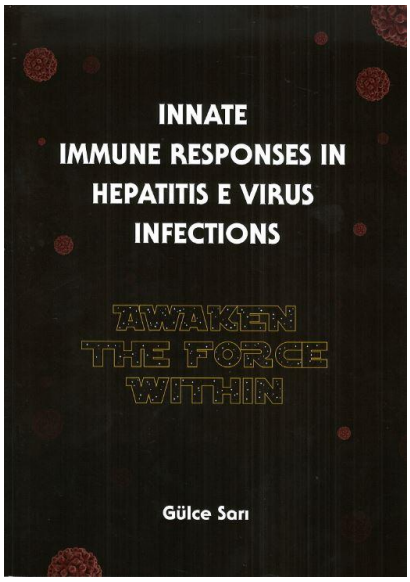

Samenvatting proefschrift G. Sari

'Innate immune responses in hepatitis E virus infections: awaken the force within"

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Hepatitis E virus (HEV) infections are the major cause of acute hepatitis worldwide with more than 3 million symptomatic cases and around 60000 fatalities. Whilst HEV infections can cause both acute and chronic infections, acute HEV cases are largely connected to outbreaks in developing countries which vary in size, but sporadically are recognized in western countries. Differently, chronic HEV infections are common in developed countries, and affect patients with an immunocompromised status, such as patients who received a solid organ transplant, or human immunodeficiency virus infection. The limitations of the model systems, the molecular biology of HEV being incompletely undeciphered and the unavailability of specific antiviral compounds hamper the fight to control HEV.
In the PART I of this thesis, our studies focused on two main subjects: 1) We examined the experimental factors associated with HEV infection and PHH engraftment in 2 xenograft systems TK-NOG and uPA-NOG; and then 2) We examined the suitability of these liver humanized models as a model for lipoprotein studies and studies on atherosclerotic plaque formation.
In the PART II of this thesis, we studied: 1) Compartmentalization of HEV in chronic HEV gt3 patients and additionally the spontaneous genomic alterations of HEV after in vitro or in vivo propagation. 2) The functions of open reading frame (ORF) 3 protein in HEV spread, replication and release in in vitro and in vivo systems. 3) The potential of pegylated (peg) IFNλ as a new treatment candidate against chronic gt3 HEV infections.
Overall, we showed that human liver chimeric mice have an undeniable role in increasing our understanding of human viruses and diseases. As scientists, we all should strive for excellence; a good design, an adequate model and all the necessary controls to obtain repeatable and universal results. Our study expanded the knowledge on HEV biology, and anti-HEV treatment strategies and further studies are required to test whether obtained data can be translated into clinical studies.

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Voor proefschriftsamenvattingen zie:
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