Personal details

Name: Steven H. L. Verhelst
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Education

2004 – present Post-doctoral training (chemical biology), Stanford University, School of Medicine (California, USA).

1999 – 2004 PhD (chemistry), Leiden University (Leiden, The Netherlands).

1994 – 1999 M.Sc. (chemistry), *cum laude*, Leiden University (Leiden, The Netherlands).

Research experience

2004 – present Post-doctoral fellow at the Department of Pathology of the Stanford University School of Medicine in the group of Dr. M. Bogyo. The development and evaluation of small molecule research tools for cysteine and serine proteases.

1999 –2004 PhD research at Leiden Institute of Chemistry in co-operation with Organon/Akzo-Nobel, with Prof. Dr. J.H. van Boom, Prof. Dr. C. A. A. van Boeckel and Dr. G. A. van der Marel. The development of novel aminoglycoside antibiotics.

1998 – 1999 Internship at the Harvard Medical School, Department of Immunology, with Prof. Dr. H. L. Ploegh. The synthesis and evaluation of inhibitors for the proteasome and cysteine proteases.

1997 – 1998 Internship at the Leiden Institute of Chemistry, in the group of Prof. Dr. J. H. van Boom (bio-organic synthesis), under supervision of Dr. H. S. Overkleeft. The synthesis of sugar amino acids as conformational restricted dipeptide isosters. Awarded with the Unilever Research Prize 1998.

Research interests

My research focuses on the development and application of small molecule probes to detect the activity and to study the biological role of cysteine and serine proteases.

My immediate future plans deal with rhomboids, a recently discovered class of intramembrane serine proteases, for which no small molecule research tools are available. I plan on using an interdisciplinary approach, combining synthetic organic chemistry, biochemistry and cell biology, to develop small molecule probes specifically targeting rhomboids and to validate this class of proteases as a potential drug target.

In the long term, I plan to extend the chemical strategies developed for rhomboids to other intramembrane proteases as well as to soluble serine proteases. Ultimately, I aim to create a line of research that chemically maps proteolytic pathways involving these proteases, discover their importance in pathological events, and determine if they are suitable targets for the development of novel drug therapies.

Awards, fellowships and honors

2006	Quantitative Chemical Biology Training Grant, Stanford University, Department of Chemical and Systems Biology.
2004	TALENT postdoctoral fellowship, Netherlands Organisation for Scientific Research (NWO).
2003	Fellinga Fund travel stipend, KNCV (Royal Dutch Chemical Society).
1999	*Cum Laude* for achievements in Master's program, Leiden University.
1998	Unilever Research Prize, awarded for the research conducted as an undergraduate at the laboratory of Prof. Dr. J. H. van Boom.
1998	LUSTRA travel stipend, Leiden University.
1998	Stipend from LUF (Leiden University Fund) for an internship at Harvard Medical School.

Teaching experience

2003	Molecular Recognition, problem-based practical undergraduate project; instructor.
2002	Organic Chemistry I, undergraduate course; teaching assistant.
2001 – 2003	Organic Synthesis, practical organic chemistry undergraduate course; instructor.
2000 – 2001	Reaction Kinetics, practical physical chemistry undergraduate course; instructor.

Courses

2006	Scientific Management – Stanford University.
2005	Instruction to Teaching and Presentation Skills – Stanford University Center for Teaching and Learning.
2001	Bio-organic Synthesis – course by Holland Research School of Molecular Chemistry.
1998	Working with Radio-isotopes – Harvard Medical School.
1997	Science & Journalism – course by the Dutch Royal Chemical Society (KNCV).

Lectures and presentations

2007	Seminar, Penn Center for Molecular Discovery, University of Pennsylvania.
2007	Oral presentation, Pacific Coast Protease meeting, California.
2006	Seminar, Medicinal Chemistry Department, Utrecht University, Utrecht, The Netherlands.
2006	Seminar, Chemistry of Biopolymers Department, Technische Universität München, Munich, Germany.
2006	Oral presentation, Stanford Mass Spectrometry Users Meeting, Stanford, California.
2006	Oral presentation, Pacific Coast Protease Workshop, Palm Springs, California.
2005	Oral presentation, Stanford Department of Pathology, Monterey, California.
2004	Oral presentation, Pacific Protease Workshop, Half Moon Bay, California.
2003	Seminar Bio-organic Synthesis, Institute for Organic Chemistry, Universität Münster, Münster, Germany.
2002	Oral presentation, Leiden/Amsterdam Center for Drug Research.

List of publications

23. Fonovic, M.; **Verhelst, S. H. L.**; Sorum, M. T.; Bogyo, M. Proteomic evaluation of chemically cleavable activity based probes. *Mol. Cell. Proteomics*, in press.

22. Sadaghiani, A. M.; **Verhelst, S. H. L.**; Gocheva, V.; Hill, K.; Majerova, E.; Stinson, S.; Joyce, J. A.; Bogyo, M. (2007) Design, synthesis and evaluation of *in vivo* potency and selectivity of epoxysuccinyl-based inhibitors of papain family cysteine proteases. *Chem. Biol.*, 14: 499-511.

21. Cuerrier, D.; Moldoveanu, T.; Campbell, R. L.; Kelly, J.; Yoruk, B.; **Verhelst, S. H. L.** ; Greenbaum, D.; Bogyo, M.; Davies, P. L. (2007) Development of calpain-specific inactivators by screening of positional-scanning epoxide libraries. *J. Biol. Chem.*, 282: 9600-9611.

20. **Verhelst, S. H. L.**; Fonovic, M.; Bogyo, M. (2007) A mild chemically cleavable linker system for functional proteomic applications. *Angew. Chem. Int. Ed.,* 46: 1284-1286.

19. Sexton, K. B.; Kato, D.; Berger, A.; Fonovic, M.; **Verhelst, S. H. L.**; Bogyo, M. (2007) Specificity of aza-peptide electrophile activity-based probes of caspases. *Cell Death Differ.*, 14: 727-732.

18. Sadaghiani, A. M.; **Verhelst, S. H. L.**; Bogyo, M. (2007) Tagging and detection strategies for activity-based proteomics. *Curr. Opin. Chem. Biol.*, 11: 20-28.

17. Sadaghiani, A. M.; **Verhelst, S. H. L.**; Bogyo, M. (2006) Solid phase methods for the preparation of epoxysuccinate-based inhibitors of cysteine proteases. *J. Comb. Chem.*, 8: 802-804.

16. Yuan, F.; **Verhelst, S. H. L.**; Blum, G.; Coussens, L. M.; Bogyo, M. (2006) A selective activity-based probe for the papain family cysteine protease dipeptidyl peptidase I/cathepsin C. *J. Am. Chem. Soc.*, 128: 5616-5617.

15. **Verhelst, S. H. L.**; Witte, M. D.; Arastu-Kapur, S.; Fonovic, M.; Bogyo, M. (2006) Novel aza peptide inhibitors and active site probes of papain family cysteine proteases. *ChemBioChem*, 7: 943-950.

14. Kato, D.;[*] **Verhelst, S. H. L.**;[*] Sexton, K. B.; Bogyo, M. (2005) A general solid phase method for the preparation of diverse azapeptide probes directed against cysteine proteases. *Org. Lett.*, 7: 5649-5652. [*] equal authorship.

13. Timmer, M. S. M.; **Verhelst, S. H. L.**; Grotenbreg, G. M.; Overhand, M.; Overkleeft, H. S. (2005) Carbohydrates as versatile platforms in the construction of small compound libraries. *Pure & Applied Chem.*, 77: 1173-1182.

12. **Verhelst, S. H. L**.; Bogyo, M. (2005) Solid phase synthesis of double headed epoxysuccinyl activity based probes for selective targeting of papain family cysteine proteases. *ChemBioChem*, 6: 824-827.

11. **Verhelst, S. H. L.**; Bogyo, M. (2005) Dissecting protein function using chemical proteomic methods. *QSAR Comb. Sci.*, 24: 261-269.

10. **Verhelst, S. H. L.**; Bogyo, M. (2005) Chemical proteomics applied to target identification and drug discovery. *Biotechniques*, 38: 175-177.

9. Chehade, K. A. H.; Baruch, A.; **Verhelst, S. H. L.**, Bogyo, M. (2005) An improved preparation of the activity-based probe JPM-OEt and in situ applications. *Synthesis*, 240-244.

8. **Verhelst, S. H. L.**; Magnée, L.; Wennekes, T.; Wiedenhof, W.; Van der Marel, G. A.; Overkleeft, H. S.; Van Boeckel, C. A. A.; Van Boom, J. H. (2004) Glycosylation of cyclitols: novel analogs of aminoglycoside antibiotics. *Eur. J. Org. Chem.* 11: 2404-2410.

7. **Verhelst, S. H. L.**; Michiels, P. J. A.; Van der Marel, G. A.; Van Boeckel, C. A. A.; Van Boom, J. H. (2004) Surface plasmon resonance evaluation of various aminoglycoside – RNA hairpin interactions reveals low degree of selectivity. *ChemBioChem,* 5: 937-942.

6. **Verhelst, S. H. L.**; Wennekes, T.; Van der Marel, G. A.; Overkleeft, H. S.; Van Boeckel, C. A. A.; Van Boom, J. H. (2004) Synthesis of orthogonally protected 2-deoxystreptamine stereoisomers. *Tetrahedron* 60: 2813-2822.

5. **Verhelst, S. H. L.**; Paez Martinez, B.; Timmer, M. S. M.; Lodder, G.; Van der Marel, G. A.; Overkleeft, H. S.; Van Boom, J. H. (2003) A short chiral route towards polyhydroxylated indolizidines and quinolizidines. *J. Org. Chem.* 68: 9598-9603.

4. **Verhelst, S. H. L.**; Wiedenhof, W.; Ovaa, H.; Van der Marel, G. A.; Overkleeft, H. S.; Van Boeckel, C. A. A.; Van Boom, J. H. (2002) A stereoselective route towards highly functionalized 4,6-diaminocyclohexene derivatives. *Tetrahedron Lett*. 43: 6451-6455.

3. Shi, G. P.; Bryant, R. A. R.; Riese, R.; **Verhelst, S.**; Driessen, C.; Li, Z. Q.; Brömme, D.; Ploegh, H. L.; Chapman, H. A. (2000) Role for cathepsin F in invariant chain processing and major histocompatability complex class II peptide loading by macrophages. *J. Exp. Med.* 191: 1177-1185.

2. Bogyo, M.; **Verhelst, S.**; Bellingard-Dubouchaud, V.; Toba, S.; Greenbaum, D. (2000) Selective targeting of lysosomal cysteine proteases with radiolabeled electrophilic substrate analogs. *Chem. Biol*. 7: 27-38.

1. Overkleeft, H. S.; **Verhelst, S. H. L.**; Pieterman, E.; Meeuwenoord, N. J.; Overhand, M.; Cohen, L. H.; Van der Marel, G. A.; Van Boom, J. H. (1999) Design and synthesis of a protein: farnesyltransferase inhibitor based on sugar amino acids. *Tetrahedron Lett.* 40: 4103-4106.

Submitted/ In preparation

Kaschani, F.; **Verhelst, S. H. L**.; Van Swieten, P. F.; Wang, Z.; Kaiser, M.; Overkleeft, H. S.; Bogyo, M.; Van der Hoorn, R. A. L. Minitags for small molecules: visualising targets of small molecules in living plant tissues by using click-chemistry. *Submitted to Plant Physiology*.

Burster, T.; Marin-Esteban, V.; Boehm, B. O.; Rotzschke, O.; Falk, K.; Weber, E.; **Verhelst, S. H. L.**; Overkleeft, H.; Kalbacher, H.; Driessen, C. Design of protease-resistant myelin basic protein-derived peptides by cleavage site directed amino acid substitutions. *Submitted to Biochem. Pharm.*

Patents

Bogyo, M.; **Verhelst, S. H. L.**; Fonovic, M. A mild chemically cleavable linker for use in affinity purification and proteomics applications. Provisional patent, July 2006.

Bogyo, M.; Sadaghiani, A. M.; **Verhelst, S. H. L.** Design and Synthesis of epoxysuccinyl inhibitors of cysteine cathepsins for cancer chemotherapy. Provisional patent, November 2005.

Bogyo, M.; **Verhelst, S. H. L**. Solid-Phase Synthesis of Small Molecule Inhibitors of Cathepsin Cysteine Proteases. US patent, no US-2006-0154325-A1, Int. patent, no WO 2006/074466.

Overkleeft, H. S.; **Verhelst, S. H. L.**; Meeuwenoord, N. J.; Pieterman, E. J.; Cohen, L. H.; Overhand, M.; Van der Marel, G. A.; Van Boom, J. H. Novel protein: prenyl transferase inhibitors. European patent, no EP1028117.