



Universiteit
Leiden
The Netherlands

Illuminating N-acylethanolamine biosynthesis with new chemical tools

Mock, E.D.

Citation

Mock, E. D. (2019, November 6). *Illuminating N-acylethanolamine biosynthesis with new chemical tools*. Retrieved from <https://hdl.handle.net/1887/80154>

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/1887/80154>

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

**Illuminating *N*-acylethanolamine biosynthesis
with new chemical tools**

PROEFSCHRIFT

ter verkrijging van

de graad van Doctor aan de Universiteit Leiden,

op gezag van Rector Magnificus prof. mr. C.J.J.M. Stolker,

volgens het besluit van het College voor Promoties

te verdedigen op woensdag 6 november 2019

klokke 15:00 uur

door

Elliot David Mock

geboren te Amsterdam in 1989

Promotiecommissie

Promotores: Prof. dr. M. van der Stelt
Prof. dr. C.A.A. van Boeckel

Overige leden: Prof. dr. H.S. Overkleeft
Prof. dr. J.M.F.G. Aerts
Prof. dr. C.J. Hillard
Medical College of Wisconsin, USA
Prof. dr. C.J. Schofield
Oxford University, UK
Dr. G.J.P. van Westen

The cover depicts the inhibitor **LEI-401** docked in a crystal structure of the enzyme NAPE-PLD (PDB: 4QN9).
Adapted from Magotti *et al.*, *Structure* (2015).

Sapere aude

Table of contents

Chapter 1	7
Therapeutic opportunities of modulating the endogenous <i>N</i> -acylethanolamine tone	
Chapter 2	45
High-throughput screening delivers new inhibitors for NAPE-PLD	
Chapter 3	63
Optimization of pyrimidine-4-carboxamide NAPE-PLD inhibitors affords LEI-401	
Chapter 4	131
Photoaffinity probes for NAPE-PLD confirm LEI-401 target engagement	
Chapter 5	175
LEI-401 is an <i>in vivo</i> active NAPE-PLD inhibitor that reduces brain anandamide levels and pain behavior	
Chapter 6	201
Discovery and optimization of α -ketoamide inhibitors for the <i>N</i> -acyltransferase PLAAT2	
Chapter 7	239
Summary and future prospects	
Nederlandse Samenvatting	264
List of publications	272
Curriculum Vitae	274
Nawoord	275

