Membrane interactions of mesoporous silica nanoparticles as carriers of antimicrobial peptides

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Membrane interactions are critical for the successful use of mesoporous silica nanoparticles as delivery systems for antimicrobial peptides (AMPs). In order to elucidate these, we here investigate effects of nanoparticle charge and porosity on AMP loading and release, as well as consequences of this for membrane interactions and antimicrobial effects. Anionic mesoporous silica particles were found to incorporate considerable amounts of the cationic AMP LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLVPRTES (LL-37), whereas loading is much lower for non-porous or positively charged silica nanoparticles. Due to preferential pore localization, anionic mesoporous particles, but not the other particles, protect LL-37 from degradation by infection-related proteases. For anionic mesoporous nanoparticles, membrane disruption is mediated almost exclusively by peptide release. In contrast, non-porous silica particles build up a resilient LL-37 surface coating due to their higher negative surface charge, and display largely particle-mediated membrane interactions and antimicrobial effects. For positively charged mesoporous silica nanoparticles, LL-37 incorporation promotes the membrane binding and disruption displayed by the particles in the absence of peptide, but also causes toxicity against human erythrocytes. Thus, the use of mesoporous silica nanoparticles as AMP delivery systems requires consideration of membrane interactions and selectivity of both free peptide and the peptide-loaded nanoparticles, the latter critically dependent on nanoparticle properties.