

University of Groningen

Targeting Aspartate Transcarbamoylase: A Versatile Approach to Multispecies Drug and Herbicide Discovery

Du, Xiaochen

DOI:
[10.33612/diss.979448168](https://doi.org/10.33612/diss.979448168)

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:
2024

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

Citation for published version (APA):

Du, X. (2024). *Targeting Aspartate Transcarbamoylase: A Versatile Approach to Multispecies Drug and Herbicide Discovery*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.979448168>

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.

**Targeting Aspartate Transcarbamoylase:
A Versatile Approach to Multispecies
Drug and Herbicide Discovery**

Xiaochen Du

2024




university of
 groningen

faculty of science
 and engineering



The research presented in this PhD thesis was performed in the group of Drug Design within the Groningen Research Institute of Pharmacy at the University of Groningen, the Netherlands. The work was financially supported by the China Scholarship Council (CSC).

Printing of this thesis was financially supported by the University Library and the Graduate School of Science, Faculty of Science and Engineering, University of Groningen, the Netherlands.

Layout	Xiaochen Du
Cover design	Xiaochen Du, Yanjie Wang (Huahua)
Printed by	
© Copyright 2024	Xiaochen Du, Groningen, the Netherlands

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



university of
 groningen

Targeting Aspartate Transcarbamoylase: A Versatile Approach to Multispecies Drug and Herbicide Discovery

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. J.M.A. Scherpen
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on

Tuesday 30 April 2024 at 14:30 hours

by

Xiaochen Du

born on 29 July 1991
in Hebei, China

Supervisor

Prof. M. R. Groves

Prof. A. S. S. Dömling

Assessment Committee

Prof. A. M. Dolga

Prof. D. Merkler

Prof. W. C Szymanski

To
Who Understand Me
And
Stands by My Side

Paranymph

Xuwen Yang

Table of Contents

CHAPTER 1 Introduction and Scope of the Thesis	1
CHAPTER 2 The Potential of Aspartate Transcarbamoylase as Drug Target in Multiple Diseases	7
CHAPTER 3 Discovery of Small Molecule Allosteric Inhibitors of <i>Pf</i> ATCase as Novel Antimalarials	35
CHAPTER 4 Fragment Screening in the Development of a Novel Anti-malarial	113
CHAPTER 5 Inhibitors of Aspartate Transcarbamoylase inhibit <i>Mycobacterium tuberculosis</i> growth	137
CHAPTER 6 Small-Molecule Allosteric Inhibitors of Human Aspartate Transcarbamoylase Suppress Proliferation of Bone Osteosarcoma Epithelial Cells	175
CHAPTER 7 Non-competitive Inhibitors of <i>Arabidopsis thaliana</i> Aspartate Transcarbamoylase lead to Impaired Root Growth	201
CHAPTER 8 Summary and Future Perspectives	233
Appendix	263

