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Robert Pola et al., J Pharm Drug Deliv Res 2017, 6:4 (Suppl)
DOI: 10.4172/2325-9604-C1-021

International Conference and Exhibition on

Nanomedicine and Drug Delivery

May 29-31, 2017 Osaka, Japan

In vivo imaging of passively tumor targeted polymer carrier and the enzymatically cleavable drug model

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Precise preclinical characterization of new polymeric prodrug candidates is important for understanding the effects of polymer prodrug structure on distribution, controlled drug release and elimination of these carrier systems. In our study, we have demonstrated the enzymatic release of a lysosomotropic model drug inside a tumor using multispectral optical imaging *in vivo* in nude mice bearing two different colorectal carcinoma xenograft models - HT-29 and DLD-1. We also clearly demonstrated the important role of the molecular weight of a polymeric drug carrier in tumor accumulation and the rate of enzymatic drug release. Our study showed a much higher rate of the model drug release *in vivo* from a linear (30 kDa) (N-2-hydroxypropyl)methacrylamide (HPMA)- based polymer compared with a high molecular weight branched (170 kDa) polymer conjugate. There was no significant difference in the relative biodistribution in the body between the 30 kDa linear and 170 kDa branched polymers, but the branched polymer circulated much longer. Both copolymers were labeled with two different fluorophores. Dyomics-676 (DY-676) dye was attached to the polymer via an enzymatically cleavable Gly-Phe-Leu-Gly spacer, which represented a lysosomotropic drug model molecule. Dyomics 782 (DY-782) dye was bound to the same polymer backbone via a non-degradable amide bond enabling the tracking of the polymer carrier itself after i.v. application to mice. We hypothesize that the increase in the molecular weight of the polymer prodrug conjugate significantly lowers the rate of release of the model drug due to steric hindrance of the cleavable spacer to enzymes.

Biography

Robert Pola has completed his PhD from Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (IMC). He is the member of Department of Biomedicinal Polymers of IMC. He has published 24 papers in reputed international journals. His research focus is based on synthesis of peptide sequences and preparation of water-soluble polymer conjugates used as drug delivery systems for effective treatment of cancer or for vaccination.

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