MicroRNAs miR-21, miR-210, miR-34a and miR-146a/b-5p are up-regulated in human atherosclerotic plaques in Tampere Vascular Study

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Rationale. MicroRNAs (miRNAs) are small non-coding RNA molecules that inversely regulate their target gene expression. The whole miRNA profile of human atherosclerotic plaques has not been previously studied.

Objective. The aim of this study was to investigate the miRNA expression profile in human atherosclerotic plaques compared to non-atherosclerotic left internal thoracic arteries (LITA) and connect this expression to the processes in atherosclerosis.

Methods. MicroRNA expression profiles were analyzed from six LITAs and twelve atherosclerotic plaques obtained from aortic, carotid, and femoral atherosclerotic arteries from Tampere Vascular Study. Analyzes were done with Agilent’s Human miRNA Microarray. Expression levels of over 4-fold up-regulated miRNAs were verified with qRT-PCR from larger population (n=50). Messenger RNA levels were analyzed with Illumina’s Expression BeadChip to study miRNA target expression.

Results. Ten miRNAs were found to be differentially expressed in atherosclerotic plaques compared to controls (P<0.05). Expression of miR-21, -34a, -146a, -146b-5p and -210 was verified with qRT-PCR and was significantly up-regulated in cases compared to LITAs (p<0.001, fold changes 4.61, 2.55, 2.87, 2.82 and 3.92, respectively). Several predicted targets of these miRNAs were down regulated and gene set enrichment analysis showed several pathways which could be differently expressed due to this miRNA profile.

Conclusions. MicroRNA expression profile differs significantly between atherosclerotic plaques and control arteries. The most up-regulated miRNAs are involved in processes known to be connected to atherosclerosis. Interfering with the miRNA expression in the artery wall may be a potential way to affect the atherosclerotic plaque and cardiovascular disease development.

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