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Poly (ethylene glycol) bisphosphonate nanoparticles for diagnosis and therapy of primary and metastatic bone cancer

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Statement of the Problem: Most primary and metastatic bone tumors demonstrate increased osteoclast activity and bone resorption. Current treatment is based on a combination of surgery, radiotherapy and chemotherapy. Severe side effects areassociated with chemotherapy due to use of high dosage and nonspecific uptake. Bisphosphonates have a strongaffinity to Ca2+ ions and are widely used in the treatment of bone disorders.The purpose of this study is to describe our biodegradable bisphosphonate nanoparticle (NPs) that can be effective treatment against OS.

Methodology & Theoretical Orientation: Our NPs bearing two functional surface groups: (1) primary amine groups for covalent attachment of a dye/drug (e.g. NIR dye Cy7 or Doxorubicin); (2) bisphosphonate groups for targeting and chelation to bone hydroxyapatite. In addition, these engineered NPs contain high polyethyleneglycol (PEG) concentration in order to increase their blood half life time. Our *in vitro* experiments were performed using Saos-2 and U2OS human osteosarcoma cell lines. Both chicken embryo and mice model were used for *in vivo* experiments.

Findings: *In vitro* experiments on Saos-2 cells, demonstrated that at a tenth of the concentration, Doxorubicin-conjugated bisphosphonate NPs achieved a similar uptake to free Doxorubicin. *In vivo* targeting experiments using the NIR fluorescence bisphosphonate NPs on both Soas-2 human osteosarcoma xenograft mouse model and orthotopic bone metastases mCherry-labeled 4T1 breast cancer mouse model confirmed specific targeting. In addition, therapeutic *in vivo* experiments using Doxorubicin-conjugated bisphosphonate NPs demonstrated a 40% greater inhibition of tumor growth in Saos-2 human osteosarcoma xenograft chicken embryo and mouse model when compared to free Doxorubicin.

Conclusion & Significance: In this research we have shown the potential use of Doxorubicin-conjugated BP NPs for the targeting and treatment of primary and metastatic bone tumors. The targeted delivery of Doxorubicin to the tumor significantly increased the efficacy of the anti-cancer drug, thus enabling the effective use of a lower concentration of Doxorubicin.

Biography

Igor Grinberg is currently pursuing post doctoral research under the supervision of Prof. Shlomo Margel, at the Bar-Ilan Institute of Nanotechnology and Advanced Materials, Bar-Ilan University, Israel. He received his B.Sc.(2002), M.Sc. (2007), and his Ph.D. (2011) in Biology and Life Sciences, at Bar-Ilan University. Igor's work involves the development of the chicken embryo model as well as *in vivo* (small animal) models for investigating various types of nanoparticles for various medical applications.

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