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Targeted Delivery of Bisphosphonates and an Anti-neoplastic Agent to Metastatic Bone Lesions

Drs. Debbie C. Crans and Stewart D. Ryan from the Departments of Chemistry and Clinical Sciences at Colorado State University and the Animal Cancer Center plan to develop microemulsion formulations incorporating a bisphosphonate (zoledronic acid (ZA)) and an anti-neoplastic agent (paclitaxel), as a model delivery vehicle for multimodal targeted therapy of metastatic bone cancer. The technology will use the bisphosphonate to target the delivery of paclitaxel to the bone microenvironment by co-emulsification.

Metastatic bone cancer is a frequent and painful sequel to primary breast, prostate, lung and colon cancer in people that is commonly multifocal. The predominant process in metastatic bone cancer is osteolytic (i.e. causes bone destruction) which can lead to bone pain, hypercalcemia and pathologic fracture. Bisphosphonates inhibit the activity of osteoclasts (the cells that destroy bone) and also have some direct anti tumor effect by induction of apoptosis and inhibition of angiogenesis. The ability to target delivery of chemotherapeutic agents such as taxanes, doxorubicin, carboplatin and methotrexate to the local metastatic tumor microenvironment will permit the use of lower doses of agent with decreased incidence and severity of adverse side effects (myelotoxicity and/or thrombocytopenia) compared to systemic administration. Microemulsion formulations as delivery vehicles for coadministration of drugs with different charges illustrates a novel drug delivery technology that goes beyond the applications of bisphosphonates and chemotherapeutic drugs for cancer therapy and has wide reaching clinical application.

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