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NEW PEPTIDE AS TARGETING AGENT FOR MOLECULAR IMAGING OF ATHEROSCLEROSIS BY SPECT.

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Atherosclerosis specific nanocarriers for molecular imaging and therapy depend on their capacity to interact with receptors expressed by target cells. We are interested in the design of nanocarriers composed of nanoparticles conjugated with peptides capable of selectively targeting atheroma. The main purpose of our work was to select phages displaying peptides able to bind to vascular markers present in human atheroma and validate their capacity to target the vascular markers in vitro and in low-density lipoprotein receptor knockout (LDLr^{-/-}) mouse model of atherosclerosis. By performing peptide fingerprinting on human atherosclerotic tissues using in vitro biopanning, we selected and isolated peptides that bind to atherosclerotic lesions, which share significant similarity to known human proteins with prominent roles in the development of atherosclerosis. Among the collection of bound peptides in human atheroma, phages displaying four different peptide sequences were selected for further studies. The CTHRSSVVC-phage peptide displayed the strongest reactivity with human carotid atherosclerotic lesions, ($P < 0.05$), when compared to tissues from normal carotid arteries. In addition, this peptide sequence shares similarity to a sequence present in the cysteine-rich fifth domain of the scavenger receptor (SRCR), CD163, which appeared to bind to CD163. Moreover, the CTHRSSVVC-phage targets atherosclerotic lesions of a lowdensity lipoprotein receptor knockout (LDLr^{-/-}) mice, in vivo, to high fat-diet group was reported as means \pm SEM 45.50, \pm S.D 13.97 versus control group. Our data shows that phage displaying the cyclic peptide sequence CTHRSSVVC binds to human atheroma and atherosclerotic lesions in LDLr^{-/-} mice. DOTA-CTHRSSVVC-peptide was synthesized and labeled with ¹¹¹InCl₃ as propose of peptide validation, at radiochemical yield of $> 95\%$ was determined by HPLC. In a pilot study to normal and high fat diet LDLr^{-/-} mice to 1 year diet, preliminary pre-clinical images by SPECT with CTHRSSVVC peptide and ¹¹¹InCl₃ showed different patterns of uptake between arteries to each group. Thus considering the important role of CD163 in macrophages and its high expression levels in inflammation, CTHRSSVVC peptide may provide a remarkable sequence to the development of theranostics approaches and nanodevices composed of a nanoparticle conjugated with peptides capable of targeting selectively, which reinforce this potential offering stability, sensitivity and signal amplification.