Versatile Single Chain Polymer Nanoparticles in Drug Delivery and Targeted Imaging

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As the area of controlled drug delivery is increasingly finding application in a variety of diseases, with different targeting sites and drug candidates, there is an urgent need for adjustable nanocarrier systems. Linear biopolymers folded into 3D-structures fulfill a wide array of complex functions and are omnipresent in biological systems; prime examples are proteins, in which the precise positioning of monomeric units (i.e. amino acids) largely determines protein morphology and therefore their remarkable variety of properties.

Due to their chemical diversity and highly modular nature polymers, and polymeric nanoparticles in particular, are popular drug carrier materials. Most polymeric nanoparticles are in the 50-200 nm size range, which is unfortunate, since proteins, enzymes and some viruses are considerably smaller in size.

In order to widen the existing polymeric drug carrier systems to the sub-20 nm size regime, we are investigating single-chain polymer nanoparticles (SCNPs) for controlled drug delivery and targeted imaging. [1] SCNPs are prepared through intramolecular crosslinking of individual polymer chains into individual nanoparticles and thus offer tremendous control over size and dispersity. Through exclusive intramolecular crosslinks, SCNPs are an order of magnitude smaller than conventional polymer nanoparticles, easily accessible in relevant quantities and without the requirement of complex synthetic strategies. Highly modular in nature, these uniquely sized polymer nanoparticles enable encapsulation and controlled release of drug molecules, irrespective of their hydro- or lipophilicity. [2]

Preparation of SCNPs from prepolymers containing pentafluorophenol activated esters, followed by functional amine substitution, allows for careful engineering of the nanoparticle surface, providing control over distribution behavior and enabling the mimicking of proteins in terms of shape, composition and even function. Current efforts focus on evaluation of these promising materials in vivo.

References

[1] Kröger, A. P. P.; Paulusse, J. M. J. “Single-Chain Polymer Nanoparticles in Controlled Drug Delivery and Targeted Imaging” *J. Control. Rel.* 286 (2018) 326–347.

[2] Kröger, A. P. P.; Hamelmann, N. M.; Juan, A.; Lindhoud, S.; Paulusse, J. M. J. “Biocompatible Single-Chain Polymer Nanoparticles for Drug Delivery-A Dual Approach” *ACS Appl. Mater. Interfaces* 37 (2018) 30946–30951.

Figures

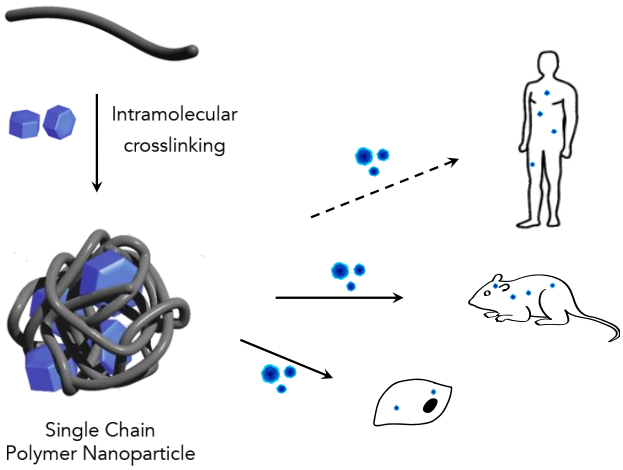

Figure 1. Intramolecular crosslinking of polymers, in the presence of therapeutics, to form single chain polymer nanoparticles for application in nanomedicine.