OFFICIAL ABSTRACT and CERTIFICATION

Electrostatic Targeting of Feraheme Using Doxorubicin Conjugates for Prostate Cancer

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Prostate cancer is a deadly disease that lacks effective treatment. Many existing chemotherapeutics are non-specific, meaning they kill off both cancerous and healthy cells. Targeting agents have been utilized in order to increase specificity of these treatments. Studies performed by Kaittanis in 2017 demonstrated the conjugation of a prostate-specific membrane antigen (PSMA) targeting peptide onto iron oxide nanoparticles followed by loading of therapy. They found increased uptake for PSMA-expressing cells after treatment with the targeting nanoparticles. Effective peptide conjugation to the particle surface was shown, but they did not show if the targeting peptide could be directly conjugated to the chemotherapeutics. In this study, a PSMA targeting agent was created and attached to Doxorubicin, a cancer treatment drug, through a peptide linker. LNCaP, 22Rv1, Du145, and PC3 prostate cancer cells were treated in order to determine uptake by these cells. The cells were treated for 24 hours with Doxorubicin, Doxorubicin loaded onto Feraheme, Doxorubicin conjugate, and the conjugate loaded onto Feraheme. LNCaP cells showed the highest fluorescence under microscopy, which was expected because they expressed the highest level of PSMA. Fluorescence signals were lower in Du145 and PC3 cells, which did not express PSMA at all. Data from flow cytometry showed that the Doxorubicin conjugate was taken up by the prostate cancer cells but did not exceed the amount of free drug taken up by the same cells. These findings suggest that more experiments need to be performed in order to determine how the targeting agent affected cell uptake.

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