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Glycolysis is a promising target for encapsulation nano-therapeutic molecules against cancer cells

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The well understanding of cancer metabolism and signaling pathways, has allowed for development of more effective therapies. For instance, the increase of glucose consumption in many types of cancer cells is regulated by overexpression of type II hexokinase (HKII). Indeed, tumor cells show active glycolysis even under aerobic conditions, which is known as the Warburg effect [1]. This unique pathway endows cancer cells with selective advantages like enhanced proliferation, invasion, and metastasis [2]. The glycolysis furthermore confers selective advantage to cancer cells by supporting uninterrupted growth. For example, a higher glycolytic rate in tumor cells has been shown to promote resistance to chemotherapeutics. In the cervical cancer cell line, HeLa for example, the enzyme pyruvate dehydrogenase kinase (PDK) isoforms PDK1 and PDK3 have been demonstrated to provide resistance to chemotherapeutics [3]. Hexokinase is a key glycolytic enzyme that catalyzes the first step in the glycolytic pathway and helps to exhibit the Warburg effect. This enzyme transfers a phosphate group from ATP to glucose to form glucose-6-phosphate. Moreover, HKII interacts with the outer membrane protein voltage dependent anion channel (VDAC). It blocks mitochondrial inter membrane space proteins release and prevents activation of the apoptotic process [4]. Whereas , HKII prevents association of pro-apoptotic BcL-2 family member proteins (Bad, Bak, Bax) with the mitochondrial permeability transition pore (mtPTP) complex; pro-apoptotic factor association is necessary for mitochondrial permeability transition and cytochrome c release (the apoptotic cascade) [5]. This observation has led to the development of therapeutic strategies such as use of small molecules for inhibition of glycolytic activity in cancer cells [6]. In this case, lonidamine, 3-bromopyruvate (3-BrPA) and 3-BrOP (3-bromo-2-oxopropionate-1 -propyl ester) [7,8], are used as HK-II inhibitors in the early stages of treatment, can effectively inhibit glycolysis. The crucial problem for using them in clinical application is related to their interaction with normal cells, especially erythrocytes [9]. Thus, there is an urgent need to encapsulate them inside smart carriers having efficient strategies from size, shape, and targeted for cancer cells [10]. In our previous report, 3BrPA attached Poly(allylamine) hydrochloride was entrapped inside $CaCO_3$ rods during their fabrication. [11]. However, non-specific, passive, targeting, carriers can result in uptake by healthy cells. This can be minimized by the active targeting of the therapy, In our recent work, targeted hybrid lipid polymer as alternate assembly structure instead of liposomes is fabricated. Their positive attributes make them a promising drug delivery vehicle for further in vivo evaluation. Hybrid polymeric protein carriers (HPPNCs) were assembled by using chitosan, oleic acid and BSA-FA to form core shell structure [12].

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