Proceedings of the 10th Chinese International Peptide Symposium

Peptides

Biology and Chemistry

Editors
Yan-Mei Li
Chuan-Guang Qin

Chemical Industry Press

Peptides

Biology and Chemistry

Proceedings of the 10th Chinese International Peptide Symposium
July 1–5, 2008, Xi'an China

Edited by

Yan-Mei Li
Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology, Tsinghua University, Beijing, China

Chuan-Guang Qin
Laboratory of Chemical Biology and Medicinal Chemistry, Northwestern Polytechnical University, Xi'an, China

Chemical Industry Press
· BeiJing ·

图书在版编目（CIP）数据

多肽生物学和多肽化学 = Peptides Biology and Chemistry: 英文/李艳梅，钦传光主编. —北京：化学工业出版社, 2009. 8
ISBN 978-7-122-05965-9

Ⅰ.多… Ⅱ.①李…②钦… Ⅲ. ①多肽-生物学②多肽-化学 Ⅳ. Q516

中国版本图书馆 CIP 数据核字（2009）第 098455 号

责任编辑：李晓红　　装帧设计：关　飞
责任校对：顾淑云

出版发行：化学工业出版社（北京市东城区青年湖南街 13 号　邮政编码 100011）
印　　刷：北京永鑫印刷有限责任公司
装　　订：三河市万龙印装有限公司
787mm×1092mm　1/16　印张 11　字数 182 千字
2010 年 1 月北京第 1 版第 1 次印刷

购书咨询：010-64518888（传真：010-64519686）　售后服务：010-64518899
网　　址：http://www.cip.com.cn
凡购买本书，如有缺损质量问题，本社销售中心负责调换。

定　　价：98.00 元

Preface

The 10th Chinese International Peptide Symposium (CPS-2008), hosted by Tsinghua University and Northwestern Polytechnical University, was held at Xi'an, China, July 1–5, 2008 with more than 200 participants. The four-day conference was both intense and spiritually rewarding. Our goal for CPS-2008 was to provide a forum for the exchange of knowledge, cooperation and friendship between the international and Chinese scientific communities in peptide sciences.

The symposium consisted of 14 sessions with 68 oral and 90 poster presentations, including synthetic methods, molecular diversity and peptide libraries, structure and conformation of peptides and proteins, bioactive peptides, peptide immunology, denovo design and synthesis of proteins and peptides, ligand-receptor interactions, the chemistry-biology-interface and challenging problems in peptides.

The enthusiastic cooperation and excellent contributions were gratifying and the active response of the speakers contributed to the success of the symposium. The presentations were of excellent caliber and represented the most current and significant aspects of peptide science.

We greatly appreciate the generous financial assistance of the sponsors and donors, especially the National Natural Science Foundation of China, whose support was indispensable to make the meeting a great success.

Yan-Mei Li
Chuan-Guang Qin

10th Chinese International Peptide Symposium (CPS-10)

July 1-5, 2008
Xi'an, China

Sponsored by
National Natural Science Foundation of China
Tsinghua University
Northwestern Polytechnical University

Organized by
Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology, Tsinghua University
Laboratory of Chemical Biology and Medicinal Chemistry, Northwestern Polytechnical University

Organizations

Symposium Chairperson
Yan-Mei Li, *Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology, Tsinghua University, Beijing, China*

Symposium Vice Chairman
Chuan-Guang Qin, *Laboratory of Chemical Biology and Medicinal Chemistry, Northwestern Polytechnical University, Xi'an, China*

Secretary General
Yuan Ma, *Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology, Tsinghua University, Beijing, China*

Consultative Committee
Zhi-Nan Chen, *The Fourth Military Medical University, China*

Xue-Yun Cui, *Hainan Zhonghe Pharmaceutical Co., Ltd., China*
Bing-Wen Liang, *中药复方新药开发国家工程研究中心 DDS 中试基地*
Gui-Chen Lu, *Institute of Materia Medica, Chinese Academy of Medical Sciences, China*
Geoffrey W. Tregear, *Howard Florey Institute, The University of Melbourne, Australia*
Hong-Yan Xu, *G L Biochem (Shanghai) Ltd.*
Yun-Hua Ye, *Peking University, China*
You-Shang Zhang, *Institute of Biochemistry and Cell Biology, Shanghai Institute for Biology Sciences, Chinese Academy of Sciences, China*
Yu-Fen Zhao, *Tsinghua University, China*
Yong-Hui Zhu, *Xi'an Kinggeng Biomedical Research Co., Ltd., China*

International Scientific Committee

Saburo Aimoto, *Institute for Protein Research, Osaka University, Japan*
Zhi-Nan Chen, *The Fourth Military Medical University*
Kyung-Soo Hahm, *Research Center for Proteinous Materials, Chosun University, Korea*
Victor J. Hruby, *Department of Chemistry, University of Arizona, USA*
Hong-Yu Hu, *Institute of Biochemistry and Cell Biology, Shanghai Institute for Biology Sciences, Chinese Academy of Sciences, China*
Zi-Wei Huang, *The Burnham Institute, University of California at San Diego, USA*
Yong Ju, *Tsinghua University, China*
Yoshiaki Kiso, *Departtment of Medicinal Chemistry, Kyoto Pharmaceutical University, Japan*
Kit S. Lam, *University of California Davis, USA*
Yan-Mei Li, *Tsinghua University, China*
Gang Liu, *Institute of Materia Medica, Chinese Academy of Medical*

Sciences, China

Ke-Liang Liu, *Beijing Institute of Pharmacology and Toxicology, China*

Lei Liu, *Tsinghua University, China*

Ya-Qiu Long, *Shanghai Institute of Materia Medica, Chinese Academy of Sciences, China*

Da-Wei Ma, *Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, China*

Jean Martinez, *Universities de Montpellier I, Faculte de Pharmacie, France*

Chuan-Guang Qin, *Northwestern Polytechnical University, China*

Ian Smith, *Monash University, Australia*

James P. Tam, *The Scripps Research Institute-Scripps Florida, USA*

Ning-Hua Tan, *Kunming Institute of Botany, Chinese Academy of Sciences, China*

John D. Wade, *Howard Florey Institute, The University of Melbourne, Australia*

Rui Wang, *Lanzhou University, China*

Jia-Xi Xu, *Beijing University of Chemical Technology, China*

Zhu-Jun Yao, *Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, China*

Local Organizing Committee (*Tsinghua University, China*)

Guo-Li Dong, Yu-Ping Feng, Yong Ju, Yuan Ma, Tian-Shu Lin, Lei Liu, Qin-Zhu Wang, Jin-Xiang Yin, Zheng Wu, Jia Hu, Lu Jin

Cathay Awarding Committee

You-Shang Zhang, *Institute of Biochemistry and Cell Biology, Shanghai Institute for Biology Sciences, Chinese Academy of Sciences, China*

Victor J. Hruby, *Department of Chemistry, University of Arizona, USA*

Kit S. Lam, *University of California Davis, USA*

Ke-Liang Liu, *Beijing Institute of Pharmacology and Toxicology, China*

Jean Martinez, *Universities de Montpellier I, Faculte de Pharmacie, France*

James P. Tam, *The Scripps Research Institute-Scripps Florida, USA*

Rui Wang, *Lanzhou University, China*
Yun-Hua Ye, *Peking University, China*

The effort and support of the following sponsors are gratefully acknowledged:

Platinum Sponsor
Hai Nan Zhonghe (Group) Ltd.
Xi'an Kingene Biomedical Research Co., Ltd.
GL Biochem (Shanghai) Ltd.

Gold Sponsor
CL Bio-Scientific Co. Ltd.

Silver Sponsor
Phoenix Biotech (Beijing) Co., Ltd.
Scilight-Peptide Inc.

Brozone Sponsor
Sichuan Sangao Biochemical Co., Ltd.
Chengdu Kaijie Bio-Pharmaceutical Co., Ltd.
C S Bio. Co.

Other Sponsor
Acta Biochimica et Biophysica Sinica

Awards
Cathy Award (Sponsored by H. H. Liu Education Fundation)
Peptide Application Special Award (Sponsored by Hainan Zhonghe Pharmaceutical Co., Ltd.)
Young Scientist Award (Sponsored by Hainan Zhonghe Pharmaceutical Co., Ltd.)
Excellent Poster Award (Sponsored by Sangao Biochemical Co., Ltd)
Outstanding student participants support (Sponsored by Hainan Zhonghe Pharmaceutical Co. Ltd.)

Contents

Session 1

Proteomics/Analytical/Structure

Interaction of Local Anesthetic Drugs and Na^+ Channel Inactivation Gate Peptide in Linker between Domain III and IV by Electrospray Tandem Mass Spectrometry and Surface Plasma Resonance

Bih-Show Lou[a], Pei-Shan Wu[a], Yuan-Chin Chen[b], and Hui-Fen Wu[b]

[a]Chemistry division, Center of Education, Chang Gung University, Tao-Yuan, Taiwan, China

[b]Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, Taiwan, China

Introduction

Ion channels are membrane proteins that play a fundamental role in cell physiology and in signal transduction and transmission. To fulfill their functional role, such as Na^+ channels of nerve and muscle cells, they must be able to complete their state transitions in vivo among resting, open and fast inactivated states in a few milliseconds[1-3]. Fast inactivation is at least partly mediated by the cytoplasmic linker between domains III and IV (L_{III-IV}). Mutations of a cluster of three hydrophobic residues within this linker, Ile^{1488}, Phe^{1489}, and Met^{1490} (IFM), result in a channel that does not inactivate, and this triplet IFM has been proposed as a part of inactivation particle that may function as a hinged lid[4,5]. In addition, Voltage-gated Na^+ channels are the primary targets of many important therapeutic drugs, including local anesthetics and anticonvulsants[6,7]. The binding of therapeutic drugs not only blocks the voltage-gated sodium ion channels and hence stop the propagation of action potentials, but may also stabilize the fast inactivated state of the sodium ion channel directly[1]. The investigation of the interaction between the inactivation particle IFM motif and therapeutic drugs may provide understanding for the fast inactivated state which can be stabilized by the drug binding. In this study, BL-1, a model of IFM containing peptide with a sequence of acetyl-GGQDIFMTEEK-OH, in the presence of an anticonvulsant diphenyl drug, phenytoin (DPH) are measured by electrospray ionization mass spectrometry (ESI-MS) and surface plasma resonance (SPR) to obtain their interactions.

Results and Discussion

The measurements of a non-covalent peptide and an organic drug complex is challenging due to the fact that they tend to dissociate easily. However, ESI is a gentle ionization method that allows intact weakly bounded complexes to be detected[8]. Direct binding specie between BL-1 and DPH has been observed in the ESI-MS spectrometry[9]. The best binding condition is determined by drug titration experiment (Fig. 1). The major peak at *m/z* 668 in Fig. 1(a) corresponds to $[M+3H_2O+2H]^{2+}$, where M (1279) is generated by the neutral loss of ammonia (−17u) from Lys (K) in the C-terminal of BL-1. A new peak at *m/z* 776.0 could be barely observed when BL-1 and DPH have a molar ratio of 1:5.6 after 18 hours of incubation at 40°C, and its abundance increased steadily while the DPH molar ratio increased up to 1:28 as shown in Fig. 1(c). This peak can be assigned as a $[M+H_2O+DPH+2H]^{2+}$ complex. At a higher drug to BL-1 ratio in Fig. 1(d), the relative abundance at peak *m/z* 776 remained and no other complex signal was detectable. The results above suggest that BL-1 complex with DPH has a 1:1 stoichiometry.

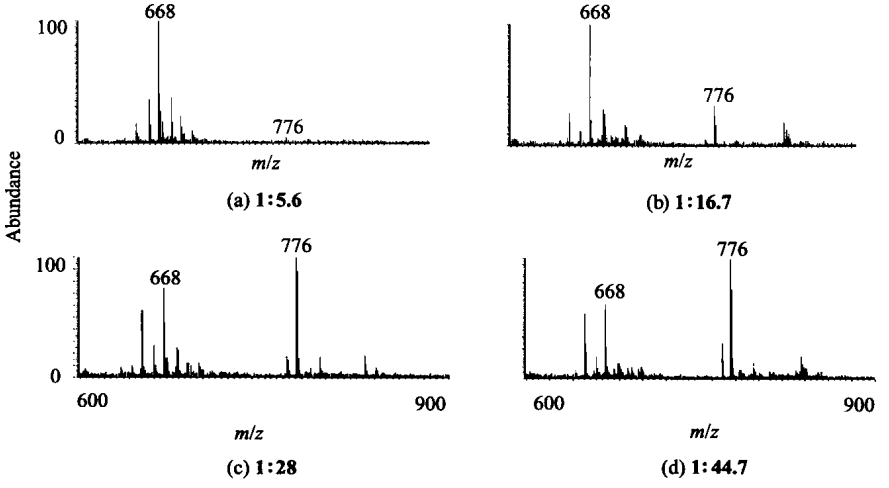

Fig. 1. ESI-MS for BL-1 complex with DPH were obtained in different molar ratios of BL-1 and DPH after 18 hours of incubation at 40 ℃.

From NMR studies[10,11], we found NH chemical shifts of BL-1 caused by DPH in phospholipid bicelles (DMPC/DHPC) are larger than in a phosphate buffer, which indicates the interaction between BL-1 and DPH is increased once an -helix is formed in the phospholipid bicelles. In

addition, the residues from Phe^{6} to Clu^{10} in the BL-1 C-terminal with remarkable chemical shift changes caused by DPH bound demonstrates that they are involved in inhibitor-receptor interaction. From SPR[12] studies, we have established the technology of the lipid system to capture L1 chip and can be observed by BIACore 3000. Soy lecithin nanoemulsion (SLN) is determined as a better lipid system for our study because its consis-

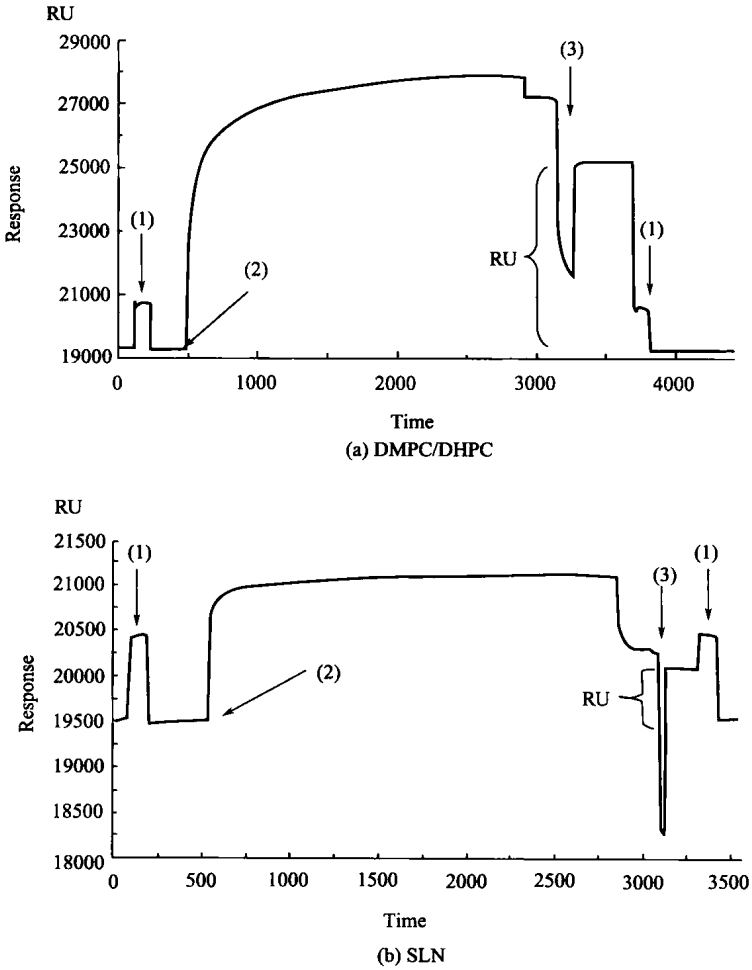

Fig. 2. Captured responses were compared in two different liposomes (resonance unite, RU). (a) DMPC/DHPC = 0.5/1 mM; (b) 1mM SLN. The capture program is (1) 20 mM CHAPS, 20 μl/min, 40 μl; (2) Liposome captured, 2 μl/min, 80 μl; and (3) 10 mM NaOH, 100 μl/min, 50 μl. DMPC: 1,2-dimyristoyl-sn-glycero-3- phosphatidylcholine, DHPC: 1,2-dihexanoy-sn- glycero-3-phosphatidylcholine. SLN: Soy Lecithin Nanoemulsion.