New Polymer-Peptide Conjugates for Targeting and Delivering Drugs to Tumor Vascular Endothelium (BGN)

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Success in the treatment of cancer with chemotherapy is often limited by the non-specific toxicity of anticancer drugs. Current therapeutic approaches to the treatment of cancer are thus focused on developing novel delivery systems to increase the therapeutic efficacy of anticancer agents by targeting them to malignant cells. A variety of strategies and carrier molecules have been used to direct therapeutic agents to tumor sites. The conjugation of anticancer drugs to polymeric carrier confers many advantages over small molecular therapeutics, including improved solubility and bioavailability, preferential accumulation of the conjugates in solid tumors due to the enhanced permeability and retention (EPR) effect, reduced systemic toxicity and enhanced therapeutic efficacy. The incorporation of a specific targeting moiety to drug carrier may result in active drug uptake by malignant cells.

The Technology

We have developed a new drug delivery system for increasing the efficacy of anticancer drugs by employing the biocompatible, non-immunogenic, and non-toxic, water-soluble N-(2-hydroxypropyl) methacrylamide (HPMA) copolymer conjugates equipped with oligopeptides as targeting ligand that can bind selectively to tumor vascular endothelial cells. These conjugates contained the anticancer drug Doxorubicin (DOX) and a specific peptide sequence (named 'Esbp', primary sequence DITWDQLWDLMK) that can selectively bind with high affinity to E- selectin, which is a molecular marker expressed exclusively by vascular endothelial cells during inflammation and cancer.

In vitro cytotoxicity of DOX- HPMA-peptide copolymers against TNFa activated (solid lines) and non-activated (dashed lines) IVECs, as determined by MTT assay. (□, red) free DOX drug; (, blue) P-(Esbp)-DOX; (, black) P-(Scrm)-DOX; and (, green) P-DOX. P-(Esbp)-DOX presented higher cytotoxicity against TNFa activated cells while all other controls, including using P-(Scrm)-DOX with scrambled peptide sequence, did not. The IC50 for P-(Esbp)-DOX in these assays was found to be 0.3 mM

Applications

Targeted anti cancer drug delivery (e.g Doxorubicin)

Patent Status

Patent Pending

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