Sarah E. O'Connor

Plants are an unrivaled source of medicines and bioactive molecules. However, the complexity of plants has hindered our ability to elucidate and engineer the metabolic pathways that are responsible for synthesis of these important molecules. Using a range of bioinformatic and experimental methods, S.E.O.'s research group has contributed to our understanding of the enzymatic and mechanistic basis for a wide variety of plant-derived molecules. A few recent examples include the discovery of the enzymes for quinine (1), vinblastine (2), strychnine (3), ibogaine (4) and kratom alkaloid (5) biosynthesis. Her group has developed new methodologies to streamline the discovery of these enzymes; recent examples include development of single cell mass spectrometry methodology (6) and single cell transcriptome-metabolomic multiplexing (7). Moreover, her work reveals the divergent evolutionary mechanisms by which chemical diversity in plants arises (*e.g.* 8, 9). Conversely, she has also shown the mechanistic basis by which the same molecular scaffold can independently evolve (*e.g.* 10, 11). Collectively, her work provides a basis for metabolic engineering of these compounds (1), thereby enabling sustainable access to these important molecular scaffolds.

References

1. Lombe, B. K., Zhou, T., Kang, G., Wood, J. C., Hamilton, JP, Gase, K., Nakamura, Y., Alam, R. M., Dirks, R. P., Caputi, L., Buell, C. R.*, O'Connor, S. E.* (2026) Biosynthesis of cinchona alkaloids. Nature. 2026 doi: 10.1038/s41586-026-10227-x.

2. Caputi, L., Franke, J., Farrow, S. C., Chung, K., Payne, R. M. E., Nguyen, T.-D., Dang, T.-T.-T., Carqueijeiro, I. S. T., Koudounas, K., Dugé de Bernonville, T., Ameyaw, B., Jones, D. M., Vieira, I. J. C., Courdavault, V.*, & O'Connor, S. E.* (2018). Missing enzymes in the biosynthesis of the anticancer drug vinblastine in Madagascar periwinkle. Science, 360, 1235-1238.

3. Hong, B., Grzech, D., Caputi, L., Sonawane, P., López, C.E.R., Kamileen, M.O., Hernández Lozada, N.J., Grabe, V., O'Connor, S.E.* (2022) Biosynthesis of strychnine. Nature. 607, 617-622.

4. Farrow, S. C., Kamileen, M. O., Caputi, L., Bussey, K., Mundy, J. E. A., McAtee, R. C., Stephenson, C. R. J., & O'Connor, S. E.* (2019). Biosynthesis of an anti-addiction agent from the iboga plant. Journal of the American Chemical Society, 141(33), 12979-12983.

5. McDonald, A., Nakamura, Y., Schotte, C., Titchiner, G. R., Lau, K., Alam, R. M., Lopes, A. A., Buell, C. R., & O'Connor, S. E.* (2025). Enzymatic epimerization of monoterpene indole alkaloids in Kratom. Nature Chemical Biology, 22, 229-238.

6. Vu, A. H., Kang, M., Wurlitzer, J., Heinicke, S., Li, C., Wood, J. C., Grabe, V., Buell, C. R., Caputi, L.*, & O'Connor, S. E.* (2024). Quantitative single-cell mass spectrometry provides a highly resolved analysis of natural product biosynthesis partitioning in plants. Journal of the American Chemical Society, 146(34), 23891-23900.

7. Kang, M., Vu, H. A., Casper, A. L., Kim, R., Wurlitzer, J., Heinicke, S., Yeroslaviz, A., Caputi, L.*, & O'Connor, S. E.* (2025). Single-cell metabolome and RNA-seq multiplexing on single plant cells. Proceedings of the National Academy of Sciences of the United States of America, 122(43): e2512828122.

8. Kamileen, M. O., Hong, B., Gase, K., Kunert, M., Caputi, L., Lichman, B. R., & O'Connor, S. E.* (2025). Oxidative rearrangements of the alkaloid intermediate geissoschizine. Angewandte Chemie, International Edition in English, 64(24): e202501323.

9. Caputi, L., Franke, J., Bussey, K., Farrow, S. C., Curcino Vieira, I. J., Stevenson, C. E. M., Lawson, D. M.*, & O'Connor, S. E.* (2020). Structural basis of cycloaddition in biosynthesis of iboga and Aspidosperma alkaloids. Nature Chemical Biology, 16, 383-386.

10. Colinas, M.*, Morweiser, C., Dittberner, O., Chioca, B., Alam, R. M., Leucke, H., Nakamura, Y., Serna Guerrero, D. A., Heinicke, S., Kunert, M., Wurlitzer, J., Ploss, K., Hong, B., Grabe, V., Lopes, A. A., & O'Connor, S. E.* (2025). Ipecac alkaloid biosynthesis in two evolutionarily distant plants. Nature Chemical Biology, 23(8), 3414-3416.

11. Koellner, T.G.*, David, A., Luck, K., Kunert, G., Beran, F., Zhou, J.-J., Caputi, L., O'Connor, S.E.* (2022) Biosynthesis of iridoid sex pheromones in aphids. Proc. Natl. Acad. Sci. USA 119, e2211254119.