CURRICULUM VITAE

NAME AND TITLE PHONE

Hermann von Grafenstein	Home:	419-531-3377
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EDUCATION

	Year		
Colleges Attended	Graduated	<u>Degree</u>	<u>Major</u>
		Diplom	
Ludwig Maximilian University, Munich	1976	(equivalent	Physics
		to M.S.)	
Ludwig Maximilian University, Munich	1982	M.D.	Medicine
Max Planck Institute for Biochemistry			
Munich and University of Konstanz	1983	Ph.D.	Biophysical Chemistry

PROFESSIONAL LICENSURE

Licensure in Medicine (in the European Community, not in U.S.)

PROFESSIONAL POSITIONS

1983-1985	EMBO-Fellowship, Department of Physiology, King's College London, UK
1985-1987	Research Associate with P.F. Baker, Department of Physiology, King's College
	London, UK
1987-1988	Research Associate, Principal Investigator of an MRC Project Grant, Department of
	Physiology, King's College London, UK
1988-1989	Research Fellow and Honorary Lecturer, King's College London, UK
1989-1992	Research Associate with C. Janeway Jr., Section of Immunobiology, Yale
	University School of Medicine, New Haven, Connecticut, USA
1992-1993	Associate Research Scientist in Medicine and Immunobiology, (non-tenure track
	faculty position) Yale University School of Medicine, New Haven, Connecticut,
	USA
1993-2000	Assistant Professor of Pharmaceutical Sciences, School of Pharmacy, University of
	Southern California, Los Angeles, California, USA
1995-2002	Joint Appointment, Department of Physiology and Biophysics, Keck School of
	Medicine, University of Southern California, Los Angeles, California, USA

- 2000-2002 Associate Professor of Research Medicine, Division of Endocrinology and Diabetes, Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA
- 2003- Associate Professor of Medicinal and Biological Chemistry and of Pharmacology, College of Pharmacy, University of Toledo, Ohio, USA

TEACHING RESPONSIBILITIES

1. <u>King's College London (1986-1989)</u>

Undergraduate/Professional

- a. Tutorials in physiology for 1st year medical students for two years. These tutorials comprise two hours per week and cover the entire field of physiology for medical students.
- b. Supervision of projects (two medical students gaining intercalated degrees in physiology).
- c. Lectures in physiology for first year medical students.
- d. Lectures in cell physiology for third year students with diverse degree requirements.
- e. Organization of practical classes for students of physiology and medicine.

2. University of Southern California (1993-2002)

Undergraduate/Professional

- a. Course developer of PHAR441, "Immunology". A new course that was introduced into the Doctor of Pharmacy curriculum in the Fall of 1997. Course coordinator in 1997, 1998, and 1999. Teaching activities include lectures, case studies (term papers) and discussion groups.
- b. Participation in teaching professional degree courses in the Schools of Pharmacy and Medicine
 - (i) Doctor of Pharmacy courses: PHAR 406, Pharmaceutics IV; PHAR 411L, Microbiology; PSCI 655, Immunopharmaceutics; Participation in the Experiential Teaching Program for Pharmacy Residents. MPTX 500, Molecular Pharmacol. and Toxicol. Core Course; PSCI 599, Drug Delivery Strategies: Mechanism and Regulation of Cellular Membrane Transport; PSCI664, Drug Discovery and Design;

(ii) Doctor of Medicine courses: General Medicine, Diabetes Mellitus (Case studies for 3rd year students of medicine); Journal club for Endocrinology fellows.

Mentoring of professional students

- 1996 Mentor of a group of incoming Pharm. D. students in the Sibling/Faculty Mentor program (3 meetings totaling approximately 6 hours).
- 1998 Participation in the Experiential Teaching Program for Pharmacy Residents (resident supervised: Suzanne Kawasaki).

Graduate

- a. Course Organizer of PSCI662L "Advanced Pharmaceutical Analysis". Teaching activities include lectures, term papers and supervision of laboratory projects.
- b. Participation in teaching of graduate courses in the Schools of Pharmacy and Medicine
 - (i) School of Medicine graduate courses: PHBI 556A, Structural Basis of Intracellular Protein Traffic; MICB 502, Molecular and Cellular Immunology, Autoimmunity
 - (ii) School of Pharmacy graduate courses: PSCI 663, Drug Dosage Form Design and Evaluation

3. University of Toledo (Jan 2003 -)

Professional/Undergraduate:

Spring 2003

MBC 3560 "Physiological Chemistry II: Chemical regulation of cells and organisms"

Lectures: Amino acid synthesis (3 hrs), Fatty acid catabolism (1 hr), Lipid biosynthesis (2 hrs), Cholesterol biosynthesis and control (2 hrs), Nucleotide biosynthesis and regulation (3 hrs), Integration of metabolism (2 hrs)

Fall 2003 - Fall 2007

MBC 3550 "Physiological Chemistry I: Structure and biology of macromolecules", a three unit course, (44 hrs)

Graduate:

MBC 6100/8100 Advanced Immunology (2003-2007, team taught, course organizer Spring 2004, 2006 and 2007)

MBC 5900/7900 Medicinal and Biological Chemistry Seminar (2003-2007 team taught, course organizer Spring 2004 and 2006)

RESEARCH INTERESTS AND ACTIVITIES

Major Areas of Research Interest

Autoimmune disease with emphasis of the pathogenesesis of Type I diabetes.

Conformational dynamics of MHC bound antigenic peptides - computational simulation and experimental tests.

Structure – function relationships of cytokine and Toll-like receptors.

Rational design of immunotherapeutics

Research in Progress

Basic Laboratory Research

- a. The role of T cell macrophage signal exchange in β -cell destruction during the development of Type 1 diabetes.
- b. Structure-function relationships of Toll-like receptors and associated proteins
- c. Experimental testing of computational predictions the structure of MHC bound peptides.
- d. Assembly of multimeric cytokine ligand receptor complexes, particularly the ligand TGF-beta receptor complex.

Clinical Research

Development of noninvasive markers of islet inflammation.

Undergraduate Research

Advisor in USC - Francisco Bravo Medical Magnet High School Science Partnership Program:

- 1993 Abby Spivack
- 1994 Chelsea Dang
- 1994 Daniel Rowen

Exchange Undergraduate students

- 2005 Magdalena Menhofer (from Technical University of Munich, Germany)
- 2006 Teresa Schäffler (from the Technical University of Munich, Germany)

B.S.P.S. Research Practicum for University of Toledo BSPS students:

- 2005 Jaqueline Kulbaga
- 2005 Eileen Kish
- 2006 Thomas Cremer.

2007 Ermias Gebremichael2007 Sucheta Sachdeva

Honors Thesis Projects

2007 Thomas Cremer: "Modified hyaluronan oligosaccharides as agonists/antagonosts of innate immune receptors and anti-inflammatory drug precursors"

Graduate Research

<u>List of Students adivised</u>:

CM = Thesis Advisory Committee membership, CC = Primary advisor/Committee chair, T = temporary advisor, USC = University of Southern California, UT = University of Toledo:

Period	Name of student	Department/University		Degree	Graduated
1993-1997	Masayuki Yuki	Pharmaceutical Sciences/USC	CM	Ph.D.	1997
1993-1997	Neill Mathias	Pharmaceutical Sciences/USC	CM	Ph.D.	1997
1993-1998	Wilson Meng	Pharmaceutical Sciences/USC	CM,T	Ph.D.	1998
1993-1998	Karin Beloussow	Pharmaceutical Sciences/USC	CM	M.S.	1998
1994-1996	Chun Zheng	Pharmaceutical Sciences/USC	CM,T	Ph.D.	*
1994-1996	Wei-Wei Huang	Pharmaceutical Sciences/USC	T	Ph.D.	*
1994-1999	Zheng Liu	Pharmaceutical Sciences/USC	CC	Ph.D.	1999
1994-1999	Sujit Basu	Pharmaceutical Sciences/USC	CM,T	Ph.D.	1999
1995-1996	Norman Lehman	Pharmaceutical Sciences/USC	CM	Ph.D.	1996
	Jr.				
1995-1998	Katherine Louie	Molecular Microbiology and	CM	Ph.D.	1998
		Immunology/USC			
1995-2001	Vidya Ganapathy	Pharmaceutical Sciences/USC	CC	Ph.D.	2001
Srping 1996	Karen Morrison	Pharmaceutical Sciences/USC	T	Ph.D.	*
1996-1999	Bill Schultz	Molecular Microbiology and	CM	Ph.D.	1999
		Immunology/USC			
1996-1997	Tao Yang	Physiology and	CM	Ph.D.	1997
		Biophysics/USC			
1996-1997	Zhijun Guo	Physiology and	CM	Ph.D.	1997
		Biophysics/USC			
1996-2000	Sharon Wu	Pharmaceutical Sciences/USC	CM	Ph.D.	2002
Fall 1996	Jun Yang	Pharmaceutical Sciences/USC	T	Ph.D.	
1997-2000	Tanya Gruber	Children's Hospital Los	CM	Ph.D.	2000
		Angeles/USC			
Fall 1997-	Gerlie de los	Pharmaceutical Sciences/USC	T	Ph.D.	
	Reyes				
Spring 1998-	Andrew Rice	Program of Interdisciplinary and Basic Biomedical	T	Ph.D.	2003
		Sciences/USC			

1998-1999	Kenneth Kawamura	Pharmaceutical Sciences/USC	T	Phar m.D./ Ph.D.	*
1998-2000	Hilde Jarstadmarken	Pharmaceutical Sciences/USC	CC	M.S.	2000
1999-2004	Adam Widera	Pharmaceutical Sciences/USC	T	Ph.D.	2004
2000-2003	Dimitrios Vatakis	Molecular Microbiology and Immunology/USC	CM	Ph.D.	2003
Fall 2003 -	Sachin Patil	Medicinal and Biol. Chem./UT	CC	Ph.D.	
Fall 2003 -	Lisa Ficke	Medicinal and Biol. Chem./UT	CC	Ph.D.	
Fall 2003 -	Stella Mayo	Biology /UT	CM	Ph.D.	2006
Summer 2004	Michael Morran	Medicinal and Biol. Chem./UT	CM	Ph.D.	2006
Summer 2004	Min Xu	Pharmacology/UT	CM	M.S.	2004
Summer 2004	Nirdesh Gupta	Medicinal and Biol. Chem./UT	CM	Ph.D.	2007
Spring 2005-	Xiaoning Li	Chemistry UT	CM	Ph.D.	
1999-2006	Marc Christensen	Medicinal and Biol. Chem. / UT	CM	Ph.D	2006
Summer 2005-	Lyudmyla Golovko	Chemistry / UT	CM	M.S.	2006
2006-	Xiaowei Lu	Chemistry / UT	CM	Ph.D.	
Spring 2006-	Jidong Liu	Medicinal and Biol.Chem. / UT	CM	Ph.D.	
Summer 2006	Sathish Arcot	Pharmacology /UT	CM	M.S.	2006
Summer 2006	Alex Kiraly	Pharmacology / UT	CM	M.S.	2006
Spring 2007	Sarah Rashe	Biological Sciences / UT	CM	M.S.	
Spring 2007	Da Xu	Biological Sciences /UT	CM	Ph.D.	
Summer 2007	Amy C. Beickelman	Pharmacology / UT	CM	M.S.	2007

^{*} Transferred to a different program or university.

Postgraduate

- Tatyana Gurlo, Ph.D. worked in my laboratory at USC form June 1993-December 2002.
- Lilly Saleena, Ph.D. worked in my laboratory at UT from September 2003 December 2005.

Trainee recognition and awards:

- Wilson Meng and Sijit Basu won Krown Fellowships with immunology related projects carried out in part in my laboratory.
- Wilson Meng was appointed Assistant Profesor of Pharmaceutical Sciences at Ducanesque University College of Pharmacy
- Wilson Meng became membier of an NIH study section
- Abby Spivac won a third price in the Science Fair.

- Ken Kawamura won a "Gateway" Research Scholarship from the American Foundation for Pharmaceutical Education.
- Zheng Liu won an award from the American Association of Pharmaceutical Scientists for "Outstanding Academic Paper" at the 1999 AAPS meeting in San Diego.
- Tatyana Gurlo was appointed Assistant Professor of Research Medicine at USC in 2003 and Assistant Adjunct Professor of Medicine at UCLA in 2004.
- Ermias Gebremichael, an undergraduate practicum student won the National Science Foundation Glenn-Stokes Internship at University of Toledo.
- Sachin Patil won the first prize in the SigmaXI competition in category "Pharmacy and related fields" in the Fall of 2007.

GRANTS

During my academic career I have received research funding exceeding one million dollars in direct costs.

Current funding

- Structure and Dynamics of MHC-bound peptides: NIH R15 grant, \$150,000 (5/1/2006-4/30 2008) PI: Hermann von Grafenstein
- Development Towards Carbohydrate-Based Cancer Vaccines: Inderdisciplinary Research Initiation Award, \$30,000 (7/1/06-5/30/2008), PI: Steven Sucheck, Co-Investigators: Xuefei Huang, Katherine Wall, Marcia McInerney, Hermann von Grafenstein

Funding History

- 1. EMBO Fellowship (European Molecular Biology Organization); \$18,840; Terminal Date: 1985.
- 2. Thyssen Foundation Travel Award; \$1,168; Terminal Date: 1986.
- 3. Identification of Tumor Antigens by Peptide Elution from Tumor MHC Class I Molecules. American Cancer Society Pilot Project; \$14,500; Terminal Date: 6/29/94; Principal Investigator: Hermann von Grafenstein.
- 4. Identification of Autoantigens in Type I Diabetes by Peptide Elution from MHC molecules. Zumberge Fellowship, University of Southern California; \$24,000; Terminal Date: 6/30/95; Principal Investigator: Hermann von Grafenstein.
- 5. Peptide Epitopes and Anti-Islet Reactivity of Bovine Serum Albumin Specific T Cell Clones in the Non Obese Diabetic Mouse. Starter Grant, American Association of Colleges of Pharmacy; \$7,500; Terminal Date: 11/30/95; Principal Investigator: Hermann von Grafenstein.

- 6. Mannosylated Peptides as Candidate Vaccines and Probes for Mannose Receptor Function. Research Starter Grant, Pharmaceutical Research and Manufacturers of America Foundation; Grant #: Starter Grant 95 3249 (USC # 53-5202-2636); \$24,000; Terminal Date:12/31/1996; Principal Investigator: Hermann von Grafenstein.
- 7. Molecular Studies Using a Protein Sequencer. NCRR-BRS Shared instrumentation Grant; Grant #: 1 S10 RR11337-01; \$115,828; Terminal Date: 1996; Principal Investigator: Minnie McMillan, Ph.D.; Co-Investigator: Hermann von Grafenstein.
- 8. Mechanism of Action of Arctic Spray. Contract with System Design Associates; Grant #: SDAI 96-97; \$10,000; Terminal Date: 1/15/1997; Principal Investigator: Hermann von Grafenstein.
- 9. MHC Class I Bound Beta Cell Peptides in NOD Mice. National Institutes of Health; Grant #: 5 R29 DK49717 First Award; \$350,000; Terminal Date: 5/31/2001; Principal Investigator: Hermann von Grafenstein.
- 10. TGF-β Rational Therapeutics. National Institutes of Health Program Project; Grant #: 5 PO1 HL060231; \$426,466; Terminal Date: 3/31/2004; Principal Investigator: Ian Haworth, Co-Principal Investigator: Hermann von Grafenstein.
- 11. Role of IFN-γ in the development and progression of Type I diabetes, University of Toledo Interdisciplinary Research Initiation Award, \$50,000, Terminal Date: 4/30/2004. Principal Investigator: Deborah Vestal, Co-Investigators: Hermann von Grafenstein, Anthony Quinn, Marcia McInerney.
- 12. Structural Studies of Membrane Proteins. University of Toledo Interdisciplinary Research Initiation Award, \$50,000, Terminal Date: 4/30/2006. Prinicpal Investigator: Ron Viola (Chemistry), Co-Investigators: Timothy Mueser (Chemistry) John Gray (Biological Sciences), Hermann von Grafenstein.

PUBLICATIONS

Peer-reviewed Papers published and in press

1. von Grafenstein H and Neumann E.

Interaction of chromaffin granules with plasma membranes mediated by Ca^{2+} and Mg-ATP using self-generating gradients of Percoll.

FEBS Letters 123: 238-240, 1981.

2. von Grafenstein H and Neumann E.

ATP-stimulated accumulation of calcium by chromaffin granules and mitochondria from the adrenal medulla.

Biochem. Biophys. Res. Comm. 117: 245-251, 1983.

3. von Grafenstein H, Roberts CS and Baker PF.

Kinetic analysis of the triggered exocytosis/endocytosis secretory cycle in cultured bovine adrenal medullary cells.

J. Cell Biol. 103: 2343-2352, 1986.

4. Borges R, Carter D, von Grafenstein H, Halliday J, and Knight DE.

Activation of sodium channels is not essential for endothelin induced vasoconstriction.

Pflüger's Archiv, Eur. J. Physiol. 413: 313-315, 1989.

5. Borges R, Carter DV, von Grafenstein H, Halliday J and Knight DE.

Ionic requirements of the endothelin response in rat aorta and protein vein.

Circulation Res. 65: 265-271, 1989.

6. <u>von Grafenstein H</u> and Powis DA.

Calcium is released by exocytosis together with catecholamine from bovine adrenal medullary cells.

J. Neurochem. 53: 428-435, 1989.

7. Borges R, von Grafenstein H, and Knight DE.

Tissue selectivity of endothelin.

Eur. J. Pharmacol. 165: 223-230, 1989.

8. Powis DA, O'Brien KJ and von Grafenstein H.

Calcium export by sodium-calcium exchange in bovine chromaffin cells.

Cell Calcium 12: 493-504, 1991.

9. Nakagawa TY, <u>von Grafenstein H</u>, Sears JE, Williams J, Janeway CA and Flavell RA.

The use of the polymerase chain reaction to map CD4⁺ T cell epitopes.

Eur. J. Immunol. 21: 2851-2855, 1991.

10. <u>von Grafenstein H</u> and Knight DE.

Membrane recapture and early triggered secretion from the newly formed endocytic compartment in bovine chromaffin cells.

J. Physiol. (Lond.) 453: 15-31, 1992.

11. von Grafenstein H, Borges R and Knight DE.

Effect of botulinum toxin type D on triggered and constitutive exocytosis/endocytosis cycles cultures of in bovine adrenal medullary cells.

FEBS Letters 298: 118-122, 1992.

12. <u>von Grafenstein H</u>, and Knight DE.

Triggered exocytosis and endocytosis have different requirements for calcium and nucleotides in permeabilized bovine chromaffin cells.

J. Membr. Biol. 134: 1-13, 1993.

13. Wolff CHJ, Hong SC, von Grafenstein H and Janeway CA.

TCR-CD4 and TCR-TCR interactions as distinctive mechanisms for the induction of increased intracellular calcium in T-cell signaling.

J. Immunol. 151: 1337-1345, 1993.

14. Reich E-P, von Grafenstein H, Barlow A, Swenson KE, Williams K and Janeway jr. CA. Peptides associated with Major Histocompatibility Complex (MHC) glycoproteins of the spontaneously diabetic NOD mouse.

J. Immunol. 152: 2279-2288, 1994.

15. Meng WS, Gallaher TK, von Grafenstein H and Haworth IS.

> Sequence Dependent Conformational Motion of a Peptide Bound to a Class I MHC molecule.

Protein and Peptide Letters 3: 51-58, 1996.

16. Zekzer D, Wong S, Altieri M, Gurlo T, von Grafenstein H and Sherwin RS.

Inhibition of diabetes mellitus by an insulin reactive CD4⁺ T cell clone in the non obese diabetic mouse.

Diabetes 46: 1124-1132, 1997.

17. Meng WS, von Grafenstein H and Haworth IS.

A model of water structure inside the HLA-A2 peptide binding groove.

International Immunology 9: 1339-1346, 1997.

18. Gurlo T, Huang W-W and von Grafenstein H.

PGE₂ inhibits IL-2 and IL-4 induced proliferation of CTLL-2 and HT-2 cells.

Cytokine 10: 265-274, 1998.

19. Basu S, Shen J, Elbert K, Okamoto C, Lee VHL and von Grafenstein H.

Development and utility of anti-PepT1 anti-peptide polyclonal antibodies.

Pharm. Res. 15: 338, 1998.

20. Meng WS, Bhavaraju AV, Haworth IS and von Grafenstein H.

Modeling of the non-obese diabetic mouse class II MHC molecule I-A^{g7}.

Protein and Peptide Letters 5: 75-82, 1998.

21. Bolger MB, Haworth IS, Yeung AK, Ann D, von Grafenstein H, Hamm-Alvarez S, Okamoto CT, Kim KJ, Basu SK, Wu S and Lee VHL.

Structure, function, and molecular modeling approaches to the study of the intestinal dipeptide transporter PepT1.

J. Pharm. Sci. 87(11): 1286-1291, 1998.

22. Yeung AK, Basu SK, Wu SK, Ann DK, Haworth IS, Bolger MB, Hamm-Alvarez S,

Okamoto CT, von Grafenstein H, Shen W-C, Kim K-J and Lee VHL.

Molecular identification of a role for tyrosine 167 in the function of the human intestinal proton-coupled dipeptide transporter (hPepT1).

Biochem. Biophys. Res. Comm. 250(1): 103-107, 1998.

23. Gurlo T, Kawamura K and von Grafenstein H.

Role of inflammatory infiltrate in activation and effector function of cloned islet-reactive NOD CD8⁺ T cells: Involvement of a nitric oxide dependent pathway **J. Immunol.** 163: 5770-5780, 1999.

24. Gurlo T, Meng WS, Bui H-H, Haworth IS and von Grafenstein H.

Experimental evidence for the presence of a water network at the peptide-MHC interface. **Immunol. Lett.** 70(3): 139-141, Dec. 1999.

25. Liu Z, Gurlo T and von Grafenstein H.

Cell-ELISA using β-galactosidase conjugated antibodies.

J. of Immunological Methods 234/1-2: 153-167, 2000.

26. Ganapathy V, Gurlo T, Jarstadmarken H and von Grafenstein H.

Regulation of IFN- γ release from islet reactive NOD CD8⁺ T cells by PGE₂ receptor signaling.

International Immunology 12(6): 851-860, 2000.

27. Meng W, von Grafenstein H and Haworth I.

Water dynamics at the binding interface of four different HLA-A2/peptide complexes. **International Immunolgy** 12(7): 949-957, 2000.

28. Gurlo T and von Grafenstein H.

Antigen-independent cross-talk between macrophages and CD8⁺ T cells facilitates their cooperation during target destruction.

International Immunology 15(9): 1063-1071, 2003.

29. Huynh-Hoa T. Bui, Alexandra J. Schiewe, <u>Hermann von Grafenstein</u>, and

Ian S. Haworth.

Structural Prediction of Peptides Binding to MHC Class I Molecules.

Proteins 63(1), 43 - 52, 2006.

30. Mohammad, K. Mohammad, Michael Morran, Brandon Slotterbeck, Douglas W.

Leaman, Yaping Sun, <u>Hermann von Grafenstein</u>, Soon-Cheol Hong, and Marcia F. McInerney.

Dysregulated Toll Like Receptors in Bone Marrow Derived Macrophages at the Onset of Diabetes in the Nonobese Diabetic Mouse.

International Immunology 18(7), 1101-1113, 2006.

Manuscripts - in Preparation or Submitted

1. Ficke, LM, Cremer, TJ, Huang, X, and <u>von Grafenstein, H</u>. Hyaluronic acid tetra- and hexasaccharides do not activate Toll-like receptor 4 in macrophages and vascular endothelial cells. **In revision**.

- 2. Patil, S., Meeresahib, LS, Haworth, IS, von Grafenstein, H. Evidence for the presence of mobile water molecules in the peptide-MHC binding interface. **In preparation**.
- 3. Patil, S and <u>von Grafenstein, H.</u>
 A method for the determination of Hydrogen-Deuterium exchange rates at single amino acid resolution. **In preparation**.
- 4. Gurlo T, Ganapathy V, Hawk R, Amilineni J, Warburton D, Haworth IS, and <u>von</u> <u>Grafenstein H</u>.

Agonist properties of a soluble form of the type II TGF- β receptor. **In preparation**.

Book Chapters

Knight DE, von Grafenstein H and Maconochie DJ.
 Intracellular requirements for exocytotic noradrenaline release.
 In: Ischemia and Myocardial Infarction, Brachmann, J., Schomig, A. (Eds.) Springer, Berlin, 1989.

Monographs

1. von Grafenstein H.

Teilschritte des Exocytosevorgangs in der Chromaffinzelle.

In: Vitro Untersuchungen zur Ca²⁺- und Mg-ATP-Induzierten Wechselwirkung zwischen Plasmamembran-Fragmenten und Chromaffin Granula und zur Rückregulation des Cytoplasmatischen Calcium-Signals. (Thesis)

Konstanzer Dissertationen 32, Hartung Gorre, Konstanz, F.R.G., 1983.

Reviews

1. von Grafenstein H.

In: The secretory and endocytic paths by A.M. Tartakoff (book review).

FEBS Letters 239:382, 1988.

2. Knight DE, von Grafenstein H and Athayde CM.

Calcium dependent and calcium independent exocytosis.

Trends in Neuroscience 12: 451-458, 1989.

POSTERS/PLATFORM PAPERS PRESENTED (selected)

Seminars and Invited Presentations

1. "In memory of Peter Baker – The secretory cycle in chromaffin cells." 5th International Symposium on Chromaffin Cell Biology, Alice Springs, Australia (1987).

- 2. "Coupling of regulated exocytosis and endocytosis in chromaffin cells." 5th Annual Meeting of the Brain Research Association, Edinburgh, Scotland, UK (1987).
- 3. "Antigen processing and cell-cell communication in the immune system." Department of Biochemistry and Molecular Biology, USC School of Medicine, Los Angeles, California (1993).
- 4. "Antigen processing and presentation in secretory systems." Department of Cell Biology and Anatomy, USC School of Medicine, Los Angeles, California (1994).
- 5. "Structure-activity relationships of MHC bound peptides." California Institute of Genetic Medicine, USC School of Medicine, Los Angeles, California (1995).
- 6. "T cells in IDDM: Disease promoting versus protective roles." Diabetes and Endocrinology Grand Rounds, USC School of Medicine, Los Angeles, California (1996).
- 7. "Towards the elusive MHC class I bound beta cell autoantigen in type I diabetes." Immunology Seminar Series, Department of Molecular Microbiology and Immunology, USC School of Medicine, Los Angeles, California (1996).
- 8. "Novel methods to detect cell surface molecules expressed at low levels. Regulation of B7 expression on macrophages." National Meeting of the American Association of Pharmaceutical Scientists, Boston, Massachusetts (1997).
- 9. "The Revolution in Drug Design." Co-chair, plenary session, Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, (1998).
- 11. "Towards computer-aided, rational design of therapeutics The merging of the biotechnology and information revolutions." Department of Pharmaceutical Technology, University of the Saarland, Germany, (1998).
- 12. "Role and education of pharmacists in the United States." Department of Pharmaceutical Technology University of the Saarland, Germany, (1998).
- 13. "Role of local accessory cells in the activation of diabetes-promoting CD8⁺⁺ T cells." Joint Immunology Conference, Department of Molecular Microbiology and Immunology, USC School of Medicine, Los Angeles, California (1999).
- 14. "Cooperation of CD8⁺ T cells and macrophages in islet destruction: role of nitric oxide." USC Diabetes Research Center Colloquium, Los Angeles, California (2000).
- 15. Mechanisms of islet destruction in type I diabetes Cooperation of CD8⁺ T cells and macrophages, USC Joint Immunology Seminar Series, January 2002.

- 16. Signaling cross-talk between CD8⁺ T cells and macrophages A mechanism of cooperative islet destruction in NOD mice. University of Toledo College of Pharmacy, May 2002.
- 17. Bi-directional communication between CD8⁺ T cells and macrophages during tissue destruction. University of Toledo, Department of Biology Seminar Series, March 2003
- 18. Signaling Cross-Talk Between CD8+ T cells and macrophages A Mechanism of Cooperative Target Destruction. Department of Pharmacology Seminar Series, February 2004
- 19. Type 1 Diabetes Future Directions in Research. College of Pharmacy, University of Szeged, Hungary, May 2006
- 20. Hydrogen-deuterium exchange as a structural tool Peptide-MHC complexes, Department of Medicinal and Biological Chemistry Seminar Series, October 2006.
- Hydrogen-deuterium exchange reveals a variable network of mobile water molecules in the peptide-MHC binding interface.
 3rd Annual Ohio Valley Crystallography and Biophysics Symposium:
 "Analyzing Macromolecular Complexes with Crystallography and Biophysical Methods"
 The University of Toledo, November 9th, 2007.

Selected Abstracts

- 1. <u>von Grafenstein H</u>, Stocker F, and Neumann E. Ca²⁺- and ATP-mediated interaction of chromaffin granules with plasma membranes of bovine adrenal medulla using self-generating Percoll-gradients. Hoppe-Seyler's Z. Physiol. Chem. 361: 1261-1362, 1980.
- von Grafenstein H, and Neumann E.
 Regulation of the calcium level by chromaffin cell organelles at exocytosis steps.
 Hoppe-Seyler's Z. Physiol. Chem. 364: 1132, 1983.
- 3. von Grafenstein, H, and Powis, D.A. Exocytosis as an export route for calcium from bovine chromaffin cells. J. Physiol. <u>358</u>, 66P, 1984.
- 4. Baker PF, von Grafenstein HRK, and Roberts CS.

 Membrane retrieval following stimulation of exocytosis in cultured bovine adrenal medullary cells: lack of effect of extracellular Ca.

 J. Physiol. 371, 156P, 1985.
- 5. Dollery CM, and von Grafenstein HRK.

The general anaesthetic urethane inhibits evoked catecholamine secretion and calcium uptake in cultured bovine adrenal medullary cells.

15

J. Physiol. <u>374</u> 40P, 1986.

6. von Grafenstein H, and Baker PF.

Kinetics of endocytosis following triggering of exocytosis in cultured bovine adrenal medullary cells.

4th International Symposium for Chromaffin Cell Biology.

7. von Grafenstein H.

Dissecting exocytosis and endocytosis in permeabilized bovine chromaffin cells. 5th International Symposium for Chromaffin Cell Biology, Alice Springs, Australia, 1987.

8. von Grafenstein H.

Endocytosis following triggered exocytosis in permeabilized bovine adrenal medullary cells is calcium-independent and blocked by non-hydrolysable analogs of ATP. J. Physiol. <u>403</u>, 94P, 1988.

9. Borges R, von Grafenstein H, and Knight DE.

Alpha-scorpion toxin and endothelin, although homologous, may act at different sites to increase tension in Sprague Dawly rat aorta and portal vein segments.

J. Physiol. 413, 24P, 1989.

10. von Grafenstein H, and Knight DE.

Endocytotic vesicles formed during triggered exocytosis/endocytosis rapidly re-enter the secretory cycle.

6th International Symposium on Chromaffin Cell Biology, Jerusalem, Israel, 1989.

11. von Grafenstein H, and C.A. Janeway, Jr. CA

A possible role of the macrophage mannose receptor in the initiation of immune responses.

FASEB meeting, Anaheim CA, USA, 1992.

12. Reich E-P, von Grafenstein H, Barlow A, and Janeway jr. C.

Sequence analysis of peptides presented by MHC class II molecules isolated from NOD spleen cells.

American Diabetes Association, 12th International Immunology and Diabetes Workshop, Orlando, Florida, USA, April 15-18, 1993.

13. Gurlo T, Spivack A, and von Grafenstein H.

Quantitation, kinetics and peptide dependence of interferon- γ induced surface expression of MHC class I molecules in the β -cell line NIT-1. Pharm. Res. 11(10), S-93: 1994.

14. Meng WS, Gallaher TK, von Grafenstein H, and Haworth IS.

Prediction of the Conformation of a Peptide in the Binding Groove of a Class I MHC Molecule.

Protein Science 4(S2): 87, 1995.

15. Meng WS, Gallaher TK, von Grafenstein H, and Haworth IS.

Prediction of the Conformation of a Peptide in the Binding Groove of a Class I MHC Molecule. J. Biomol. Struct. Dyn. 12: A160, 1995

16. Zekzer D, Gurlo T, Wong S, and von Grafenstein H.

Islet-reactive Th1 cell line protects against adoptive transfer of IDDM into NOD mice. Diabetes 44 (Suppl. 1): 163A, 1995.

17. Meng WS, von Grafenstein H, and Haworth IS.

Molecular dynamics simulations of the conformation of a peptide in the binding groove of a class I MHC molecule.

Protein Science 4(S2): 86, 1995.

18. Prostaglandin E₂ inhibits interleukin-2 dependent proliferation of T-cells.

Gurlo T, Huang W-W, and von Grafenstein, H.

Pharm. Res. 12(9): S-88, 1995

19. Meng WS, von Grafenstein H, and Haworth IS.

Computer simulation of peptides bound to class I MHC molecules.

Pharm. Res. 12(9): S-131, 1995.

20. Basu S, Shen J, Elbert KJ, Gurlo T, Okamoto CT, von Grafenstein H, and Lee VHL.

Screening of anti-PepT1 antibodies using indirect ELISA.

Pharm. Res. 13(9): S-37, 1996.

21. Zekzer D, Wong S, von Grafenstein H, and Sherwin, R.

An insulin-reactive T cell clone prevents IDDM in NOD mice by blocking homing of diabetogenic splenocytes to the islet. (oral presentation)

Diabetes 45 (Suppl. 2): 53A, 1996.

22. Meng WS, von Grafenstein H, and Haworth IS.

Analysis of the role of water inside the binding groove of HLA-A2.

Protein Science 5(S1): 96, 1996.

23. Meng WS, von Grafenstein H, and Haworth IS.

Rational design of nonnatural peptide ligands for class I MHC molecules.

Pharm. Res. 13(9): S-139, 1996.

24. Yeung AK, Ann D, Bolger MB, von Grafenstein H, Hamm-Alvarez S, Shen W-C, Okamoto CT, Kim KJ, Basu SK, Haworth IS, and Lee VHL.

Expression of dipeptide transporter PepT-1 in NIH3T3 cells for structure-function studies.

Pharm. Res. 13(9), S-243, 1996.

25. Meng WS, von Grafenstein H, and Haworth IS.

Molecular modeling of the non-obese diabetic (NOD) mouse class II MHC molecule $I-A^{g7}$.

AAPS Western Regional Meeting, San Francisco, 1997.

26. Meng WS, von Grafenstein H, and Haworth IS.

Computational studies of non-natural peptides for the for the human class I MHC molecule HLA-A2.

AAPS Western Regional Meeting, San Francisco, 1997.

27. Meng WS, von Grafenstein H, and Haworth IS.

The role of water in complex formation between peptides and the MHC molecule HLA-A2.

J. Biomol. Struct. Dyn. 14: 847-848, 1997.

28. Meng WS, von Grafenstein H, and Haworth IS.

Contrasting the role of water in the complexes of the MHC molecule HLA-A2 with the peptides GILGFVFTL and TLTSCNTSV.

Protein Science 6(S2): 90, 1997.

29. Liu Z, Gurlo T, and von Grafenstein H.

Novel methods to detect cell surface molecules expressed at low levels. Regulation of B7 expression on macrophages. AAPS Annual Meeting, November 2-6, 1997, Boston, MA (Podium presentation).

Pharm. Res. 14(11), S-428, 1997.

30. Yeung AK, Ann DK, Bolger MB, Haworth IS, Hamm-Alvarez S, Okamoto CT, Shen WC, von Grafenstein H, Basu S, Wu S, and Lee VHL.

Functional analysis of human dipeptide transporter (hPepT1) by site directed mutagenesis.

Pharm. Res. 14(11): S154, 1997.

31. Meng W, Bhavaraju A, von Grafenstein H, and Haworth I.

Computational studies of the non-obese diabetic mouse class II MHC molecule I-A^{g7}. Pharm. Res. 14(11): S390, 1997.

32. Meng WS, von Grafenstein H, and Haworth IS.

Water is an integral part of peptide binding to the class I MHC molecule HLA-A2: A theoretical and experimental study.

Western Regional Meeting of AAPS, San Francsco, 1998.

33. Ganapathy V, Gurlo T, and von Grafenstein H.

Effect of PGE₂ on IFN-γ release from diabetes promoting CD8⁺ T cell clones.

Western Regional Meeting of AAPS, San Francisco, 1998.

34. Haworth IS, Warburton D, and von Grafenstein H.

Peptide inhibitors of TGF β based on computer models of TGF β receptor structure. Western Regional Meeting of AAPS, San Francisco, 1998.

35. Gurlo T, and von Grafenstein H.

Islet destruction and IFN-γ production by NOD CD8⁺ T cells have different requirements for specific MHC molecules. 3rd Immunology of Diabetes Society Conference, Oak Brook, Illinois, USA, June 10-12, 1998. Oak Brooks, Illinois. Diabetes 47(Suppl. 1): A206, 1998.

36. Gurlo T, and von Grafenstein H.

Islet destruction and IFN-γ production by NOD CD8⁺ T cells have different requirements for specific MHC molecules.

3rd Immunology of Diabetes Society Conference, Oak Brook, Illinois, USA, 1998.

37. Liu Z, Gurlo T, and von Grafenstein H.

Regulation of B7 expression on antigen presenting cells.

Pharm. Sci. 1(Suppl. 1): S-230, 1998.

38. Gurlo T, Liu Z, and von Grafenstein H.

Abnormally persistent activation signaling in T cells of the Non-Obese Diabetic mouse. Pharm. Sci. 1(Suppl. 1): S-231, 1998.

39. Liu Z, Gurlo T, and von Grafenstein H.

Different sensitivity of alveolar and peritoneal macrophages to exogenous stimuli: Implications for the selection of drug delivery routes. (Podium presentation). Western Regional Meeting of AAPS, San Diego, 1999.

40. Gurlo T, and von Grafenstein H.

Influence of islet mononuclear infiltrate on function of islet destructive CD8⁺ T cells. Diabetes 48 (Suppl. 1): A205, 1999

41. Liu Z, Gurlo T, and von Grafenstein H.

Reactivity of macrophage subpopulations and its implication in drug delivery, Conference on Frontiers of Drug Development, Pasadena, CA, July 26-28, 1999.

42. Liu Z, Gurlo T, and von Grafenstein H.

Comparison of costimulatory signal regulation in macrophage subpopulations. PharmSci $^{\text{TM}}$ 1(4, Suppl.): S-1201, 1999.

43. Gurlo T, Kawamura K, Jarstadmarken HO, and von Grafenstein H.

Cooperation of CD8⁺ T cells and macrophages in islet destruction: Role of nitric oxide Midwinter Conference of Immunologists, Asilomar CA, January 2000.

44. Gurlo T, Jarstadmarken H, and von Grafenstein H.

Cooperation of CD8⁺ T cells and macrophages in islet destruction: Role of nitric oxide. Diabetes 49(Suppl. 1): 971-P, 2000.

45. Gurlo T, and von Grafenstein H.

Signal exchange between CD8 $^{\scriptscriptstyle +}$ T cells and macrophages triggers nitric oxide synthesis in macrophages - A novel pathway of β -cell destruction in NOD mice.

Midwinter Conference of Immunologists, Asilomar CA, January 2001.

46. Gurlo T, and von Grafenstein H.

 $CD8^+$ T cells trigger macrophage nitric oxide synthesis - A novel pathway of β -cell destruction in T1DM.

Experimental Biology (FASEB - AAI) 2001, Orlando FL, March 31-April 4, 2001.

47. Gurlo T, and von Grafenstein H.

NOD CD8⁺ T cells cooperate with macrophages in islet destruction by triggering nitric oxide synthesis (Oral poster discussion session).

Diabetes 50(Suppl. 2): 1068-P, 2001.

48. Gurlo T, and von Grafenstein H.

Signal exchange of NOD CD8⁺ T cells with macrophages and its role in islet destruction (oral presentation).

Western Region Islet Study Group, Marconi Conference Center, Marshall, CA. September 28-30, 2001

49. Gurlo, T. and von Grafenstein, H.

Antigen-Independent And ICAM-1/LFA-1-Dependent Cross-Talk Between Macrophages and CD8⁺ T Cells - A Mechanism Of Cooperative Islet Destruction In NOD Mice. Diabetes 51(Suppl. 2) 1160-P, 2002.

50. Patil, S., Saleena, L.M., and von Grafenstein, H.

Hydrogen-deuterium exchange provides evidence for presence of mobile water molecules at the MHC-Peptide binding interface. Annual Conference of the American Society for Mass Spectrometry, Indianapolis, IN, June 2 – June 7, 2007

51. Patil, S., Saleena, L.M., and von Grafenstein, H.

Hydrogen-deuterium exchange provides evidence for presence of mobile water molecules at the MHC-Peptide binding interface.

Oral Presentation (S. Patil), Mid-Atlantic Graduate Student Symposium in Medicinal Chemistry, West Virginia University, Morgantown, WV, June 12-12, 2007

51. Patil, S., Saleena, L.M., and von Grafenstein, H.

Evidence for the presence of mobile water molecules in the peptide-HLA-A2.1 binding interface. 13th International Congress of Immunology, August 21-25, 2007, Rio de Janeiro, Brazil

SERVICE RESPONSIBILITIES

1. <u>University of Southern California</u>:

Department

Departmental Secretary, School of Pharmacy Department of Pharmaceutical Sciences, 1998, 1999

Member, Faculty Search Committee, Department of Pharmaceutical Sciences, 1994

Member, Department of Pharmaceutical Sciences Graduate Affairs Committee, 1994/1995, 1995/1996, 1996/1997, 1997/1998

College (and outside home department)

Member, School of Pharmacy Curriculum Reform Committee for Harmonizing Clinical and Basic Sciences, 1993

Member, School of Pharmacy Curriculum Reform Committee, 1994

Member, School of Pharmacy Faculty Search Committee, Department of Molecular Pharmacology and Toxicology, 1996

Elected Departmental Representative in the School of Pharmacy's Academic Planning and Budget Advisory committee 1995/1996

Member, Ad hoc Committee for the Formulation of the USC School of Pharmacy's Vision and Mission Statements, 1996

Member, School of Pharmacy Faculty Search Committee to fill two faculty positions in the Department of Clinical Pharmacy, 1996/1997

Participation in School of Pharmacy First year Faculty-Mentor/Student-Sibling Program, 1996, 1997

Interviews of applicants to the Professional Pharm.D. Program. 1993, 1994, 1995, 1996, 1997.

Postgraduate Pharmaceutical Care Course Development Task Force, 1998

Facilitator during the 1998 retreat of the School of Pharmacy. Conference Subtopic "Team Building, Faculty-Administration-Student-Staff-Relationships"

Elected Departmental Representative in the School of Pharmacy Faculty Assembly Executive Committee, 1998/99

Member of an ad hoc committee charged by the Provost with the evaluation of the Dean, Spring 1999

University

Senate Task Force on the Future of Health Sciences at USC, 1997

2. University of Toledo

Department

Organization of Medicinal and Biological Chemistry (MBC) Seminar Series, Spring 2004, Spring 2006.

MBC Graduate Affairs Committee member, Fall 2003, Spring 2004, Fall 2004, Spring 2005, Fall 2005, Spring 2006, Spring 2007

MBC Graduate Affairs Committee chair. Fall 2007

Department of Medicinal and Biological Chemistry Faculty Search Committee to fill a tenure track position, Summer/Fall 2006. Appointment of Amanda Bryant-Friedrich

Mentor for newly appointed faculty: Amanda Bryant-Friedrich

MBC Personnel Committee, Fall 2007

College (and outside home department)

ACPE Committee on Faculty (charged to revise College of Pharmacy documents related to promotion and tenure), Spring 2004.

College of Pharmacy Admissions Committee for the Pharm.D. progran, Spring 2005 – Summer 2007.

Participation in Professional Division Applicant Interviews, Spring 2004, 2005, 2006, 2007.

Department of Pharmacology Search Committee to fill a tenure track position, Summer 2004 - Summer 2005 Dr. Nauli was appointed in the Summer of 2006.

Department of Pharmacology Search Commettee to fill a tenure track position, Fall 2006. Appointment of Ming-Cheh Liu, Fall 2007.

UT College of Pharmacy delegate to the Faculty of Pharmacy at the University of Szeged to establish programs of research collaboration and student exchange, April / May 2006

College Personnel Committee, Member-at-large, Spring 2007 -

College of Pharmacy Search Committee (member) to fill a position of Chair of the Department of Medicinal and Biological Chemistry, Summer 2007 -.

Department of Pharmacology and Toxicology Personnel Committee (member), Fall 2007 -

<u>University</u>

Membership Committee of the Graduate Council (2005/2006 academic year).

IUCAC Committee (member), Fall 2007 -

Graduate Executive Committe Fall 2007 -

3. Scientific Community

Peer Review Activities and Consensus Committees

FEBS Letters (ad hoc reviewer)

Biochem. Biophys. Acta (ad hoc reviewer)

J. Drug Targeting (ad hoc reviewer) 1998

Pharm. Res. (ad hoc reviewer) 1997, 1998, 1999, 2000

Member, Krown Fellowship Selection Committee, 1997, 1998

NIH (ad hoc reviewer) 1998, 1999, 2000

Judge for selection of best academic and industrial posters at the Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, USA, 1998.

Diabetes and Endocrinology Research Center a the University of Colorado at Bolder (ad hoc) 1999.

Member, Study Section for review of Career Development Fellowships at Children's Hospital of Los Angeles (1999).

Wellcome Trust, U.K. (2000).

Diabetes and Endocrinology Research Center, Washington University, Seattle, U.S.A. (2000).

Vaccine (ad hoc reviewer), 2004.

Meetings Organized

Co-organizer, together with Tom Zioncheck of the plenary session of the Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, USA, 1998.

Co-chair, podium presentations of posters, Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, (1998).

Co-Chair of Plenary Session, "The Revolution of Drug Design", Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, USA, 1998.

Moderator, Afternoon Podium Session, Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Francisco, California, USA, 1998.

Moderator, Contributed Papers Podium Session, Western Regional Meeting of the American Association of Pharmaceutical Scientists, San Diego Concourse, San Diego, California, USA, 1999.

Co-Chair, "Session #3: Cell signaling" Conference on Frontiers of Drug Development, July 26-28, 1999, Pasadena, California, USA, 1999.

Member of USC team at the American Association of Colleges of Pharmacy Institute on Pedagogical and Curricular Change, Leesburg, Virginia, USA, 1999.

Society Memberships:

American Association of Immunologists
American Diabetes Association
American Association for the Advancement of Science
American Association of Colleges of Pharmacy
American Society of Mass Spectrometry