A Nanomedicine Approach for Targeted Thrombolysis

Ravichandran, Kavya

In occlusive vascular pathologies like heart attack and stroke, rapid thrombolysis is necessary for restoring blood flow to critical organs. It is advantageous to localize the delivery and action of thrombolytic drugs specifically at the clot site to minimize risk of systemic coagulopathy and hemorrhage from indiscriminate drug action. Thus, it is hypothesized that site-specific thrombolytic delivery can be achieved by engineering nanoparticles that specifically target the thrombus by actively binding to thrombus-associated active platelets and allow controlled drug release via thrombus-relevant enzyme trigger. Liposomal nanovehicles that bind to active platelets were previously developed in the Sen Gupta laboratory by decorating liposome surface with peptides that specifically bind integrin GPIIb-IIIa and P-selectin. Building on this work, the current study investigated the encapsulation and enzyme-triggered release of a model payload from such liposomal vehicles and in vitro clot lysis. A model payload carboxyfluorescein (CF) was encapsulated in the aqueous core of liposomes and the encapsulation efficiency (EE) was measured by fluorescence spectrometry to be 74.70%±0.97. Subsequently the CF-loaded liposomes were incubated with the thrombus-relevant enzyme phospholipase A2 (PLA2) at physiologically-relevant conditions and monitored over time. These studies showed a twofold increase in CF release when triggered by PLA2. Subsequently, a relevant thrombolytic drug, streptokinase (SK), was encapsulated in platelet-targeted liposomes and PLA2-triggered targeted thrombolysis was evaluated in vitro, using platelet-rich thrombi. The results show feasibility of platelet-targeted enzyme-triggerable vehicles as a novel nanomedicine technology for site–specific thrombolysis.