Curriculum Vitae
Patricia M. Flatt, Ph.D.

Department of Chemistry
Western Oregon University
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Appointments

Assistant Professor (2008 – present) Department of Chemistry, Western Oregon University, Monmouth, OR

Assistant Professor of Sr. Research (2003-2010) College of Pharmacy, Oregon State University, Corvallis, OR

Professional Preparation

2000 – 2003: Postdoctoral Fellow, Marine Natural Products Research, College of Pharmacy, Oregon State University, Corvallis, OR.

1994-2000: Ph.D. in Biochemistry, Vanderbilt University, Nashville, TN. GPA = 3.5.

1992-1994: M.S. in Plant Ecology, University of Denver, Denver, CO. GPA = 3.9.

1988-1992: Bachelor of Science in Biology at University of Denver, Denver, CO. Magna Cum Laude. GPA = 3.9. Minors in Chemistry and Geography.

Teaching Experience:

Fall 2008 – Present: Assistant Professor of Chemistry at Western Oregon University, Monmouth, OR. Responsible for teaching CH 450, 451, 452 Biochemistry Series, CH 320 and CH 420 Forensic Sciences Courses, CH322 Medicinal Chemistry and Pharmacology, CH345 Introduction to Toxicology, CH 347 Biochemistry of Complementary and Alternative Medicines, CH 100 Introductory Chemistry, CH 200 General Chemistry Courses, and CH409 Applications of Traditional Chinese Medicine Study Abroad Class.

Spring 2004 – Spring 2008: Adjunct Faculty at Lane Community College, Eugene, OR. Responsible for teaching Genetics and Society, Biobonds BI 112, and a hybrid on-line/on-site course entitled Evolution and the Diversity of Life, BI 103. Biobonds is a cell biology class for health occupations majors (especially nursing). (For Reference Call: Kyle Hammon: 541-463-5447).

Winter 2005: Guest Lecturer at OSU in Veterinary Medicine Course VM762. Topics covered included small animal oncology: analysis of the disease state and treatment.

Fall 2003 to Fall 2004: Adjunct Faculty, Linn Benton Community College, Albany, OR

Responsible for teaching Biology 101(Diversity and Ecology) and Biology 102 (Cell Biology) Prepared lectures and lab section associated with the class, as well as grading and preparation of exams. (For Reference Call: Carolyn Lebsack: 541-917-4762)

Fall 2000; Winter 2001; Spring 2003: Research Assistant Professor, Oregon State University
Responsible for teaching guest lectures in the medicinal chemistry section of PHR753 class in the areas of cancer and cardiovascular biology. This course is required for the completion of the education of second year pharmacy students at Oregon State University. (For Reference Call: Dr. Gary DeLander: 541-737-5805)

Spring 1998: Adjunct Faculty, Freewill Baptist Bible College, Nashville, TN
Responsible for teaching an environmental science course with two laboratory sections. Prepared lectures and graded exams. Designed wet labs and organized regional field trips to waste management / natural resource facilities and wildlife refuges.

1989-1994: Teaching Assistant, University of Denver, Denver, CO
Prepared lectures and exams, graded laboratory notebooks and supervised two laboratory sections per week for the following courses: Concepts in Biology, Molecules to Mankind, and Plant Ecology. Topics covered: Genetics, cell structure and function, physiology, ecology, and experimental field design. (For Reference Call: Lisa Nelson 307-634-9221)

1992-1994: Lab Manager, Plant and Soils Lab, University of Denver, Denver, CO
Trained and organized projects for undergraduate students. Oversaw experimental design and troubleshooting of undergraduate thesis projects. Ordered laboratory materials, disposed of biohazardous waste, and maintained general lab organization. (For Reference Call: Dr. Robert Sanford Jr. 303-871-3534)

Research Experience
Dec 2003 – Present : Assistant Professor of Chemistry at Western Oregon University, Monmouth, OR. Previously as a research assistant professor with the College of Pharmacy, I have worked with Dr. William Gerwick and Dr. Taifo Mahmud on the biosynthesis of secondary metabolites from marine cyanobacteria and soil-derived actinomycete species. Current collaborative studies with Dr. Mahmud are focused on the isolation and characterization of the pyralomicin biosynthetic gene cluster. The pyralomicins are a class of antibacterial natural products derived from a combination of non-ribosomal peptide and ketide extended units, related to the plant-protective compound pyoluteorin. Pyoluteorin is an antibiotic compound that protects plants from seed- and root-rotting pathogens. In pyralomicin biosynthesis, unique tailoring reactions are required for the incorporation of a cyclitol or glucose ring structure, several chlorinations, and the intramolecular rearrangement of the carbonyl group of proline from the 2-position to the 3-position in the final product. Our hope is to use combined molecular genetic- and semi-synthetic-methodologies to enhance production of the pyralomicin class of antibiotics and to generate novel derivatives of this class of metabolites for further testing as pharmaceutical lead compounds. Independent research includes the study of cyanobacterial biosynthetic pathways leading to the production of UV-protective compounds known at mycosporine-like amino acids. This work is funded through a Faculty Development Grant at WOU. Additional support through the WOU Foundation has enabled the initiation of an additional research project designed to study the diversity and metabolic potential of soil bacteria from a diverse array of habitats within Oregon.

> *Techniques include:* Culturing of bacterial strains, genomic DNA isolation and library construction, PCR, Southern blotting, protein expression and purification, biosynthetic feeding experiments, HPLC, column chromatography, TLC, LC-MS, GC-MS and NMR. (For Reference call: Dr. Taifo Mahmud, (541)-737-9679

May 2000 – Dec 2003: Postdoctoral Fellow, Oregon State University, Corvallis, OR
A current goal in biosynthetic chemistry is to understand the mechanisms that microorganisms use to produce structurally complex, biologically active natural products and then to utilize these tools in a laboratory setting to improve the activity and production of therapeutically relevant compounds. The biosynthetic pathway of barbamide, a molluscicidal agent that shares structural homology with the

antitubulin agent, dolastatin 10, is of considerable interest because it is the product of a novel tailoring reaction that results in the addition of three chlorine atoms to one peripheral carbon atom. The techniques of molecular biology were to isolate and purify the enzymes required for barbamide biosynthesis. Several recombinant enzymes from the pathway have been expressed characterized for their role in barbamide biosynthesis. In addition, genes involved in the biosynthesis of related metabolites were also isolated in strain-variants of the cyanobacteria, *Lyngbya majuscula* and the symbiotic species *Oscillatoria spongelliae.*

Techniques include: Collection and culturing of marine cyanobacteria, isolation of genomic DNA and library production, PCR, recombinant DNA technologies, protein expression and purification, biosynthetic feeding experiments and the structural isolation of secondary metabolites, HPLC, GC-MS, column chromatography, TLC, NMR, Phylogenetic Analysis, FISH-analysis. (For Reference Call: Dr. William Gerwick, 858-822-4900)

Sept 1994 – Feb 2000: Graduate Student, Vanderbilt University, Nashville, TN
Conducted Ph.D. thesis research in the Center in Molecular Toxicology and Department of Biochemistry at Vanderbilt University with the goal of (1) elucidating the biochemical mechanisms involved in p53-mediated G2 cell cycle arrest, (2) determining the mammalian protein expression and function of a novel p53-regulated gene, PIG3, and (3) determining how primary cell types of different origin (epithelial vs. mesenchymal) respond to genotoxic stress. Major conclusions include: (1) Expression of p53 after genotoxic stress-induced G2 arrest prolongs the duration of the G2 checkpoint. The mechanism of p53 prolonged G2 arrest was found to be dependent on the transactivation of the cyclin dependent kinase inhibitor, p21, and on the activity of the retinoblastoma protein. (2) PIG3 expression after genotoxic stress is p53-dependent and occurs with delayed kinetics when compared with the transactivation of other p53 downstream targets. PIG3 protein is localized to the cytoplasm and expression of the protein in the absence of genotoxic stress does not effect cell proliferation or survival. (3) The position of cell cycle arrest in response to genotoxic stress differs between primary human keratinocytes and fibroblasts. Human keratinocytes display a predominant G2 arrest in response to treatment with ionizing radiation or adriamycin, whereas the majority of fibroblast cells arrest at the G1 phase of the cell cycle. These results correlated with differential activation of the p53 tumor suppressor protein, and differential inhibition of cdk2 and cdc2 kinase activity.

Techniques include: Preparation of human tissue culture lines that contain inducible expression of several p53 deletion constructs; preparation of normal human and mouse keratinocytes and fibroblasts from tissue samples; RT-PCR, DNA cloning and sequencing; retroviral infection; antibody production and purification; Western and Northern analysis; FACS analysis; CAT-, luciferase, and kinase assays; DNA gel-shift assays, recombinant protein expression and purification; fluorescence spectroscopy, subcellular fractionation, and immunohistochemistry. (For Reference Call: Jennifer Pietenpol 615-936-1512)

Sept 1992 - June 1994: Graduate Student, University of Denver, Denver, CO
Completed my M.S. in ecology conducting research on nutrient cycling in a tropical wet forest. In addition to the main thesis topic, I contributed to the evaluation of tropical ecosystem dynamics pre- and post- fire, and two Colorado-based projects; one focusing on the requirements of rare and endangered plants, and the other focusing on the anthropological impact on nutrient pools in the Colorado Front Range.

Techniques included: Soil sampling, litter harvesting and decomposition, elemental analysis of leaf litter and soil, measuring rates of photosynthesis, measuring soil emission of nitric and nitrous oxide, carbohydrate analysis of leaves and stem xylem/phloem, and ecological computer modeling. Geographical areas of research included: the Big Island of Hawaii; La Selva, Costa Rica; San Mateo, Mexico; and the Colorado Rocky Mountains. (For Reference Call: Dr. Robert Sanford Jr. 303-871-3435)

Grants and Fellowships:

Current:

Flatt, P.M. (Co-PI) (Awarded 06/01/2011) Collaborative Grant Proposal Submitted with Steve Taylor (PI) and Paul Measeles (PI) at Oregon Department of Agriculture. 'Surface Water Quality Monitoring in the Mid-Willamette Valley.' Submitted to Oregon Watershed Enhancement Board (OWEB). $14,000.

Flatt, P.M. (Awarded 01/01/2011) Faculty Development Grant awarded by WOU. Deciphering Secondary Metabolic Pathways in Microorganisms. $3,000

Participating as a Vertical Leader in a five-year NSF funded grant entitled, 'ASAP - Advancing the careers of women in STEM at predominantly undergraduate institutions'. PI: Joanne Smieja at Gonzaga University (2011-2016).

Completed:

Flatt, P.M., Latham, K. and Courtney, A. (April 2010) $9,500 grant award from WOU Academic Infrastructure Committee for the purchase of a shaker incubator.

Flatt, P.M., and Allen, W. (April 2010) $650 grant award from WOU Student Technology Committee for the development of distance learning resources.

Flatt, P.M. (Dec, 2008 – Dec, 2009) $500 grant award from WOU Foundation Grant entitled, 'Profiling Oregon Soil Microbes for Use in the Production of Biofuels and Medicines.'

Flatt, P.M. (Jan, 2009 – June, 2010) $3,500 grant award from WOU Faculty Development entitled, 'The Biosynthesis of Photoprotective Mycosporine-like Amino Acids.'

Flatt, P.M. (July 2007-June 2009) "Genetic engineering of *Pseudomonas fluorescens* as biocontrol agents." Agricultural Research Foundation Grant. Grant amount: $12,000

Flatt, P.M. (May 2006 – April 2007) "Characterization of the pyralomicin halogenases for use in drug design." General Research Fund Grant from OSU. Grant amount: $10,000

Flatt, P.M. (Feb 2006-Feb 2007) "Molecular Evolution of the Pyralomicin N-Glycosyltransferase for use in Drug Design." Medical Research Foundation of Oregon. Grant amount: $30,000

Flatt, P.M. and Gerwick, W.H., (Dec 2000 – Dec 2003) "Isolation of halogenating enzymes for drug design." *NRSA-F32 NIH Postdoctoral Fellowship*

Professional Associations:

American Society of Pharmacognosy (2008 – Present)
Oregon Academy of Science (2008 – 2010)
Council on Undergraduate Research (2009 – 2010)
American Association of Cancer Research (1999-2000)
International Society for the Study of Xenobiotics (1999-2000)

Publications

Flatt, P.M., Walters, M., Perry, S. and Mahmud, T. (In Preparation) Isolation and characterization of the pyralomicin biosynthetic gene cluster from *Nonomuraea spiralis*. To be submitted to Microbiology by the end of the summer.

Asamizu, S., Xie, P., Brumsted, C., **Flatt, P.M.,** Mahmud, T. (Accepted) Evolutionary Divergence of Sedoheptulose 7-Phosphate Cyclases Leads to Several Distinct Cyclic Products. *Submitted to JACS.*

Andrianasolo, E., **Flatt, P.M.,** McPhail, K.L., Simmons T. L., and Gerwick, W.H. (2011) Pivotal Connections: Tracing Support by the Natural Products Branch to Drug Discovery from Marine Organisms. To be published in Bruce Ponman's Ed: *Realizing Natures Potential: Proceedings of the William L Brown Symposium Honoring Dr. Gordon Cragg.* MGB Press.

Ito, T., Roongsawang, N., Shirasaka, N., Lu, W., **Flatt, P.M.**, Kasanah, N., Miranda, C., and Mahmud, T. (2009) Deciphering pactamycin biosynthesis and engineered production of new pactamycin analogues. *ChemBioChem.* 10: 2253-2265.

Fosto, S., Zabriskie, T.M., Proteau, P.J., **Flatt, P.M.**, Santosa, D.A., Sulastri, and Mahmud, T. (2009) Limazepines A-F, Pyrrolo[1,4]benzodiazepine Antibiotics from an Indonesian *Micrococcus* sp. *J. Nat. Prod.* 72(4): 690-695.

Wu, X., **Flatt, P.M.**, and Mahmud, T. (2009) Biosynthetic gene cluster of Cetoniacytone A, an unusual aminocyclitol from the endosymbiotic bacterium, *Actinomyctes* sp. LU9419. *ChemBioChem* 10(2):304-314.

Mahmud, T., **Flatt, P. M**., and Wu, X. (2007) Biosynthesis of Unusual Aminocyclitol-containing Natural Products. *J. Nat. Prod.*, *70*, 1384-1391.

Wu, X., **Flatt, P.M.**, Schlorke, O., Zeeck, A. Dairi, T., Mahmud, T. (2007) A comparative analysis of the sugar phosphate cyclase superfamily involved in primary and secondary metabolism. *Chembiochem.* 8(2):239-48.

Flatt, P.M., Mahmud, T. (2007) Biosynthesis of aminocyclitol-aminoglycoside antibiotics and related compounds. *Nat Prod Rep*. 24(2):358-92.

Ramaswamy, A.V., **Flatt, P.M.,** Edwards, D.J., Simmons, T.L., Han, B., Gerwick, W.H. (2006) "The secondary metabolites and biosynthetic gene clusters of marine cyanobacteria. Applications in biotechnology." In Proksch, P. and Müller, W.E.G. eds. of Frontiers of Marine Biotechnology. Horizon Scientific Press, Norfolk, UK.

Flatt,P.M., O'Connell, S.J., McPhail, K., Zeller, G., Willis, C., Sherman, D.H. and Gerwick, W.H. (2006) Characterization of the Initial Steps in Barbamide Biosynthesis. *J. Nat. Prod*. 69(6):938-44.

Flatt, P.M., Gautschi, J.T., Thacker, R.W., Musafija-Girt, M., Crews, P. and Gerwick, W.H. (2005) Identification of the Cellular Site of Polychlorinated Peptide Biosynthesis in the Marine Sponge *Dysidea* (*Lamellodysidea*) *herbacea* and Symbiotic Cyanobacterium *Oscillatoria spongeliae* by CARD-FISH analysis. *Marine Biology* 147(3):761-774.

Simmons, T.L., Andrianasolo, E., McPhail, K., **Flatt, P.M.** and Gerwick, W.H. (2005) Marine natural products as anticancer drugs. *Molecular and Cancer Therapeutics* 4:333-342.

Chang, Z., Sitichitta, N., Rossi, J.V., Roberts, M.A., **Flatt, P.M.,** Jia, J., Sherman, D.H. and Gerwick, W.H. Biosynthetic pathway and gene cluster analysis of curacin A, an anti-tubulin natural product form the tropical marine cyanobacterium *Lyngbya majuscula*. *J Nat Prod* 67(8):1356-67 (2004).

Chang, Z*., **Flatt, P.M.***., Gerwick, W.H., Nguyen, V-A., Willis, C.L., and Sherman, D.H. (2002). The barbamide biosynthetic gene cluster: A novel marine cyanobacterial system of mixed polyketide synthase (PKS)-non-ribosomal peptide synthetase (NRPS) origin involving an unusual trichloroleucyl starter unit. *Gene*. 296:235-247. *Authors with equal contribution to this work.

Flatt, P.M. and Pietenpol, J.A. (2000). Mechanisms of cell cycle checkpoints: At the crossroads of carcinogenesis and drug discovery. *Drug Metabolism Reviews*. 32(3&4), 283-305.

Flatt, P.M., Tan, L. J., Scatena, C.D., Szak, S.T., Pietenpol, J.A., (2000). p53 regulation of G2 checkpoint is retinoblastoma protein dependent. *Mol Cell Biol* 20(12): 4210-4223.

Flatt, P.M., Polyak, K., Tang, L.J., Scatena, C.D., Westfall, M.D., Rubenstein, L.A., Yu, J., Kinzler, K. W., Vogelstein, B., Hill, D., and Pietenpol, J.A. (2000) p53-dependent expression of PIG3 during proliferation, genotoxic stress, and reversible growth arrest. *Cancer Letters* 156:63-72

Flatt, P.M., Price, J.O., Shaw, A., and Pietenpol, J.A. (1998). Differential cell cycle checkpoint response in normal human keratinocytes and fibroblasts. *Cell Growth and Differentiation.* 9:535-543.

Herrmann, L.M., **Flatt, P**., and Bowler, B.E. (1996). Site-directed replacement of the invariant lysine73 of Saccharomyces cervisiae iso-1-cytochrome c with all ribosomally encoded amino acids. *Inorganica Chimica Acta*. 242(1):97-103.

Synergistic Activities

(i) Participation as a Vertical Leader in an NSF sponsored project to advance the careers of women in STEM at predominantly undergraduate institutes.

(ii) Curriculum development and replacement of aging equipment in the Chemistry Dept. at WOU through the development of an AIC grant in collaboration with Dr. Latham in Biology and Dr. Courtney in Chemistry.

(iii) Development of the Watershed Grant Application with Dr. Steve Taylor in Earth Sciences and Paul Measeles at Oregon Department of Agriculture.

(ii) Curriculum development and teaching of an Evolution and Diversity 100-level course at Lane Community College, Eugene, OR. This involved the integration of internet and computer technologies within the classroom.

(ii) Participation in the training of students from foreign nations (Papua New Guinea) as part of an NIH PO1 project grant. This involved field collection and processing techniques for the analysis of natural products from marine natural resources.

(iii) Participation in the Women in Science Workshop sponsored by dedicated female scientists at OSU. This workshop is local program used to introduce and encourage high school aged women to pursue careers in the biological and physical sciences

Collaborators and Other Affiliations

(i) Additional Collaborators and Co-Editors

a. Dr. Taifo Mahmud, College of Pharmacy, Oregon State University, Corvallis, OR
b. Dr. John Meeks, Department of Chemistry, UC Davis, Davis, CA
c. Dr. Phil Crews, Professor of Chemistry, UC Santa Cruz, Department of Chemistry, Santa Cruz, CA
d. Dr. Philip J. Proteau, Associate Professor, Oregon State University, College of Pharmacy, Corvallis, OR

e. Dr. David Sherman, The John G. Searle Professor of Medicinal Chemistry, University of Michigan, College of Pharmacy, Ann Arbor, MI
f. Dr. Robert Thacker, Assistant Professor, University of Alabama at Birmingham, Department of Biology, Birmingham, AL
g. Dr. Christine Willis, Professor of Organic Chemistry, Director of the Graduate School, University of Bristol, School of Chemistry, Bristol, UK

(ii) Graduate and Postdoctoral Advisors

a. Dr. Jennifer A. Pietenpol, Associate Professor, Vanderbilt University, Department of Biochemistry, Nashville, TN
b. Dr. William H. Gerwick, Professor of Marine Natural Products Chemistry, Oregon State University, College of Pharmacy, Corvallis, OR

(iii) Student Training and Mentoring

a. Involved with Training 4 Graduate Students
    - Chloe'Mae Abott (WOU)
    - Aishwarya Ramaswamy (OSU)
    - Rashel Grindberg (OSU)
    - Xiumei Wu (OSU)
b. Involved in the Training of 19 Undergraduate Students
    - Troy Vaden (WOU graduate - currently accepted as a graduate student in Organic Chemsitry at OSU)
    - Roger Shoemaker (Current WOU Student)
    - Nyssa Hicks (WOU graduate 2012)
    - Yijun Su (Current WOU Student)
    - Terry Siewart (WOU graduate 2012)
    - Christopher Rule (WOU graduate 2011)
    - Samantha Cunningham (WOU graduate 2011)
    - Justin Hoagland (WOU graduate 2011)
    - James Kramer (WOU graduate 2011 - applying to Medical School)
    - Autumn Hughes (WOU graduate 2011)
    - Jeff Sigrist (WOU graduate 2011)
    - Jennifer East (WOU graduate 2010)
    - Ted Bolstadt (WOU undergraduate 2009 - WOU Masters of Education 2010 - Currently teaching in the Dominican Republic)
    - Amanda Lakamp ((WOU undergraduate 2009 - Currently in graduate school at University of Nebraska)
    - Mathew McCrary (WOU student; transfer to CU Health Sciences in Denver, CO)
    - Travis Hoagland (WOU graduate 2010 - currently in Pharmacy School at OSU)
    - Heather Cruise (OSU graduate 2009 - currently on a botony fellowship in Tanzania)
    - Steven Perry (OSU graduate 2007)
    - Micah Walters (OSU graduate 2007 - attended Pharmacy School at OSU)
c. Visiting Scholars
    - Hosted Linnan Zhang, a visiting scholar from China Chinese visiting scholar in 2010-2011; and in the Winter and Spring of 2012
    - Hosted Chenyuan Li, a visiting scholar from China in 2009-2010

References:

Taifo Mahmud, Ph.D. Assistant Professor. College of Pharmacy. Oregon State University, Corvallis, OR 97331 (541)-737-9679.

William H. Gerwick, Ph.D. Professor of Natural Products Chemistry. Skaggs School of Pharmacy and Pharmaceutical Sciences and Scripps Institute of Oceanography. San Diego, CA 92093 (858)-822-4900.

Jennifer Pietenpol, Ph.D. Ingram Professor of Cancer Research, Vanderbilt University, Department of Biochemistry, Nashville, TN (615)-936-1512

Kyle Hammon, Ph.D. Previous Division Chair of Science and Math. Current Director of Distance Learning, Lane Community College, Eugene, OR. Phone: (541)-463-5893