5.1x10e-15)	90.0 (4.5x10e-38)
<b>Down Regulated Pathways</b>			
<b>Flagellum</b>	3.6 (3.4x10e-14)	3.0 (1.2x10e-19)	--
<b>Cell projection</b>	4.6 (4.6x10e-11)	3.2 (1.2x10e-9)	--
<b>Flagellar motility</b>	4.0 (7.4x10e-9)	3.5 (3.2x10e-12)	--
<b>Organelle inner membrane</b>	--	--	54.4 (2.0x10e-89)
<b>Taxis</b>	3.5 (7.8x10e-14)	3.2 (5.1x10e-20)	12.3 (7.8x10e-15)
<b>Pathways Enriched for Genes in C227 Harboring CTGCAG Modifications</b>			
<b>Flagellum</b>	1.9 (4.1x10e-5)		
<b>Pathways Enriched for Genes in K12+<math>\phi</math>Stx104 Harboring CTGCAG Modifications</b>			
<b>Organelle inner membrane</b>	33.7 (1.2x10e-187)		
<b>Taxis</b>	4.9 (2.6x10e-11)		

<sup>†</sup>Nominal p-values represent the significance of the Fisher Exact Test statistic under the null hypothesis that the frequency of the indicated signature gene set is the same between a reference set of genes consisting of the intersection of the genes in each strain for the indicated comparison and the set of genes comprising the signature.

-- Indicates the p value was not < 5% FDR