

University of Groningen

## Molecular identification of the uptake carriers for organic cations in liver

Montfoort, Jessica Edith van

**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:*

2001

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

*Citation for published version (APA):*

Montfoort, J. E. V. (2001). Molecular identification of the uptake carriers for organic cations in liver Groningen: s.n.

**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).

**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.

# **Molecular identification of the uptake carriers for organic cations in liver**

Jessica van Montfoort



RIJKSUNIVERSITEIT GRONINGEN

**Molecular identification of the uptake carriers for organic cations in liver**

PROEFSCHRIFT

ter verkrijging van het doctoraat in de  
Wiskunde en Natuurwetenschappen  
aan de Rijksuniversiteit Groningen  
op gezag van de Rector Magnificus, dr. D.F.J. Bosscher,  
in het openbaar te verdedigen op  
maandag 17 december 2001  
om 14.15 uur

door

Jessica Edith van Montfoort

geboren op 25 mei 1970  
te Zürich (Zwitserland)

**Promotores:**

Prof. dr. D.K.F. Meijer  
Prof. dr. P.J. Meier-Abt

**Co-promotores:**

Prof. dr. M. Müller  
Prof. dr. H. Koepsell

**Referenten:**

dr. G.M.M. Groothuis  
dr. B. Hagenbuch

**Beoordelingscommissie:**

Prof. dr. F. Kuipers  
Prof. dr. R.P.J. Oude Elferink  
Prof. dr. F.G.M. Russel

**ISBN:** 90-6464-048-3

Voor Cornelia en Niels

## **Paranimfen:**

Esther Kroodsma  
Emiel Scheffer

This PhD project was performed in the framework of the “Ubbo Emmius” internationalization program of the University of Groningen, The Netherlands. In total, four different laboratories participated in the project and provided specific expertise:

- Research group Pharmacokinetics and Drug Delivery (Univ. Centre for Pharmacy, Univ. Groningen, The Netherlands)
- Division of Clinical Pharmacology and Toxicology (Univ. Zürich, Switzerland)
- Department of Anatomy (Univ. Würzburg, Germany)
- Division of Gastroenterology and Hepatology (Faculty of Medical Sciences, Univ. Groningen, The Netherlands).

Experimental work was done in Zürich and Groningen in the research school “Groningen University Institute for Drug Exploration (GUIDE)”.

The printing of this thesis was financially supported by grants of the Faculty of Mathematics en Sciences of the University of Groningen and the Groningen University Institute for Drug Exploration (GUIDE).

Printed by Ponsen & Looien BV, Wageningen, The Netherlands.

© 2001 by Jessica van Montfoort

All rights are reserved. No part of this publication may be produced, stored in a retrieval system, or transmitted in any form or by any means, mechanically, by photocopying, recording, or otherwise, without the written permission of the author.

The cover depicts the first slide of my oral presentation at the 49<sup>th</sup> Annual Meeting of the American Association for the Study of Liver Diseases, AASLD, in Chicago on November 10, 1998.

# CONTENTS

CHAPTER 1	Aim and outline of the thesis	1
CHAPTER 2	General introduction: Drug uptake systems in liver and kidney	3
CHAPTER 3	Hepatic uptake of the magnetic resonance imaging contrast agent gadoxetate by the organic anion transporting polypeptide Oatp1	37
CHAPTER 4	Polyspecific organic anion transporting polypeptides mediate hepatic uptake of amphipathic type II organic cations	49
CHAPTER 5	Comparison of “type I” and “type II” organic cation transport by organic cation transporters and organic anion transporting polypeptides	63
CHAPTER 6	Localization of organic anion transporting polypeptide 4 (Oatp4) in rat liver and comparison of its substrate specificity with Oatp1, Oatp2, and Oatp3	77
CHAPTER 7	Molecular cloning and functional characterization of the mouse organic anion transporting polypeptide 2 (Oatp2)	91
CHAPTER 8	General discussion and perspectives	101
	Summary	109
	Samenvatting	113
	Publications	117
	Dankwoord	119



