
In the search for markers and modulators of vascular disease, microRNAs (miRNAs) have emerged as potent therapeutic targets. To investigate miRNAs of clinical interest in patients with unstable carotid stenosis at risk of stroke. Using patient material from the BiKE (Biobank of Karolinska Endarterectomies), we profiled miRNA expression in patients with stable versus unstable carotid plaque. A polymerase chain reaction-based miRNA array of plasma, sampled at the carotid lesion site, identified 8 deregulated miRNAs (miR-15b, miR-29c, miR-30c/d, miR-150, miR-191, miR-210, and miR-500). miR-210 was the most significantly downregulated miRNA in local plasma material. Laser capture microdissection and in situ hybridization revealed a distinct localization of miR-210 in fibrous caps. We confirmed that miR-210 directly targets the tumor suppressor gene APC (adenomatous polyposis coli), thereby affecting Wnt (Wingless-related integration site) signaling and regulating smooth
muscle cell survival, as well as differentiation in advanced atherosclerotic lesions. Substantial changes in arterial miR-210 were detectable in 2 rodent models of vascular remodeling and plaque rupture. Modulating miR-210 in vitro and in vivo improved fibrous cap stability with implications for vascular disease. An unstable carotid plaque at risk of stroke is characterized by low expression of miR-210. miR-210 contributes to stabilizing carotid plaques through inhibition of APC, ensuring smooth muscle cell survival. We present local delivery of miR-210 as a therapeutic approach for prevention of atherothrombotic vascular events.