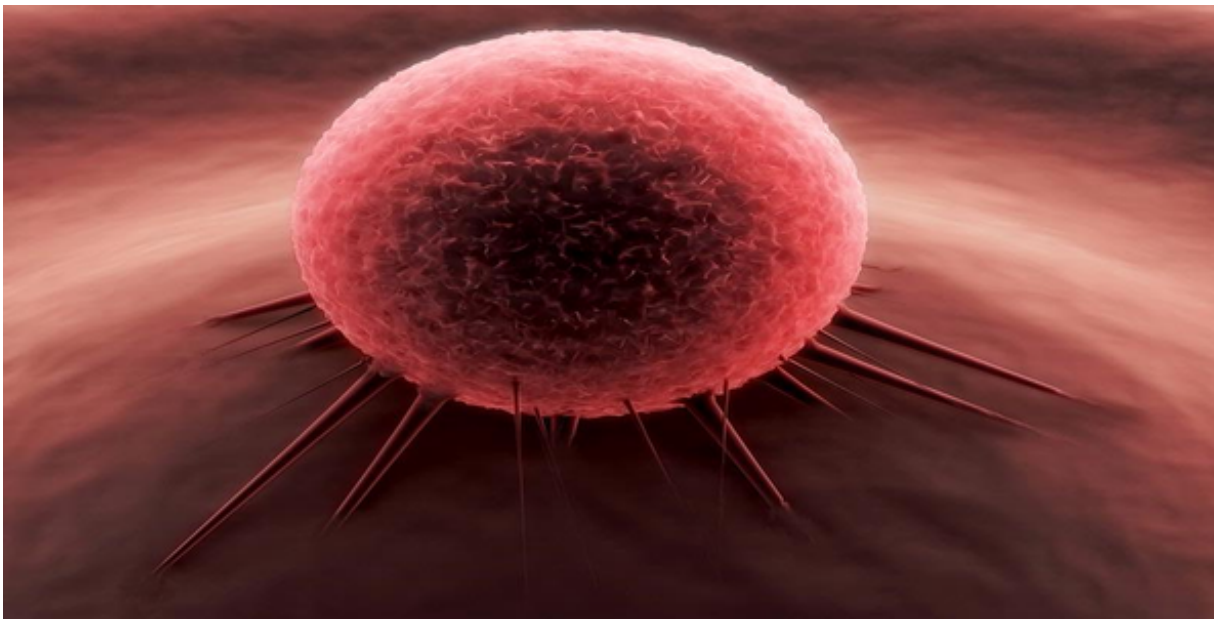
THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Cancer

Antofine Derivatives, A New Class of Anti-Cancer Agents



Phenanthroindolizidines and phenanthroquinolizidines are a series of plant-derived natural alkaloids primarily found in the Asclepiadaceae and Moracea plant family. R-tylophorine, R-antofine, and R-cryptopleurine are well known representatives in the family having been reported to have potent antitumor activity. A major side effect of these natural alkaloids impacting their use as therapeutic agents is their severe CNS toxicity. Analogs with higher polarity may be desirable to manipulate such side effects by preventing them from entering the blood brain barrier. Previous methodologies to achieve these analogs have focused on modifications on rings -A, -C, and -D. There has been no synthetic method reported by far for making analogs with modifications on the ring-E, especially with practically versatile, efficient, and facile E-ring-derivatized advancements. Unlike conventional syntheses in which the formation of the E ring occurred prior to the conjugation of the D ring; in this innovative approach, the construction of the E ring takes place after the D ring has been conjugated to the phenanthrene scaffold allowing for the generation of antofine analogs with E-ring modifications.

Benefits

- Reduced toxicity
- Simplified synthesis

carolina blue™ opportunity

For More Information

If you would like more information about this technology or UNC - Chapel Hill's technology transfer program, please contact:

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The Technology

The clinical use of chemotherapeutic agents against malignant tumors is successful in many cases, but suffers from major drawbacks. One drawback is lack of selectivity, which leads to severe systemic side effects and limited efficacy. Another major problem is the emergence/selection of drug-resistance. The drug development failure of tylocrebrine a positional isomer of tylophorine, in 1966 was due to a central nervous system toxicity, manifested by ataxia and disorientation. This disappointing clinical result discouraged further consideration of these alkaloids for drug development. However, in the 1990s, tylophorine analogs deemed previously not to warrant further research were re-screened for antitumor potential by the National Cancer Institute (NCI) using a 60-tumor cell line panel. These compounds showed potent and uniform activity against 54 human tumor cell lines.

- Chemotherapy

Opportunity

UNC's Office of Technology Development seeks to stimulate development and commercial use of UNC-developed technologies. UNC is flexible in its agreements, and opportunities exist for joint development, academic or commercial licensing (exclusive, non-exclusive, and field-of-use), publishing, or other mutually beneficial relationships. UNC is pursuing U.S. and international intellectual property protection for this innovation.