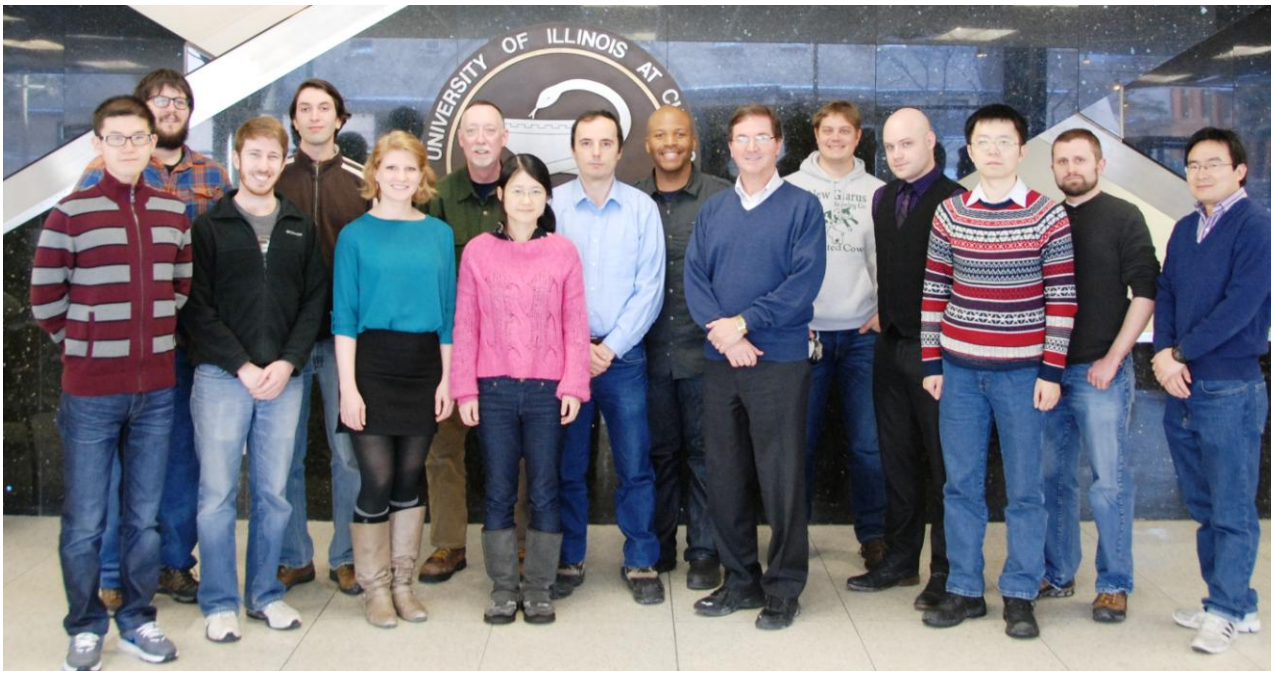
The van Breemen Research Group and Chicago Mass Spectrometry Laboratory 2014 Newsletter

Highlights of 2013

February, 2014
Volume 3, Issue 1

This is the third edition of the van Breemen research group newsletter. Highlights this year included the awarding of two new NIH grants, 1) a T32 training grant in natural products research; and 2) an R01 grant to support our studies of natural products mass spectrometry. Other highlights included 16 papers, and two new mass spectrometers (Shimadzu LCMS-8050 and AB Sciex 6500). Two graduate students and one visiting international scholar completed their studies in our laboratory during 2013. Read on for details of these achievements as well as awards to lab members.

Inside this issue:



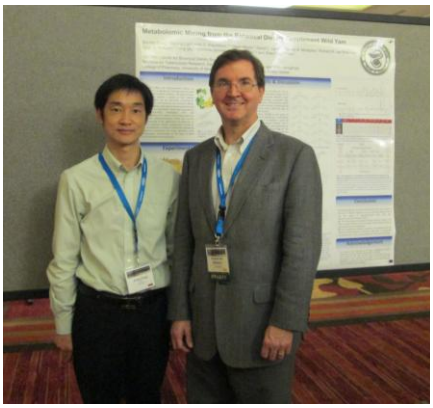
2013-2014 van Breemen Research Group in the College of Pharmacy Lobby. *Front row:* Lingyi Huang, Daniel May, Elisabeth Hersman, Guannan Li, Dejan Nikolic, Richard van Breemen, Ke Huang, Yongchao Li. *Back row:* Josh Henkin, Andrew Newsome, Richard Morrissy, Brian Wright, Zane Hauck, Michael Rush, Caleb Nienow. (*Not pictured:* Tristesse Jones)

New Instrumentation

We were fortunate in 2013 to install two new mass spectrometers. An AB Sciex 6500 QTrap replaced the Thermo Quantum triple quad and was acquired with the help of the Research Resources Center and a shared instrument grant from the NIH. In addition, Shimadzu generously replaced the LCMS-8080 in our lab with its latest triple quadrupole, the LCMS-8050. This instrument is even faster and more sensitive than the LCMS-8040 or LCMS-8080. Sigrid Baumgarten (Postdoctoral 2011) joined Shimadzu in France while alumni Jeff Dahl (PhD 2010) and Kevin Krock (Ph.D. 2013) continue to work for Shimadzu in MD and CA.

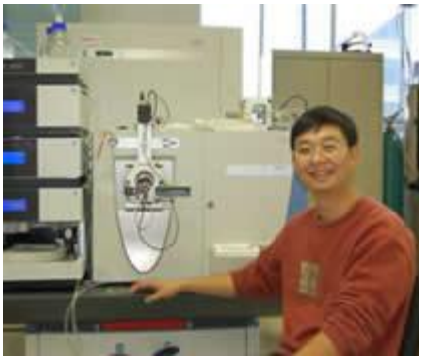
Lab Graduates of 2013

Dr. Jinbo Fang was a visiting scholar in our laboratory from the summer of 2012 until August 2013. He then returned to China where he holds the position of lecturer in the Department of Chinese Medicine at the School of Pharmacy of Huazhong University of Science and Technology. Previously, he had received his Ph.D in Natural Product Chemistry from Tianjin University of China. While in Chicago, Jinbo determined the structures of glucuronides of 8-prenylnaringenin, which is the estrogenic prenylated flavonoid in hops. This work required not only LC-MS/MS but also semi-preparative HPLC and high field NMR in collaboration with David Lankin in our Botanical Center.



Kevin Krock and Linlin Dong became the 44th and 45th students, respectively, to graduate from our laboratory. Kevin was our 27th Ph.D. graduate in Medicinal Chemistry, and Linlin became the 9th Pharmacogngosy student to receive a Ph.D. in our laboratory.

Medicinal Chemistry graduate student Kevin Krock received his Ph.D. in 2013. The title of his dissertation was, “Investigation of two potential treatments for frontotemporal dementia by LC-MS.” This project concerned the development of a new MS-based drug discovery assay based on the prevention of tau peptide aggregation and was fundamentally different from our pulsed ultrafiltration LCMS screening approach. Prior to graduation, Kevin had already accepted his current position as a Scientist at the west coast facility of Shimadzu Instruments in Pleasanton, CA. - Look for him at the 2014 ASMS Conference that will be held in Baltimore, Maryland this year.



Linlin Dong received his Ph.D. in Pharmacognosy during 2013. His dissertation was entitled, “Analysis of carotenoids using LC-MS-MS with ion mobility spectrometry and photoionization.” His studies extended our laboratory tradition of applying innovative mass spectrometry techniques to the study of carotenoids. After graduation, Linlin joined Millenium Pharmaceuticals in Cambridge, MA. Several of our lab graduates have worked at Millenium, including Chao-Ran Huang (postdoctoral fellow 1994-1996) and, currently, Xiaofeng Yang (Ph.D. 2005).

Historic Group Photo 1990

Back row: Johnny Creech, Rod Davis, Roy Martin
Front row: Richard van Breemen, Chien-Hua Huang, Yinhsien Tsou (posthumous Ph.D. 1993), David Goodlett
Updates: David is at the University of Maryland (Pharmacy), Rod is at the University of Illinois (Chicago), and Roy is at Waters (MA). Lost touch with John and Chien-Hua.

Grants in 2013

In a year of national budget rescission, we were fortunate to receive two new NIH grants, both of which were sponsored by the National Center for Complementary and Alternative Medicine. NCCAM co-funds our Botanical (which I continue to direct) along with the NIH Office of Dietary Supplements.

1. Our first new grant of 2013 was a training grant (1T32AT007533) entitled, "Research training in natural product complementary and alternative medicine." This 5-year grant supported 2 graduate students and 2 postdocs in 2013 and will eventually support 6 students and 3 postdocs each year. Since I joined UIC in 1994, this has been the only training grant in the College of Pharmacy. Currently, Mike Rush of our group is supported by this grant. I am using the other slots to fund trainees of other research groups.

2. The other new NIH grant of 2013 was 1R01CA79870, entitled, "Rapid identification of active agents and metabolomics of botanical supplements". During this 5-year grant, we hope to enhance the throughput of ultrafiltration mass spectrometry over 100-fold for faster identification of active natural products and to develop fast validated approaches to chemical standardization of botanical dietary supplements.

3. We continue to work with PepsiCo and Hershey, and we are investigators on several other NIH grants. Last year marked the 15th anniversary of our UIC/NIH Center for Botanical Dietary Supplements Research (NIH grant P50AT0155). Here is our latest Center photo:

Awards

1. At the 4rd Annual College of Pharmacy Research Day last spring, Pharmacognosy graduate student Tristesse Jones received a W. E. van Doren Scholar Award. She is working with our group as well as with Botanical Center botanist Prof. Soejarto.

2. Ke Huang, a graduate student in Medicinal Chemistry and our group, also received a W. E. van Doren Scholar Award.

***Chemical & Engineering News*, the weekly news magazine of the American Chemical Society, featured the work of our Botanical Center and others in helping to improve the safety of botanical dietary supplements through analytical testing & standardization.**

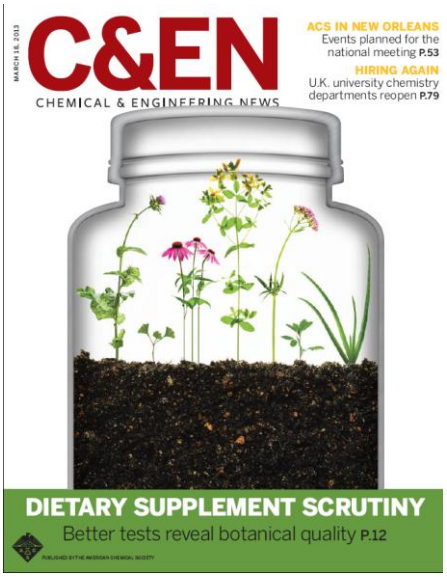
Meetings and Press

Our group presented 20 talks and posters at international and national meetings in 2013.

I presented talks in Shanghai and Beijing, China, as part of the Sino-American Pharmaceutical Association Symposia during March. In October, I spoke at the famous Dohme Lecture series of the Johns Hopkins University Pharmacology Department which was dedicated this year to the late Robert Cotter. Bob had been my postdoctoral advisor at Hopkins.

Our proteomics paper on lycopene mechanisms of action of in human prostate cells (paper #5, 2013) received special attention when Michael Sporn (who coined "chemoprevention") of Dartmouth wrote an editorial praising us. Our paper was then cited by the popular press including the *Daily Mail* and the *Wall Street Journal.*

Finally, our Botanical Center work was featured in a cover article of *Chemical & Engineering News* (91(11): 12-17, March 18, 2013.



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http://www.uic.edu/labs/breemen/

2013 Publications

For more than 12 years, our laboratory has been publishing between 10 and 20 peer-reviewed papers and book chapters per year. In 2013, our group published 15 peer-reviewed papers and one book chapter, which exceeded our 2012 total of 15 papers and book chapters.

1. Nikolic D, van Breemen RB. Analytical methods for quantitation of prenylated flavonoids from hops. *Curr. Anal. Chem.* **9**, 71-85 (2013).
2. Zhao G, Yu R, Deng J, Zhao Q, Li Y, Joo M, van Breemen RB, Christman JW, Xiao L. Pivotal role of reactive oxygen species in differential regulation of lipopolysaccharide-induced prostaglandins production in macrophages. *Mol. Pharmacol.* **83**, 167-178 (2013).
3. Kabirov KK, Kapetanovic IM, Benbrook DM, Dinger N, Mankovskaya I, Zakharov A, Detrisac C, Pereira M, Martín-Jiménez T, Onua E, Banerjee A, van Breemen RB, Nikolić D, Chen L, Lyubimov AV. Oral toxicity and pharmacokinetic studies of SHetA2, a new chemopreventive agent, in rats and dogs. *Drug Chem Toxicol*. **36**, 284-295 (2013).
4. Yuan Y, Yu L-F, Qiu X, Kozikowski AP, van Breemen RB. Pharmacokinetics and brain penetration of LF-3-88, (2-[5-[5-(2(S)-azetidinylmethoxyl)-3-pyridyl]-3-isoxazolyl]-ethanol, a selective α4β2-nAChR partial agonist and promising antidepressant. *J. Chromatogr. B* **912**, 38-42 (2013).
5. Qiu X, Yuan Y, Vaishnav A, Tessel MA, Nonn L, van Breemen RB. Effects of lycopene on protein expression in human primary prostatic epithelial cells *Cancer Prev. Res. (Phila.)* **6**, 419-427 (2013). NIHMS 446802 Featured in a "Perspective" editorial in this issue by Sporn and Liby, p 384.
6. van Breemen RB. Robert J. Cotter (1943 – 2012). *J. Am. Soc. Mass Spectrom.* **24**, 655-656 (2013).
7. Gaba RC, Yap FY, Martinez EM, Li Y, Guzman G, Parvinian A, van Breemen RB, Kumar N. Transarterial sorafenib chemoembolization: preliminary study of technical feasibility in a rabbit model. *J. Vasc. Interv. Radiol.* **24**, 744-750 (2013).
8. Conda-Sheridan M, Park EJ, Beck DE, Reddy PV, Nguyen TX, Hu B, Chen L, White JJ, van Breemen RB, Pezzuto JM, Cushman M. Design, synthesis, and biological evaluation of indenoisoquinoline rexinoids with chemopreventive potential. *J. Med. Chem.* **56**, 2581-2605 (2013).
9. Yu R, Zhao G, Christman JW, Xiao L, van Breemen RB. Method development and validation for ultra-high pressure liquid chromatography/tandem mass spectrometry determination of multiple prostanoids in biological samples. *J. AOAC Intl.* **96**, 67-76 (2013).
10. Dong SH, Cai G, Napolitano JG, Nikolić D, Lankin DC, McAlpine JB, van Breemen RB, Soejarto DD, Pauli GF, Chen SN. Lipidated steroid saponins from *Dioscorea villosa* (wild yam). *Fitoterapia* **91C**, 113-124 (2013).
11. Hajirahimkhan A, Simmler C, Yuan Y, Anderson JR, Chen SN, Nikolić D, Dietz BM, Pauli GF, van Breemen RB, Bolton JL. Evaluation of estrogenic activity of licorice species in comparison with hops used in botanicals for menopausal symptoms. *PLoS One* 8(7):e67947 Jul 12 (2013). doi: 10.1371/journal.pone.0067947
12. Mo S, Dong L, Hurst WJ, van Breemen RB. Quantitative analysis of phytosterols in edible oils using APCI liquid chromatography-tandem mass spectrometry. *Lipids* **48**, 949-956 (2013).
13. Andreani A, Leoni A, Locatelli A, Morigi R, Rambaldi M, Cervellati R, Greco E, Kondratyuk TP, Park E-J, Huang K, van Breemen RB, Pezzuto JM. Chemopreventive and antioxidant activity of 6-substituted imidazo[2,1-b]thiazoles, *Eur. J. Med. Chem*. **68C**, 412-421 (2013).
14. Jana A, Modi KK, Roy A, Anderson JA, van Breemen RB, Pahan K. Up-regulation of neurotrophic factors by cinnamon and its metabolite sodium benzoate: therapeutic implications for neurodegenerative disorders. *J. Neuroimmune Pharmacol.* **8**, 739-755 (2013).
15. Eilati E, Hales K, Zhuge Y, Ansenberger Fricano K, Yu R, van Breemen RB, Hales DB. Flaxseed enriched diet-mediated reduction in ovarian cancer severity is correlated to the reduction of prostaglandin E2 in laying hen ovaries. *Prostaglandins Leukot. Essent. Fatty Acids*, **89**, 179-187 (2013).
16. Abdelkarim H, Brunsteiner M, Neelarapu R, Bai H, Madriaga A, van Breemen RB, Blond SY, Gaponenko V, Petukhov PA. Photoreactive "nanorulers" detect a novel conformation of full length HDAC3-SMRT complex in solution. *ACS Chem. Biol.* **8**, 2538–2549 (2013).