

Study of Bioactive Natural Products in Medicine and Biology

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Bioactive natural products are a rich source of drug candidates as well as important tools for investigating biological systems. Ipomoeassin F is a flagship congener of a plant-derived macrolide resin glycoside family with an embedded carbohydrate core. It possesses potent cell growth inhibition activity with IC₅₀ values in the single-digit nanomolar range against many cancer cell lines. In the NCI 60-cell line screen, ipomoeassin A, a structural homolog of ipomoeassin F, demonstrated a unique cytotoxicity profile; however, its mode of action remained largely unexplored before 2019. To date, we have accomplished the gram-scale production of ipomoeassin F and have been carrying out systematic studies to understand its structure-activity relationship. More importantly, we identified Sec61alpha as the specific protein target of ipomoeassin F in live cells, which makes it a good lead compound for future target-based drug discovery to explore pharmaceutical potential of both the natural product and the target protein.

