



Universiteit  
Leiden  
The Netherlands

## Activity-based protein profiling of diacylglycerol lipases

Baggelaar, M.P.

### Citation

Baggelaar, M. P. (2017, April 6). *Activity-based protein profiling of diacylglycerol lipases*. Retrieved from <https://hdl.handle.net/1887/48284>

Version: Not Applicable (or Unknown)

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

Downloaded from: <https://hdl.handle.net/1887/48284>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/48284> holds various files of this Leiden University dissertation

**Author:** Baggelaar, M.P.

**Title:** Activity-based protein profiling of diacylglycerol lipases

**Issue Date:** 2017-04-06

# **Activity-based Protein Profiling of Diacylglycerol Lipases**

**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 6 April 2016  
klokke 15:00 uur

door

**Marc Pieter Baggelaar**

Geboren te Harlingen in 1984

## **Promotiecommissie**

Promotor                      Prof. dr. H. S. Overkleeft

Co-promotor                  Dr. M. van der Stelt

Overige leden :              Prof. dr. B. F. Cravatt

                                  Prof. dr. H. Ovaa

                                  Prof. dr. C. A. A. van Boeckel

                                  Prof. dr. G. A. van der Marel

                                  Prof. dr J. Brouwer

                                  Dr. K. Bonger

Printed by Ridderprint

Cover picture: Robert van Sluis

ISBN 978-94-6299-551-2



# **Table of contents**

## **Chapter 1**

Activity-based Protein Profiling Drives Inhibitor Discovery	<b>7</b>
---	----------

## **Chapter 2**

2-Arachidonoylglycerol: a Signaling Lipid	<b>15</b>
---	-----------

## **Chapter 3**

Development of an Activity-Based Probe and Focused Library Screening Reveal Highly Selective Inhibitors for DAG-lipase- $\alpha$ in Brain	<b>49</b>
---	-----------

## **Chapter 4**

A highly Selective, Reversible Inhibitor Identified by Comparative Chemoproteomics Modulates Diacylglycerol Lipase Activity in Neurons	<b>81</b>
--	-----------

## **Chapter 5**

Structure Activity Relationship of LEI105	<b>113</b>
---	------------

## **Chapter 6**

Chemical Proteomics Maps Brain Region Dependent Activity of Endocannabinoid Hydrolases	<b>139</b>
---	------------

**Chapter 7**

Focused Library Screening Using Activity-based Probes Reveals **159**  
Novel Inhibitors of the  $\alpha,\beta$ -hydrolase Fold Family

**Chapter 8**

Summary and Future Prospects **177**

**Samenvatting** **191**

**List of publications** **195**

**Curriculum Vitae** **198**

