Table S5.6 Metabolites and their relevant information

Metabolite	Properties	References
2-Aminopimelic acid	- forms lysine and contributes to cell wall structure in bacteria. - involved in plant morphogenesis. - likely associated with the cnidarian microbiome or translocated from the symbionts.	(Berges et al., 1986; Valmaseda et al., 2005; Tabeta and Hirai, 2024)
2-Hydroxyglutaric acid	- high levels in humans are associated with metabolic disorders. - metabolite is differentially expressed in Aiptasia colonised with different symbiont types. - implications for T-cell differentiation.	(Tyrakis et al., 2016; Yamada et al., 2019; Du and Hu, 2021 Lust, 2022; Tsang Min Ching et al., 2022)
3-Aminoglutaric acid	- the precursor of glutamine synthase which is important for nitrogen assimilation, amino acid synthesis and cellular metabolism. - commonly found in bacteria and plants. - likely associated with the cnidarian microbiome or translocated from the symbionts.	(Patrice et al., 2001; Ito et al., 2022)
Galacturonic acid	- found in plants and has anti-inflammatory properties. - produced by Symbiodiniaceae and may be important in symbiosis establishment and recognition. - likely translocated from the symbiont to the host.	(Gerschenson, 2017; Tortorelli et al., 2022)
Gluconic acid	- involved in glucose metabolism, and antioxidant NADPH production through the pentose phosphate pathway. - found in the Aiptasia metabolome. - increased only at T4 and not T16 in the current study.	(MIETTINEN and LESKINEN, 1970; Matthews et al., 2017)
Glycolic acid	- increases in aposymbiotic *vs.* symbiotic Aiptasia. - has anti-inflammatory properties by modulation of NFkB pathways and pro-inflammatory cytokines, however it can also induce apoptosis.	(Yang et al., 2004; Tang et al., 2017; Lust, 2022)
Pantothenic acid	- increases in aposymbiotic Aiptasia and Aiptasia colonised with heterologous symbionts *vs.* Aiptasia colonised with homologous symbionts. - precursor of CoA. - CoA can lead to the formation of triglycerides, phospholipids, antioxidants, cysteine and methionine.	(Wada and Takagi, 2006; Matthews, 2017; Aloum et al., 2019; Chandel, 2021; Mignani et al., 2021; Filonenko and Gout, 2023)
Phosphoric acid	- increases in aposymbiotic Aiptasia. - involved in cellular signalling, and the production of ATP, phospholipids and triglycerides.	(Stillwell, 2016; Matthews, 2017; Kritmetapak and Kumar, 2021; Choi et al., 2023)
Rhamnose	- usually found in bacteria, plants and fungi. - likely associated with the cnidarian microbiome or translocated from the symbionts. - found in plant and bacterial cell walls and increases in bacteria and plants under stressful conditions to adapt membrane structure or as an antioxidant defense.	(Williams et al., 2004; Hillyer, 2016; Dastogeer et al., 2017; Jiang et al., 2021; Nguyen et al., 2021; Song et al., 2021)
Ribonic acid	- sugar involved in ribose metabolism and production of nucleotides. - found in coral *Montipora capitata* metabolome. - increases in humans with diabetes	(Ding et al., 2017; Matthews, 2017; Tofte et al., 2019; Curovic et al., 2020)
Sedoheptulose	- sugar that is important for the production of nucleotides and is an intermediate in the pentose phosphate pathway. - mainly produced in plants. - likely translocated from the symbionts. - increased only at T4 and not T16 in the current study.	(Benson et al., 1951)
Tryptamine	- a group of monoamines that includes serotonin and melatonin that are well-studied in vertebrates but less studied in invertebrates. - increases in marine invertebrates, including cnidarians under stressful conditions	(da Silveira et al., 2007; Liu et al., 2018)

References

Aloum, L., Brimson, C. A., Zhyvoloup, A., Baines, R., Baković, J., Filonenko, V., et al. (2019). Coenzyme A and protein CoAlation levels are regulated in response to oxidative stress and during morphogenesis in Dictyostelium discoideum. *Biochem. Biophys. Res. Commun.* 511, 294–299. doi:10.1016/j.bbrc.2019.02.031.

Benson, A. A., Bassham, J. A., and Calvin, M. (1951). Sedoheptulose in photosynthesis by plants. *J. Am. Chem. Soc.* 73, 2970. doi:10.1021/ja01150a543.

Berges, D. A., DeWolf, W. E., Dunn, G. L., Taggart, J. J., Grappel, S. F., Newman, D. J., et al. (1986). Peptides of 2-Aminopimelic Acid: Antibacterial Agents That Inhibit Diaminopimelic Acid Biosynthesis. *J. Med. Chem.* 29, 89–95. doi:10.1021/jm00151a015.

Chandel, N. S. (2021). Lipid Metabolism. *Cold Spring Harb. Perspect. Biol.* 13. doi:10.1101/cshperspect.a040576.

Choi, Y. M., Ajjaji, D., Fleming, K. D., Borbat, P. P., Jenkins, M. L., Moeller, B. E., et al. (2023). Structural insights into perilipin 3 membrane association in response to diacylglycerol accumulation. *Nat. Commun.* 14. doi:10.1038/s41467-023-38725-w.

Curovic, V. R., Suvitaival, T., Mattila, I., Ahonen, L., Trošt, K., Theilade, S., et al. (2020). Circulating Metabolites and Lipids Are Associated to Diabetic Retinopathy in Individuals With Type 1 Diabetes. *Diabetes* 69, 2217–2226. doi:10.2337/db20-0104.

da Silveira, R. B., Wille, A. C. M., Chaim, O. M., Appel, M. H., Silva, D. T., Franco, C. R. C., et al. (2007). Identification, cloning, expression and functional characterization of an astacin-like metalloprotease toxin from Loxosceles intermedia (brown spider) venom. *Biochem. J.* 406, 355–363. doi:10.1042/BJ20070363.

Dastogeer, K. M. G., Li, H., Sivasithamparam, K., Jones, M. G. K., Du, X., Ren, Y., et al. (2017). Metabolic responses of endophytic Nicotiana benthamiana plants experiencing water stress. *Environ. Exp. Bot.* 143, 59–71. doi:https://doi.org/10.1016/j.envexpbot.2017.08.008.

Ding, Z., Jia, S., Wang, Y., Xiao, J., and Zhang, Y. (2017). Phosphate stresses affect ionome and metabolome in tea plants. *Plant Physiol. Biochem.* 120, 30–39. doi:https://doi.org/10.1016/j.plaphy.2017.09.007.

Du, X., and Hu, H. (2021). The Roles of 2-Hydroxyglutarate. *Front. Cell Dev. Biol.* 9, 1–13. doi:10.3389/fcell.2021.651317.

Filonenko, V., and Gout, I. (2023). Discovery and functional characterisation of protein CoAlation and the antioxidant function of coenzyme A. *BBA Adv.* 3, 100075. doi:10.1016/j.bbadva.2023.100075.

Gerschenson, L. N. (2017). The production of galacturonic acid enriched fractions and their functionality. *Food Hydrocoll.* 68, 23–30. doi:https://doi.org/10.1016/j.foodhyd.2016.11.030.

Hillyer, K. E. (2016). Thermal Stress and Bleaching in the Cnidarian-Dinoflagellate Symbiosis: The Application of Metabolomics. 53.

Ito, K., Miyamoto, H., Matsuura, M., Ishii, C., Tsuboi, A., Tsuji, N., et al. (2022). Noninvasive fecal metabolic profiling for the evaluation of characteristics of thermostable lactic acid bacteria, Weizmannia coagulans SANK70258, for broiler chickens. *J. Biosci. Bioeng.* 134, 105–115. doi:10.1016/j.jbiosc.2022.05.006.

Jiang, N., Dillon, F. M., Silva, A., Gomez-Cano, L., and Grotewold, E. (2021). Rhamnose in plants - from biosynthesis to diverse functions. *Plant Sci.* 302, 110687. doi:10.1016/j.plantsci.2020.110687.

Kritmetapak, K., and Kumar, R. (2021). Phosphate as a Signaling Molecule. *Calcif. Tissue Int.* 108, 16–31. doi:10.1007/s00223-019-00636-8.

Liu, W., Mo, F., Jiang, G., Liang, H., Ma, C., Li, T., et al. (2018). Stress-induced mucus secretion and its composition by a combination of proteomics and metabolomics of the jellyfish aurelia coerulea. *Mar. Drugs* 16. doi:10.3390/md16090341.

Matthews, J. L. (2017). The Nutritional Implications of Partner Switching in the Cnidarian-Dinoflagellate Symbiosis.

Matthews, J. L., Crowder, C. M., Oakley, C. A., Lutz, A., Roessner, U., Meyer, E., et al. (2017). Optimal nutrient exchange and immune responses operate in partner specificity in the cnidarian-dinoflagellate symbiosis. *Proc. Natl. Acad. Sci. U. S. A.* 114, 13194–13199. doi:10.1073/pnas.1710733114.

MIETTINEN, T. A., and LESKINEN, E. (1970). “GLUCURONIC ACID PATHWAY,” in *Metabolic Conjugation and Metabolic Hydrolysis*, ed. W. H. FISHMAN (Academic Press), 157–237. doi:https://doi.org/10.1016/B978-0-12-257601-0.50011-6.

Mignani, L., Gnutti, B., Zizioli, D., and Finazzi, D. (2021). Coenzyme a Biochemistry: From Neurodevelopment to Neurodegeneration. *Brain Sci.* 11. doi:10.3390/brainsci11081031.

Nguyen, P. T., Nguyen, T. T., Vo, T. N. T., Nguyen, T. T. X., Hoang, Q. K., and Nguyen, H. T. (2021). Response of Lactobacillus plantarum VAL6 to challenges of pH and sodium chloride stresses. *Sci. Rep.* 11, 1–9. doi:10.1038/s41598-020-80634-1.

Patrice, R., Kelly, N., J., S. H., and F., R. M. (2001). β-Glutamate as a Substrate for Glutamine Synthetase. *Appl. Environ. Microbiol.* 67, 4458–4463. doi:10.1128/AEM.67.10.4458-4463.2001.

Song, M., Liu, Y., Li, T., Liu, X., Hao, Z., Ding, S., et al. (2021). Plant Natural Flavonoids Against Multidrug Resistant Pathogens. *Adv. Sci.* 8, 1–11. doi:10.1002/advs.202100749.

Stillwell, W. (2016). “Chapter 5 - Membrane Polar Lipids,” in *An Introduction to Biological Membranes (Second Edition)*, ed. W. Stillwell (Elsevier), 63–87. doi:https://doi.org/10.1016/B978-0-444-63772-7.00005-1.

Tabeta, H., and Hirai, M. Y. (2024). l-2-Aminopimelic acid acts as an auxin mimic to induce lateral root formation across diverse plant species. *FEBS Lett.* doi:10.1002/1873-3468.14908.

Tofte, N., Suvitaival, T., Trost, K., Mattila, I. M., Theilade, S., Winther, S. A., et al. (2019). Metabolomic Assessment Reveals Alteration in Polyols and Branched Chain Amino Acids Associated With Present and Future Renal Impairment in a Discovery Cohort of 637 Persons With Type 1 Diabetes. *Front. Endocrinol. (Lausanne).* 10, 1–11. doi:10.3389/fendo.2019.00818.

Tyrakis, P. A., Palazon, A., Macias, D., Lee, K. L., Phan, A. T., Veliça, P., et al. (2016). S-2-hydroxyglutarate regulates CD8+ T-lymphocyte fate. *Nature* 540, 236–241.

doi:10.1038/nature20165.

Valmaseda, E. M. M. de, Campoy, S., Naranjo, L., Casqueiro, J., and Martín, J. F. (2005). Lysine is catabolized to 2-aminoadipic acid in Penicillium chrysogenum by an omega-aminotransferase and to saccharopine by a lysine 2-ketoglutarate reductase. Characterization of the omega-aminotransferase. *Mol. Genet. Genomics* 274, 272–282. doi:10.1007/s00438-005-0018-3.

Wada, M., and Takagi, H. (2006). Metabolic pathways and biotechnological production of L-cysteine. *Appl. Microbiol. Biotechnol.* 73, 48–54. doi:10.1007/s00253-006-0587-z.

Williams, R. J., Spencer, J. P. E., and Rice-Evans, C. (2004). Flavonoids: antioxidants or signalling molecules? *Free Radic. Biol. Med.* 36, 838–849. doi:https://doi.org/10.1016/j.freeradbiomed.2004.01.001.

Yamada, T., Nabe, S., Toriyama, K., Suzuki, J., Inoue, K., Imai, Y., et al. (2019). Histone H3K27 Demethylase Negatively Controls the Memory Formation of Antigen-Stimulated CD8+ T Cells. *J. Immunol.* 202, 1088–1098. doi:10.4049/jimmunol.1801083.

Yang, J.-H., Chou, C.-C., Cheng, Y.-W., Sheen, L.-Y., Chou, M.-C., Yu, H.-S., et al. (2004). Effects of glycolic acid on the induction of apoptosis via caspase-3 activation in human leukemia cell line (HL-60). *Food Chem. Toxicol. an Int. J. Publ. Br. Ind. Biol. Res. Assoc.* 42, 1777–1784. doi:10.1016/j.fct.2004.07.004.