LIVER

N^ε-(Carboxymethyl)lysine is involved in hepatic steatosis

N^ε-(Carboxymethyl)lysine (CML) accumulates in the livers of obese patients with hepatic steatosis and could be involved in the pathogenesis of nonalcoholic fatty liver disease (NAFLD), according to a recent paper.

CML is an end product of lipid peroxidation reactions, which are known to occur more frequently in patients with NAFLD. Therefore, Gaens *et al.* suggested that increased endogenous formation and accumulation of CML might take place in the livers of patients with steatosis. The authors used two approaches to test this hypothesis; tests in humans and *in vitro*.

Liver biopsy samples were taken from 74 severely obese individuals who were categorized according to their degree of hepatic steatosis (low, moderate or severe). Immunohistochemical staining showed that CML accumulation was greater in patients with severe or moderate grade steatosis than in those with low grade steatosis. The authors also found that increased CML accumulation was associated with hepatic inflammation, which can lead to NAFLD.

Immunohistochemical staining of N^ε-(Carboxymethyl)lysine (CML) in liver biopsy samples of controls (left panel) showed no staining of CML-modified proteins; a strong CML staining was detected in the cytoplasmic fraction of the hepatocytes of liver biopsy samples of severely obese patients with severe hepatic steatosis (right panel). Courtesy of C. G. Schalkwijk.

By inducing steatosis in two hepatic cell lines, the researchers demonstrated that the development of steatosis increased endogenous formation of CML and the expression of inflammatory markers, such as the receptor for advanced glycation end products.

These findings suggest that CML formation could be targeted to interfere with the development of NAFLD. “A major question to be addressed is whether

the adipose tissue in obesity reacts similarly to the liver,” concludes author Casper Schalkwijk.

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Original article Gaens, K. H. J. *et al.* Endogenous formation of N^ε-(Carboxymethyl)lysine is increased in fatty livers and induces inflammatory markers in an *in vitro* model of hepatic steatosis. *J. Hepatol.* doi:10.1016/j.jhep.2011.07.028.