PLATELET-MIMICKING MULTI-LIGAND NANO PARTICLES INHIBIT ENDOTHELIAL CELL INFLAMMATION AND NEOINTIMAL RESTENOSIS

Oral Contributions
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Authors: Hao Xu, Emmanouil Brilakis, Kytai T. Nguyen, Subhash Banerjee, UT Southwestern Medical Center, Dallas, TX, USA, UT Arlington, Arlington, TX, USA

Background: Endothelial cells (EC) activation and inflammation is a key step in initiation and progression of many cardiovascular diseases such as atherosclerosis. Targeted-delivery of therapeutic reagents to inflamed EC using nanoparticles is promising but challenging, as nanoparticles do not arrest on EC efficiently under shear stress in blood circulation. The purpose of this study is to develop a novel platelet-mimicking nanoparticle for strong particle adhesion on activated EC and enhanced particle internalization.

Methods and Results: The platelet-mimicking biodegradable polymeric PLGA-PEG-GP1b/TAT multi-ligand nanoparticles (MLNP) were synthesized using poly(L-lactic-co-glycolic) acid with dexamethasone encapsulated as the anti-inflammatory drug, and conjugated with polyethylene glycol (PEG), glycoprotein 1b (GP1b), and trans-activating transcriptional peptide (TAT) on particle surface (Figure A-B). Compared to unmodified nanoparticles, MLNP showed significantly greater adhesion on P-selectin and von Willebrand Factor (vWF) in vitro under both static and flow condition (Figure C), as well as increased uptake by activated EC in vitro (Figure D) and angioplasty balloon-injured rat carotid artery ex vivo (Figure E). MLNP also suppressed angioplasty balloon-injured rat carotid artery neointimal proliferation in vivo (Figure F).

Conclusions: These results indicate that our MLNP construct delivers anti-inflammatory drugs to injured vessel wall and inhibit restenosis.