Multifunctional oxygen non-stoichiometric bismuth (Bi)-based nanospheres for melanoma theragnostic

Marcela L. Chaki Borrás, Philip J. Barker, Ronald Sluyter, Konstantin Konstantinov**

Northfields Avenue
University of Wollongong
Wollongong, NSW 2500, Australia
mlcb986@uowmail.edu.au, *konstan@uow.edu.au*

Melanoma is the most aggressive form of skin cancer. Unfortunately, conventional treatment regimens, such as radiotherapy, chemotherapy, immunotherapy and targeted therapy, lack selectivity for the cancer cells or do not eradicate the cancer. As such, new therapeutic platforms are needed. Herein, oxygen non-stoichiometric bismuth (Bi)-based nanospheres ($Bi@BiO_x$ and Bi_2O_{3-x}) were synthesised as cancer theragnostic agents. First, a hydrothermal method was used to synthesize $Bi@BiO_x$, which was then annealed under atmospheric conditions to obtain Bi_2O_{3-x}. Both materials were composed of uniform nanospheres (115 ± 17 nm and 113 ± 20 nm, respectively) and multivalent Bi atoms. The materials possessed X-ray computed tomography (CT) imaging properties with a CT contrast enhance efficiency of 12.9 and 8.2 Hounsfield Units mL mg^{-1} for $Bi@BiO_x$ and Bi_2O_{3-x}, respectively. Both samples of nanospheres displayed selectivity towards the human A375 melanoma cell line as determined with the MTT and proliferation clonogenic assays. The MTT assay revealed that $Bi@BiO_x$ and Bi_2O_{3-x} reduced A375 cell numbers in a concentration- and time-dependent manner. The clonogenic assay showed that 50 µg mL^{-1} $Bi@BiO_x$ and Bi_2O_{3-x} significantly reduced A375 cell proliferation by 93% and 63% compared to untreated control cells, respectively. Additional studies revealed $Bi@BiO_x$ and Bi_2O_{3-x} to exert A375 cell death in a time-dependent manner, which correlated with a selective augmentation of intracellular ROS amounts in A375 cells. This work highlights the potential of $Bi@BiO_x$ and Bi_2O_{3-x} nanospheres as versatile theragnostic agents for CT imaging and selective therapy.