Total and Biosynthesis of Natural Products and their bioactive analogs as P-gp Inhibitors of Human ABCB1

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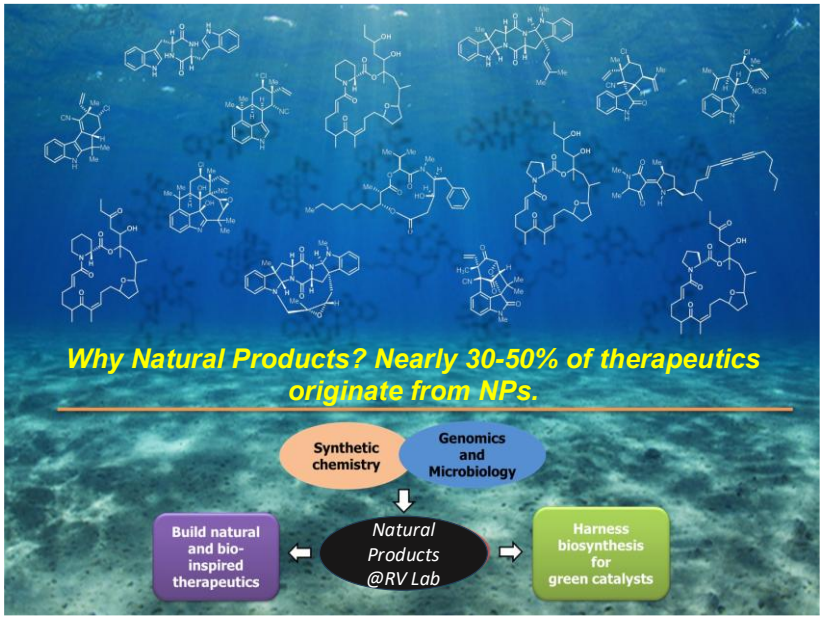
Rise in antibiotic and chemotherapeutic resistance challenge us to develop new age therapeutics. By developing tools to understand Nature's mechanisms of assembling natural products, and by implementing biomimetic chemistry, we create approaches to expanding chemical diversity of bioactive molecules. In this presentation, I will present our recent studies on the biosynthesis of marine nocardioazine alkaloids that are anti-cancer natural products and their bioactive analogs. Genetically-templated biomimetic synthesis of (+)-nocardioazine B alkaloid family and their analogues afford concise, enantiospecific and scalable pathways.

Our approach offers leads to turn endogenous substrates into non-toxic inhibitors of P-glycoprotein (PgP) mediated drug efflux pumps. Through a combination of organic synthesis, genomics and enzymology tools, we have prepared a platform for better understanding of unique biosynthetic mechanisms leading to marine anticancer *Nocardiopsis* alkaloids.



Recent Publications and Patents:

- Vincent, D.M.; Viswanathan R. *et al. Chem. Eur. J.* **2024**, *30, e202401782*; and *Comms. Chem.* **2024**.
- Pradhan, S.;Viswanathan, R. *Organic and Biomolecular Chem.* **2025**, *23, 5086-5090.*
- Deletti, Swapnil Joshi, Tushar M. Khopade, Amy L. Lane* and **Rajesh Viswanathan*** *Nature Communications*, **2023**, *14*, 2558.
- Khopade, T. M.; Viswanathan, R. *et al. J. Org. Chem.*, **2022,** *87,* 11519-11533.
- Khopade, T. M.; Viswanathan, R. *et al. ACS Omega*, **2021,** *6*, 10840–10858.
- Method of modulating ribonucleotide reductase, C. G. Dealwis, R. Viswanathan, S. E. Huff, W. Harte - US Patent 11,439,623, 2022. [co-inventor]