BIOGRAPHICAL SKETCH of Beat Ernst

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion	FIELD OF STUDY
ETH Zürich, Switzerland	Master	05/1973	Chemical synthesis
ETH Zürich, Switzerland	PhD	06/1979	Chemical synthesis
California Institute of Technology, Pasadena, CA, USA	Postdoctoral Fellow	12/1980	Natural product synthesis

A. PERSONAL STATEMENT

Beat Ernst's research interests are at the interface between carbohydrate chemistry and glycobiology, with a particular focus on the synthesis of glycomimetics and their pharmacological profiling. His research on one hand aims at understanding the conformational and structural requirements for biological activity of glycomimetics, and on the other hand, in collaboration with academic and industrial groups, he explores the therapeutic potential of such compounds in disease models, and in one case, in the clinic (Rivipansel, currently in clinical phase III for the treatment of sickle cell disease) with the ultimate goal to discover new therapeutics.

Besides his research on glycomimetics, in the past 8 years he developed a PADMET (physico-chemical, absorption, distribution, metabolisme, elimination, toxicity) platform, allowing the determination of physico-chemical and pharmacokinetic properies of small molecules at an early stage in their development. A wide range of parameters are measured by the platform: logP/D, pKa, logS, CMC, PAMPA, Caco-2, PPB, stability in the GIT, stability in the CNS, stability in plasma, metabolic stability, excretion via OAT-1 and other transporters, P-gp transport, Ames test, and cell toxicity. This wide-ranging information enabled him to develop a FimH antagonist for the treatment of urinary tract infections that was ready for preclinical development.

Beat Ernst is engaged in the synthesis of glycomimetics for numerous lectin targets (E-, P- and L-selectin, Siglec-2, -4, -7, -8 and -9 and FimH), and second evaluates and optimizes the pharmacokinetic properties of test compounds.

B. POSITIONS AND HONORS

Positions and Employment

1981	Lab head in the Central Research Laboratory of Ciba-Geigy Ltd, Basel, Switzerland
1986	Authorized representative (Handlungsbevollmächtigter), Ciba-Geigy Ltd. Basel Switzerland
1986	Group leader "Carbocyclic Cemistry", Ciba-Geigy Ltd. Basel Switzerland
1990	Authorized officer, Ciba-Geigy AG
1992	Head of section "Carbohydrate Chemistry and Biology" at Ciba-Geigy AG
1996	Head of the Selectin project at Transplantation Research, Novartis Pharma AG, Basel, Switzerland
1998 -	Professor of Molecular Pharmacy, Department of Pharmaceutical Sciences, University of Basel, Switzerland
2004 - 2008	Head of the Department of Pharmaceutical Sciences
2017	Professor Emeritus, with lab and office at the University of Basel

Professional Memberships

1981 -	Swiss Chemical Society
1999 -	American Chemical Society
2002 -	Swiss Society of Biochemistry
2010 -	American Society of Microbiology
2016 -	Fellow of the Swiss Academy of Pharmaceutical Sciences

Honors

1986	Werner-Price of the Swiss Chemical Society
1993	CIBA-Fellow for his contributions to natural product synthesis
2003	LearnTechNet Prize of the University of Basel
2003	MedidaPrix, European academic award for media didactics
2003	Novartis Lecturer
2013	PHOENIX Pharmaceutical Science Award
2015	Peter Speiser Award, ETH Zürich, Switzerland

Editorial Boards

International Advisory Board of *ChemMedChem*

Editorial Board of International Journal of Carbohydrate Chemistry

Editorial Advisory Board of ACS Medicinal Chemistry Letters.

C. CONTRIBUTION TO SCIENCE

Beat Ernst has been a professor of Molecular Pharmacy in the Department of Pharmaceutical Sciences at the University of Basel since 1998. Professor Ernst studied chemistry at the ETH Zürich, where he also completed his Ph.D. in the area of tricyclic hydrocarbons supervised by Prof. Oskar Jeger and Camille Ganter. He spent the following two years as a post-doctoral associate at the California Institute of Technology, Pasadena, CA, in the research group of Prof. Robert E. Ireland, where he synthesized tirandamycin C, a member of the tetramic acid family of natural products. In 1981, he joined Ciba-Geigy's Central Research Laboratories in Basel, where he first worked on small ring compounds, and later on carbohydrates and the design of glycomimetics as potential drug candidates. After his promotion to section head Carbohydrate Chemistry and Biology in 1992, he initiated the Selectin program. From 1996, he headed the Selectin project at Transplantation Research of Novartis Pharma AG, which had been formed through the merger between Ciba-Geigy and Sandoz. In 1998, he was appointed Professor of Molecular Pharmacy at the University of Basel. His research interests are at the interface between carbohydrate chemistry and glycobiology, with a particular focus on the synthesis of glycomimetics and their pharmacological profiling. Finally, in 2014 he and two colleagues (Prof. A. Steck and Dr. R. Herrendorff) founded the company Polyneuron Pharmaceuticals (http://polyneuron.com) to target carbohydrate-related autoimmune diseases.

The goal of Beat Ernst's work is to gain improved insight into carbohydrate-lectin interactions and to use this information for the development of carbohydrate-based therapeutics (see selected publications below).

1. Developing glycomimetics with appropriate pharmacodynamic and pharmacokinetic properties as potential drug candidates

- Chang J, Patton JT, Sarkar A, Ernst B, Magnani JL, Frenette PS, GMI-1070, a novel pan-selectin antagonist, reverses acute vascular occlusions in sickle cell mice. *Blood* **2010**, *116*, 1779-1786.
- Egger J, Weckerle C., Cutting B, Schwardt O, Rabbani R, Lemme K, Ernst B. Nanomolar E-selectin Antagonists with Prolonged Half-lives by a Fragment-based Approach. *J. Am. Chem. Soc.* **2013**, *135*, 9820-9828.
- Klein T, Abgottspon D, Wittwer M, Rabbani S, Herold J, Jiang X, Kleeb S, Lüthi C, Scharenberg M, Bezençon J, Gubler E, Pang L, Smiesko M, Cutting B, Schwardt O, Ernst B. FimH Antagonists for the Oral Treatment of Urinary Tract Infections: From Design and Synthesis to In Vitro and In Vivo Evaluation. *J. Med. Chem.* **2010**, *53*, 8627-8641.
- Kleeb S, Pang L, Mayer K, Eris D, Sigl A, Preston RC, Zihlmann P, Sharpe T, Jakob RP, Abgottspon D, Hutter AS, Scharenberg M, Jiang X, Navarra G, Rabbani S, Smiesko M, Lüdin N, Bezençon J, Schwardt O, Maier T, Ernst B. FimH Antagonists - Bioisosteres to Improve the *in vitro* and *in vivo* PK/PD Profile, *J. Med. Chem.* **2015**, *58*, 2221-2239.
- Kleeb S, Jiang X, Frei P, Sigl A, Bezencon B, Bamberger K, Schwardt O, Ernst B. FimH Antagonists – Phosphate Prodrugs Improve Oral Bioavailability. *J. Med. Chem.* **2016**, *59*, 3163-3182.

- Herrendorff R, Hänggi P, Pfister H, Yang F, Demeestere D, Hunziker F, Frey S, Schaeren-Wiemers N, Steck AJ, Ernst B. Selective in vivo removal of pathogenic anti-MAG autoantibodies, an antigen-specific treatment option for anti-MAG neuropathy. *PNAS* **2017**, *114*, E3689-E3698.

2. Conformational issues of carbohydrates and mimetics thereof

- Kolb HC, Ernst B. Development of Tools for the Design of Selectin Antagonists. *Chem. Eur. J.* **1997**, *3*, 1571.
- Jahnke W, Kolb HC, Blommers MJJ, Magnani JL, Ernst B. Comparison of the Bioactive Conformations of Sialyl Lewisx and a Potent Sialyl Lewisx Mimic. *Angew. Chem. Int. Ed.* **1997**, *36*, 2603.
- Su Z, Wagner B, Cocinero EJ, Ernst B, Simons J. The intrinsic conformation of a Lewis antigen: The Lewisx trisaccharide. *Chem. Phys. Lett.* **2009**, *477*, 365-368.
- Zierke M, Smieško M, Rabbani S, Aeschbacher T, Cutting B, Allain FHT, Schubert M, Ernst B. Stabilization of branched oligosaccharides: Lewisx benefits from a non-conventional C-H•••O hydrogen bond. *J. Am. Chem. Soc.* **2013**, *135*, 13464-13472.
- Eris D, Preston RC, Scharenberg M, Hilliger F, Abgottspon D, Pang L, Jiang X, Schwardt O, Ernst B. The Conformational Variability of FimH - Which Conformation Represents the Therapeutic Target?"ChemBioChem **2016**, *11*, 1012-1020.
- Mayer K, Eris D, Schwardt O, Sager CP, Rabbani S, Kleeb S, Ernst B. Urinary Tract Infection: Which Conformation of the Bacterial Lectin FimH Is Therapeutically Relevant? *J. Med. Chem.* **2017**, *60*, 5646-5662.
- Sager CP, Fiege B, Zihlmann P, Vannam R, Rabbani S, Jakob RP, Preston RC, Zalewski A, Maier T, Peczuh MW, Ernst B. The price of flexibility – a case study on septanoses as pyranose mimetics. *Chemical Science* **2018**, DOI: 10.1039/C7SC04289B.

3. Catch bond mechanism of carbohydrate-lectin interactions

- Sauer MM, Jakob RP, Eras J, Baday S, Eris D, Navarra G, Bernèche S, Ernst B, Maier T, Glockhuber R. Catch-bond mechanism of the bacterial adhesion FimH. *Nature Commun.* **2016**, *7*, 10738.
- Eris D, Preston RC, Scharenber M, Hilliger F, Abgottspon D, Pang G, Jiang X, Schwardt O, Ernst B. The Conformational Variability of FimH - Which Conformation Represents the Therapeutic Target? *ChemBioChem* **2016**, *11*, 1012-1020.
- Preston RC, Jakob RP, Binder, Sager CP, Ernst B, Maier T. E-Selectin Ligand Complexes Adopt an Extended High-Affinity Conformation. *J. Mol. Cell Biol.* **2015**, *290*, 21213-21230.

4. Thermodynamic and kinetic issues of carbohydrate-lectin interactions

- Mesch S, Lemme K, Koliwer-Brandl H, Strasser DS, Schwardt O, Kelm S, Ernst B. Kinetic and thermodynamic properties of MAG antagonists. *Carbohydr. Res.* **2010**, *345*, 1348-1359.
- Binder FPC, Lemme K, Preston RC, Ernst B. Sialyl Lewisx – a "Pre-organized Water Oligomer"? *Angew. Chem. Int. Ed.* **2012**, *51*, 7327-7331 [selected as Very Important Paper (VIP)].
- Pang L, Kleeb S, Lemme K, Rabbani S, Scharenberg M, Zalewski A, Schädler F, Schwardt O, Ernst B. FimH Antagonists: Structure-Activity and Structure-Property Relationships for Biphenyl α-D-Mannopyranosides. *ChemMedChem* **2012**, *7*, 1404-1422 [selected as Very Important Paper (VIP)].
- Scharenberg M, Jiang X, Pang L, Navarra G, Rabbani S, Binder F, Schwardt O, Ernst B. Kinetic Properties of Carbohydrate-Lectin Interactions: FimH Antagonists. *ChemMedChem* **2014**, *9*, 78-83.

5. Assay development

- Rabbani S, Jiang X, Schwardt O, Ernst B. Expression of the Carbohydrate Recognition Domain of FimH and Development of a Competitive Binding Assay. *Anal. Biochem.* **2010**, *407*, 188-195.
- Abgottspon D, Rölli G, Hosch L, Steinhuber A, Jiang X, Schwardt O, Cutting B, Smiesko M, Jenal U, Ernst B, Trampuz A. Development of an Aggregation Assay to Screen FimH Antagonists *J. Microbiol. Meth.* **2010**, *82*, 249-255.
- Scharenberg M, Abgottspon D, Cicek E, Jiang X, Schwardt O, Rabbani S, Ernst B. A Flow Cytometry-based Assay for Screening FimH Antagonists. *Assays Drug Dev. Technol.* **2011**, *9*, 455-464.
- Wipf M, Stoop RL, Navarra G, Rabbani S, Ernst B, Bedner K, Schönenberger C, Calame M. Label-Free FimH Protein Interaction Analysis Using Silicon Nanoribbon BioFETs. *ACS Sens.* **2016**, *6*, 781-788.