

University of Groningen

## Novel strategies targeting hepatic stellate cells to reverse liver fibrosis

Shajari, Shiva

DOI:  
[10.33612/diss.144700577](https://doi.org/10.33612/diss.144700577)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2020

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
Shajari, S. (2020). *Novel strategies targeting hepatic stellate cells to reverse liver fibrosis*. University of Groningen. <https://doi.org/10.33612/diss.144700577>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

**Novel strategies targeting hepatic stellate cells  
to reverse liver fibrosis**

Shiva Koets-Shajari

This work is supported by The Groningen University Institute for Drug Exploration (GUIDE).

For printing of this thesis, financial support of the following institutions and companies is gratefully acknowledged:

Graduate School of Medical Sciences (GSMS)

Nederlandse vereniging voor Hepatologie (NVH)

Shiva Koets-Shajari

Novel strategies targeting hepatic stellate cells to reverse liver fibrosis

Copyright 2020, Shiva Koets-Shajari, The Netherlands

All rights reserved. No part of this book may be reproduced, stored in a retrieval system or transmitted in any form or by any means, without the written permission of the author.

Cover photo by: Banafsheh Ashrafi

Layout by: Publiss.nl

Printed by: Ridderprint.nl



**university of  
 groningen**

**Novel strategies targeting hepatic stellate cells  
 to reverse liver fibrosis**

**PhD Thesis**

to obtain the degree of PhD at the  
 University of Groningen  
 on the authority of the  
 Rector Magnificus Prof. C. Wijmenga  
 and in accordance with  
 the decision by the College of Deans.

This thesis will be defended in public on  
 Wednesday, 25 November 2020 at 16:00.

by

**Shiva Koets-Shajari**

born on 27 December 1980

in Kermanshah, Iran

## **Supervisors**

Prof. dr. Klaas Nico Faber

Prof. dr. Han Moshage

## Table of contents

|                   |   |     |
|-------------------|---|-----|
| <b>Chapter 1:</b> | Introduction and aim of the thesis  | 7   |
| <b>Chapter 2:</b> | Hormone-sensitive lipase is a retinyl ester hydrolase in human and rat quiescent hepatic stellate cells   | 23  |
|                   | <i>Shajari S*, Saeed A*, Smith-Cortinez NF, Heegsma J, Sydor S, Faber KN, Biochim Biophys Acta Mol Cell Biol Lipids. 2019 Sep;1864(9):1258-1267. doi: 10.1016/j.bbaliip.2019.05.012. Epub 2019 May 28.</i>    |     |
|                   | <i>*equal authors</i>   |     |
| <b>Chapter 3:</b> | Melatonin suppresses activation of hepatic stellate cells through ROR $\alpha$ -mediated inhibition of 5-lipoxygenase   | 49  |
|                   | <i>Shajari S, Laliena A, Heegsma J, Tuñón MJ, Moshage H, Faber KN, J Pineal Res. 2015 Oct;59(3):391-401. doi: 10.1111/jpi.12271. Epub 2015 Sep 15.</i>  |     |
| <b>Chapter 4:</b> | Multifaceted esculetin suppresses human hepatic stellate cell activation and CCl <sub>4</sub> -induced liver fibrosis in mice   | 71  |
|                   | <i>Bai X, Shajari S, Yang P, Cai B, Zhou Q, Smith-Cortínez NF, Buist-Homan M, Heegsma J, Sydor S, Bechmann LP, Shen D, Wu Y, Luo X, Chen Y, Niu Y, Zhang Y, Gao F, Moshage H, Shi G, Faber KN, Submitted.</i> |     |
| <b>Chapter 5:</b> | Hydroxyurea attenuates hepatic stellate cell proliferation <i>in vitro</i> and liver fibrogenesis <i>in vivo</i>  | 99  |
|                   | <i>Haijer F, Koets-Shajari S, Heegsma J, Blokzijl T, Buist-Homan M, Moshage H, Faber KN, Submitted.</i>   |     |
| <b>Chapter 6:</b> | Discussion  | 123 |
| <b>Chapter 7:</b> | Samenvatting  | 136 |
| <b>Chapter 8:</b> | Acknowledgements  | 140 |

