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Discovery and development of synthetic tricyclic pyrroloquinone alkaloid analogs for human cancer therapy

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Marine natural products have established themselves as an important source of novel chemical entities that are unlikely to be found in the terrestrial environment. For the past half century, global marine sources have proven to be a rich source of a vast array of new medicinally valuable compounds. In the recent past, there has been an increase in the number of anticancer alkaloids isolated from marine sources, with sponges being an abundant source of chemically and biologically diverse natural products. This is largely due to the improvements in the deep-sea sample collection technology.In this talk, I will present a story of the discovery, synthesis and evaluation of three marine derived tricyclic pyrroloquinone (TPQ) alkaloid analogs ascancer therapeutic agents. Chemical synthesis of these compounds (BA-TPQ, TBA-TPQ, and TCBA-TPQ) has been accomplished and the mechanisms of action (MOA) and structure-activity relationships (SAR) have been investigated. In the past, the complexity of chemical synthesis and the lack of well-defined mechanism of action have dampened the enthusiasm for the development of this class of marine alkaloids. Recent discovery of novel molecular targets for these alkaloids warrant further consideration of these compounds as pre-clinical candidates. We have successfully demonstrated that these compoundsattackseveralkey molecular targets, including the MDM2-p53 pathway. In addition to the establishment of synthetic methods and mechanism of action, *in vitro* and *in vivo* anticancer activities of these compounds are also demonstrated.

Biography

Sadanandan E Velu has received his PhD in Organic Chemistry at the University of Madras in 1993. He did his Postdoctoral research at the University of Alabama and at Clemson University. Currently, he is working as a Tenured Associate Professor in the University of Alabama at Birmingham. He also holds co-appointments as an Associate Scientist in Comprehensive Cancer Center and Center for Clinical and Translational Sciences of the University of Alabama at Birmingham. He has authored 63 research articles and is an inventor/co-inventor of US 5 patents. He is a member of American Chemical Society, American Association of Cancer Research and American Heart Association.

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