Histone acetylation and methylation significantly change with severity of atherosclerosis in human carotid plaques.

The aim of the study was to analyze histone acetylation, methylation, and the expression of their corresponding transferases in atherosclerotic plaques of patients with carotid artery stenosis. Atherosclerotic tissue from our biobank (n=80) was divided into various segments covering all plaque stages and classified according to the American Heart Association. The plaques were assigned to early (types I-III) or advanced (types V-VII) stage group of atherosclerosis. Ten healthy carotid arteries from transplant donors served as controls. The expression of histone acetyltransferases (GNAT group: GCN5L, P300/CBP group: P300, MYST group: MYST1 and MYST2) and histone methyltransferases (H3K4: MLL2/4, SET7/9, and hSET1A; H3K9: SUV39H1, SUV39H2, ESET/SETDB1, and EHMT1; H3K27: EZH2 and G9a) was analyzed by SYBR-green-based real-time polymerase chain reaction. Histone acetylation/methylation in the cells within atherosclerotic plaques was determined by immunohistochemistry. Increased histone acetylation was observed on H3K9 and H3K27 in smooth muscle cells (SMCs) in advanced atherosclerotic lesions compared to healthy vessels (P=.002 and .034). H3K9 acetylation in SMCs and macrophages was associated with plaque severity of atherosclerosis (P=.048 and <.001). Expression of
GCN5L and MYST1 also correlated with the severity of atherosclerosis (P<.001). Methylation of H3K9 and H3K27 was significantly reduced in atherosclerotic plaques in SMCs and inflammatory cells (P<.001 and .026). Methylation on H3K4 was significantly associated with the severity of atherosclerosis. Expression of methyltransferase MLL2/4 was increased in advanced stages of atherosclerosis (P<.001). Histone acetylation and methylation seem to play a decisive role in atherosclerosis, showing significant differences between healthy vessels and vessels at different stages of atherosclerosis.

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