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Bio-inspired anionic polymers as a platform for designing novel nanoscale intracellular drug delivery systems

It remains a major challenge to effectively deliver therapeutic agents, in particular macromolecules, through negatively charged lipid membrane barriers. It is the most limiting step preventing successful implementation of macromolecule-based cell modification and intracellular therapies. This is due to endosomal entrapment of macromolecules and their degradation in lysosomes. Many researchers have used cationic delivery systems to address this challenge. However, the positive charge could cause some issues, such as unfavorable biodistribution, rapid renal clearance and high non-specific cytotoxicity. This presentation presents an alternative delivery strategy based on an anionic drug delivery platform. It covers our recent efforts on design and synthesis of novel anionic, viral-peptide-mimicking, pH-responsive, metabolite-derived polymers, and evaluation of their use in intracellular drug delivery *in vitro* and *in vivo*. Strict control over the size, structure, hydrophobicity-hydrophilicity balance and sequence of the polymers can effectively manipulate interactions with lipid membrane, cell and tissue models. It has been demonstrated that the biomimetic polymers can successfully traverse the extracellular matrix in three-dimensional multicellular spheroids, and also enable efficient loading of a wide range of macromolecules into the cell interior. This can represent a versatile delivery platform, suitable for targeted therapeutic delivery and cell therapy for treatment of various diseases including but not limited to cancer.

Recent Publications

1. Wang S and Chen R (2017) pH-responsive, lysine-based, hyperbranched polymers mimicking endosomolytic cell-penetrating peptides for efficient intracellular delivery. Chemistry of Materials. 29(14):5806-5815.
2. Chen S et al. (2017) Membrane-anchoring, comb-like pseudopeptides for efficient, pH-mediated membrane destabilization and intracellular delivery. ACS Applied Materials & Interfaces. 9(9):8021-8029.
3. Chen S and Chen R (2016) A virus-mimicking, endosomolytic liposomal system for efficient, pH-triggered intracellular drug delivery. ACS Applied Materials & Interfaces. 8(34):22457-22467.
4. Zhang W et al. (2016) pH and near-infrared light dual-stimuli responsive drug delivery using DNA-conjugated gold nanorods for effective treatment of multidrug resistant cancer cells. Journal of Controlled Release. 232:9-19.
5. Khormaee S et al. (2013) Endosomolytic anionic polymer for the cytoplasmic delivery of siRNAs in localized *in vivo*. Advanced Functional Materials. 23(5):565-574.

Biography

Rongjun Chen obtained his MSc Degree in Materials Science from Tsinghua University (P R China) in 2003; pursued PhD Degree at Cambridge University (UK) during the period 2003-2007, with focus on polymer drug delivery. He carried out his Postdoctoral Research at Cambridge University first on lyophilisation of pharmaceuticals and then on manufacture of clinical-grade lentiviral vectors for gene therapy during the period October 2006 to September 2009. In May 2013, he moved to Imperial College London as a Lecturer and is currently a Senior Lecturer since 2016. From October 2009 to April 2013, he started his independent academic career by taking a tenure-track faculty position as the Group Leader and BHRC Senior Translational Research Fellow at the University of Leeds. His research interests focuses on biomaterials, nano-medicine, drug delivery and cell therapy.

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