

Nanomedicine Approach for Targeting the Tumor Microenvironment

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Abstract

Tumor metastases are the principal cause of mortality in the majority of cancer patients. A hospitable tumor microenvironment, of which the vascular system is a significant component, is crucial in the implantation of disseminated tumor cells. Angiogenesis, the formation of new blood vessels, is a multifactorial process that is critical for tumor progression and metastasis. Anti-angiogenic compounds, has been widely investigated as a strategy to treat cancer. However, several of these drugs are limited by poor pharmacological properties, such as low bioavailability, undesired biodistribution and short half-life necessitating their use in high intravenous doses which expose the patients to adverse side-effects due to off-target activity. To overcome these drug limitations, we developed a formulation of self-assembled nanomicelles composed of short di-block polymers, polyethylene glycol-poly(lactic acid) (PEG-PLA), for conjugating small molecule drugs. We present a case of re-formulating a broad spectrum anti-angiogenic drug from the fumagillin family which originally had several clinical limitations. In the new formulation, unlike the free compound, the drug showed high oral availability, improved tumor targeting and reduced toxicity. Dramatic anti-cancer activity was obtained in eight different tumor types (60-90% growth inhibition) in mice, and, importantly, the treatment was able to prevent liver metastases due to the shift from intravenous to oral administration. The activity was associated with reduction of microvessel density and increased tumor apoptosis. Nanomicelle drug delivery system has been shown to be an efficient approach for improving pharmacological properties of drugs and

Polymeric Nanomicelles Delivery System

