

## Atherosclerosis - Specific microRNAs promote inflammation

**Atherosclerosis, an inflammatory reaction, is at the root of the most common forms of cardiovascular disease. LMU researchers have now identified a microRNA that plays a prominent role in the process, and offers a promising target for new therapies.**

Atherosclerosis – otherwise known as hardening of the arteries – is a prevalent cause of death in modern societies. The condition arises from the build-up of localized fatty deposits called plaques in the arteries. Macrophages, the phagocytic cells of the immune system, migrate to these sites, inducing chronic inflammation which exacerbates the accumulation of the atherosclerotic lesions. These can lead to obstruction of major vessels, causing heart attack and stroke. A team of medical researchers led by LMU's Professor Andreas Schober has now identified a microRNA (miRNA) that helps initiate the inflammatory process.

miRNAs are short segments of RNA derived from longer precursors transcribed from defined stretches of the genomic DNA. They act as versatile regulators of gene expression in cells, and also control the function of macrophages, in which patterns of gene activity must respond rapidly to changes in the extracellular environment. "However, the miRNAs that control the inflammation process during the various stages of atherosclerosis had not been identified up to now," says Schober.

In an earlier study, Schober and his team had shown that the microRNA *miR-155* is a prominent member of the miRNA population in macrophages. The molecule prevents the synthesis of a protein that inhibits the inflammatory reaction, and thus promotes the progression of atherosclerosis. However, *miR-155* does not serve as the initiator of inflammation. Schober and his colleagues have now looked at the patterns of microRNA expression in atherosclerotic lesions in the mouse, and noted that levels of a different miRNA, called *miR-342-5p*, increase in very early plaques.

### New therapeutic approaches

"The newly identified *miR-342-5p* is actually expressed constitutively in macrophages, but it is activated by pro-inflammatory signals. This activation process then induces production of *miR-155*," Schober explains. The results of the new study thus make *miR-342-5p* an interesting target for new therapeutic agents. Indeed, in their animal model, the researchers have been able to demonstrate that inhibition of the action of *miR-342-5p* by means of a specific antagonist retards the progression of atherosclerosis.

“Atherosclerosis in humans should also be susceptible to treatment with inhibitors of microRNAs,” Schober suggests. “Synthetic inhibitors are available for each and every microRNA, and could be used for therapeutic purposes as soon as their efficacy and safety has been demonstrated in clinical tests.” Hence the researchers now plan to collaborate with biotechnology companies on the development of their own specific microRNA inhibitor for future clinical use.

The work was supported by grants from the *Deutsche Forschungsgemeinschaft* (DFG) to DFG Research Unit FOR809.

göd

Publication:

The *microRNA-342-5p* fosters inflammatory macrophage activation through an Akt1- and *microRNA-155*-dependent pathway during atherosclerosis

Yuanyuan Wei, Maliheh Nazari-Jahantigh, Lily Chan, Mengyu Zhu, Kathrin Heyll, Judit Corbalán-Campos, Petra Hartmann, Anna Thiemann, Christian Weber, Andreas Schober

Circulation, published online 19. March, 2013

doi: 10.1161/CIRCULATIONAHA.112.000736