



Special Technical Report

**AMRI Contributions to Science:
Review of Scientific Publications in 2009**

**Margarita Kirova-Snover, Ph.D. and R. Jason Herr, Ph.D.
Medicinal Chemistry Department**

Abstract: *As we have drawn the year 2009 to a close, we would like to take a moment to sum up the number of technological communications that AMRI scientists have contributed to the scientific community during this year. Please read through this document for a full list of abstracts (as they appear either with the original documents or taken from the SciFinder database) for all of the publications, presentations and patent applications that appeared during the year. We hope to make this bibliographical summary a regular year-end contribution.*

2009 AMRI Research Publications

During 2009, 23 research articles have appeared in peer-reviewed scientific journals that described innovations conceived by AMRI scientists. In most of these cases, these manuscripts were written by AMRI lead authors to communicate independent research, or were co-authored with customers to communicate research in collaboration with AMRI. Below are the bibliographies for these publications, including the abstracts, as they appeared with the original documents. The lead author name(s) are indicated.

1. "Synthesis and SAR of vinca alkaloid analogues," *Bioorganic and Medicinal Chemistry Letters* **2009**, 19(4), 1245-1249.

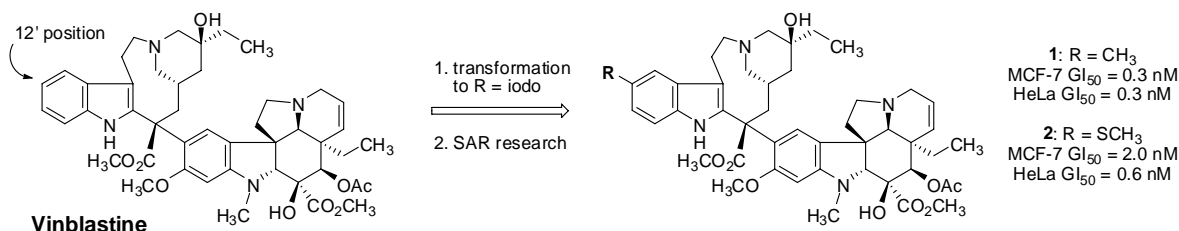
Matthew E. Voss,*¹ Jeffery M. Ralph,¹ Dejian Xie,¹ David D. Manning,¹ Xinchao Chen,¹ Anthony J. Frank,¹ Andrew J. Leyhane,¹ Lei Liu,² Jason M. Stevens,² Cheryl Budde,¹ Matthew D. Surman,¹ Thomas Friedrich,³ Denise Peace,³ Ian L. Scott,¹ Mark Wolf¹ and Randall Johnson⁴

¹Medicinal Chemistry Department, AMRI, Albany, NY, USA

²Chemical Development Department, AMRI, North Syracuse, NY, USA

³Albany Medical College, Albany, NY, USA

⁴Santa Fe, NM, USA

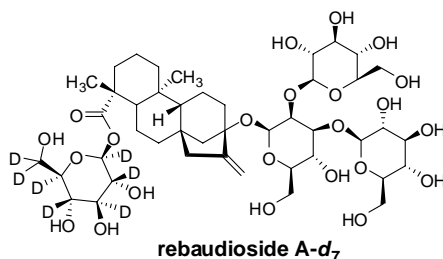


2. "Gas-phase intramolecular elimination reaction studies of steviol glycosides in positive electrospray and tandem mass spectrometry," *European Journal of Mass Spectrometry* **2009**, 15(1), 11-21.

Mani Upreti,¹ John F. Clos,¹ Kasi V. Somayajula,¹ Dennis J. Milanowski,² Ulla Mocek,² Grant E. DuBois¹ and Indra Prakash*¹

¹The Coca-Cola Company, Atlanta, GA, USA

²Bothell Research Center, AMRI, Bothell, WA, USA

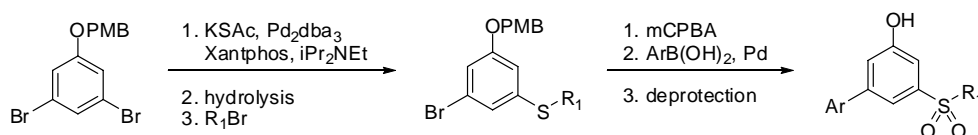


3. “Practical synthesis of 5-aryl-3-alkylsulfonylphenol and 5-aryl-3-arylsulfonylphenol libraries,” *Journal of Combinatorial Chemistry* **2009**, *11*(2), 327-334.

György Jeges*,¹ Tamás Nagy,¹ Tamás Mészáros,¹ József Kovács,¹ György Dormán,¹ Agnieszka Kowalczyk² and Robert A. Goodnow²

¹AMRI, Budapest, Hungary

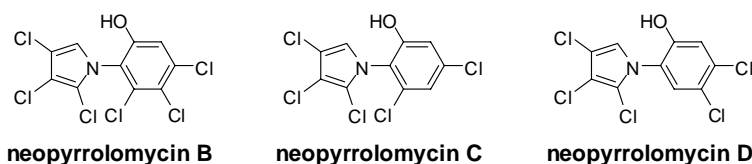
²Roche Research Center, Hoffmann-La Roche Inc., Nutley, NJ, USA



4. “Neopyrrolomycins with broad spectrum antibacterial activity,” *Journal of Natural Products* **2009**, *72*(2), 276-279.

D. Craig Hopp, Joshua Rhea, Daniel Jacobsen, Khadidja Romari, Chris Smith, John Rabenstein, Macarena Irigoyen, Midori Clarke, Linda Francis, Michele Luche, Grant J. Carr and Ulla Mocek*

Bothell Research Center, AMRI, Bothell, WA, USA

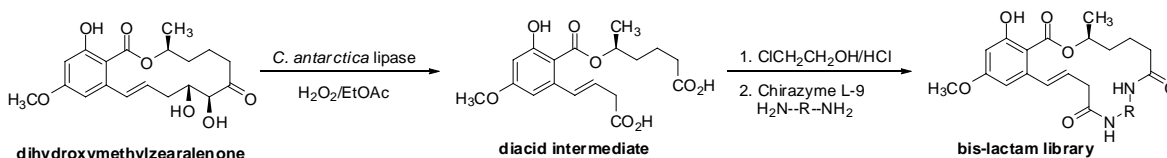


5. “Application of combinatorial biocatalysis for a unique ring expansion of dihydroxymethylzearalenone,” *Bioorganic & Medicinal Chemistry Letters* **2009**, *19*(11), 3059-3062.

Joseph O. Rich*,¹ Cheryl L. Budde,¹ Luke D. McConeghey,¹ Ian C. Cotterill,¹ Vadim V. Mozhaev,¹ Sheo B. Singh,² Michael A. Goetz,² Annie Zhao,² Peter C. Michels¹ and Yuri L. Khmelnsky*,¹

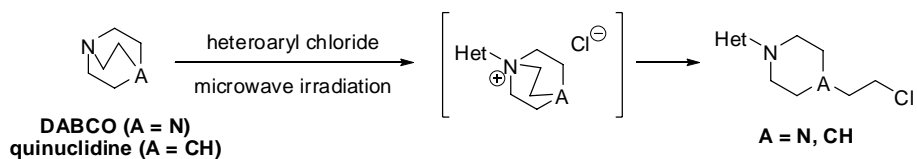
¹Department of Metabolism and Biotransformations, AMRI, Albany, NY, USA

²Merck Research Laboratories, Rahway, NJ, USA



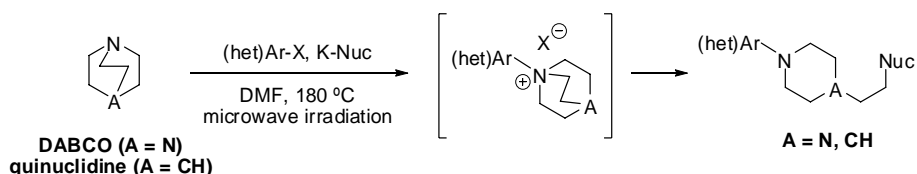
6. “Efficient *N*-arylation/dealkylation of electron deficient heteroaryl chlorides and bicyclic tertiary amines under microwave irradiation,” *Journal of Combinatorial Chemistry* **2009**, *11*(3), 355-363.

Hong-Jun Wang,* Yi Wang, Adam J. Csakai, William G. Earley and R. Jason Herr
Medicinal Chemistry Department, AMRI, Albany, NY, USA



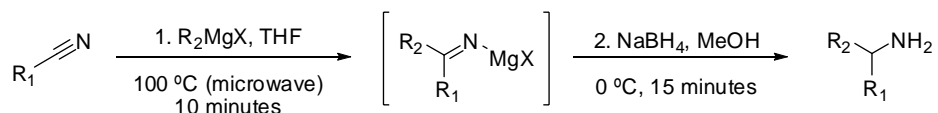
7. “Efficient microwave-assisted three-component one-pot preparation of 1-aryl-4-(2-acetoxyethyl)piperazines and 1-aryl-4-(2-acetoxyethyl)piperidines,” *Tetrahedron Letters* **2009**, *50*(27), 3813-3816.

S. Gabrielle Gladstone, William G. Earley,* Jared K. Acker and Gregory S. Martin
Medicinal Chemistry Department, AMRI, Albany, NY, USA



8. “Rapid, one-pot synthesis of α,α -disubstituted primary amines by the addition of Grignard reagents to nitriles under microwave heating conditions,” *Tetrahedron Letters* **2009**, *50*(27), 3978-3981.

Brian T. Gregg,* Kathryn C. Golden, John F. Quinn, Hong-Jun Wang, Wei Zhang, Ruifang Wang, Francis Wekesa and Dmytro O. Tymoshenko
Medicinal Chemistry Department, AMRI, Albany, NY, USA



9. “Design, selection, and evaluation of a general kinase-focused library,” *ChemMedChem* **2009**, *4*(8), 1273-1278.

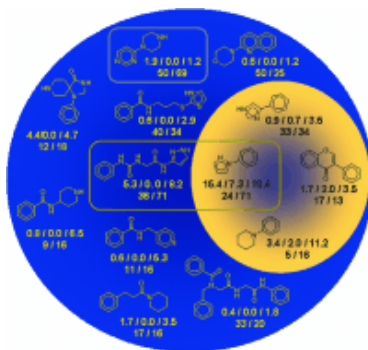
Hélène Decornez,¹ Anna Gulyás-Forró,² Ákos Papp,² Miklós Szabó,² Gabriella Sármay,³ István Hajdú,⁴ Sándor Cseh,⁴ György Dormán² and Douglas B. Kitchen*¹

¹Computer Aided Drug Discovery, AMRI, Albany, NY, USA

²Computer Aided Drug Discovery, AMRI, Budapest, Hungary

³Department of Immunology, Eötvös Loránd University, Budapest, Hungary

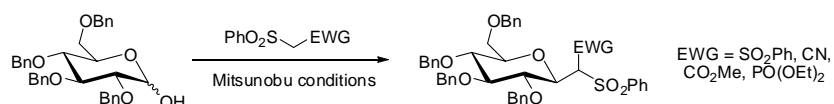
⁴TargetEx, Dunakeszi, Hungary



10. “A Mitsunobu route to C-glycosides,” *Tetrahedron* **2009**, 65(41), 8468-8477.

Paolo Pasetto* and Matthew C. Walczak

Medicinal Chemistry Department, AMRI, Albany, NY, USA



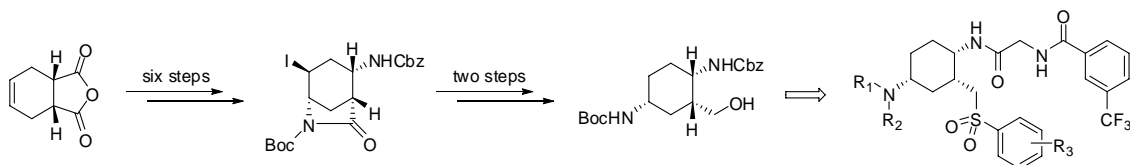
11. “Enantioselective synthesis of benzyl (1*S*,2*R*,4*R*)-4-(*tert*-butoxycarbonylamino)-2-(hydroxymethyl)cyclohexylcarbamate using an iodolactamization as the key step,”

Journal of Organic Chemistry **2009**, 74(16), 6368-6370.

Carlton L. Campbell,² Carla Hassler,² Soo S. Ko,¹ Matthew E. Voss,¹ Michael A. Guaciaro,² Percy H. Carter¹ and Robert J. Cherney*¹

¹Research and Development, Bristol-Myers Squibb Company, Princeton, NJ, USA

²Medicinal Chemistry Department, AMRI, Albany, NY, USA



12. “Controlling the genotoxins ethyl chloride and methyl chloride formed during the preparation of amine hydrochloride salts from solutions of ethanol and methanol,” *Organic Process Research & Development* **2009**, 13(4), 786-791.

Qiang Yang,¹ Brian P. Haney,*¹ Alexander Vaux,¹ Dean A. Riley,¹ Linda Heidrich,²

Ping He,² Paul Mason,*² Ashok Tehim,³ Lawrence E. Fisher,⁴ Hans Maag⁴ and Neal G. Anderson⁵

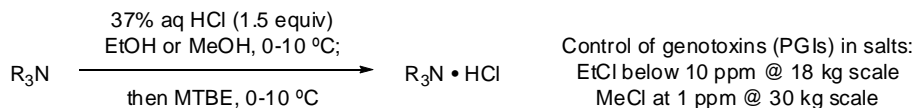
¹Chemical Development Department, AMRI, Albany, NY, USA

²Analytical and Quality Services, AMRI, Albany, NY, USA

³Memory Pharmaceuticals Corp., Montvale, NJ, USA

⁴Roche Palo Alto, LLC, Palo Alto, CA, USA

⁵Anderson's Process Solutions, Jacksonville, OR USA



13. “Aminoimidazoles as potent and selective human β -secretase (BACE1) inhibitors,” *Journal of Medicinal Chemistry* **2009**, 52(20), 6314-6323.

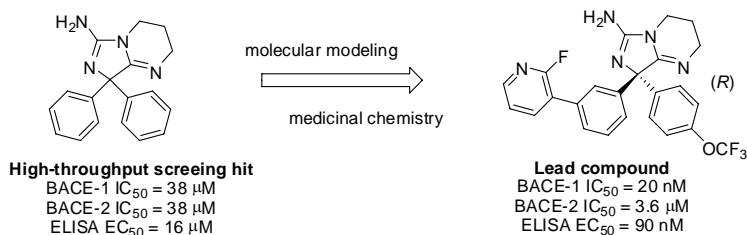
Michael S. Malamas,^{*,1} Jim Erdei,¹ Iwan Gunawan,¹ Keith Barnes,² Matthew Johnson,² Yu Hui,² Jim Turner,³ Yun Hu,³ Erik Wagner,³ Kristi Fan,¹ Andrea Olland,⁴ Jonathan Bard³ and Albert J. Robichaud¹

¹Department of Chemical Sciences, Wyeth Research, Princeton, NJ, USA

²Medicinal Chemistry Department, AMRI, Albany, NY, USA

³Neuroscience Department, Wyeth Research, Princeton, NJ, USA

⁴Department of Chemical Sciences, Wyeth Research, Cambridge, MA, USA

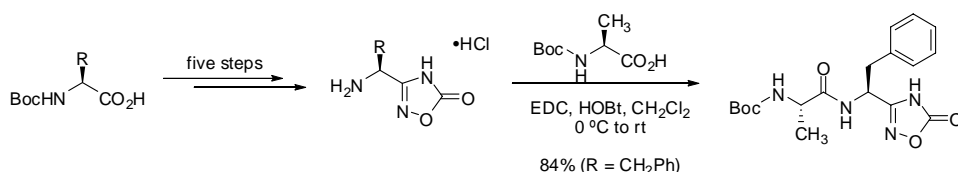


14. “The preparation of optically active α -amino 4H-[1,2,4]oxadiazol-5-ones from optically active α -amino acids,” *Tetrahedron* **2009**, 65(46), 9536-9541.

John E. Mangette,^{*,1} Matthew R. Johnson,¹ Van-Duc Le,¹ Rajesh A. Shenoy,¹ Howard Roark,² Michael Stier,² Thomas Belliotti,² Thomas Capiris² and Peter R. Guzzo¹

¹AMRI, Albany, NY, USA

²Pfizer, Inc., Ann Arbor, MI, USA

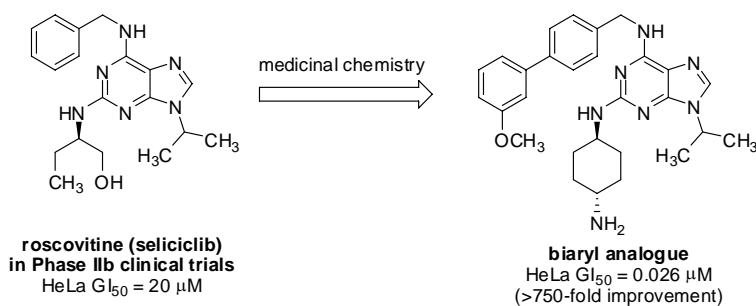


15. “Biaryl purine derivatives as potent antiproliferative agents: Inhibitors of cyclin dependent kinases. Part I,” *Bioorganic & Medicinal Chemistry Letters* **2009**, 19(23), 6608-6612.

Michael P. Trova,¹ Keith D. Barnes,^{*,1} Curt Barford,¹ Travis Benanti,¹ Mark Bielaska,¹ Lori Burry,¹ John M. Lehman,² Christine Murphy,¹ Harold O’Grady,¹ Denise Peace,² Susan Salamone,² Jennifer Smith,¹ Patricia Snider,¹ Joseph Toporowski,¹ Steven Tregay,¹ Alison Wilson,¹ Michael Wyle,¹ Xiaozhang Zheng¹ and Thomas D. Friedrich²

¹Medicinal Chemistry Department, AMRI, Albany, NY, USA

²Albany Medical College, Center for Immunology and Microbial Disease, Albany, NY, USA

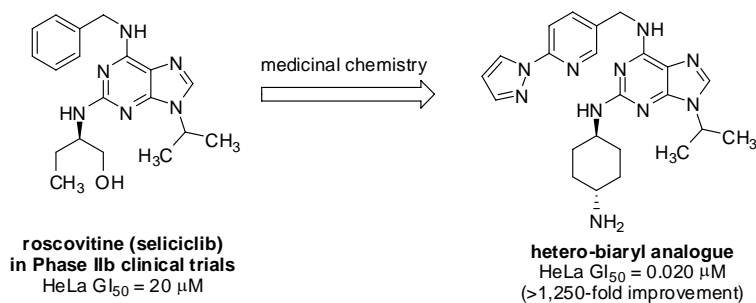


16. “Heterobiaryl purine derivatives as potent antiproliferative agents: Inhibitors of cyclin dependent kinases. Part II,” *Bioorganic & Medicinal Chemistry Letters* **2009**, 19(23), 6613-6617.

Michael P. Trova,¹ Keith D. Barnes,^{*1} Luis Alicea,¹ Travis Benanti,¹ Mark Bielaska,¹ Joseph Bilotta,¹ Brian Bliss,¹ Thuy Nguyen Duong,¹ Simon Haydar,¹ R. Jason Herr,¹ Yu Hui,¹ Matthew Johnson,¹ John M. Lehman,² Denise Peace,² Matthew Rainka,¹ Patricia Snider,¹ Susan Salamone,² Steven Tregay,¹ Xiaozhang Zheng¹ and Thomas D. Friedrich²

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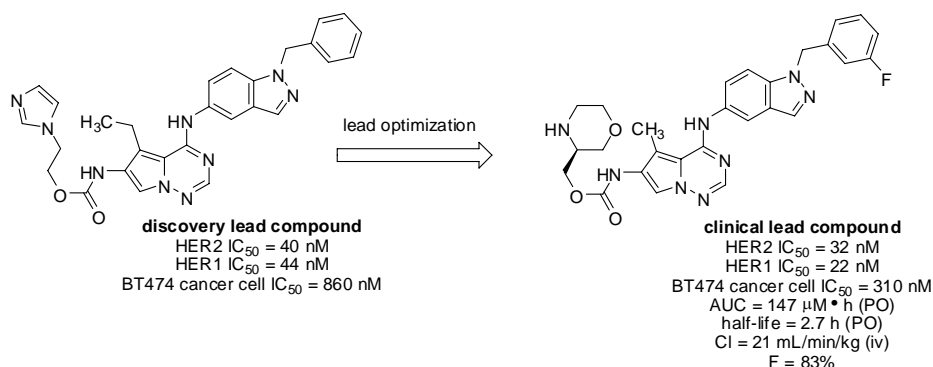


17. “Discovery and preclinical evaluation of [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid, (3S)-3-morpholinylmethyl ester (BMS-599626), a selective and orally efficacious inhibitor of human epidermal growth factor receptor 1 and 2 kinases,” *Journal of Medicinal Chemistry* **2009**, 52(21), 6527-6530.

Ashvinikumar V. Gavai,^{*1} Brian E. Fink,¹ David J. Fairfax,² Gregory S. Martin,² Lana M. Rossiter,² Christian L. Holst,² Soong-Hoon Kim,¹ Kenneth J. Leavitt,¹ Harold Mastalerz,¹ Wen-Ching Han,¹ Derek Norris,¹ Bindu Goyal,¹ Shankar Swaminathan,¹ Bharat Patel,¹ Arvind Mathur,¹ Dolatrai M. Vyas,¹ John S. Tokarski,¹ Chiang Yu,¹ Simone Oppenheimer,¹ Hongjian Zhang,¹ Punit Marathe,¹ Joseph Fargnoli,¹ Francis Y. Lee,¹ Tai W. Wong¹ and Gregory D. Vite¹

¹Bristol-Myers Squibb Research and Development, P.O. Box 4000, Princeton, New Jersey 08543

²Medicinal Chemistry Department, AMRI, Albany, NY, USA



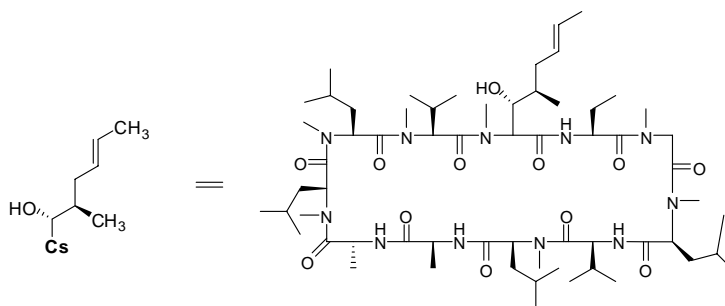
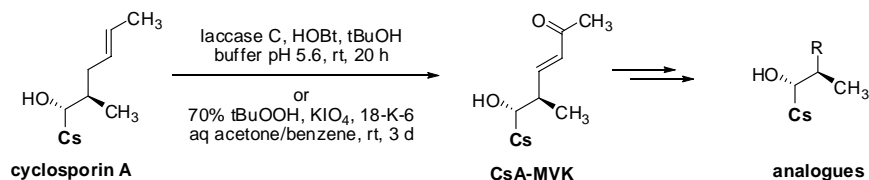
18. “Novel oxidation of cyclosporin A: Preparation of cyclosporin methyl vinyl ketone (Cs-MVK),” *Synlett* **2009**, 18, 2935-2938.

Zhicai Yang,¹ Kevin Pattamana,¹ Bruce F. Molino*,¹ Simon N. Haydar,¹ Yeyu Cao,¹ Frederic Bois,¹ Jun-Ho Maeng,² Michael S. Hemenway,² Joseph O. Rich,² Yuri L. Khmel'nitsky,² Thomas D. Friedrich,³ Denise Peace³ and Peter C. Michels²

¹Medicinal Chemistry Department, AMRI, Albany, NY, USA

²Discovery Research and Development, AMRI, Albany, NY, USA

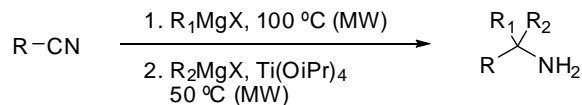
³Albany Medical College, Center for Immunology & Microbial Disease, Albany, NY, USA



19. “Rapid Ti(Oi-Pr)₄ facilitated synthesis of α,α,α -trisubstituted primary amines by the addition of Grignard reagents to nitriles under microwave heating conditions,” *Tetrahedron Letters* **2009**, 50(50), 7070–7073.

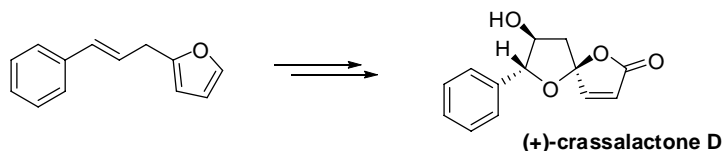
Ruifang Wang, Brian T. Gregg,* Wei Zhang, Kathryn C. Golden, John F. Quinn, Peng Cui and Dmytro O. Tymoshenko

Medicinal Chemistry Department, AMRI, Albany, NY, USA



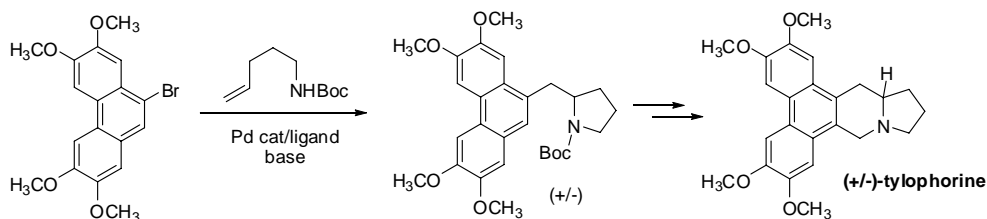
20. “Asymmetric total synthesis of (+)-crassalactone D,” *Journal of Organic Chemistry* **2009**, 74(24), 9546-9549.

Zhicai Yang,* Phung Tang, Jolicia F. Gauuan, and Bruce F. Molino
Medicinal Chemistry Department, AMRI, Albany, NY, USA



21. “A concise palladium-catalyzed carboamination route to (+/-)-tylophorine,” *Journal of Organic Chemistry* **2009**, 74(24), 9554-9557.

Lana M. Rossiter, Meagan L. Slater, Rachel E. Giessert, Samuel A. Sakwa and R. Jason Herr*
Medicinal Chemistry Department, AMRI, Albany, NY, USA

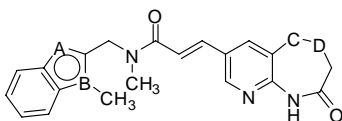


22. “2,3,4,5-Tetrahydro-1H-pyrido[2,3-*b* and *e*][1,4]diazepines as inhibitors of the bacterial enoyl ACP reductase, FabI,” *Bioorganic & Medicinal Chemistry Letters* **2009**, 19(18), 5359-5362.

Jailall Ramnauth*¹ Mathew D. Surman,² Peter B. Sampson,¹ Bryan Forrest,¹ Jeff Wilson,¹ Emily Freeman,² David D. Manning,² Fernando Martin,¹ Andras Toro,¹ Megan Domagala,¹ Donald E. Awrey,¹ Elias Bardouniotis,¹ Nachum Kaplan,¹ Judd Berman¹ and Henry W. Pauls*¹

¹Affinium Pharmaceuticals Inc., Toronto, Ontario, Canada

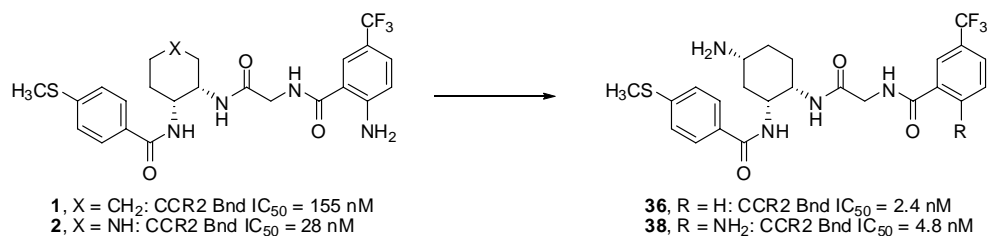
²Discovery Research and Development, AMRI, Albany, NY, USA



23. “Discovery of trisubstituted cyclohexanes as potent CCR2 chemokine receptor 2 (CCR2) antagonists,” *Bioorganic & Medicinal Chemistry Letters* **2009**, *19*(3), 597-601. Robert J. Cherney,^{*,1} John B. Brogan,² Ruowei Mo,¹ Yvonne C. Lo,¹ Gengjie Yang,¹ Persymphonie B. Miller,¹ Peggy A. Scherle,¹ Bruce F. Molino,² Percy H. Carter¹ and Carl P. Decicco¹

¹Research and Development, Bristol-Myers Squibb Company, Princeton, NJ, USA

²Medicinal Chemistry Department, AMRI



2009 AMRI Review Publications (including Book Chapters)

AMRI scientists were also lead authors on several review publications during 2009, many appearing as chapters in serial book series or in scientific journals, and are abstracted in scientific databases.

1. **“Five-membered ring systems: with more than one N atom,”** *Progress in Heterocyclic Chemistry* **2009**, 20, 190-219.

Larry Yet

Singapore Research Centre, AMRI

2. **“Hiyama cross-coupling reaction,”** *Name Reactions for Homologations, Pt. 1* **2009**, 33-46.

“Negishi cross-coupling reaction,” *Name Reactions for Homologations, Pt. 1* **2009**, 70-99.

“Nozaki-Hiyama-Kishi reaction,” *Name Reactions for Homologations, Pt. 1* **2009**, 299-318.

Larry Yet

Singapore Research Centre, AMRI

3. **“The evolution of microbial transformations for industrial applications,”** *Society for Industrial Microbiology News* **2009**, 59(2), 36-53.

Pete Michels¹ and John Rosazza²

¹Department of Metabolism and Biotransformations, AMRI

²Division of Medicinal and Natural Products Chemistry, University of Iowa, Iowa City, IA, USA

4. **“Palladium(II)-catalyzed C-H activation/C-C cross-coupling reactions: Versatility and practicality,”** *Angewandte Chemie International Edition* **2009**, 48(28), 5094–5115.

Xiao Chen,² Keary M. Engle,¹ Dong-Hui Wang¹ and Jin-Quan Yu*¹

¹Department of Chemistry, The Scripps Research Institute, La Jolla, CA, USA

²Chemical Development Department, AMRI

5. **“New central targets for the treatment of obesity,”** *British Journal of Clinical Pharmacology* **2009**, 68(6), 852-860.

Bruce J. Sargent and Nicholas A. Moore

Discovery Research & Development, AMRI

6. **“4-N-, 4-S-, and 4-O-Chloroquine analogues: Influence of side chain length and quinolyl nitrogen pKa on activity vs chloroquine resistant malaria,”** *Chemtracts Organic Chemistry* **2009**, 21, 172-178.

R. Jason Herr

Medicinal Chemistry Department, AMRI

7. “**L-Cysteine, S-[(2-nitrophenyl)methyl],**” *e-EROS Encyclopedia of Reagents for Organic Synthesis*, Crich, D., Ed., John Wiley & Sons, Ltd. **2009**.

Jitendra D. Belani

Medicinal Chemistry Department, AMRI

8. “**The influence of lead discovery strategies on the properties of drug candidates,**” *Nature Reviews Drug Discovery* **2009**, 8(3), 203-212.

Gyöergy M. Keserü¹ and Gergely M. Makara²

¹Discovery Chemistry, Gedeon Richter, Budapest, Hungary

²AMRI, Budapest, Hungary

AMRI Research Presented (Oral Papers and Posters)

Several presentations were given by AMRI scientists during the year 2009, some as talks given at scientific meetings or invited lectures at universities and some presented as posters at a scientific meeting.

1. Poster Presentation: “5-(Furo[3,2-*c*]pyridin-4(5*H*)-on-5-yl)indazoles as MCH1 antagonists,” MEDI-086: Abstracts of Papers, 238th ACS National Meeting, Washington, DC, USA, August 16-20, 2009.

James Grabowski,^{*1} Emily E. Freeman,¹ Matthew D. Surman,¹ Peter R. Guzzo,¹ Michele Luche,² Yuri Khmelnsky,³ John Lindsay,³ Julianne Zaremba,³ Steven Vickers,⁴ Jean Viggers⁴ and Sharon Cheetham⁴

¹Discovery Research & Development, Chemistry Department, AMRI

²Lead Discovery, Bothell Research Center, AMRI

³Metabolism and Biotransformation Department, AMRI

⁴RenaSci Consultancy Ltd, Biocity, Nottingham, United Kingdom

2. Poster Presentation: “ALB-109564, a novel tubulin inhibitor with improved efficacy over vinorelbine, is better tolerated when dosed iv versus ip, leading to improved activity in human tumor xenograft studies,” AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Conference, November 14-19, 2009.

Mark A. Wolf, Randall K. Johnson, Dejian Xie, Anna Avrutskaya, Robert Mullin, Beverly Godfrey, Mary Anne Mead, Erin E. Trachet, Wilbur R. Leopold, Peter Guzzo and Ian Scott

Discovery Research & Development, Chemistry Department, AMRI

3. Poster Presentation: “Pharmacology of AMR-MCH-14, an antagonist of the MCH1 receptor for the treatment of obesity,” 39th Annual Meeting of the Society for Neuroscience, Chicago, IL, October 17-21, 2009.

Bruce Sargent, Matthew Surman, Michele Luche, Emily Freeman, Mark Hadden, Alan Henderson, Peter Michels, Yuri Khmelnsky, John Lindsay, Jiffry Ismail, Lyuda Mozhaeva, Julianne Zaremba, Steven Vickers, Jean Viggers, Sharon Cheetham and Peter Guzzo

Discovery Research & Development, Chemistry Department, AMRI

4. Poster Presentation: “Pharmacology of AMR-MCH-14, an antagonist of the MCH1 receptor for the treatment of obesity,” Keystone Symposium on Obesity, Banff, Alberta, Canada, January 20-25, 2009.

Michele Luche, Matthew Surman, Peter Guzzo, Xiao-Wu (May) Jiang, Guowei Jiang, Alan Henderson, Mark Hadden, Emily Freeman, Yuri Khmelnsky, John Lindsay, Julianne Zaremba, Steve Vickers, Jean Viggers and Sharon Cheetham

Discovery Research & Development, Chemistry and Bothell Research Center, AMRI

5. Poster Presentation: “Identification of CFTR correctors and potentiators from AMRI natural product libraries,” North American Cystic Fibrosis Conference, Minneapolis, MN, October 15-17, 2009.

Janet Adolphson, Ursula Mocek, Kathryn Waikins, Joshua Rhea, Ricardo Reategui, Michele Luche and Grant Carr
Discovery Research & Development, Bothell Research Center, AMRI

6. Poster Presentation: “The SMA Project: A Progress Report,” 13th Annual International SMA Research Group Meeting/FSMA, Cincinnati, OH, June 18-19, 2009. Amelie K. Gubitz, John M. McCall, Keith D. Barnes, Sangeeta P. Chitnis, Svetlana V. Dobritsa, Chris L. Lorson, Monique A. Lorson, Michele M. Luche, Graham Johnson, John Lippert, Virginia B. Mattis, Nick Mayhew, Amy R. Noe, Sabina I. Robinson, James A. Romano, Jr., Donna L. Romero and Jill Heemsker
Discovery Research & Development, Bothell Research Center and Medicinal Chemistry Department, AMRI

7. Oral Presentation: “A natural opportunity,” Society for Biomolecular Sciences 15th Annual Conference and Exhibition, Lille, France, April 26-30, 2009.
Grant Carr
Discovery Research & Development, Bothell Research Center

8. Invited Lecture: “Discovery and advancement to clinic of ALB 109564,” Albany College of Pharmacy Pharmaceutical Research Institute, May 7, 2009.
Matthew Voss
Medicinal Chemistry Department, AMRI

9. Invited Lecture: “Post-Graduate Research Summary,” Homecoming Weekend Chemistry Symposium, Utica College, September 19, 2009.
Joseph Raker
Medicinal Chemistry Department, AMRI

10. Invited Lecture: “Small adventures in total synthesis,” Gordon Research Conference on Heterocyclic Compounds, Newport, Rhode Island, July 2, 2009.
R. Jason Herr
Medicinal Chemistry Department, AMRI

11. Invited Lectures: “Palladium-catalyzed synthesis of (S)-(+) and **(R)-(-)-coniine from enantiopure allylic alcohols,”** St. Lawrence University, Canton, New York and State University of New York at Potsdam, Potsdam, New York, both on April 7, 2009.
R. Jason Herr
Medicinal Chemistry Department, AMRI

12. Invited Lecture: “Bioprocess strategies impacting pharmaceutical discovery and development,” Advances in BioProcessing 2009, Syracuse, New York, March 22, 2009.
Peter C. Michels
Department of Metabolism and Biotransformations, AMRI

13. Poster Presentation: “High-throughput screening of 30,000 diverse small molecules for the discovery of tumor cell specific cytotoxic agents: Results and

structural analysis,” Joint Meeting on Medicinal Chemistry, Budapest, Hungary, June 24-27, 2009.

Beata Flachner, Zsolt Lorincz, David Marcus, Anwar Rayan, Amiram Goldblum, Orazio Nicolotti, Angelo Carotti, Jordi Mestres, Miklos Szabo, Bela Bertok, Istvan Bagyi, Sandor Cseh and Gyorgy Dorman
AMRI, Budapest, Hungary

14. Poster Presentation: “Grid aided computer system for accelerated anti-cancer drug design: CancerGrid,” Fifth International Symposium on Computational Methods in Toxicology and Pharmacology Integrating Internet Resources(CMTPI 2009), Istanbul, Turkey, July 4-8, 2009.

Gyorgy Dorman, Peter Kacsuk, Jozsef Kovacs, Istvan Bagyi, Angelo Carotti, Sandor Cseh, Simona Distinto, Amiram Goldblum, Johannes Kirchmair, David Marcus, Alfons Nonell-Canals, Jordi Mestres, Andre Lomaka, Mikios J. Szabo, Gabor Pocze and Bela Bertok
AMRI, Budapest, Hungary

15. Invited Lecture: “Affinity screening and optimization--A review,” Hungarian Biochemical Society Meeting, Balatonoszod, Hungary, May 2009.

Gergely Makara
AMRI, Budapest, Hungary

Patent Applications Filed and Issued containing AMRI Scientists

The process of obtaining a patent for an invention often takes several years, from the filing of the application through the subsequent review and issuance by various national patent offices. During this year, seven patent applications were filed by AMR Technology, Inc, USA (our corporate holding company for patents assigning all rights to AMRI as the owner of the intellectual property), either as the sole owner of IP or in collaboration with others. In addition, four previously filed patent applications were issued as full US patents. In all cases, AMRI scientists were named as co-inventors. Several other patent applications filed by customers and collaborators were also published during the year, in which AMRI scientists were named as co-inventors (six listed below).

Patent applications filed by AMRI covering novel intellectual property (IP) owned completely or in part by AMR Technology, Inc., USA:

1. **“Aryl- and heteroaryl-substituted tetrahydrobenzazepines and use thereof to block reuptake of norepinephrine, dopamine, and serotonin,”** US Application Publication US 2009/0118260 A1 (AMR Technology, Inc. and Bristol-Myers Squibb).
Bruce Molino, Shuang Liu, Peter Guzzo, Min Hu, David Manning, Matthew Isherwood, Kristen Fleming and Wenge Cui
Discovery R&D, Chemistry Department, AMRI

2. **“Preparation of 5-pyridinone substituted indazoles as melanin-concentrating hormone (MCH1) receptor selective antagonists,”** US Application Publication US 2009/0082359 A1 and PCT International Application Publication WO 2009/015037 A2 (AMR Technology, Inc.)
Peter Guzzo, Matthew Surman, Alan Henderson and Mark Hadden
Discovery R&D, Chemistry Department, AMRI

3. **“Processes for preparing tetrahydroisoquinolines,”** PCT International Application Publication WO 2009/149259 A2 (Bristol-Myers Squibb Company, USA and AMR Technology, Inc.)
Paul Lobben,¹ Rulin Zhao,¹ Bei Wang,¹ Bang-Chi Chen,¹ Shuang Liu,² Min Hu,² Yuh-Lin Allen Yang,² Matthew Isherwood,² Rasidul Amin² and Wenge Cui²
¹Bristol-Myers Squibb Company, USA
²Discovery R&D Chemistry Department, AMRI

4. **“Crystalline form of 6-[(4S)-2-methyl-4-(2-naphthyl)-1,2,3,4-tetrahydroisoquinolin-7-yl]pyridazin-3-amine,”** PCT International Application Publication WO 2009/149258 A2 (Bristol-Myers Squibb Company, USA and AMR Technology, Inc.)
Jun Qiu,¹ Qi Gao,¹ Shuang Liu,² Min Hu,² Yuh-Lin Allen Yang,² Matthew Isherwood² and Rasidul Amin²
¹Bristol-Myers Squibb Company, USA
²Discovery R&D Chemistry Department, AMRI

5. **“5-HT₃ receptor modulators, methods of making and use thereof,”** US Application Publication 2009/0298809 A1 (AMR Technology, Inc.)
David D. Manning and Christopher L. Cioffi
Discovery R&D, Chemistry Department, AMRI
6. **“Pyridoindole derivatives as MCH antagonists and their preparation, pharmaceutical compositions and use in the treatment of diseases,”** US Application Publication US 2009/0275590 A1 and PCT International Application Publication WO 2009/089482 (AMR Technology, Inc.)
Guzzo, Peter; Surman, Matthew David; Henderson, Alan John; Jiang, May Xiaowu; Hadden, Mark; Grabowski, James
Discovery R&D, Chemistry Department, AMRI
7. **“Preparation of isoindoline compounds for the treatment of spinal muscular atrophy and other uses,”** PCT International Application Publication WO 2009/042907 A1 (Department of Health and Human Services, USA, Science Applications International Corporation (SAIC) and AMR Technology, Inc.)
Jill E. Heemskerck,¹ John M. McCall² and Keith D. Barnes³
¹National Institute of Neurological Disorders and Stroke, National Institutes of Health, USA
²PharMac LLC, USA
³Medicinal Chemistry Department, AMRI

Issued patents previously filed as applications by AMRI:

1. **“Process for production of piperidine derivatives,”** US Patent 7,498,345: filed September 14, 2004, issued March 3, 2009.
Harold Meckler, Benjamin J. Littler, Prasad Raje, Michael Van Brunt and Paul F. Vogt
Chemical Development Department, AMRI
2. **“Process for production of carebastine,”** US Patent 7,498,443: filed September 17, 2004, issued March 3, 2009.
Harold Meckler, Benjamin J. Littler, Prasad Raje, Michael Van Brunt and Paul F. Vogt
Chemical Development Department, AMRI
3. **“Cyclosporin alkynes and their utility as pharmaceutical agents,”** US Patent 7,632,807: filed March 12, 2008, issued December 15, 2009 (AMR Technology, Inc.)
Bruce F. Molino and Zhicai Yang
Discovery R&D, Chemistry Department, AMRI
4. **“Cyclosporin analogues and their pharmaceutical uses,”** US Patent 7,511,013: filed September 21, 2005, issued March 31, 2009 (AMR Technology, Inc.)
Bruce F. Molino and Zhicai Yang
Discovery R&D, Chemistry Department, AMRI

5. **“Aryl- and heteroaryl-substituted tetrahydroisoquinoline and use thereof to block reuptake of norepinephrine, dopamine, and serotonin,”** US Patent 7,541,357: filed July 15, 200r, issued June 2, 2009 (AMR Technology, Inc.)

Bruce F. Molino,¹ Shuang Liu,¹ Peter Guzzo¹ and James P. Beck²

¹Discovery R&D, Chemistry Department, AMRI

²Bristol-Myers Squibb Company, USA

6. **“Preparation of novel cyclosporins,”** US Patent 7,538,084: filed November 25, 2004, issued May 26, 2009 (AMR Technology, Inc.)

Bruce F. Molino, Simon N. Haydar, Peter C. Michels, Zhichai Yang, Michael S.

Hemenway, Joseph O. Rich and Yuri Khmelnsky

Discovery R&D, Chemistry and Metabolism and Biotransformations Departments, AMRI

Some patents issued or patent applications filed by collaborators/customers of AMRI containing AMRI scientists as co-inventors, but for which AMRI is not a co-assignee (NOT a fully inclusive list):

1. **“Biphenylalkylbenzamide derivatives as CCR10 antagonists and their preparation, pharmaceutical compositions and use in the treatment of diseases,”**

PCT International Application Publication WO 2009/052078 A1 (Boehringer Ingelheim Pharmaceuticals, Inc.)

Kaka Dey,² Donghong Amy Gao,¹ Daniel R. Goldberg,¹ Alexander Heim-Riether,¹ John E. Mangette,² Ingo Andreas Mugge,¹ Roger Snow,¹ Alan David Swinamer,¹ Jiang-Ping Wu,¹ Zhaoming Xiong¹ and Yu Yang¹

¹Boehringer Ingelheim Pharmaceuticals, Inc.

²Medicinal Chemistry Department, AMRI

2. **“Preparation of heterocyclic amides as cytokine inhibitors for treating various diseases,”** US Application Publication US 2009/0023701 A1 (Boehringer Ingelheim Pharmaceuticals, Inc.)

Ronald A. Aungst,² Derek Cogan,¹ Amy L. Davis,² Daniel R. Goldberg,¹ Ming-Hong Hao¹ and Zhaoming Xiong¹

¹Boehringer Ingelheim Pharmaceuticals, Inc.

²Medicinal Chemistry Department, AMRI

3. **“Preparation of pyrazinone substituted amides as Btk inhibitors,”** US Application Publication US 2009/0082330 A1 and PCT International Application Publication WO 2009/039397 A2 (CGI Pharmaceuticals, Inc.)

Peter A. Blomgren,¹ Kevin S. Currie,¹ Seung H. Lee,¹ Scott A. Mitchell,¹ Jianjun Xu,¹ Aaron C. Schmitt,¹ Zhongdong Zhao,¹ Paul E. Zhichkin,² Douglas G. Stafford² and Jeffrey E. Kroft¹

¹CGI Pharmaceuticals, Inc.

²Medicinal Chemistry Department, AMRI

4. **“Preparation of methano- or ethanobenzo[*b*]thiophene-2-carboxamides and related analogous as BTK inhibitors,”** PCT International Application Publication WO 2009/137596 A1 (CGI Pharmaceuticals, Inc. and Genentech, Inc.)

Peter A. Blomgren,¹ David R. Brittelli,¹ Kevin S. Currie,¹ Seung H. Lee,¹ Jeffrey E. Kropf,¹ Scott A. Mitchell,¹ Aaron C. Schmitt,¹ Xiaojing Wang,² Jianjun Xi,¹ Zhongdong Zhao¹ and Paul E. Zhichkin³

¹CGI Pharmaceuticals, Inc.

²Genentech, Inc.

³Medicinal Chemistry Department, AMRI

5. **“Polycyclic guanine derivatives and methods of use thereof,”** PCT International Application Publication WO 2009/002423 A2 (Schering Corporation, USA).

Deen Tulshian,¹ William B. Geiss,² Gregory S. Martin,² Van-Duc Le,² James C. Haber, Jr.,² Julius J. Matasi,¹ Michael F. Czarniecki¹ and Stephanie N. Cooke¹

¹Chemistry Technologies Department, Schering-Plough Research Institute

²Medicinal Chemistry Department, AMRI

6. **“Preparation of imidazopyrazines as protein kinase inhibitors,”** PCT International Application Publication WO 2009/097233 A1 (Schering Corporation, USA)

Matthew Paul Rainka,² Matthew Ernst Voss,² Lisa Helen Peterson,² Mike Fleming,² David B. Belanger,¹ Patrick J. Curran,¹ Bheemashankar A. Kulkarni,¹ Tao Yu,¹ Yonglian Zhang,¹ Yushi Xiao,¹ Angela D. Kerekes,¹ Jayaram R. Tagat,¹ Ronald J. Doll¹ and M. Arshad Siddiqui¹

¹Chemistry Technologies Department, Schering-Plough Research Institute

²Medicinal Chemistry Department, AMRI

7. **“Preparation of (S)-N-methylnaltrexones with opioid receptor binding activity for use in pharmaceutical compositions,”** US Patent 7,563,899: filed May 25, 2006, issued July 21, 2009 (Progenics Pharmaceuticals, Inc.)

Howard Wagoner,¹ Suketu P. Sanghvi,¹ Thomas A. Boyd,¹ Christopher Verbicky² and Stephen Andruski²

¹Progenics Pharmaceuticals, Inc., Tarrytown, NY USA

²Chemical Development Department, AMRI