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Chemical tools to monitor and control human proteasome activities

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Citation

Bruin, G. de. (2016, June 1). *Chemical tools to monitor and control human proteasome activities*. Retrieved from <https://hdl.handle.net/1887/39834>

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Author: Bruin, G. de

Title: Chemical tools to monitor and control human proteasome activities

Issue Date: 2016-06-01

List of publications

- 1. Proteasome subunit selective activity-based probes report on proteasome core particle composition in a native-PAGE FRET assay**
de Bruin, G.; Florea, B.I.; Overkleeft, H.S.; *manuscript in preparation.*
- 2. Structure-based design of β 5c selective inhibitors of human constitutive proteasomes**
Xin, B.T.; de Bruin, G.; Huber, E. M.; Besse, A.; Florea, B.I.; Filippov, D.V.; van der Marel, G.A.; Kisselev, A.F; van der Stelt, M.; Driessen, C.; Groll, M.; Overkleeft, H. S.; *manuscript in preparation.*
- 3. Towards β 2 selective inhibitors with reduced basicity**
de Bruin, G.; Wesseling, C.M.J.; Ward, D.J.; van Rooden, E.J.; Florea, B.I.; van der Marel, G. A. Overkleeft, H.S.; *manuscript in preparation.*
- 4. Tools and strategies to monitor and quantify proteasome activities**
de Bruin, G.; Florea, B.I.; Overkleeft, H.S.; *manuscript in preparation.*
- 5. Enantioselective synthesis of adamantylalanine and carboranylalanine and their incorporation into the proteasome inhibitor bortezomib**
de Bruin, G.; Mock, E.; Hoogendoorn, S.; van den Nieuwendijk, A. M. C. H.; Mazurek, J.; van der Marel, G. A.; Florea, B. I.; Overkleeft, H. S., *Chemical Communications* **2016**, 52 (21), 4064-4067.
- 6. 5-Methylpyridin-2-one into peptide vinyl sulfones and peptide epoxyketones is detrimental for proteasome inhibition**
Xin, B.-T.; de Bruin, G.; Plomp, J.-W.; Florea, B. I.; van der Marel, G. A.; Overkleeft, H. S., *European Journal of Organic Chemistry* **2016**, 6, 1132-1144.

7. **A set of activity-based probes to visualize human (immuno)proteasome activities**
de Bruin, G.; Xin, B. T.; Kraus, M.; van der Stelt, M.; van der Marel, G. A.; Kisselev, A. F.; Driessen, C.; Florea, B. I.; Overkleeft, H. S., *Angewandte Chemistry International Edition* **2016**, 55 (13), 4199-4203.

8. **Systematic analyses of substrate preferences of 20S proteasomes using peptidic epoxyketone inhibitors**
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9. **The novel β 2-selective proteasome inhibitor LU-102 decreases phosphorylation of I kappa B and induces highly synergistic cytotoxicity in combination with ibrutinib in multiple myeloma cells**
Kraus, J.; Kraus, M.; Liu, N.; Besse, L.; Bader, J.; Geurink, P.; de Bruin, G.; Kisselev, A.; Overkleeft, H.; Driessen, C., *Cancer Chemotherapy and Pharmacology*, **2015**, 76 (2), 383-396.

10. **The novel β 2-selective proteasome inhibitor LU-102 synergizes with bortezomib and carfilzomib to overcome proteasome inhibitor resistance of myeloma cells**
Kraus, M.; Bader, J.; Geurink, P. P.; Weyburne, E. S.; Mirabella, A. C.; Silzle, T.; Shabaneh, T. B.; van der Linden, W. A.; de Bruin, G.; Haile, S. R.; van Rooden, E.; Appenzeller, C.; Li, N.; Kisselev, A. F.; Overkleeft, H.; Driessen, C., *Haematologica* **2015**, 100 (10), 1350–1360

11. **Structure-based design of β 1i or β 5i specific inhibitors of human immunoproteasomes**
de Bruin, G.; Huber, E. M.; Xin, B.-T.; van Rooden, E. J.; Al-Ayed, K.; Kim, K.-B.; Kisselev, A. F.; Driessen, C.; van der Stelt, M.; van der Marel, G. A.; Groll, M.; Overkleeft, H. S., *Journal of Medicinal Chemistry* **2014**, 57 (14), 6197-6209.

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13. **Activity-based proteasome profiling in medicinal chemistry and chemical biology**
de Bruin, G.; Li, N.; Paniagua, G.; Willems, L.; Xin, B.-T.; Verdoes, M.; Geurink, P.; Linden, W. v. d.; Stelt, M. v. d.; Marel, G. v. d.; Overkleeft, H.; Florea, B., *In Concepts and Case Studies in Chemical Biology*, Wiley-VCH Verlag GmbH & Co. KGaA, **2014**, 177-190

14. Proteasome inhibitors with photocontrolled activity

Hansen, M. J.; Velema, W. A.; de Bruin, G.; Overkleeft, H. S.; Szymanski, W.; Feringa, B. L., *ChemBioChem* **2014**, 15 (14), 2053-2057.

15. Exploring dual electrophiles in peptide-based proteasome inhibitors: carbonyls and epoxides

Xin, B.-T.; de Bruin, G.; Verdoes, M.; Filippov, D. V.; van der Marel, G. A.; Overkleeft, H. S., *Organic & Biomolecular Chemistry* **2014**, 12 (30), 5710-5718.

16. A combined solid- and solution-phase approach provides convenient access to analogues of the calcium-dependent lipopeptide antibiotics

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18. Incorporation of non-natural amino acids improves cell permeability and potency of specific inhibitors of proteasome trypsin-like sites

Geurink, P. P.; van der Linden, W. A.; Mirabella, A. C.; Gallastegui, N.; de Bruin, G.; Blom, A. E. M.; Voges, M. J.; Mock, E. D.; Florea, B. I.; van der Marel, G. A.; Driessen, C.; van der Stelt, M.; Groll, M.; Overkleeft, H. S.; Kisselev, A. F., *Journal of Medicinal Chemistry* **2013**, 56 (3), 1262-1275.

19. A concise preparation of the non-proteinogenic amino acid L-kynurenine

Kleijn, L. H. J.; Müskens, F. M.; Oppedijk, S. F.; de Bruin, G.; Martin, N. I., *Tetrahedron Letters* **2012**, 53 (47), 6430-6432.

Curriculum Vitae

Nederlands

Gerjan de Bruin werd geboren op 7 januari 1988 te Nunspeet. Hij behaalde in 2006 het Gymnasium diploma (profiel Natuur & Gezondheid) aan de 'Jacobus Fruijtjer Scholengemeenschap' te Apeldoorn. In datzelfde jaar begon hij aan de bachelor opleiding Scheikunde aan de Universiteit van Utrecht, welke hij in 2009 *cum laude* afrondde. Tijdens de bachelor opleiding heeft hij zich gespecialiseerd in de richting van organische chemie en biochemie.

In 2009 begon hij met de master *Drug Innovation* aan de Universiteit van Utrecht, in het kader waarvan hij twee onderzoekstages voltooide. Het *major research project* voerde hij uit onder de supervisie van dr. N.I. Martin en prof. dr. R.M.J. Liskamp in de vakgroep *Medicinal Chemistry & Chemical Biology* in Utrecht. Tijdens dit onderzoek synthetiseerde hij verschillende cyclische peptiden en onnatuurlijk aminozuren met als doel het ophelderen van het werkingsmechanisme van het peptidisch antibioticum daptomycine. Het *minor research project* heeft hij gedaan bij het Nederlands Kanker Instituut (NKI) in de vakgroep *Cell Biology II* onder de supervisie van dr. R. Merkx en prof. dr. H. Ovaa. In dit onderzoek werd de synthese van di-ubiquitine moleculen door middel van natieve chemische ligatie geoptimaliseerd. In 2011 behaalde hij het Master of Science diploma *cum laude*.

In september 2011 begon hij als promovendus aan de Universiteit Leiden in de vakgroep Bio-organische Synthese. Het onderzoek vond plaats onder supervisie van prof. dr. H.S. Overkleeft, prof. dr. G.A. van der Marel en dr. B.I. Florea. Op verschillende nationale en internationale conferenties werden delen van het onderzoek gepresenteerd. Zo gaf hij mondelinge presentaties op de COST *Chemical Proteomics Meeting* in Berlijn (Duitsland, 2013) en Oxford (Engeland, 2015), op het *Dutch Peptide Symposium* in Utrecht (2014) en op de nationale chemische conferentie CHAINS in Veldhoven (2015). Binnen de Universiteit Leiden gaf hij presentaties als onderdeel van de *Chemical Biology Lectures* (2015) en *This Weeks Discoveries* (2016). In 2015 werd hij genomineerd als 'Onderzoeker van het Jaar' van de Faculteit der Wiskunde en Natuurwetenschappen van de Universiteit Leiden.

Curriculum Vitae

English

Gerjan de Bruin was born on January 7th 1988 in Nunspeet, the Netherlands. He obtained his high school diploma (Gymnasium) at the 'Jacobus Fruijtier Scholengemeenschap' in Apeldoorn (major Nature & Health) in 2006. In the same year he started with the bachelor's program Chemistry at Utrecht University, which he completed with distinction in 2009. During the bachelor education he specialized in organic chemistry and biochemistry.

In 2009 he started the master's program Drug Innovation at Utrecht University, as part of which he did two research internships. He performed his Major Research Project under the supervision of dr. N.I. Martin and prof. dr. R.M.J. Liskamp in the group of Medicinal Chemistry & Chemical Biology. During this research he synthesized several cyclic peptides and unnatural amino acids with the aim to elucidate the mechanism of action of the peptidic antibiotic daptomycin. Subsequently, he performed his Minor Research Project at the Dutch Cancer Institute (NKI) in the Cell Biology II group under the supervision of dr. R. Merckx and prof. dr. H. Ovaas. In this research the synthesis of di-ubiquitins via native chemical ligation was optimized. In 2011 he obtained his Master of Science degree with distinction.

In September 2011, he started as PhD-student at Leiden University in the Bio-organic Synthesis group. The research was conducted under the supervision of prof. dr. H.S. Overkleeft, prof. dr. G.A. van der Marel and dr. B.I. Florea. Parts of the research have been presented on various conferences. He gave oral presentations at the COST Chemical Proteomics Meeting in Berlin (Germany, 2013) and Oxford (England, 2015), at the Dutch Peptide Symposium in Utrecht (2014) and at the Dutch national chemistry conference CHAINS in Veldhoven (2015). At Leiden University, he gave presentations as part of the Chemical Biology Lectures (2015) and This Week's Discoveries (2016). In 2015 he was nominated as 'Researcher of the Year' of the Faculty of Science of Leiden University.