



Universiteit
Leiden
The Netherlands

Sensing transport: label-free in vitro assays as an atTRACTive alternative for solute carrier transporter drug discovery

Sijben, H.J.

Citation

Sijben, H. J. (2022, November 23). *Sensing transport: label-free in vitro assays as an atTRACTive alternative for solute carrier transporter drug discovery*. Retrieved from <https://hdl.handle.net/1887/3487027>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3487027>

Note: To cite this publication please use the final published version (if applicable).

The research in this thesis was performed at the Division of Drug Discovery and Safety of the Leiden Academic Centre for Drug Research (LACDR), Leiden University, The Netherlands. This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777372. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Cover design and thesis layout by Huub Sijben

This thesis was printed by GildePrint (www.gildeprint.nl)

© Huub Sijben 2022

ISBN: 978-94-6419-539-2

All rights reserved. No part of this thesis may be reproduced in any form or by any means without permission of the author.



SENSING TRANSPORT

Label-free *in vitro* assays as an attractive alternative
for solute carrier transporter drug discovery

PROEFSCHRIFT

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof. dr. ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op woensdag 23 november 2022
klokke 16:15 uur

door

Hubert Jacob Sijben
geboren te Woerden, Nederland
in 1993

Promotores

Prof. dr. A.P. IJzerman
Prof. dr. L.H. Heitman

Promotiecommissie

Prof. dr. H. Irth
Prof. dr. J.A. Bouwstra
Prof. dr. D.J. Slotboom (Rijksuniversiteit Groningen)
Prof. dr. U. Gether (University of Copenhagen)
Dr. S. Sucic (Medical University of Vienna)
Dr. J.M. Zweemer

SENSING TRANSPORT

TABLE OF CONTENTS

Chapter 1

General introduction	9
----------------------------	---

Chapter 2

Targeting solute carriers to modulate receptor–ligand interactions.....	31
---	----

Chapter 3

A study of the dopamine transporter using the TRACT assay: a novel <i>in vitro</i> tool for solute carrier drug discovery.....	39
---	----

Chapter 4

Label-free high-throughput screening assay for the identification of norepinephrine transporter inhibitors	67
---	----

Chapter 5

Proteochemometric modeling identifies chemically diverse norepinephrine transporter inhibitors	93
---	----

Chapter 6

Impedance-based phenotypic readout of transporter function: a case for glutamate transporters.....	119
---	-----

Chapter 7

Molecular insights into disease-associated glutamate transporter variants using <i>in silico</i> and <i>in vitro</i> approaches.....	155
---	-----

Chapter 8

General discussion, conclusions and future perspectives	185
---	-----

Appendix

Table A.1–A.2.....	219
--------------------	-----

Summary.....	239
--------------	-----

Nederlandse samenvatting.....	243
-------------------------------	-----

List of publications.....	247
---------------------------	-----

Curriculum vitae.....	249
-----------------------	-----

Acknowledgements.....	251
-----------------------	-----