Preparation, Characterization and Biological Evaluation of Multifunctional Nanoscale Drug Delivery System for Prostate Cancer Therapy and Imaging

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Prostate cancer (CaP) is the commonest diagnosed malignancy and the second main cause of cancer mortality in males in the United States. Thus, there is an urgent need to develop novel drug delivery systems to improve the chemotherapy option for CaP patients. The goal of this research was to develop novel magnetically and molecularly guided nanoscale drug delivery systems with dual functionality for treatment and imaging of CaP. First, we investigated the preparation and physical characterization of magnetic polymeric nanoparticles (NPs) for the site directed delivery of Noscapine (Nos) to invasive CaP. We synthesized and characterized monodisperse superparamagnetic iron oxide NPs which was subsequently used to prepare Nos loaded magnetic polymeric nanoparticles (NMNP). Elemental analysis and fourier-transform infrared (FT-IR) spectroscopy confirmed the encapsulation of IO NPs and Nos on the surface of the polymer matrix, respectively.

Next, we developed and optimized a molecularly guided nanoscale drug delivery system which is also MRI (Fe3O4 core) and optically imageable (NIR-dye Cy5.5). This targeted system takes advantage of over-expression of the urokinase plasminogen activator receptor (uPAR), the receptor in CaP cells, compared to normal epithelia. Specifically, we employed the human-type 135 amino-acid amino-terminal fragment (hATF) of the urokinase plasminogen activator (uPA), which is a high-affinity natural ligand for uPAR. Prussian blue staining elucidated that these uPAR-targeted NPs can bind to the receptors and are internalized by PC-3 cells. The efficient internalization of these uPAR-targeted NPs in PC-3 cells was translated to 6-fold stronger inhibitory effect compared to the free drug.

Lastly, we have developed for targeted delivery system of toxic chemotherapeutic agents to CaP cells. This drug delivery system composes of a polymer coated iron oxide nanoparticles which are guided by the 9-mer peptide AE105 which is a potent antagonist for the uPA/uPAR interaction. Our results demonstrate that these uPAR-targeted NPs were capable of binding to the receptor and were internalized by PC-3 cells. The drugs vinblastine (VIN) and doxorubicin (DOX) were efficiently encapsulated onto the polymer coating the IO NPs. The targeted NPs loaded with either VIN or DOX were uniformly compact-sized, stable at physiological pH, and efficiently released the drug at pH 4 to 5 within a span of 4 h. Both VIN and DOX-loaded AE105-Io NPs showed slim enhancement in the inhibition of PC-3 cells proliferation in comparison to the same amount of the free drug. The similarity in the size between the targeting moiety and the drugs may have contributed to the reduction in binding affinity between the drug-loaded AE105-Io NPs and the uPAR in the tumor cells.

Dr. Mohamed O. Abdalla is an assistant professor in the Department of Chemistry at Tuskegee University. Dr. Abdalla is also affiliated with the Center for Cancer Research at Tuskegee University. Dr. Abdalla received his doctorate in Integrative Biosciences and a master’s degree in Chemistry from Tuskegee University. He completed his undergraduate studies majoring in Chemistry/Zoology at the University of Khartoum in Khartoum, Sudan. Dr. Abdalla
had experience working as a Chemistry instructor and research associate in the field of Materials Science and Engineering. The research interest of Dr. Abdalla is to develop nanomaterials for various biomedical applications with special focus on cancer’s nanomedicine. His area of specialty is development of bio-conjugated nanoparticles for simultaneous imaging and treatment of prostate cancer. Currently, Dr. Abdalla work involves design, synthesis, characterization, and biological evaluation of solid and porous magnetic iron oxide nanoparticles. These nanoparticles have the potential to be used for important medical applications such as in vivo cancer imaging, multiplexed molecular profiling, correlation of biomolecular signatures (biomarkers) with clinical outcome, early cancer detection, and targeted drug delivery. Dr. Abdalla is an active member/officer in several Professional Scientific Societies at Tuskegee University.

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