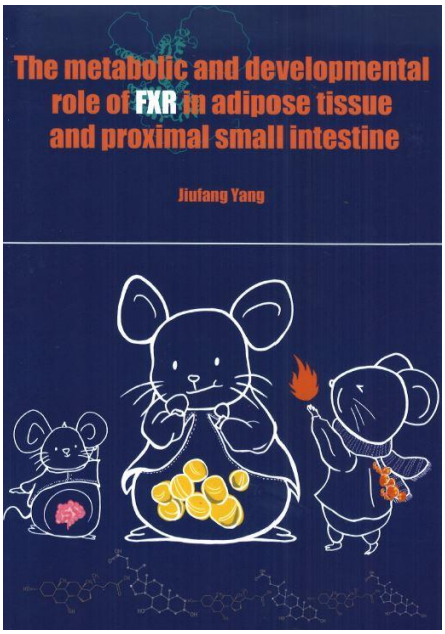

Samenvatting proefschrift
J. Yang

'The metabolic and developmental role of FXR in adipose tissue and proximal small intestine'

Promotiedatum: 2 maart 2022
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Promotor:
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Bile acids act not only as natural detergents to facilitate fat absorption but also as signalling molecules, regulating different metabolic processes such as glucose, lipid and energy metabolism. Many effects of bile acids mediated by farnesoid X receptor (FXR), a transcription factor that is specifically activated by bile acids and derivatives thereof. FXR is highly expressed in liver and intestine, and several FXR agonists have been developed and tested in clinical trials for the treatment of bile acid-related liver disorders. FXR is also lowly expressed in other organs and tissues such as adipose tissues. However, the role of FXR in adipose tissues and how FXR regulates the cross-talk between liver and adipose tissues remains unclear.

In this thesis, we investigated the role of FXR in white and brown adipose tissues by using adipose specific $FXR^{-/-}$ or overexpression mice. We found that deletion of FXR in adipocytes does not affect glucose metabolism while overexpression of FXR in adipose tissues has adverse metabolic consequences such as limited lipid storage capacity, ectopic lipid accumulation in liver, whole-body insulin resistance and whitened brown fat. The function of brown adipose tissue is also partially impaired. It suggests that treatment with FXR agonists might trigger fat-specific actions and current chronic use of FXR agonists for the treatment of liver and metabolic diseases deserve careful evaluation of their effects in adipose tissues.

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