

CANCER

Nanoliposomal delivery of ceramide prevents growth of hepatocellular carcinoma

Mark Kester and colleagues from Pennsylvania State University have demonstrated that nanoliposomal ceramide is able to prevent *in vivo* growth of hepatocellular carcinoma (HCC). These findings are important because the incidence of HCC continues to increase

worldwide, and treatment options for this disease are limited.

Ceramide is already known to have antiproliferative and proapoptotic effects *in vivo* and *in vitro*. "One of the more exciting aspects of utilizing exogenous ceramide as a chemotherapeutic is the observation that ceramide is inherently selective in inducing apoptosis in cancer as compared to nontransformed cells," explains Kester. "However, the use of ceramide as an antineoplastic chemotherapeutic agent has been limited due to its inherent insolubility and impermeability."

A nanoscale delivery system, using liposomes, has been developed for ceramide. This delivery system is able to overcome solubility issues whilst retaining the nontoxic profile of ceramide to normal cells, and has already been shown to induce remission in a mouse model of leukemia. Kester and colleagues

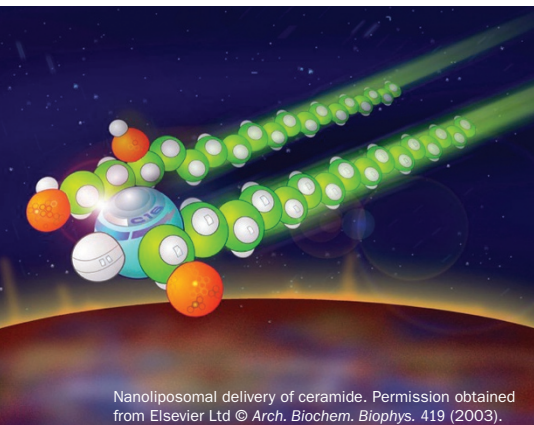
thus investigated the antiangiogenic and antineoplastic efficacy of nanoliposomal ceramide using *in vitro* and *in vivo* models of HCC.

This agent was found to contribute to widespread tumor apoptosis, cell cycle blockade at the G1/S and G2/M checkpoints, reduced tumor vascularization and, ultimately, to reduced tumor growth in mice.

"There is a continuing need for innovative and alternative therapies for HCC," says Kester. "On the basis of these mechanistic studies, ceramide nanoliposomes are being developed for future clinical evaluation in patients with HCC."

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Original article Tagaram, H. R. *et al.* Nanoliposomal ceramide prevents *in vivo* growth of hepatocellular carcinoma. *Gut* doi:10.1136/gut.2010.216671



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