Accumulation of trace elements in atherosclerotic lesions in LDL Receptor Deficient Mice

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The onset of atherosclerosis is characterized by a subendothelial accumulation of low density lipoproteins (LDL) in the vessel wall. The oxidation of LDL in the intima is a crucial step. Oxidized LDL exhibits many atherogenic properties. It acts as a chemo attractant of circulating monocytes and T-cells and it is cytotoxic for many cell types, including the endothelial cells. Macrophages are attracted to the lesion site, where they take up the oxidized LDL. This results in the formation of a fatty streak, which is an important feature in the chronic inflammation process of atherosclerosis.

In cell cultures it has been observed that Fe and Cu are important parameters in the oxidation of LDL and redox-active metals were found in atherosclerotic plaques. Possibly Fe and Cu play a role as catalysts in this oxidation process. Zn is known for its anti-oxidant properties. Though, it is still not clear at which stage these trace elements play a role e.g. in the onset of a plaque or in more advanced stages. In more advanced lesions it is known that calcifications of lesion areas can occur.

Homozygous LDL receptor deficient mice were used as a model of atherosclerosis. The experimental groups were put on a high fat diet and the control groups were put on a reference diet. Aortas were studied at different stages of the disease process; from onset to advanced lesions.

A 3 MeV proton microbeam with a resolution of 1x1 μm^2 was used to analyze 10 µm thick cross-sections of aortas.

Iron accumulations in the fatty streak were observed. The role of Fe, Zn, Cu and Ca in disease process of atherosclerosis, as well as their spatial correlations will be discussed.