

## PERSONAL INFORMATION

**Mario van der Stelt, prof.dr.**

Researcher unique identifier: ORCID ID 0000-0002-1029-5717

Date of birth: 20-09-1975

Nationality: Dutch

Position: Chair and Professor of Molecular Physiology, Leiden Institute of Chemistry, Universiteit Leiden

[www.universiteitleiden.nl/en/science/chemistry/molphys](http://www.universiteitleiden.nl/en/science/chemistry/molphys)

Mario van der Stelt is chair and professor of Molecular Physiology at the Leiden Institute of Chemistry and is elected as senior investigator of Onco Institute. He is a medicinal chemist and worked as a group- and project leader for almost eight years in the pharmaceutical industry (Merck Research Laboratories, Oss). In 2016 he founded the department of Molecular Physiology, which is embedded in the Chemical Biology division of Leiden University and the NWO Gravity Institute of Chemical Immunology. His research interests are focused on the design, synthesis and application of chemical tools in lipid and kinase signaling in neurodegenerative diseases and cancer. The group has developed strong expertise in organic synthesis, molecular biology, enzymology, activity-based protein profiling, drug discovery and chemical proteomics, enabling the discovery and optimization of new molecules to study biological processes in the brain and cancer cells. Specifically, his group is worldwide recognized for the discovery and profiling of modulators of the endocannabinoid system in the brain. Using chemical proteomics his group revealed the off-target profile of the covalent, irreversible FAAH inhibitor BIA 10-2474 that killed a healthy volunteer in a clinical phase 1 study in France (Van Esbroeck et al., Science, 2017; Van Rooden et al., Nature Prot, 2018). In addition, his group developed the first brain active inhibitors of endocannabinoid biosynthesis, which were shown to possess anti-neuroinflammatory properties (Ogasawara et al., PNAS, 2016). The discovery of drug candidates to treat neuroinflammation and cancer are high on the group's wish list.

### • EDUCATION

2002            PhD (cum laude, top 5%); Bio-organic Chemistry, Utrecht University (NL)  
1998            Master; Chemistry (cum laude), Utrecht University (NL)

### • CURRENT POSITION(S)

2019 – now    Senior Investigator, Onco Institute  
2017 – now    Full professor and chair of Molecular Physiology, Leiden University (NL)

### • PREVIOUS POSITIONS

2012 – 2017   Associate professor of Medicinal Chemistry, Leiden University (NL)  
2004 – 2012   Group- and project leader, Merck Research Laboratories (former Organon)  
2003 – 2004   Post-doctoral fellow, Institute for Bio-molecular Chemistry (Italy)

- **Selection of FELLOWSHIPS AND AWARDS**

- 2019 Elected member Oncode Institute
- 2018 VICI-grant NWO (Netherlands Science Foundation)
- 2017 Prix Galien Research for best preclinical drug discovery research in the Netherlands
- 2017 Young Investigator Award of the International Cannabinoid Research Society
- 2005 Young Investigator Award of the International Association for Cannabis as Medicine
- 2003 Young Investigator Award (European Society for Neuroscience)
- 2001 Coy W. Waller Award (ICRS, Spain)

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS**

- 2012 – now 6 Postdocs / 24 PhD-students / 40 Master students  
Department of Molecular Physiology, Leiden University (NL)  
(10 PhD awarded)

- **TEACHING ACTIVITIES**

- 2012 – now Advanced Medicinal Chemistry (35 students/year); Chemical Biology (120 students/year); Honours class (10 students/year); Bachelor research projects (10 students/year), Master research projects (10 students/year),
- 2019 Visiting Professor in Medicinal Chemistry, University of Rome (Italy)

- **Selection of ORGANISATION OF SCIENTIFIC MEETINGS**

- 2020 Co-organizer of the first Medicinal Chemistry & Chemical Biology Symposium, KNCV, Eindhoven
- 2019 Elected (vice)-chair of the Gordon Research Conference on Cannabinoid Function in the CNS (2021-2023)
- 2018 Organizer Symposium of the International Cannabinoid Research Society (550 participants; 33 countries) in Leiden
- 2016 Member program committee of CHAINS, 1500 participants, largest chemistry conference in the Netherlands

- **Selection of INSTITUTIONAL RESPONSIBILITIES**

- 2016 – now Chair of Molecular Physiology, Leiden Institute of Chemistry, Leiden University
- 2016 – now Member exam committee, Life Science & Technology, Leiden University
- 2014 – now Board member Cell Observatory
- 2013 – 2018 Coordinator Faculty Profiling Programme “Endocannabinoids”

- **Selection of REVIEWING ACTIVITIES**

- 2018 – now Concise guide to pharmacology, British Pharmacological Society, Endocannabinoid section reviewer,
- 2014 – now Scientific advisor Hoffman-LaRoche and small biotech companies
- 2013 – now Member of several management committees (e.g. CDDI, European Lead Factory, Oncode)
- 2012 – now Reviewer for various scientific societies (e.g. NWO, Belgium, Finland, Israel, Canada)
- 2002 – now Reviewer for many scientific journals (e.g. ACS, Wiley-VCH, RSC, Elsevier and NPG journals)

- **Selection of (INTER)NATIONAL LEADERSHIP**

- 2019 – now Board member Research Management Committee Oncode Institute
- 2019 – 2023 (Vice-)Chair Gordon Research Conference on Cannabinoid Function in CNS
- 2018 – now Board member NWO Werkgeenschapscommissie Chemistry of Life
- 2016 Member organizational committee CHAINS 2016
- 2016 – now Board member of the Havinga Foundation
- 2015 – 2018 Board Member studygroup Farmacochemistry of Netherlands Science Foundation
- 2014 – 2018 Chairman of Cancer Drug Discovery Initiative
- 2013 – 2018 Founding member European Lead Factory

- **MAJOR COLLABORATIONS**

- Oncode Institute
- Institute of Chemical Immunology (NWO Gravity program)
- My group has extensive contacts, collaborations and joint publications with industrial partners including, but not limited to: Hoffman-LaRoche (Switzerland), GSK (UK), Mercachem-Syncom (NL), NTRC (NL), Covalution Bioscience (NL)
- My group has collaborations and joint publications with international academic partners, but not limited to: the Scripps Research Institute (USA), Yale University (USA), Hotchkiss Brain Institute (Canada), Virginia Commonwealth University (USA), National Institute of Health (Bethesda, USA), ETH (Switzerland)
- Joint chemical biology PhD-program with prof.dr. H. Overkleeft and Prof. dr. H. Aerts (UL)
- Joint drug discovery PhD-program with Leiden University Medical Center (LUMC)
- Several joint projects & publications with the Netherlands Cancer Institute, Amsterdam Medical Center and Utrecht Medical Center

- **VALORIZATION**

- Co-inventor of patents licensed to Abide Therapeutics and Lycera
- Co-inventor of patents filed by Organon & Merck Research Laboratories

- **FUNDING**

*Personal grants*

- 2019 – 2022 Senior Investigator Oncode (€ 1.0M)
- 2018 - 2022 VICI-award (€ 1.5M) from NWO

### *Netherlands Organisation for Scientific Research (NWO) grants*

2018 - 2022 TTW – Navistroke, co-PI with Prof. dr. W. Mulder (AMC) and others  
2018 - 2022 TTW- NACTAR, co-PI with Prof. dr. T. Ottenhof (LUMC) and others  
2016 ZonMW, middelgroot, co-PI with Dr. R. Pannu (UL) and others  
2015 - 2019 OncoDrugs, New Chemical Innovations, Topsector Chemistry, lead PI  
2014 - 2019 ECHO (NWO-Chemical Sciences)  
2013 - 2018 ECHO-STIP (NWO-Chemical Sciences)

### *Industrial & other (inter)national collaborations*

2020 - 2021 Roche ROADS program  
2018 - 2019 Dutch Arthritis Foundation, co-PI with Prof. dr. R. Toes (LUMC)  
2016 - 2020 Roche  
2015 - 2017 Roche Post-doc Fellowship Programme, co-PI with Prof. dr. IJzerman (UL)  
2013 - 2019 Institute of Chemical Immunology, Gravitation Program, participant  
2013 - 2018 Innovative Medicines Initiative - European Lead Factory, co-founder & participant

### • 5 KEY PUBLICATIONS (chronological order)

Koenders, S.T.A, Wijaya, L.S., Erkelens, M.N., Bakker, A.T., Van der Noord, V.A., Van Rooden, E.J., Burggraaff, L., Putter, P.C., Botter, E., Wals, K., Van den Elst, H., Den Dulk, H., Florea, B.I, Van de Water, B., Van Westen, G.P.J., Mebius, R.E., Overkleeft, H.S., Le Dévédec, S.E. and **Van der Stelt, M.** Development of a retinal-based probe for the profiling of retinaldehyde dehydrogenases in cancer cells., *ACS. Central Sci.*, **2019**, *in press*

*This paper describes the first-in-class activity-based probe that visualizes and quantifies aldehyde dehydrogenases, a family of drug targets that function as biomarkers for cancer (stem) cells.*

Soethoudt, M.; Stolze, S. C.; Westphal, M. V.; van Stralen, L.; Martella, A.; van Rooden, E. J.; Guba, W.; Varga, Z. V.; Deng, H.; van Kasteren, S. I.; Grether, U.; AP, I. J.; Pacher, P.; Carreira, E. M.; Overkleeft, H. S.; Ioan-Facsinay, A.; Heitman, L. H.; **van der Stelt, M.**, Selective Photoaffinity Probe That Enables Assessment of Cannabinoid CB2 Receptor Expression and Ligand Engagement in Human Cells. *J Am Chem Soc*, **140**, 6067-6075 (2018)

*This paper describes the first bifunctional, photoreactive GPCR-probe that visualizes the cannabinoid CB2 receptor on primary human immune cells. The paper was selected by the JACS editors to feature in the "Spotlights".*

van Rooden, E. J.; Florea, B. I.; Deng, H.; Baggelaar, M. P.; van Esbroeck, A. C. M.; Zhou, J.; Overkleeft, H. S.; **van der Stelt, M.**, Mapping in vivo target interaction profiles of covalent inhibitors using chemical proteomics with label-free quantification. *Nature Protoc*, **13**, 752-767 (2018)

*This paper describes a detailed method for label-free quantification of inhibitor-protein interaction landscapes in tissues using chemical proteomics.*

van Esbroeck, A. C. M.; Janssen, A. P. A.; Cognetta, A. B., 3rd; Ogasawara, D.; Shpak, G.; van der Kroeg, M.; Kantae, V.; Baggelaar, M. P.; de Vrij, F. M. S.; Deng, H.; Allara, M.; Fezza, F.; Lin, Z.; van der Wel, T.; Soethoudt, M.; Mock, E. D.; den Dulk, H.; Baak, I. L.; Florea, B. I.; Hendriks, G.; De Petrocellis, L.; Overkleeft, H. S.; Hankemeier, T.; De Zeeuw, C. I.; Di Marzo, V.; Maccarrone, M.; Cravatt, B. F.; Kushner, S. A.; **van der Stelt, M.**, Activity-based protein profiling reveals off-target proteins of the FAAH inhibitor BIA 10-2474. *Science*, **356**, 1084-1087 (2017)

*This paper is the first to show the off-target profile of the fatal FAAH inhibitor BIA 10-2474 that may potentially explain the molecular causes of the adverse neurological effects observed in human volunteers during a phase 1 clinical trial, which led to the death of one volunteer and hospitalization of four others in Rennes (France) in 2016. The paper generated comments in other journals and (social) media attention, including comments in Science, Nature Reviews Drug Discovery, Nature Chemical Biology, F1000, C&EN, Chemistry World, BioWorld, Le Figaro, NRC Handelsblad and Nemo Kennislink.nl; Altmetric attention score: 144 (top 5% of all research output scored by altmetric.com).*

Soethoudt, M.; Grether, U.; Fingerle, J.; Grim, T. W.; Fezza, F.; de Petrocellis, L.; Ullmer, C.; Rothenhausler, B.; Perret, C.; van Gils, N.; Finlay, D.; MacDonald, C.; Chicca, A.; Gens, M. D.; Stuart,

J.; de Vries, H.; Mastrangelo, N.; Xia, L.; Alachouzos, G.; Baggelaar, M. P.; Martella, A.; Mock, E. D.; Deng, H.; Heitman, L. H.; Connor, M.; Di Marzo, V.; Gertsch, J.; Lichtman, A. H.; Maccarrone, M.; Pacher, P.; Glass, M.; **van der Stelt, M.**, Cannabinoid CB2 receptor ligand profiling reveals biased signalling and off-target activity. *Nature Commun*, 8, 13958 (2017)

*In this paper the results are reported of a multinational collaboration that I coordinated with 13 academic and industry laboratories worldwide in which the most extended molecular pharmacology, off-target and pharmacokinetic profile of a set of 19 reference ligands of the cannabinoid CB2 and CB1 receptor have been determined. The paper reaches consensus on the best three selective CB2 ligands to be used in preclinical target validation studies. The paper generated (social) media attention, including an animation made by the Netherlands public broadcasting organisation (NOSop3) published on Twitter (<https://t.co/VmPASom2d?ssr=true>) and an article on *newscientist.nl*. Altmetric attention score: 88 (top 5% of all research output scored by altmetric.com).*

Ogasawara, D.; Deng, H.; Viader, A.; Baggelaar, M. P.; Breman, A.; den Dulk, H.; van den Nieuwendijk, A. M.; Soethoudt, M.; van der Wel, T.; Zhou, J.; Overkleeft, H. S.; Sanchez-Alavez, M.; Mo, S.; Nguyen, W.; Conti, B.; Liu, X.; Chen, Y.; Liu, Q. S.; Cravatt, B. F.; **van der Stelt, M.**, Rapid and profound rewiring of brain lipid signalling networks by acute diacylglycerol lipase inhibition. *Proc. Natl. Acad. Sci. USA*, 113, 26-33 (2016)

*This paper describes the first CNS-active DAGL inhibitors that can be used to block endocannabinoid biosynthesis in the brain. Using these inhibitors it was also found that arachidonic acid and pro-inflammatory prostaglandins pools are derived from diacylglycerol and dependent on DAGL activity. DAGL was found to have a short half life (< 4h). The inhibitors described in this paper are currently used by the scientific community to investigate the role of DAGL in food intake and various neurological and neuroinflammatory conditions (e.g. Bluett et al., *Nature Comm.*, 2017; Deng et al., *J. Med. Chem*, 2017).*

- **TOP-5 INVITED PRESENTATIONS (chronological order)**

1. Gordon Research Conference on Cannabinoids, Barcelona, Spain, 2019
2. Young Investigator Award Lecture ICRS, Leiden, The Netherlands, 2018
3. International Singapore Lipid Symposium, Singapore, 2018
4. Gordon Research Conference on Cannabinoids, Waterville, USA, 2015 & 2017
5. European Federation of Medicinal Chemistry, Manchester, UK, 2016

- **KEY OUTPUT PARAMETERS**

Total Publications: 100

h-index: 32

Average citations per item: 57 (17 articles > 100 citations)

Sum of times cited: 5701

Science (2x), Nature Comm. (2x), ACS Cent. Sci. (1x), Nature Protoc. (1x), PNAS (2x), EMBO J. (1x), JACS (3x), Angew. Chemie (2x), J. Neurosci. (3x), J. Med. Chem (13x)

Book chapters: 3

Patent applications: 8

- **Selection of Awards for my PhD-students**

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|------|--|
| 2019 | T. van der Wel, best oral presentation at the Dutch Medicine Days (FIGON), Leiden, NL      |
| 2019 | M. Baggelaar, best thesis in Medicinal Chemistry in the Netherlands (2016-2018)            |
| 2019 | A. Janssen, JACS poster prize, ABPP-symposium, Leuven, Belgium                             |
| 2019 | B. Gagestein, poster prize, ICI-symposium, Amsterdam, NL                                   |
| 2018 | A. Janssen, public prize Young European Medicinal Chemist Symposium, EFMC, Slovenia        |
| 2018 | T. van der Wel, best poster presentation, EMBL Chemical Biology meeting, Germany           |
| 2018 | M. Jiang, best poster presentation at the ICRS meeting, Leiden, The Netherlands            |
| 2017 | A. Janssen, best oral presentation at the Dutch Medicine Days (FIGON), Ede, (NL)           |
| 2017 | A. van Esbroeck, best oral presentation at the British Pharmacological Society Meeting, UK |
| 2017 | A. van Esbroeck, best oral presentation at the ICRS meeting, Montreal, Canada              |
| 2016 | M. Baggelaar, Marie Curie Fellowship   |
| 2016 | F. Janssen, Young European Medicinal Chemist of the Year, EFMC, Manchester, UK             |