The Role of Medicinal Chemistry in the Search for New Therapeutic Agents: Natural Products vs Peptides

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Natural products have long been regarded as "Nature's medicine chest" providing invaluable platforms for developing front-line drugs. The chemical structures of natural products have evolved over several millennia for a specific biochemical purpose and their molecular frameworks can be considered "privileged scaffolds." The synthesis of several bioactive natural products as "privileged scaffolds" for drug discovery will be described. This lecture will also showcase some of our research on the synthesis of peptidomimetics, lipopeptides and glycopeptides as a platform for the discovery and development of peptide therapeutics as agents to treat neurogenetic disorders, infectious disease, cancer and diabetes. One example includes the peptidomimetic drug candidate trofinetide (NNZ2566) that was approved by the US FDA in 2023 as the first drug for the treatment of Rett Syndrome (tradename Daybue™).