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A cyclic-RGD-BioShuttle functionalized with TMZ by DARinv “Click Chemistry” targeted to ?v?3 integrin for therapy

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Abstarc :

Clinical experiences often document, that a successful tumor control requires high doses of drug applications. It is widely believed that unavoidable adverse reactions could be minimized by using gene-therapeutic strategies protecting the tumor-surrounding healthy tissue as well as the bone-marrow. One new approach in this direction is the use of “Targeted Therapies” realizing a selective drug targeting to gain effectual amounts at the target site, even with drastically reduced application doses. MCF-7 breast cancer cells expressing the $?_v?_3$ [alpha(v)beta(3)] integrin receptor are considered as appropriate candidates for such a targeted therapy. The modularly composed BioShuttle carrier consisting of different units designed to facilitate the passage across the cell membranes and for subcellular addressing of diagnostic and/or therapeutic molecules could be considered as an eligible delivery platform. Here we used the cyclic RGD-BioShuttle as a carrier for temozolomide (TMZ) at the $?_v?_3$ integrin receptor realizing local TMZ concentrations sufficient for cell killing. The IC50 values are 12 µMol/L in the case of cRGD-BioShuttle-TMZ and 100 µMol/L for underivatized TMZ, which confirms the advantage of TMZ reformulation to realize local concentrations sufficient for cell killing.

Key Word :

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