BIOGRAPHICAL SKETCH

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NAME Ploegh, Hidde	POSITION TITLE Member, The Whitehead Institute for Biomedical Research
eRA COMMONS USER NAME Hidde Ploegh	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
State University of Grogningen, The Netherlands	B.Sc.	1975	Biology
State University of Grogningen, The Netherlands	M Sc.	1977	Biology & Chemistry
State University of Leiden, The Netherlands	Ph.D.	1981	Biochemistry

A. Positions and Honors.

Positions and Employment

1977 - 1980 Research Assistant, Harvard University
1979 - 1980 Tutor in Biochemical Sciences, Harvard University
1981 - 1984 Staff Scientist, Institute of Genetics, University of Cologne (Germany)
1984 - 1992 Staff Scientist, The Netherlands Cancer Institute
1986 - 1992 Head of Department of Cellular Biochemistry, Netherlands Cancer Institute,
1990 - 1992 Professor of Oncobiochemistry, Free University, Amsterdam
1992 - 1997 Professor of Biology, Center for Cancer Research and Dept. of Biology, MIT, Cambridge MA
1997 - 2005 Mallinckrodt Professor of Immunopathology, Harvard Medical School, Boston, MA
1997- 2005 Director of the Graduate Program in Immunology, Harvard Medical School, Boston, MA
2005-present Member, The Whitehead Institute for Biomedical Research, Cambridge, MA
2005-present Professor of Biology, Massachusetts Institute of Technology, Cambridge, MA

Editorial boards:

1990-present European Journal of Immunology
1990-present Member of the Executive Committee,
1991-present Trends in Cell Biology,
1994-present Annual review of Cell and Developmental Biology
1992-present Journal of Experimental Medicine,
1994-present Immunity (editor until 1996),
1996-present Immunity member editorial board.

Honors and Awards

1981 Visiting Professor Etranger au Collège de France
1982 Litchfield Lecturer in Medical Sciences, Oxford University
1983 Annual prize Dutch Society for Biochemistry
1986 Elected Member EMBOVan Loghem Lecturer
1990 Dutch Society for Immunology,
1994 Ceppellini Lecturer, European Federation of Immunological Societies
1995 Elected Royal Dutch Academy of Sciences
1996 NIH MERIT award
1997 Lamb Professorship, Vanderbilt University
1998 Kroc Lecturer Medical University of South Carolina
1999 Avery Landsteiner Prize
2000 Fellow, American Academy of Arts and Sciences,
2001 Philip Levine Lecturer, Rockefeller University April 13, 2001
2001 Wellcome visiting Professor, Loyola University, 2001.

B. Selected peer-reviewed publications (from a total of 300)

Schott, E., R. Bonasio, and **H. L. Ploegh**. 2003. Elimination in vivo of developing T cells by natural killer cells. *J Exp Med 198:1213*.
Tirosh, B., M. H. Furman, D. Tortorella, and **H. L. Ploegh**. 2003. Protein unfolding is not a prerequisite for endoplasmic reticulum-to-cytosol dislocation. *J Biol Chem 278:6664*.
Blom, D., C. Hirsch, P. Stern, D. Tortorella, and **H. L. Ploegh**. 2004. A glycosylated type I membrane protein becomes cytosolic when peptide: N-glycanase is compromised. *Embo J 23:650*.
Boes, M., and **H. L. Ploegh**. 2004. Translating cell biology in vitro to immunity in vivo. *Nature 430:264*.
Boes, M., A. Cuvillier, and **H. Ploegh**. 2004. Membrane specializations and endosome maturation in dendritic cells and B cells. *Trends Cell Biol 14:175*.
Bryant, P., and **H. Ploegh**. 2004. Class II MHC peptide loading by the professionals. *Curr Opin Immunol 16:96*.
Catic, A., C. Collins, G. M. Church, and **H. L. Ploegh**. 2004. Preferred in vivo ubiquitination sites. *Bioinformatics 20:3302*.
Cohen, H. Y., S. Lavu, K. J. Bitterman, B. Hekking, T. A. Imahiyerobo, C. Miller, R. Frye, **H. Ploegh**, B. M. Kessler, and D. A. Sinclair. 2004. Acetylation of the C terminus of Ku70 by CBP and PCAF controls Bax-mediated apoptosis. *Mol Cell 13:627*.
Fiebiger, E., C. Hirsch, J. M. Vyas, E. Gordon, **H. L. Ploegh**, and D. Tortorella. 2004. Dissection of the dislocation pathway for type I membrane proteins with a new small molecule inhibitor, eeyarestatin. *Mol Biol Cell 15:1635.*
Gil-Torregrosa, B. C., A. M. Lennon-Dumenil, B. Kessler, P. Guermonprez, **H. L. Ploegh**, D. Fruci, P. van Endert, and S. Amigorena. 2004. Control of cross-presentation during dendritic cell maturation. *Eur J Immunol 34:398.*
Hang, H. C., and **H. Ploegh**. 2004. Catching proteases in action with microarrays. *Chem Biol 11:1328*.
Harrison, S. C., B. Alberts, E. Ehrenfeld, L. Enquist, H. Fineberg, S. L. McKnight, B. Moss, M. O'Donnell, **H. Ploegh**, S. L. Schmid, K. P. Walter, and J. Theriot. 2004. Discovery of antivirals against smallpox. *Proc Natl Acad Sci U S A 101:11178*.
Hemelaar, J., A. Borodovsky, B. M. Kessler, D. Reverter, J. Cook, N. Kolli, T. Gan-Erdene, K. D. Wilkinson, G. Gill, C. D. Lima, **H. L. Ploegh**, and H. Ovaa. 2004. Specific and covalent targeting of conjugating and deconjugating enzymes of ubiquitin-like proteins. *Mol Cell Biol 24:84*.
Hirsch, C., S. Misaghi, D. Blom, M. E. Pacold, and **H. L. Ploegh**. 2004. Yeast N-glycanase distinguishes between native and non-native glycoproteins. *EMBO Rep 5:201*.
Kattenhorn, L. M., R. Mills, M. Wagner, A. Lomsadze, V. Makeev, M. Borodovsky, **H. L. Ploegh**, and B. M. Kessler. 2004. Identification of proteins associated with murine cytomegalovirus virions. *J Virol 78:11187*.
Lilley, B.N., and H.L. Ploegh. 2004. A membrane protein required for dislocation of misfolded proteins from the ER. *Nature 429:834.*
Maehr, R., M Kraus, and H.L. Ploegh. 2004. Mice deficient in invariant-chain and MHC class II exhibit a normal mature B2 cell compartment. *Eur J Immunol 34:2230.*
Mintern, J. D., M. M. Maurice, **H. L. Ploegh**, and E. Schott. 2004. Thymic selection and peripheral activation of CD8 T cells by the same class I MHC/peptide complex. *J Immunol 172:699*.
Misaghi, S., M. E. Pacold, D. Blom, **H. L. Ploegh**, and G. A. Korbel. 2004. Using a small molecule inhibitor of Peptide: N-glycanase to probe its role in glycoprotein turnover. *Chem Biol 11:1677*.
Misaghi, S., Z. Y. Sun, P. Stern, R. Gaudet, G. Wagner, and **H. Ploegh**. 2004. Structural and functional analysis of human cytomegalovirus US3 protein. *J Virol 78:413.*.
Ovaa, H., B. M. Kessler, U. Rolen, P. J. Galardy, **H. L. Ploegh**, and M. G. Masucci. 2004. Activity-based ubiquitin-specific protease (USP) profiling of virus-infected and malignant human cells. *Proc Natl Acad Sci U S A 101:2253*.
Palliser, D., **H. Ploegh**, and M. Boes. 2004. Myeloid differentiation factor 88 is required for cross-priming in vivo. *J Immunol 172:3415.*
Ploegh, H. L. 2004. Immunology. Nothing 'gainst time's scythe can make defense. *Science 304:1262*.
Rohn, T. A., M. Boes, D. Wolters, S. Spindeldreher, B. Muller, H. Langen, **H. Ploegh**, A. B. Vogt, and H. Kropshofer. 2004. Upregulation of the CLIP self peptide on mature dendritic cells antagonizes T helper type 1 polarization. *Nat Immunol 5:909*.

Schmidt-Supprian, M., J. Tian, E. P. Grant, M. Pasparakis, R. Maehr, H. Ovaa, **H. L. Ploegh**, A. J. Coyle, and K. Rajewsky. 2004. Differential dependence of CD4+CD25+ regulatory and natural killer-like T cells on signals leading to NF-kappaB activation. *Proc Natl Acad Sci U S A 101:4566*.
Fiebiger, E., D. Tortorella, M. H. Jouvin, J. P. Kinet, and **H. L. Ploegh**. 2005. Cotranslational endoplasmic reticulum assembly of Fc{varepsilon}RI controls the formation of functional IgE-binding receptors. *J Exp Med 201:267*.
Misaghi, S., P. J. Galardy, W. J. Meester, H. Ovaa, **H. L. Ploegh**, and R. Gaudet. 2005. Structure of the Ubiquitin Hydrolase UCH-L3 Complexed with a Suicide Substrate. *J Biol Chem 280:1512*
Niess, J. H., S. Brand, X. Gu, L. Landsman, S. Jung, B. A. McCormick, J. M. Vyas, M. Boes, **H. L. Ploegh**, J. G. Fox, D. R. Littman, and H. C. Reinecker. 2005. CX3CR1-mediated dendritic cell access to the intestinal lumen and bacterial clearance. *Science 307:254*
Lilley BN, **Ploegh HL**. Viral modulation of antigen presentation: manipulation of cellular targets in the ER and beyond. *Immunol Rev. 2005 Oct;207:126-44.*
Maehr R, Mintern JD, Herman AE, Lennon-Dumenil AM, Mathis D, Benoist C**, Ploegh HL**. Cathepsin L is essential for onset of autoimmune diabetes in NOD mice. *J Clin Invest. 2005 Oct;115(10):2934-43*.
Catic A, **Ploegh HL**.Ubiquitin--conserved protein or selfish gene?*Trends Biochem Sci. 2005 Nov;30(11):600-4*.
Lilley BN, **Ploegh HL**. Multiprotein complexes that link dislocation, ubiquitination, and extraction of misfolded proteins from the endoplasmic reticulum membrane. *Proc Natl Acad Sci U S A. 2005 Oct 4;102(40):14296-301*.
Tirosh B, Iwakoshi NN, Glimcher LH, **Ploegh HL**. Rapid turnover of unspliced XBP-1 as a factor that modulates the unfolded protein response. *J Biol Chem. 2005 Dec 6.*
Galardy P, **Ploegh HL**, Ovaa H. Mechanism-based proteomics tools based on ubiquitin and ubiquitin-like proteins: crystallography, activity profiling, and protease identification. *Methods Enzymol. 2005;399:120-31.*
Kim YM, Pan JY, Korbel GA, Peperzak V, Boes M**, Ploegh HL**. Monovalent ligation of the B cell receptor induces receptor activation but fails to promote antigen presentation. *Proc Natl Acad Sci U S A. 2006 Feb 28;103(9):3327-32.*
Groll M, Berkers CR, **Ploegh HL**, Ovaa H. Crystal Structure of the Boronic Acid-Based Proteasome Inhibitor Bortezomib in Complex with the Yeast 20S Proteasome. *Structure. 2006 Mar;14(3):451-6.*
Huang TT, Nijman SM, Mirchandani KD, Galardy PJ, Cohn MA, Haas W, Gygi SP, **Ploegh HL**, Bernards R, D'Andrea AD. Regulation of monoubiquitinated PCNA by DUB autocleavage. *Nat Cell Biol. 2006 Mar 12.*

C. Research Support:

Ongoing Research Support

2 RO1 AI34893 (Ploegh) 1/15/2004-12/31/2008
National Institute of Health
Assembly and trafficking of MHC Class II molecules

The specific aims are 1) to develop a chemical strategy based on the incorporation of azido-substituted peptides and amino acids into antigen entities as a new means to study Class II MHC restricted antigen presentation; 2) to study trafficking of Class II MHC molecules in live antigen-presenting cells, and 3) to analyze the contribution of CatS, CatL and CatB to immune responses in vivo.

5 R01 GM62502 (Ploegh) 7/1/2001-6/30/2005
National Institute of Health
Degradation of membrane proteins: new chemical probes

This project is aimed at generating new chemical tools for cell biology. The various reagents to be synthesized will be used primarily to dissect the degradation pathway of type I membrane proteins in the endoplasmic reticulum (ER).

4 R37 AI33456 (Ploegh) 2/1/2003-1/31/2008

National Institute of Health
Assembly of MHC class I molecules *in vitro* and *in vivo*

This project explores the aspects of MHC class I biosynthesis and MHC class I-restricted antigen presentation using the tools of biochemistry, cell biology and immunology.

1 R01 AI057182 (Ploegh) 4/1/2003-3/31/2008
National Institute of Health

Viral Evasion Strategies: Analysis of the Herpes Viruses HSV, VZV and HHV-6, -7
The specific aim of this grant is to provide a biological rationale for the multiplicity of Herpesvirus genes that encode proteins with immunoevasive properties (immunoevasins).

PHS 398 OTHER SUPPORT *(continued)*

AstraZeneca (Ploegh) 6/19/2003-12/1/2006
Ubiquitin-specific proteases: development of specificity assays and high-throughput screens for novel anti-cancer targets

The specific aims are 1) to express, in a functionally active form, all known Ub-specific proteases and their close relatives; 2) to develop activity assays for the proteases listed in aim 1, based on the use of irreversible covalent probes generated by means of chemical ligation in an intein-based approach; and 3) to establish synthetic methods for the generation of branched Ub derivatives, suitable for determination of the substrate specificity of the Ub-specific proteases proven active in aims 1 and 2.

1 P50 CA100707 (Anderson, PI) 9/1/2003-6/30/2008
National Institute of Health
Proteasome-directed novel myeloma therapies
The specific aim of this project is to define the role of the ubiquitin-proteasome pathway in Multiple Myeloma (MM) pathogenesis and therapy.

03-0023 (Ploegh) 7/1/2003-6/30/2006
Sandler Program for Asthma Research
Application of a new cell biological and chemical strategy to the study of asthma He takes no salary from this grant.

5 PO1 AI045757 (Wucherpfennig, PI) 9/1/2003-2/28/2007
National Institute of Health
Molecular aspects of antigen presentation in multiple sclerosis

The specific aims of this project are 1) to determine the antigen-presenting capabilities of micoglia isolated from DR-2 transgenic animals as compared to professional antigen presenting cells, 2) to assess the relative contribution of lysosomal proteases in the generation of the offending class II-peptide complexes responsible for MS, 3) to define trafficking and peptide-presentations properties of MHC calss II molecules in microglia obtained from human nervous tissue and 4) to determine the intracellular distribution of MHC class II products and antigen presenting intermediates in microglial cells.