

Cover Page



Universiteit Leiden



The following handle holds various files of this Leiden University dissertation:

<http://hdl.handle.net/1887/71808>

Author: Janssen, A.P.A.

Title: Inhibitor selectivity: profiling and prediction

Issue Date: 2019-05-01

Inhibitor Selectivity: Profiling and Prediction

PROEFSCHRIFT

ter verkrijging van
de graad van Doctor aan de Universiteit van Leiden,
op gezag van Rector Magnificus Prof. Dr. C.J.J.M. Stolker,
volgens het besluit van het College voor Promoties
te verdedigen op woensdag 1 mei 2019
klokke 15:00 uur

door

Antonius Petrus Arnoldus Janssen

Geboren te Nootdorp op 7 december 1989

Promotiecommissie

Promotor: Prof. Dr. M. van der Stelt

Co-promotor: Dr. G.J.P. van Westen

Overige leden: Prof. Dr. H.S. Overkleeft

Prof. Dr. C.A.A. van Boeckel

Prof. Dr. H. van Vlijmen

Prof. Dr. A.P. IJzerman

Prof. Dr. M. Kaiser

Universität Duisburg-Essen, Essen, Germany

Dr. I. Dijkgraaf

Maastricht University, Maastricht, The Netherlands

ISBN: 978-94-028-1465-1

© The copyright of this thesis rests with author.

No quotation from it should be published without author's prior consent and information derived from it should be acknowledged.

Cover image: *Sharpest ever view of the Andromeda Galaxy* - NASA, ESA, J. Dalcanton (University of Washington, USA), B. F. Williams (University of Washington, USA), L. C. Johnson (University of Washington, USA), the PHAT team, and R. Gendler. Constellations overlaid by the author.

| *You're only given a little spark of madness, if you lose that...
you're nothing.*
Robin Williams.

Table of Contents

<i>Chapter 1</i>	
General introduction.....	7
<i>Chapter 2</i>	
Hit-to-lead optimization of triazole sulfonamide DAGL- α inhibitors	17
<i>Chapter 3</i>	
Towards drug-like peripherally restricted DAGL-inhibitors.....	35
<i>Chapter 4</i>	
Structure Kinetics Relationships for irreversible DAGL inhibitors.....	63
<i>Chapter 5</i>	
BIA 10-2474 is a non-selective FAAH inhibitor that disrupts lipid metabolism	83
<i>Chapter 6</i>	
Development of a multiplexed ABPP assay to evaluate activity of endocannabinoid hydrolase inhibitors.....	109
<i>Chapter 7</i>	
t-Distributed Stochastic Neighbour Embeddings applied to drug discovery	133
<i>Chapter 8</i>	
Drug Discovery Maps visualizes and predicts kinome-inhibitor interaction landscapes	151
<i>Chapter 9</i>	
Summary and Future Prospects.....	177
Nederlandse Samenvatting	193
List of Publications	200
Curriculum Vitae	202

