Responsive nanogels as carriers for antimicrobial peptides

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Due to increasing resistance development against conventional antibiotics, antimicrobial peptides (AMPs) are receiving considerable attention as potential therapeutics. Through lysis of bacterial membranes, AMPs provide fast and broad-spectrum antimicrobial effects. While there have been considerable efforts to identify potent and selective AMPs, drug delivery aspects of such compounds have been rarely investigated. For example, infected tissue is often characterized by high proteolytic activity. Thus, administration of AMPs to chronic wounds, infected eyes, or cystic fibrosis lungs is likely to result in rapid degradation of the peptide and in corresponding activity loss. Furthermore AMPs bind to serum proteins and are rapidly cleared from bloodstream circulation, which risks translating into reduced efficacy, as well as toxicity effects, related to accumulation in the reticuloendothelial system. In addition, some infections, such as tuberculosis, are characterized by intracellular bacteria localization, which poses a challenge in how to reach the intracellular bacteria without lysing and killing the host macrophages. Yet other challenges relate to need for sustained or triggered AMP release, e.g., for implants and recurring infection. In these and other contexts, it would therefore be advantageous to combine AMPs with delivery systems designed for the application at hand.

Nanogels are lightly cross-linked polymer colloids, frequently displaying dramatic swelling/deswelling transitions in response to different stimuli. They are of particularly interesting as carriers for biomacromolecular drugs, such as peptides and proteins, since they offer a water-rich environment, thus reducing detrimental conformational changes and aggregation, at the same time providing protection against enzymatic degradation and allowing controlled or triggered release. In order to elucidate key properties of AMP-loaded nanogels, we here investigate effects of nanogel charge density on AMP loading and release, using a nanogel library of poly(ethyl acrylate-co-methacrylic acid) nanogels, investigated with ellipsometry, confocal microscopy, particle size- and z-potential measurements. In addition, membrane interactions of peptide-loaded nanogels are addressed, translating from biophysical studies to antimicrobial activity.