



Universiteit  
Leiden  
The Netherlands

## Computational modeling of pharmacokinetics and tumor dynamics to guide anti-cancer treatment

Yin, A.

### Citation

Yin, A. (2024, February 1). *Computational modeling of pharmacokinetics and tumor dynamics to guide anti-cancer treatment*. Retrieved from <https://hdl.handle.net/1887/3715801>

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/1887/3715801>

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

**Computational modeling of  
pharmacokinetics and tumor dynamics  
to guide anti-cancer treatment**

**Anyue Yin**  
尹安玥

The research presented in this thesis was performed at the department of Clinical Pharmacy and Toxicology of Leiden University Medical Center, Leiden, the Netherlands. Financial support for the publication of this thesis was provided by Afdelingsfonds Klinische Farmacie & Toxicologie.

|                   |                                 |
|-------------------|---------------------------------|
| <b>Cover</b>      | Anyue Yin                       |
| <b>Layout</b>     | Renate Siebes   Proefschrift.nu |
| <b>Printed by</b> | Proefschriftmaken.nl   De Bilt  |
| <b>ISBN</b>       | 978-94-6469-730-8               |

© 2023 Anyue Yin

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronically or mechanically, including photocopying, recording or in any information storage or retrieval system, without prior permission of the author.

# **Computational modeling of pharmacokinetics and tumor dynamics to guide anti-cancer treatment**

## **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 donderdag 1 februari 2024  
klokke 10:00 uur

door

**Anyue Yin**

geboren te Beijing, China  
in 1992

|                          |                                                                                                          |
|--------------------------|----------------------------------------------------------------------------------------------------------|
| <b>Promotor</b>          | Prof. dr. H.-J. Guchelaar                                                                                |
| <b>Copromotor</b>        | Dr. D.J.A.R. Moes                                                                                        |
| <b>Promotiecommissie</b> | Prof. dr. A.J. Gelderblom<br>Prof. dr. C.A.J. Knibbe<br>Prof. dr. E.F. Smit<br>Dr. K. Staňková, TU Delft |

# Contents

|                   |                                                                                                                                                                                                  |            |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Chapter 1</b>  | General introduction                                                                                                                                                                             | <b>7</b>   |
| <b>Section I</b>  | <b>Modeling tumor dynamics including treatment resistance</b>                                                                                                                                    |            |
| <b>Chapter 2</b>  | A review of mathematical models for tumor dynamics and treatment resistance evolution of solid tumors<br><i>CPT Pharmacometrics Syst Pharmacol. 2019 Oct;8(10):720-737</i>                       | <b>19</b>  |
| <b>Chapter 3</b>  | Anti-cancer treatment schedule optimization based on tumor dynamics modelling incorporating evolving resistance<br><i>Sci Rep. 2022 Mar 10;12(1):4206</i>                                        | <b>65</b>  |
| <b>Chapter 4</b>  | Quantitative modeling of tumor dynamics and development of drug resistance in non-small cell lung cancer patients treated with erlotinib<br><i>Submitted</i>                                     | <b>109</b> |
| <b>Section II</b> | <b>Modeling pharmacokinetics &amp; pharmacodynamics</b>                                                                                                                                          |            |
| <b>Chapter 5</b>  | Model-informed precision dosing in oncology<br><i>In preparation</i>                                                                                                                             | <b>143</b> |
| <b>Chapter 6</b>  | Population pharmacokinetic and pharmacogenetic analysis of mitotane in patients with adrenocortical carcinoma: towards individualized dosing<br><i>Clin Pharmacokinet. 2021 Jan;60(1):89-102</i> | <b>155</b> |
| <b>Chapter 7</b>  | Population pharmacokinetic and toxicity analysis of high-dose methotrexate in patients with central nervous system lymphoma<br><i>In preparation</i>                                             | <b>193</b> |
| <b>Chapter 8</b>  | General discussion                                                                                                                                                                               | <b>221</b> |
| <b>Chapter 9</b>  | Summary                                                                                                                                                                                          | <b>247</b> |
|                   | Nederlands Samenvatting                                                                                                                                                                          | <b>251</b> |
| <b>Appendices</b> | Curriculum Vitae                                                                                                                                                                                 | <b>259</b> |
|                   | List of publications                                                                                                                                                                             | <b>260</b> |
|                   | Acknowledgement                                                                                                                                                                                  | <b>261</b> |