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Enhanced Imaging of Atherosclerotic Lesions in ApoE-deficient Mice using Nanotechnology

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Atherosclerosis is the major cause of mortality in the western world today. The main objective for the use of nanotechnology is to address prospects of imaging atherosclerotic (AS) plaques, which lead to clinical endpoints. Today various biomarkers are known to be involved in the pathophysiologic scenario of AS-plaques. For the targeting the biomarker globular Adiponectin (gAd) [1] was coupled to two different nanoparticles (NP). The gAd-targeted NPs were investigated towards their potency to characterize critical scenarios within early and advanced AS-plaque lesions applying an AS-mouse model. Aortas of wt and ApoE-deficient mice, fed a high fat diet, were dissected and first stained with fluorescence-labelled gAd. *Ex vivo* imaging was performed using confocal laser-scanning microscopy (CLSM). Second, gAd was coupled to fluorescence-labelled protamine-oligonucleotide nanoparticles (proticles), respectively flu-labelled Stealth®-liposomes to enhance the imaging performance. The gAd-proticle constructs were characterized using scanning electron microscopy. Modified native gel electrophoresis was used for the characterization of the gAd-targeted Stealth®-liposomes. Successful fluorescence labelling of gAd was achieved. According to WB analysis no critical structural changes occurred. *Ex vivo* CLSM imaging showed that flu-gAd binds to the AS-plaque but not to the lesser injured aortic surface. Both, successful coupling of gAd to proticles, respectively to the reactive PEGylated lipids exposed on the liposomal surface of Stealth®-liposomes, was achieved. Compared to the plaque-staining using only flu-labelled gAd, the gAd targeted, flu-labelled Stealth®-liposomes showed a strong signal enhancement in CLSM imaging, while the gAd targeted, flu-labelled proticles generated a different, more spotty-like staining on the surface of the AS-plaques. Results by now suggest a promising role of the applied gAd-targeted NPs for enhanced AS-imaging *in vivo* and their potential use for new targeted therapeutic strategies in cardiovascular medicine.

[1] Yamauchi T, Kamon J, Waki H, Imai Y, Shimozawa N, Hioki K, Uchida S, Ito Y, Takakuwa K, Matsui J, Takata M, Eto K, Terauchi Y, Komeda K, Tsunoda M, Murakami K, Ohnishi Y, Naitoh T, Yamamura K, Ueyama Y, Froguel P, Kimura S, Nagai R, Kadowaki T. Globular adiponectin protected ob/ob mice from diabetes and ApoE-deficient mice from atherosclerosis. J Biol Chem. 2003; 278: 2461–2468. doi:10.1074/jbc.M209033200