Treating Melanoma with [^{225}Ac]cdots nanoparticles

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Current cancer treatment modalities include surgery, chemotherapy, radiotherapy, and hormone therapy. Unfortunately, none of these approaches is sufficient on its own due to non-specificity and inadequate efficacy. Nanotechnology offers necessary tools which aim to ensure optimal delivery of the desired drug to the target tissue with minimal off-target toxicity to adjacent tissues. Radiotherapy in combination with nanotechnology offers a potentially unique anti-cancer approach. We used Actinium-225, an α particle emitting radionuclide with a 10d half-life and a yield of 4 α particles in its decay chain. Our nanoparticles, cDOTs, are tumor-selective, ultrasmall Cy5 containing, poly(ethylene glycol)-coated silica constructs functionalized with melanoma-targeting peptides. They were approved for a first-in-human clinical trial in 2011 for melanoma patients. To enhance cDOTs specificity and improve oncological use, we conjugated cDOTS to an α melanocyte-stimulating hormone (αMSH)-modified ligand. MSH is an endogenous peptide hormone and neuropeptide of the melanocortin family. First we confirmed the uptake of these cDOTs by B16/F10 melanoma cell line using imaging and FACS. The complete uptake was observed after 72h. We performed a biodistribution study of [^{225}Ac]cDOTs-MSH in naïve and tumor bearing mice. Moreover, we evaluated the maximum tolerated dose (MTD) in melanoma tumors bearing mice. Four doses were tested, 0, 625, 1250 and 2500 nCi and a dose of 625 nCi was determined to be the MTD. A radiotherapy treatment study using melanoma tumor in immune competent mice was conducted using a dose of 300 nCi. The overall survival was improved in specific and non-specific treatment groups compared to vehicle group. In addition, the tumor size was significantly reduced in specific group when compared to a vehicle group after 30 days of treatment. We also evaluated the changes in T cell and macrophage infiltrates in tumor bearing mice and repot that the greatest infiltration was observed after 96h post treatment.

Speaker Biography

Aleksandra M. Urbanska has completed her PhD from the Department of Biomedical Engineering summa cum laude, Faculty of Medicine at McGill University in Montreal, Canada. She was trained as a postdoctoral fellow at Massachusetts Institute of Technology under supervision of prof. Robert S. Langer as well as at Columbia University Medical Center where she applied her multidisciplinary skills in nanotechnology, stem cells, tissue engineering, biomaterials and drug delivery. She has over 40 publications that have been cited over 800 times. Currently she is a fellow researcher at Memorial Sloan Kettering Cancer Center in New York City.

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