Currículo Resumido em Português

Prof. Dr. Patrick Woster

O Dr. Woster possui graduação em Farmácia (1978) pelo Centro Médico da Universidade de Nebraska, Omaha, EUA. Em 1986 concluiu o doutorado em Química Medicinal pela Universidade de Nebraska. Em seguida realizou dois pós-doutoramentos, um pelo Instituto Politécnico Rensselaer (Química) e outro pela Universidade de Michigan (Química Medicinal). Em 1989 assumiu o cargo de professor assistente do departamento de Ciências Farmacêuticas, Universidade Estadual Wayne e em 1995, como professor associado deste mesmo departamento. No período de 2001 a 2011, desempenhou suas atividades como Professor do Departamento de Ciências Farmacêuticas, Universidade Estadual Wayne, e desde então foi promovido assumiu funções como professor titular em Descoberta de Fármacos, Departamento de Descoberta de Fármacos & Ciências Biomédicas da Universidade Médica da Carolina do Sul. O grupo do Prof. Woster é particularmente interessado no planejamento, síntese e avaliação de agentes antitumorais que produzem efeitos epigenéticos através da inibição da histonas desacetilases e histonas desmetilases específicas. Uma segunda área de foco no laboratório Woster é a descoberta de novos compostos que atuam como agentes anti-malária. Woster atua como diretor do Núcleo de planejamento e síntese de fármacos (Drug Design and Synthesis Core - DDSC) da Universidade Médica da Carolina do Sul (Medical University of South Carolina - MUSC), que combina a química sintética e poderosos recursos computacionais para apoiar High-Throughput Screening (HTS) e a terapêutica experimental pré-clínica, facilitando assim uma estrutura interdisciplinar interativa para a descoberta de fármacos. O Prof. Woster possui 111 artigos científicos publicados.

Curriculum

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Woster, Patrick M.	Professor and SmartState™ Endowed Chair in Drug Discovery
eRA COMMONS USER NAME (credential, e.g., agency login) ad5526	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Univ. Nebraska Med. Ctr., Omaha, NE	B.S.	1978	Pharmacy
University of Nebraska, Lincoln NE	Ph.D.	1986	Medicinal Chemistry
Rensselaer Polytechnic Inst., Troy, NY	Postdoctoral	1986	Chemistry
University of Michigan, Ann Arbor	Postdoctoral	1987	Medicinal Chemistry

A. Personal Statement

The Woster group is particularly interested in the design, synthesis and evaluation of antitumor agents that produce epigenetic effects through inhibition of histone deacetylases and specific histone demethylases typified by lysine specific demethylase 1 (LSD1). This project grew out of our long-standing interest in the design and development of a variety of analogues with potent activity against a variety of cancer cell lines. A second area of focus in the Woster laboratory is the discovery of novel compounds that act as antimalarial agents, including aryl substituted (bis)biguanides, (bis)guanidines, (bis)ureas and (bis)thioureas, as well as peptidomimetic inhibitors of the plasmepsin II. These studies have led to preliminary elucidation of the antiparasitic structure/activity relationships for these chemical classes. More recently, we have collaborated with Dr. Kovari to design and synthesize peptidomimetic compounds that act as HIV protease inhibitors. I serve as Director for the MUSC Drug Design and Synthesis Core (DDSC), which combines synthetic chemistry and powerful computational resources to support high-throughput screening and pre-clinical experimental therapeutics, thus facilitating an iterative interdisciplinary framework for drug discovery. The DDSC is equipped to provide a full range of discovery chemistry services including synthetic method development, peptide synthesis, hit-to-lead structure optimization, scale-up synthesis, virtual screening, virtual docking, fragment-based drug discovery and QSAR. My role in the present project is to serve as Principal Investigator for this multiple PI project, and to oversee the design, synthesis and characterization of the proposed peptidomimetic protease inhibitors.

B. Positions and Honors

Positions and Employment

1988-1989 Lecturer, Dept. of Pharmaceutical Sciences, Wayne State University, Detroit, MI.
1989-1995 Assistant Professor, Dept. of Pharmaceutical Sciences, Wayne State University, Detroit, MI.
1995-2001 Associate Professor, Dept. of Pharmaceutical Sciences, Wayne State University, Detroit, MI.
2001-2011 Professor, Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI.
2007-2011 Professor (Adjunct), Dept. of Biochemistry & Molecular Biology, Wayne State Univ., Detroit, MI.
2011 - Professor and SmartState™ Endowed Chair in Drug Discovery, Dept. of Drug Discovery & Biomedical Sciences, Medical University of South Carolina

Other Experience and Professional Memberships

1988-	Member, American Association for the Advancement of Science
1980-	Member, American Chemical Society
1994-2011	Member, Barbara Ann Karmanos Cancer Center, Detroit, MI
2010-	NIH Special Emphasis Panel (SEP) for R13 Conference Grants Review
2011-	Member, Hollings Cancer Center (Developmental Cancer Therapeutics Section)
2011-	Director, MUSC Drug Design and Synthesis Core

Honors

1993	Wayne State University President's Award for Excellence in Teaching
1998 & 2006	Eugene Applebaum College of Pharmacy & Health Sci. Teaching Excellence Award
1998-1999	Wayne State University Career Development Chair
2008	Chair and Organizer, 5th Biennial Symposium on Polyamines in Parasites
2009	Chair, Gordon Research Conference on Polyamines
2010	Wayne State College of Pharmacy & Health Sciences Research Excellence Award
2011	Named Chair and Organizer, 2014 National Medicinal Chemistry Symposium

C. Peer-reviewed Publications (Selected from 111 peer-reviewed publications)

Most relevant to the current application

1. Gupta, D.; Yedidi, R.; Varghese, S.; Kovari, L.; Woster, P.M.: Mechanism-based inhibitors of the aspartyl protease plasmepsin II as potential antimalarial agents. *J. Med. Chem.* **2010**, *53*, 4234-4247, DOI: 10.1021/jm100233b. PMID: 20438064
2. Goodwin, A.C.; Destafano-Shields, C.E.; Wu, S.; Huso, D.L.; Wu, X.Q.; Murray-Stewart, T.R.; Hacker-
   Prietz, A.; Rabizadeh, S.; Woster, P.M.; Sears, C.; Casero, Jr., R.A.: Polyamine catabolism contributes
   to enterotoxigenic Bacteroides fragilis-induced colon tumorigenesis. *Proc. Nat'l. Acad. Sci. U.S.A.* **2011**,
   108, 15354-15359. PMID: 21876161
3. Zhu, Q.; Huang, Y.; Marton, L.J.; Woster, P.M.; Davidson, N.E.; Casero, Jr., R.A.: Polyamine analogues modulate gene expression by inhibiting lysine-specific demethylase 1 (LSD1) and altering chromatin structure in human breast cancer cells. *Amino Acids*, **2012**, *42*, 887-898. PMID: 21805138
4. Sharma, S.K.; Hazeldine, S.; Crowley, M.L.; Hanson, A.; Beattie, R.; Varghese, S.; Senanayake, T.M.D.;
   Hirata, A.; Hirata, F.; Wu, Y.; Steinbergs, N.; Murray-Stweart, T.; Bytheway, I.; Casero, R.A.; Woster, P.M.: Polyamine-based Small Molecule Epigenetic Modulators. *Med. Chem. Comm.* **2012**, *3*,
   14-21. PMID: 23293738
5. Schenk, T.; Howell, L.; Göllner, S.; Woster, P.M.; Marton, L.; Casero, R.A.; Dick, J.; Mills, K.; Burnett, A.; Müller-Tidow, C.; Petrie, K.; Zelent, A.: Inhibition of the LSD1/KDM1 histone demethylase reactivates the all-*trans*-retinoic acid differentiation pathway in acute myeloid leukemia. *Nature Medicine*, **2012**, *18*, 605-611. PMID: 22406747.
6. Hazeldine, S.; Pachaiyappan, B.; Steinbergs, N.; Hanson, A.S.; Casero, Jr., R.A.; Woster, P.M.: Low molecular weight amidoximes that act as potent epigenetic modulators. *J. Med. Chem.,* **2012**, *55*, 7378-7391. PMID: 22876979
7. Yedidi, R.; Liu, Z.; Wang, Y.; Brunzelle, J.S.; Kovari, J.A.; Woster, P.M.; Kovari, L.C.; Gupta, D.: Crystal structures of multidrug-resistant HIV-1 protease in complex with two potent anti- malarial compounds. *Biochem. Biophys. Res. Comm.* **2012**, *421*, 413-417. PMID: 22469467
8. Dewdney, T.G.; Wang, Y.; Liu, Z.; Reiter, S.J.; Brunzelle, J.S.; Kovari, I.A.; Woster, P.M.; Kovari, L.C.: Ligand modifications to reduce the relative resistance of multi-drug resistant HIV-1 protease. *Bioorg. Med. Chem.*, **2013**, 21, 7430-7434, DOI:pii: S0968-0896(13)00825-0. 10.1016/j.bmc.2013.09.045. PMID: 24128815
9. Wang, Y.; Liu, Z.; Reiter, S.J.; Brunzelle, J.S.; Kovari, I.A.; Woster, P.M.; Kovari, L.C.: Ligand modifications to reduce the relative resistance of multi-drug resistant HIV-1

protease. *Bioorg. Med. Chem.*, **2013**, 21, 7430-7434, DOI:pii: S0968-0896(13)00825-0. 10.1016/j.bmc.2013.09.045. PMID: 24291501

10. Yedidi, R.S.; Liu, Z.; Kovari, I.; Woster, P.M.; Kovari, L.C.: P1 and P1' *para*-fluoro phenyl groups show enhanced binding and favorable predicted pharmacological properties: structure-based virtual screening of extended lopinavir analogs against multi-drug resistant HIV-1 protease. *J. Molec. Graph. Model*. **2014**, *47*, 18-24, doi: 10.1016/j.jmgm.2013.10.010. PMID: 24291501

Additional recent publications of importance to the field (in chronological order)

11. Jin, L.; Hanigan, C.L.; Wu, Y; Wang, W.; Park, B.H,; Woster, P.M., Casero, Jr., R.A.: Loss of lysine-
specific demethylase 1 (LSD1) suppresses growth and alters gene expression of human colon cancer cells
in a p53 and DNA methyltransferase 1 (DNMT1) independent manners. *Biochem. J.*, **2013**, *449*, 459-
468. PMID: 23072722
12. Nowotarski, S.L.; Woster, P.M.; Casero, Jr., R.A.: Polyamines and cancer: Implications for chemoprevention and chemotherapy. *Exp. Rev. Molec. Med*. **2013,** *15*, e3 (15 pages). PMID: 23432971105.
13. Pachaiyappan, B.; Woster, P.M.: Design of small-molecule epigenetic modulators. *Bioorg. Med. Chem. Lett*., **2013**, epub ahead of print, 10.1016/j.bmcl.2013.11.001. PMID 24300735.
15. Kumarasinghe, I.; Woster, P.M.: Synthesis and evaluation of novel cyclic peptide inhibitors of lysine-specific demethylase 1*. ACS Med. Chem. Lett*. **2014**, *5(1)*, 29-33. DOI: 10.1021/ml4002997. NIHMS ID: NIHMS551633
15. Murray-Stewart, T.; Woster, P.M.; Casero, R.A.: The re-expression of the epigenetically silenced *e-*
cadherin gene by a polyamine analogue lysine-specific demethylase-1 (LSD1) inhibitor in human acute myeloid leukemia cell lines. *Amino Acids*, **2014**, *46*, 585-594, DOI 10.1007/s00726-013-
1485-1. PMID 23508577

D. Research Support

Ongoing Research Support

NIH RO1-CA149095. Woster (PI) 04/01/2010 - 01/31/2015
Identification of LSD1 inhibitors targeting epigenetic regulation in tumor cells.
The goal of this study is to synthesize and evaluate multiple series of small-molecule LSD1 inhibitors as epigenetic modulators for the treatment of cancer.
Role: PI

Completed Research Support

RO1-AI 041398-06 Wittner (PI) 08/01/2003-07/31/2009
Polyamine Inhibitors Targeting Microsporidia
The goal of this study is to synthesize and evaluate alkylpolyamine analogues as potential agents for the treatment of opportunistic microsporidia infection.
Role: Co-investigator

Waxman Cancer Research Foundation Casero (PI) 08/01/2007-07/31/2009
Novel Therapies Targeting Epigenetic Silencing of Tumor Suppressors
The goal of this study is to synthesize and evaluate multiple series of small-molecule LSD1 inhibitors as epigenetic modulators for the treatment of cancer.
Role: PI

R13AI080052-01 Woster (PI) 07/01/2008 - 06/30/2009

5th Biennial Symposium on Polyamines in Parasites
The goal of this proposal is to provide travel funds for for graduate students and postdocs attending the 2008 Biennial Symposium on Polyamines in Parasites
Role: PI

R13CA139648-01 Woster (PI) 03/01/2009-02/28/2010
2009 Polyamines Gordon Research Conference and Graduate Research Seminar
The goal of this proposal is to provide travel funds for for graduate students and postdocs attending the 2009 Gordon Research Conference on Polyamines

Role: PI
Progen Pharmaceuticals Research Contract Woster (PI) 10/01/2009-9/30/2010
Lysine-Specific Demethylase 1 Inhibitors.
The goal of this study is to synthesize, optimize and evaluate small-molecule LSD1 inhibitors identified from virtual screening as epigenetic modulators for the treatment of cancer.
Role: PI

Progen Pharmaceuticals Research Award. Woster (PI) 04/01/2008-12/31/2011
Lysine-Specific Demethylase 1 Inhibitors as Potential Antitumor Agents.
The goal of this study is to synthesize and evaluate (bis)biguanidine and (bis)biguanide LSD1 inhibitors as epigenetic modulators for the treatment of cancer.
Role: PI

RO1-CA109711 Oupicky (PI) 05/01/2005-04/30/2011
Gene Delivery Modulated by Redox
The goal of this study is to develop and evaluate polyamine-based gene and drug delivery vectors that are modulated by cellular redox systems for use in the treatment of cancer
Role: Co-investigator

NIH CTSA project
South Carolina Translational Research Woster (PI) 04/05/2012 – 7/31/2013
The MUSC Drug Design and Synthesis Core
The goal of this study is to establish a drug design and synthesis core at the Medical Univ. of South Carolina
Role: PI