



CONSTANTINOS MIKELIS
University of Patras
Greece

Modulating a small GTPase in the endothelium via targeted nanodelivery

Abstract:

Existing Vascular Endothelial Growth Factor (VEGF)-oriented anti-angiogenic approaches are known for their high potency. However, significant side effects associated with their use drive the need for novel anti-angiogenic strategies. The small GTPase RhoA is an established regulator of actin cytoskeletal dynamics. Previous studies have highlighted the impact of endothelial RhoA pathway on angiogenesis. Rho-associate kinase (ROCK), a direct RhoA effector, is potently inhibited by Fasudil, a clinically-relevant ROCK inhibitor. Here, we aimed to target the RhoA signaling in endothelial cells by generating Fasudil-encapsulated CD31-targeting liposomes as a potential antiangiogenic therapy. The liposomes presented desirable characteristics, preferential binding to CD31-expressing HEK293T cells and to endothelial cells, inhibited stress fiber formation and cytoskeletal-related morphometric parameters and inhibited in vitro angiogenic functions. Overall, this work shows that the nanodelivery-mediated endothelial targeting of RhoA signaling can offer a promising strategy for angiogenesis inhibition in vascular-related diseases.

Biography

Mikelis is an Associate Professor at the Department of Pharmacy at the University of Patras, in Greece. Till 2021 he was an Associate Professor at the School of Pharmacy of Texas Tech University Health Sciences Center, where he keeps an adjunct appointment. He was trained on vascular and cancer biology, with a focus on GPCR signaling at the National Institute of Dental and Craniofacial Research (NIDRC) at NIH, while his PhD at the University of Patras was focused on angiogenesis. His current research program is focused on investigating the role of small GTPases on endothelial physiology and cellular communication. By utilizing a repertoire of in vitro and in vivo models and innovative approaches his team is trying to elucidate their functional significance in human physiology and vascular-related pathological conditions.