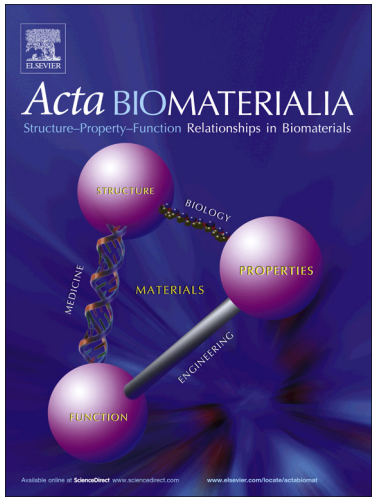

Full length article

Repurposing Disulfiram for Cancer Therapy via Targeted Nanotechnology through Enhanced Tumor Mass Penetration and Disassembly

Huacheng He, Eleni Markoutsa, Jing Li, Peisheng Xu

PII: S1742-7061(17)30789-4
DOI: https://doi.org/10.1016/j.actbio.2017.12.023
Reference: ACTBIO 5235

To appear in: *Acta Biomaterialia*

Received Date: 3 September 2017
Revised Date: 21 November 2017
Accepted Date: 18 December 2017

Please cite this article as: He, H., Markoutsa, E., Li, J., Xu, P., Repurposing Disulfiram for Cancer Therapy via Targeted Nanotechnology through Enhanced Tumor Mass Penetration and Disassembly, *Acta Biomaterialia* (2017), doi: https://doi.org/10.1016/j.actbio.2017.12.023

Article type: Original Research

Repurposing Disulfiram for Cancer Therapy via Targeted Nanotechnology through Enhanced Tumor Mass Penetration and Disassembly

Huacheng He,[‡] Eleni Markoutsa,[‡] Jing Li,[‡] and Peisheng Xu[‡,]*

H. He, Dr. E. Markoutsa, Jing Li, and Dr. Prof. P. Xu
Department of Drug Discovery and Biomedical Sciences
College of Pharmacy
University of South Carolina
715 Sumter St., Columbia, SC 29208, United States
E-mail: xup@cop.sc.edu

Abstract: Disulfiram (DSF), an FDA approved drug for the treatment of alcoholism, degrades to therapeutically active diethyldithiocarbamate (DDTC) in the body by reduction. Hereby, we developed a redox sensitive DDTC-polymer conjugate for targeted cancer therapy. It was found that the DDTC-polymer conjugate modified with a β-D-galactose receptor targeting ligand can self-assemble into LDNP nanoparticle and efficiently enter cancer cells by receptor-mediated endocytosis. Upon cellular uptake, the LDNP nanoparticle degrades and releases DDTC due to the cleavage of disulfide bonds, and subsequently forms copper (II) DDTC complex to kill a broad spectrum of cancer cells. 3D cell culture revealed that this nanoparticle shows much stronger tumor mass penetrating and destructive capacity. Furthermore, LDNP nanoparticles exhibited much greater potency in inhibiting tumor growth in a peritoneal metastatic ovarian tumor model.

Keywords: repurpose, disulfiram, cancer, polymer-drug conjugate, nanoparticle