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Design of low-molecular-weight prodrugs for targeted delivery of anticancer agents

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Abstract

Majority of the clinically used anticancer drugs display a narrow therapeutic window due to high systemic toxicity and lack of selectivity towards cancer cells. As a result, prodrug delivery approach is being explored extensively to improve the selectivity and efficacy of the existing anticancer agents. Recent prodrug designs mostly involve the conjugation of a carrier (targeting moiety) to an active drug. These prodrugs are designed to achieve an efficient and selective drug delivery system into the target tumor, where the active anticancer agents are released either extra- or intracellularly. Some of these targeting strategies take advantage of the overexpression of enzymes, receptors or other proteins in tumor tissues. Active anticancer agents are then released when the predetermined cleavage points are cleaved by the elevated tumor-associated enzymes, in the lowered extracellular pH and in lysosomes, and/or in the reducing environment of hypoxic cells in tumor tissues. Active and passive targeting strategies using antibody and polymers are some of the prodrug designs that have been explored with great promise. In contrast to these macromolecular designs, low molecular weight (MW) prodrugs also offer certain advantages in the targeted prodrug approach, especially in improving cell permeability and ease of production. Therefore, this presentation will highlight the recent trends and advances made in the design of low MW prodrugs, specifically in the conjugation of small molecules to an existing anticancer agent. Each conjugate design will be analyzed in terms of their targeting strategies and bioactivation, along with a comparison of their advantages and disadvantages.

Biography

Shengquan Liu completed his Ph.D in Medicinal Chemistry from Louisiana University, Monroe in 1997 and postdoctoral studies in Oklahoma State University and The University of Texas at Austin from 1997 to 2001. He was a senior research scientist at Albany Research Inc. from 1991 to 2005 and assistant professor in Touro University – California since 2006. He has published more than 14 papers in reputed journals, 7 US patents and contributed to 2 book chapters.