

Identified metabolites of the ancestral and evolved strains by gas chromatography-mass spectrometry. Response ratios of metabolites having  $P$ -Value  $\leq 0.05$  are shown in bold. Metabolites having correlation coefficient  $\geq 0.5$  are underlined. Response ratios of metabolites having  $P$ -Value  $\leq 0.05$  and correlation coefficient  $\geq 0.5$  are shown in bold underline.

Metabolites	MG / MG_Gal	MG / MG_Adip	MG / MG_AdipGal	MG / MG_stat	MG_Gal / MG_AdipGal	MG_Adip / MG_AdipGal	MG_Adip / MG_stat	DH / DH_Gal	DH / DH_Adip	DH / DH_AdipGal	DH / DH_stat	DH_Gal / DH_AdipGal	DH_Adip / DH_AdipGal	DH_Adip / DH_stat
2-Aminoadipate (260)	1.26	1.08	0.50	1.03	0.40	<u>0.46</u>	0.96	0.78	1.56	0.99	0.59	1.27	<u>0.64</u>	0.38
2-Hydroxyglutarate (203,247)	<u>1.38</u>	<u>0.69</u>	0.91	1.24	<b><u>0.66</u></b>	1.33	<u>1.81</u>	<u>1.34</u>	<b><u>1.84</u></b>	1.41	1.53	<u>1.05</u>	0.77	<u>0.83</u>
2-Isopropylmalate (275)	<u>0.99</u>	<u>0.63</u>	0.59	1.33	0.60	0.94	2.12	<u>0.95</u>	<u>0.75</u>	<b>0.44</b>	0.75	<b>0.47</b>	0.59	1.00
2-Ketoisocaproate (216)	1.00	0.45	0.52	<u>0.32</u>	<u>0.52</u>	<u>1.16</u>	<u>0.71</u>	0.95	0.87	0.55	<u>0.67</u>	<u>0.59</u>	<u>0.64</u>	<u>0.77</u>
2-Methylcitrate (287)	<u>0.52</u>	0.54	0.53	0.99	1.03	0.99	1.85	<u>0.35</u>	0.72	<b>0.21</b>	0.78	0.59	<b>0.28</b>	1.08
2-Methylisocitrate (259)	<u>3.02</u>	0.75	<u>3.02</u>	1.21	<u>1.00</u>	<b>4.04</b>	1.62	<u>2.64</u>	0.69	<u>1.25</u>	0.53	<u>0.47</u>	1.80	0.77
4-Aminobutyrate (174)	2.29	<u>1.44</u>	<u>2.60</u>	0.96	1.14	<b>1.81</b>	0.66	<b>2.62</b>	<u>0.44</u>	<b>2.94</b>	0.83	1.12	<b>6.61</b>	1.87
5-Methyl-thioadenosine (236)	<u>0.72</u>	<b><u>0.43</u></b>	<b>0.57</b>	0.78	0.79	1.33	1.82	<u>1.36</u>	<b><u>0.68</u></b>	1.16	1.13	0.85	<b>1.69</b>	<b>1.66</b>
Adenine (264)	0.71	<b>0.47</b>	0.66	0.41	0.92	1.40	0.88	1.22	<b>0.53</b>	0.92	0.76	0.75	<b>1.75</b>	1.44
Adenosine (236)	1.10	<u>1.05</u>	1.50	2.09	1.36	1.42	1.99	0.84	<u>1.35</u>	2.70	1.06	3.20	1.99	0.78
a-Glycerophosphate (357)	0.97	0.66	0.85	0.55	0.88	<u>1.30</u>	0.84	0.99	<b>0.67</b>	0.99	0.91	1.00	<b>1.49</b>	<b>1.36</b>
a-Ketoglutarate (198)	0.54	<u>0.20</u>	<u>0.73</u>	0.15	<u>1.34</u>	3.65	0.78	1.41	<b><u>0.19</u></b>	<u>2.03</u>	<b>0.26</b>	<u>1.45</u>	<b>10.94</b>	1.41
Alanine (116)	0.67	0.55	0.73	0.54	<u>1.08</u>	1.33	1.00	1.58	<b>0.51</b>	1.01	0.89	<u>0.64</u>	<b>1.96</b>	<b>1.73</b>
Arabinose (217)	1.42	<u>1.04</u>	0.83	<b>1.57</b>	<b>0.59</b>	0.80	1.51	1.13	<u>1.74</u>	1.56	1.37	1.38	0.90	0.79
Arginine (256)	1.58	0.52	0.92	0.76	0.58	1.75	1.45	<b>1.58</b>	0.69	1.21	1.10	0.77	1.76	1.59
Asparagine (216)	0.65	<b>0.33</b>	0.53	<b>0.41</b>	0.83	1.62	1.25	1.16	<b>0.37</b>	0.66	0.81	0.57	1.79	2.19
b-Alanine (248)	1.80	<u>0.81</u>	1.13	1.39	0.63	1.39	1.71	1.01	<u>1.08</u>	1.23	1.23	1.21	1.13	1.13
Citrate (257)	1.06	<u>0.52</u>	<b>0.62</b>	1.25	<b><u>0.59</u></b>	<u>1.20</u>	<b>2.41</b>	1.24	<u>1.01</u>	1.11	0.77	<u>0.89</u>	<u>1.10</u>	0.76
Cystathionine (128)	0.91	<b>0.19</b>	<u>0.28</u>	0.61	<u>0.31</u>	1.44	<b>3.17</b>	0.87	0.35	<u>0.54</u>	1.41	<u>0.62</u>	1.54	4.07
DHAP (400)	0.88	<u>0.75</u>	0.87	0.82	0.98	1.16	<u>1.09</u>	1.70	<u>0.51</u>	1.98	0.83	1.16	3.91	<u>1.65</u>
Diaminopimelate (200,272)	1.33	0.57	<u>1.03</u>	0.47	<u>0.77</u>	1.81	0.83	1.13	1.01	<u>1.62</u>	1.50	<u>1.43</u>	1.60	1.48
Erythrose-4-P (357)	3.04	4.45	<u>3.45</u>	4.83	1.13	0.78	<u>1.09</u>	0.17	1.85	<u>0.80</u>	2.48	4.84	0.43	<u>1.34</u>
Fructose-6-P (315)	0.75	<u>0.86</u>	0.61	<u>0.81</u>	0.82	0.71	0.94	0.91	<b>0.38</b>	0.81	<b>0.56</b>	0.89	<b>2.15</b>	1.49
Fructose (307)	<b>0.66</b>	1.01	<b>0.53</b>	1.31	0.81	<b>0.52</b>	1.30	<b>0.45</b>	0.62	<b>0.46</b>	0.93	1.01	0.73	1.49

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Fumarate (245)	<u>2.38</u>	<u>0.75</u>	1.98	0.47	<u>0.83</u>	<u>2.64</u>	0.63	<u>2.58</u>	<u>0.51</u>	3.68	0.88	<u>1.43</u>	<u>7.28</u>	1.74
Gluconate-6-P (387)	1.20	1.02	0.91	1.06	<u>0.76</u>	0.89	1.03	0.89	1.28	0.90	1.51	<u>1.01</u>	0.71	1.18
Gluconate (333)	3.22	<u>1.24</u>	2.32	1.21	0.72	1.87	0.98	1.09	<u>1.18</u>	1.97	1.63	1.81	1.67	1.38
Glucose (319)	1.47	<u>2.03</u>	<u>0.35</u>	<u>0.55</u>	0.24	0.17	<u>0.27</u>	0.85	<u>0.70</u>	<u>0.70</u>	<u>0.80</u>	0.82	0.99	<u>1.13</u>
Glucose-6-P (387)	0.77	<u>0.74</u>	0.68	<u>1.13</u>	<u>0.88</u>	0.91	<u>1.52</u>	0.86	<u>0.56</u>	0.74	<u>0.62</u>	<u>0.86</u>	1.30	<u>1.10</u>
Glucuronicacid (333)	1.12	0.17	0.71	1.71	0.63	4.09	9.83	3.07	1.99	3.04	1.43	0.99	1.53	0.72
Glutamate (230,246)	0.90	<u>0.50</u>	0.71	<u>0.58</u>	0.79	1.42	1.17	1.70	<b>0.55</b>	1.18	<u>0.95</u>	0.69	<b>2.12</b>	<b>1.71</b>
Glutamine (155)	0.93	<u>0.91</u>	<u>0.90</u>	<u>0.72</u>	<u>0.98</u>	0.99	0.79	1.34	<u>0.92</u>	<u>1.18</u>	<u>1.07</u>	<u>0.88</u>	1.29	1.16
Glycerate-2-P (299,315,459)	1.00	<b>0.58</b>	0.68	0.62	<u>0.68</u>	1.16	1.06	1.12	<b>0.65</b>	1.13	0.99	<u>1.02</u>	<b>1.74</b>	<b>1.52</b>
Glycerate (189,192)	1.56	1.17	1.20	0.91	0.77	<u>1.03</u>	0.78	1.36	0.66	0.99	0.76	0.73	<u>1.48</u>	1.14
Glycerate-3-P (227,299,459)	1.29	1.04	1.35	1.33	1.05	1.30	1.28	1.17	0.98	0.76	0.56	0.65	0.77	0.57
Glycine (174)	1.30	0.72	1.00	0.68	<u>0.77</u>	<u>1.39</u>	0.95	0.94	0.63	1.10	0.95	<u>1.17</u>	<b>1.74</b>	1.50
Isocitrate (245,319)	<u>1.00</u>	<u>0.53</u>	0.64	1.15	<b>0.64</b>	<u>1.20</u>	<b>2.18</b>	<u>0.86</u>	<u>1.04</u>	1.10	0.89	1.29	<u>1.07</u>	0.86
Isoleucine (158)	<u>2.12</u>	0.90	1.15	0.92	0.54	1.28	1.02	<u>1.02</u>	0.51	1.36	0.87	1.33	<b>2.67</b>	1.70
L,L-Cystathionine (218)	<b>0.38</b>	<b>0.39</b>	<b>0.37</b>	0.65	0.96	<u>0.93</u>	1.66	0.59	0.92	<u>0.46</u>	0.66	0.78	<u>0.50</u>	0.71
Lactate (191)	<u>1.03</u>	0.80	<u>0.66</u>	0.54	<u>0.64</u>	<u>0.83</u>	0.67	<u>1.01</u>	<b>0.61</b>	<u>0.89</u>	0.93	<u>0.88</u>	<u>1.46</u>	<b>1.52</b>
L-Aspartate (232)	0.93	1.05	0.95	0.85	1.02	0.90	0.81	1.26	0.75	1.08	0.90	0.85	1.44	1.20
L-Cysteine (220)	1.28	0.71	<b>0.54</b>	1.40	<b>0.42</b>	0.76	1.99	0.97	1.02	0.95	1.54	0.97	0.93	1.50
Leucine (158)	<u>0.72</u>	0.82	1.01	<u>0.25</u>	1.41	1.23	<u>0.31</u>	<u>0.86</u>	<b>0.07</b>	0.37	<u>0.20</u>	0.43	<b>5.37</b>	<b>2.93</b>
L-Homocysteine (234)	1.39	0.54	<u>0.60</u>	1.02	0.43	1.11	1.90	0.59	1.15	<u>0.74</u>	1.47	1.24	0.64	1.28
L-Homoserine (218)	<u>3.62</u>	1.27	<u>2.12</u>	0.52	0.59	1.68	0.41	<u>0.58</u>	2.69	<u>5.84</u>	2.72	<b>10.00</b>	2.17	1.01
Lysine (156)	0.50	0.36	0.37	1.43	0.73	1.01	3.95	2.69	<b>0.36</b>	0.84	1.20	0.31	<b>2.30</b>	<b>3.28</b>
Malate (245,307)	<u>1.21</u>	<b>0.51</b>	0.91	0.43	<u>0.75</u>	<b>1.78</b>	0.85	<u>1.92</u>	<b>0.45</b>	1.33	0.71	<u>0.69</u>	<b>2.94</b>	1.56
Maleicacid (245)	<u>0.24</u>	ND	<u>0.51</u>	ND	<u>2.12</u>	0.00	ND	<u>1.27</u>	ND	<u>1.37</u>	ND	<u>1.08</u>	0.00	ND
Methionine (176)	0.90	<b>0.49</b>	<b>0.58</b>	0.51	<b>0.64</b>	<u>1.18</u>	1.03	1.06	<b>0.58</b>	0.86	0.87	<u>0.81</u>	<u>1.49</u>	<b>1.51</b>
myo-Inositol (305)	1.01	0.67	<u>1.53</u>	0.87	1.52	2.29	1.31	2.73	4.60	<u>6.82</u>	4.52	2.49	1.48	0.98
Myo-Inositol-P (318)	1.08	1.13	1.20	1.28	1.11	1.06	1.13	0.40	0.74	1.85	0.67	<b>4.66</b>	2.52	0.92
N-Acetyl-Aspartate (274)	<b>2.31</b>	<b>3.71</b>	<b>11.68</b>	0.57	<b>5.05</b>	<b>3.15</b>	<b>0.15</b>	<b>4.82</b>	<b>19.18</b>	<b>61.43</b>	1.11	<b>12.73</b>	<b>3.20</b>	<b>0.06</b>
N-Acetyl-L-Serine (261)	3.06	<u>1.02</u>	0.89	2.48	<b>0.29</b>	<u>0.87</u>	2.42	1.20	<u>1.47</u>	1.18	1.25	0.98	<u>0.80</u>	0.85
o-acetyl-L-Homoserine (202)	1.69	<u>0.83</u>	<u>0.56</u>	0.45	<u>0.33</u>	0.68	0.54	1.15	<u>0.90</u>	<u>1.08</u>	1.29	<u>0.94</u>	1.20	1.44
o-acetyl-L-Serine (132)	1.55	0.72	ND	<u>6.55</u>	ND	ND	<u>9.07</u>	3.39	1.28	1.21	<u>0.97</u>	0.36	0.95	<u>0.76</u>
Ornithine (142)	1.03	<b>0.48</b>	0.68	0.55	<u>0.66</u>	<u>1.40</u>	1.15	1.06	<u>0.73</u>	1.06	0.90	<u>1.00</u>	<u>1.45</u>	1.24
Oroticacid (254)	1.84	<u>2.75</u>	5.63	1.29	<u>3.06</u>	<u>2.04</u>	0.47	1.96	<b>31.00</b>	<b>88.75</b>	1.25	<b>45.22</b>	<b>2.86</b>	<b>0.04</b>
Panhotenic acid (201)	2.28	1.11	0.97	<u>1.43</u>	<b>0.42</b>	0.87	<u>1.29</u>	2.35	0.93	1.10	<u>1.11</u>	<b>0.47</b>	1.18	<u>1.19</u>
PEP (369)	6.36	1.34	0.48	ND	0.08	0.36	ND	1.15	0.53	2.14	0.25	1.86	4.05	0.47

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Phenylalanine (192)	2.46	<u>1.10</u>	2.30	1.88	0.94	2.09	1.70	1.31	<u>1.21</u>	2.20	1.88	1.68	1.82	1.56
Phosphate19.28 (299)	0.94	0.45	0.51	5.95	0.54	1.14	13.29	0.75	<b>14.23</b>	1.22	4.38	1.64	0.09	0.31
Proline (142)	1.27	<u>0.53</u>	1.28	<u>0.63</u>	<u>1.01</u>	<b>2.41</b>	1.18	1.71	<u>0.62</u>	1.41	<u>1.27</u>	<u>0.83</u>	<b>2.28</b>	<b>2.06</b>
Putrescine (142,174)	0.33	<b>0.41</b>	<b>0.43</b>	0.38	1.30	1.04	0.92	0.70	0.95	0.91	1.12	1.29	0.95	1.17
Pyruvate (174)	1.05	<b>0.47</b>	0.82	0.33	0.78	1.74	0.69	1.19	0.87	1.84	0.87	1.55	<b>2.11</b>	0.99
Ribitol	0.86	0.76	0.91	0.66	<u>1.06</u>	<u>1.19</u>	0.86	0.94	0.78	0.90	0.94	<u>0.96</u>	<u>1.15</u>	1.20
Ribose (217)	<u>0.69</u>	<b>0.39</b>	<b>0.47</b>	1.08	0.68	1.21	<b>2.80</b>	<u>0.86</u>	<u>0.42</u>	0.90	1.05	1.05	2.14	2.49
Ribose-5-P (315,299)	1.04	<b>0.55</b>	0.69	0.80	0.66	1.24	1.44	1.08	0.68	1.13	0.86	1.04	1.65	1.26
Salicylicacid (267)	1.03	<b>0.43</b>	0.72	0.40	0.70	<u>1.67</u>	0.92	1.51	<b>0.48</b>	1.21	0.57	0.80	<b>2.55</b>	1.19
Serine (204)	1.22	0.65	0.92	0.53	<u>0.75</u>	1.41	0.81	1.45	0.84	1.26	1.20	<u>0.87</u>	1.50	1.42
Shikimate (204)	0.42	0.51	<b>0.38</b>	0.11	<u>0.91</u>	<u>0.75</u>	0.22	0.52	0.55	0.37	0.11	<u>0.72</u>	<u>0.68</u>	0.21
Spermidine (144)	1.05	0.67	<b>0.60</b>	0.93	0.58	0.90	1.39	0.83	0.94	0.93	0.92	1.12	0.99	0.98
Spermine (144)	0.93	0.81	<u>1.01</u>	1.10	<u>1.09</u>	1.25	1.36	1.24	1.15	<u>0.90</u>	0.88	<u>0.72</u>	0.78	0.77
Succinate (247,409)	0.97	<u>0.45</u>	0.97	0.85	<u>1.01</u>	<u>2.17</u>	1.89	1.72	<u>0.64</u>	1.31	1.08	<u>0.76</u>	<b>2.03</b>	1.68
Sucrose (361)	0.85	0.71	0.78	0.78	<u>0.92</u>	1.10	1.10	1.06	0.77	0.89	0.77	<u>0.84</u>	1.15	1.00
Threonine (101)	<b>2.97</b>	<u>0.92</u>	<u>1.62</u>	0.71	<u>0.54</u>	1.75	0.77	<u>0.60</u>	<u>0.70</u>	<u>4.26</u>	2.33	<b>7.12</b>	6.07	3.32
Thymine (255)	<b>0.53</b>	<u>0.63</u>	0.66	<u>0.47</u>	<u>1.23</u>	1.03	0.74	<b>0.67</b>	<b>0.36</b>	<b>0.55</b>	<b>0.69</b>	<u>0.82</u>	<u>1.51</u>	<b>1.91</b>
Trehalose (361)	<b>2.39</b>	<b>2.00</b>	<b>6.63</b>	0.59	2.77	<b>3.32</b>	<b>0.29</b>	<b>2.01</b>	0.85	<b>3.97</b>	<b>0.53</b>	1.98	<u>4.69</u>	0.63
Tryptophan (202)	0.77	0.71	0.82	0.67	<u>1.05</u>	1.14	0.94	0.72	0.65	0.56	0.67	<u>0.77</u>	0.86	1.04
Tyrosine (218)	1.46	1.05	<u>0.69</u>	1.67	0.47	0.66	1.59	0.92	3.58	<u>0.62</u>	1.03	0.67	0.17	0.29
Unknown14.80 (228)	1.09	0.73	0.82	0.26	0.75	<u>1.12</u>	0.36	1.09	<b>0.32</b>	1.44	0.66	1.31	<b>4.46</b>	<b>2.06</b>
Unknown32.96 (361)	<b>183.88</b>	<u>1.32</u>	<b>231.43</b>	1.88	<u>1.26</u>	<b>175.44</b>	1.42	<b>196.78</b>	<b>4.59</b>	<b>255.29</b>	1.43	<u>1.30</u>	<b>55.62</b>	0.31
Uracil (255,241)	1.09	<b>0.46</b>	1.03	0.70	<u>0.95</u>	<b>2.24</b>	1.50	1.42	<b>0.49</b>	<b>1.88</b>	1.11	<u>1.33</u>	<b>3.83</b>	<b>2.27</b>
Urea (189)	0.60	0.06	<u>0.17</u>	0.06	<u>0.29</u>	2.81	0.99	1.43	0.30	<u>0.25</u>	0.44	<u>0.18</u>	0.84	1.46
Valine (144)	0.36	0.66	<b>0.53</b>	0.53	<u>1.47</u>	0.80	0.81	0.99	<b>0.54</b>	<b>0.44</b>	0.64	<b>0.44</b>	0.81	1.19



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