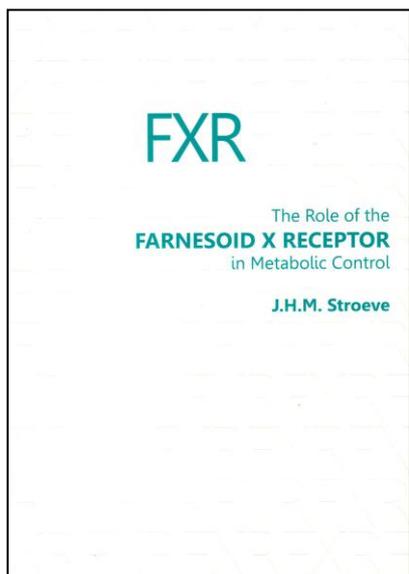




Nederlandse
Vereniging voor
Hepatology



Samenvatting proefschrift Jeroen H.M. Stroeve

'The Role of the Farnesoid X Receptor in Metabolic Control'

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Obesity or overweight is a serious public health problem in the 21st century. The current obesity epidemic, which particularly affects children, is largely the result of a lifestyle change (less physical activity) and changes in dietary habits (high intake of energy-dense food). Obesity is associated with serious health problems, including metabolic diseases such as metabolic syndrome, cardiovascular disease and type 2 diabetes.

Bile acids are synthesized from cholesterol by the liver. After ingestion of a meal, bile acids are secreted from the gallbladder, where they are stored, into the small intestine. Here they function as a kind of "detergent" to facilitate the absorption of fats in the diet. In addition, it becomes more and more evident that bile acids, by binding and activating the protein called the farnesoid X receptor (FXR), play a role in regulating various metabolic processes, including those of bile acids, sugars and fats. FXR is present in many tissues including the liver, intestine, kidney and adipose tissue. Because of its broad functionality, FXR is considered a promising therapeutic target for new therapies in the treatment of metabolic diseases such as obesity and type 2 diabetes. In recent years, our knowledge of FXR function increased significantly. There is, however, still a lot unknown about FXR functioning. In this dissertation we aim to unravel certain specific functions of FXR. First, the relative contribution of FXR in the intestine to the regulation of hepatic bile acid synthesis has been determined in mice. Then we studied the consequences of lack of FXR on the metabolism of bile acids, sugars and fats in a mouse model of obesity. Finally, the role of FXR in the development and functioning of adipose tissue was examined. Together, the results described in this dissertation provided novel insights in the role of FXR in the regulation of various metabolic processes. ◀

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