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New Insights in the etiology of fatty liver disease

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Due to the obesity epidemic, the incidence of non-alcoholic steatohepatitis (NASH) has risen, and NASH is becoming the major cause of liver transplantations in the western world. The aetiology of NASH is commonly explained by the "two-hit model" where the fatty liver develops first, and then progresses towards NASH. We tested this model in the LDLR knockout mouse, i.e. a mouse with a human like lipoprotein profile. In the LDLR knock-out mouse, given a western type diet, inflammation develops independent of the fatty liver. We also found that the major cause of inflammation are the oxidised lipoproteins, that accumulate in the Kupffer cells. Hence, the two-hit model should be replaced by other models whereby the fatty liver and the hepatic inflammation develop independently. As there are currently no therapies for NASH, this novel insight is crucial to develop novel diagnostic tools and treatments.

CURRICULUM VITAE

Marten Hofker studied Biology in Leiden, where he received his PhD degree in 1987 on the basis of the development of genetic markers for the detection of inherited diseases, and in particular the application in the diagnosis of X-linked diseases such as Duchenne muscular dystrophy. During 1987-1989, he received a fellowship of the Medical Research Council of Canada, and worked at the genetics department of the Hospital for Sick Children, Toronto. At the end of 1989, he returned to the department of Human and Clinical Genetics in Leiden. During 1989-1994, he received a fellowship of the Royal Dutch Society of Arts and Sciences, which allowed him to start his work on the genetics of cardiovascular diseases using transgenic mice. Subsequently, he became an Established Investigator of the Dutch Heart Association (1997). In 2000, he was appointed as a professor of Molecular Genetics, and founded the laboratory of Molecular Genetics at the Maastricht University. Since January 2007, he is appointed as head of the laboratory of Molecular Genetics at the UMCG. His main field of interest is mechanisms of metabolic diseases, diabetes and atherosclerosis.