Naomi Cotton-Munn, PhD
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EDUCATION*

Doctorate of Philosophy, Biochemistry (2000-2004)
University of Washington, Biochemistry Department, Seattle, WA 98195

Education focus on characterization of oxidative chemical effects on enzymatic function. Structure based drug/inhibitor/accelerator design. Structure-function characterization studies.
Thesis Advisor: Professor Bill Parson

Bachelors of Science, Biochemistry & Molecular Biology (1995 to 2000)
University of California, Biochemistry & Molecular Biology Department, Santa Cruz, CA 95064

Education focus on biochemistry and molecular biology. Laboratory positions in Environmental Toxicology, Santa Cruz Institute for Particle Physics and Immunology departments. SCUBA (NAUI), basic to advanced diver training certifications.

WORK/RESEARCH EXPERIENCE*

Quality Assurance Assistant (REMOTE), www.peopoli.com (2/2026 to present)
Reference: Robert Munn, robert@robertmunn.com
Testing and reporting bugs for deployment of internet software

Educational Outreach, www.mineralchemistry.com (2/2025 to present)
Reference: Self-employment
Consultations include structural chemistry and molecular biology to unravel the known molecular mechanisms medication, supplements or addictive substances. We search for alternatives based on molecular structure and literature review of mechanism of action.

Board Member, Compressed Earth Block Materials, Santa Fe NM 87505 (6/2022 to 6/2024)
Reference: Robert Munn, robert@robertmunn.com
Masonry (development of soil-based bricks for sustainable building construction). Administration, business-related assistance

Board Member, Medicinal Research Institute, Santa Cruz CA 95060 (8/2009 to 1/2013)
Reference: Self-employment
Founder and board member of research institute focused on the molecular characterization of cannabis for medicinal purposes

Post-doctoral Associate, University of California San Diego (10/2006 to 10/2008)
Research Advisors: Prof. Ed Dennis edennis@ucsd,edu; Prof. Partho Ghosh, pghosh@ucsd.edu
Phospholipid plasma membrane-associated enzymatics via isotopic LC-MS assay (C(14) labeled lipids), Lipid Maps database laboratory member. Structure-function studies on pathogen enzymes.

Post-doc; Burnham Institute for Medical Research, La Jolla, CA 92037 (11/2005 to 10/2006)
Director: Prof. Pellecchia, maurizio.pellecchia@ucr.edu
Structure function analysis of mitochondrial membrane-associated Bcl-2 proteins. Existing inhibitor/pharmaceutical re-purposing studies. Structure, functional bioinformatics

Postdoc; University of California Santa Cruz, Santa Cruz, CA 95064 (10/2004 to 11/2005)
Director: Professor Phil Crews, pcrews@ucsc.edu
Department of Chemistry and Biochemistry; Purification (Extraction, HPLC) and identification (MS, NMR) of biologically active molecules from marine sponges. Assay development. SCUBA diving training and Masters certification

Ph.D. Candidate University of Washington Seattle, WA 98195 (9/2000 to 6/2004)
Research Advisor: Professor Bill Parson, parsonb@u.washington.edu
UV spectoscopy, enzyme kinetics, gas chromatography, mass spectrometry, designed websites for BMSD department, SGPP proteomics project, laboratory websites; staff member, instructor at UW rock wall facility. Thesis: structure-function characterization of catechol-O-methyltransferase (COMT)

Quality Assurance Engineer; Pumatech Santa Cruz CA (9/1995 to 6/1997)
Tested and reported bugs for scientific internet software

Computer Consultant, Manager; University of California Santa Cruz (9/1995 to 6/1997)
Manager: Alicia Marquez, Reference: Philip Stark philip@ucsc.edu
University computer lab student support. Promoted to manager, trained new consultants and provided support to UCSC lab consultants. Managed and trained new employees

Other employment titles (1995 to 2010)
Quality Assurance Engineer, Web Designer, Laboratory Assistant, Teachers Assistant, Restaurant Server, Cashier, Lifeguard, Swimming instructor, Rock climbing Instructor, Model

PUBLICATIONS, W/ ABSTRACTS*

J Nat Prod. 2007 Mar;70(3):383-90. doi: 10.1021/np060555t. Epub 2007 Feb 10

Accelerating the discovery of biologically active small molecules using a high-throughput yeast halo assay

Gassner NC(1), Tamble CM, Bock JE, Cotton N, White KN, Tenney K, St Onge RP, Proctor MJ, Giaever G, Nislow C, Davis RW, Crews P, Holman TR, Lokey RS. Author information:(1)Department of Chemistry and Biochemistry, University of California, Santa Cruz, CA 95064, USA

The budding yeast Saccharomyces cerevisiae, a powerful model system for the study of basic eukaryotic cell biology, has been used increasingly as a screening tool for the identification of bioactive small molecules. We have developed a novel yeast toxicity screen that is easily automated and compatible with high-throughput screening robotics. The new screen is quantitative and allows inhibitory potencies to be determined, since the diffusion of the sample provides a concentration gradient and a corresponding toxicity halo. The efficacy of this new screen was illustrated by testing materials including 3104 compounds from the NCI libraries, 167 marine sponge crude extracts, and 149 crude marine-derived fungal extracts. There were 46 active compounds among the NCI set. One very active extract was selected for bioactivity-guided fractionation, resulting in the identification of crambescidin 800 as a potent antifungal agent.

J Med Chem. 2008 Dec 25;51(24):8027-37. doi: 10.1021/jm800649q

Synthesis of polyfluoro ketones for selective inhibition of human phospholipase A2 enzymes

Baskakis C(1), Magrioti V, Cotton N, Stephens D, Constantinou-Kokotou V, Dennis EA, Kokotos G. Author information: (1)Laboratory of Organic Chemistry, Department of Chemistry, University of Athens, Panepistimiopolis, Athens 15771, Greece

The development of selective inhibitors for individual PLA(2) enzymes is necessary in order to target PLA(2)-specific signaling pathways, but it is challenging due to the observed promiscuity of known PLA(2) inhibitors. In the current work, we present the development and application of a variety of synthetic routes to produce pentafluoro, tetrafluoro, and trifluoro derivatives of activated carbonyl groups in order to screen for selective inhibitors and characterize the chemical properties that can lead to selective inhibition. Our results demonstrate that the pentafluoroethyl ketone functionality favors selective inhibition of the GVIA iPLA(2), a very important enzyme for which specific, potent, reversible inhibitors are needed. We find that 1,1,1,2,2-pentafluoro-7-phenyl-heptan-3-one (FKGK11) is a selective inhibitor of GVIA iPLA(2) (X(I)(50) = 0.0073). Furthermore, we conclude that the introduction of an additional fluorine atom at the alpha' position of a trifluoromethyl ketone constitutes an important strategy for the development of new potent GVIA iPLA(2) inhibitors.

J Biol Chem. 2004 May 28;279(22):23710-8. doi: 10.1074/jbc.M401086200. Epub 2004 Mar 18
Oxidative inhibition of human soluble catechol-O-methyltransferase
Cotton NJ(1), Stoddard B, Parson WW. Author information: (1)Department of Biochemistry, University of Washington, Seattle, Washington 98195-7350, USA

A common polymorphism in the human gene for catechol-O-methyltransferase results in replacement of Val-108 by Met in the soluble form of the protein (s-COMT) and has been linked to breast cancer and neuropsychiatric disorders. The 108M and 108V variants are reported to differ in their thermal stability, with 108M COMT losing catalytic activity more rapidly. Because human s-COMT contains seven cysteine residues and includes CXXC and CXXS motifs that are associated with thiol-disulfide redox reactions, we examined the effects of reducing and oxidizing conditions on the enzyme. In the absence of a reductant 108M s-COMT lost activity more rapidly than 108V, whereas in the presence of 4 mm dithiothreitol (DTT) we found no significant differences in the stability of the two variants at 37 degrees C. DTT also restored most of the activity that was lost upon incubation at 37 degrees C in the absence of DTT. Mass spectrometry showed that cysteines 188 and 191 formed an intramolecular disulfide bond when s-COMT was incubated with oxidized glutathione, whereas cysteines 69, 95, 157, and 173 formed protein-glutathione adducts. Replacing Cys-95 by serine protected 108M s-COMT against inactivation in the absence of a reductant; C33S and Cys-188 mutations had little effect, and C69S was destabilizing. The sequences surrounding the reactive cysteine residues of human s-COMT and other proteins that form glutathione adducts at identified sites all include Pro and/or Gly and most include a hydrogen-bonding residue, suggesting that glutathiolation at conserved sites plays a physiologically important role.

Chem Biol Drug Des. 2008 Feb;71(2):131-9. doi: 10.1111/j.1747-0285.2007.00617.x. Epub 2008 Jan 19
Rhodanine derivatives as selective protease inhibitors against bacterial toxins
Johnson SL(1), Chen LH, Harbach R, Sabet M, Savinov A, Cotton NJ, Strongin A, Guiney D, Pellecchia M. Author information: (1) Burnham Institute for Medical Research, 10901 North Torrey Pines Rd, La Jolla, CA 92037, USA

In this study, we analyzed a series of rhodanine derivatives, as potential inhibitors of bacterial toxins, namely the proteases anthrax lethal factor and the botulinum neurotoxin type A. Conducting an extensive structure-activity relationship study on rhodanine derivatives, we profiled their selectivity against the two bacterial toxins and two related human metalloproteases using in vitro assays. In addition, we examined initial in vitro ADME-Tox properties of selected compounds and their ability to protect lethal factor-induced cell death of macrophages. These data allowed the selection of one additional drug candidate for which preliminary in vivo efficacy studies against anthrax spores were conducted. Integration of these results with our structure-activity relationship studies provides a framework for the development of potential drug candidates against anthrax and botulinum.

Bioorg Med Chem. 2008 Dec 15;16(24):10257-69. doi: 10.1016/j.bmc.2008.10.046. Epub 2008 Nov 1
Structure-activity relationships of natural and non-natural amino acid-based amide and 2-oxoamide inhibitors of human phospholipase A(2) enzymes
Antonopoulou G(1), Barbayianni E, Magrioti V, Cotton N, Stephens D, Constantinou-Kokotou V, Dennis EA, Kokotos G. Author information: (1)Laboratory of Organic Chemistry, Department of Chemistry, University of Athens, Panepistimiopolis, Athens 15771, Greece

A variety of 2-oxoamides and related amides based on natural and non-natural amino acids were synthesized. Their activity on two human intracellular phospholipases (GIVA cPLA(2) and GVIA iPLA(2)) and one human secretory phospholipase (GV sPLA(2)) was evaluated. We show that an amide based on (R)-gamma-norleucine is a highly selective inhibitor of GV sPLA(2).

Bioorg Chem. 2007 Aug;35(4):344-53. doi: 10.1016/j.bioorg.2007.03.001. Epub 2007 May 21
Structure-based discovery of a new class of Bcl-xL antagonists
Rega MF(1), Leone M, Jung D, Cotton NJ, Stebbins JL, Pellecchia M. Author information: (1) Burnham Institute for Medical Research, La Jolla, CA 92037, USA

Apoptosis, or programmed cell death, plays a key role in normal tissue homeostasis ensuring a proper balance between cell production and cell loss. Anti-apoptotic Bcl-2-family proteins are central regulators of the apoptotic pathway and due to their ability to confer tumor resistance to chemotherapy or radiation, have been recently validated as targets for cancer drug discovery. Since the crucial interaction between pro- and anti-apoptotic members occurs via a conserved region located on the surface of the protein, a viable way to inhibit the anti-death activity of Bcl-2 proteins is to design small molecule inhibitors that occupy this cavity. Here, we describe a structure-based approach that led to the identification of four small molecule inhibitors directed at the hydrophobic groove on the surface of the Bcl-2 family protein Bcl-xL. The compounds were characterized in a number of assays including in vitro binding using 15N-labeled protein, a displacement DELFIA assay, and a cell-based viability assay with human cancer cells.