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Discovery of a novel tubulin-targeting scaffold derived from the rigidin family of marine alkaloids

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We developed synthetic chemistry to access the marine alkaloid rigidins and over forty synthetic analogues based on the 7-deazaxanthine, 7-deazaadenine, 7-deazapurine and 7-deazahypoxanthine skeletons. Analogues based on the 7-deazahypoxanthine skeleton exhibit ednanomolar potencies against cell lines representing cancers with dismal prognoses, tumor metastases and multidrug resistant cells. Studies aimed at elucidating the mode(s) of action of the 7-deazahypoxanthines in cancer cells revealed that they inhibited *in vitro* tubulin polymerization and disorganized microtubules in live HeLa cells. Experiments evaluating the effects of the 7-deazahypoxanthines on the binding of [^{3}H]colchicine to tubulin identified the colchicine site on tubulin as the most likely target for these compounds in cancer cells. Because many microtubule-targeting compounds are successfully used to fight cancer in the clinic, we believe the new chemical class of antitubulin agents represented by the 7-deazahypoxanthine rigidin analogues have significant potential as new anticancer agents.

Biography

Alexander Kornienko has recently accepted a position of an Associate Professor of Chemistry at Texas State University after having held an academic position at New Mexico Tech since 2001. His teaching and research interests encompass the discovery of new reactions and methods in synthetic organic chemistry, natural product isolation and derivatization, and cancer drug development. Professor Kornienko has published 70 research papers and trained numerous students in research disciplines on the chemistry-biology interface. His current projects focus on applying synthetic chemistry toward advancing a number of anticancer natural products, specifically active against apoptosis-resistant tumors, to human clinical trials.

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