



**ANDREA A. STIERLE, Ph.D., Research Professor**  
Natural Products Organic Chemistry/ Drug Discovery  
Department Biomedical and Pharmaceutical Sciences  
The University of Montana  
Missoula, Montana 59812

### ***Education***

- California Western University-USIU, B.A., Biology/ Chemistry, 1971-1975, *summa cum laude*.
- Montana State University, Doctor of Philosophy in Chemistry (major area- Organic Chemistry, minor area - Biochemistry), 1984-1988.
- Scripps Institution of Oceanography, Postdoctoral Fellow, 1988-1989
- Montana State University, Department of Plant Pathology, Postdoctoral Fellow, 1989-1991.

### ***Personal Statement***

The Stierle lab focuses on the isolation and characterization of small molecules produced by microorganisms from unique ecological niches. One of strengths of Natural Products Chemistry is its adaptability. Diverse biological assays can direct isolation efforts from diverse source organisms. We are currently studying several different organisms, including the extremophilic microbes residing in Berkeley Pit Lake, an abandoned open pit copper mine and part of the largest EPA Superfund site in North America. Although it is not a logical location for a drug discovery program, this unusual ecosystem has selected for microbes that produce unique secondary metabolites. It is a reminder that even the most undesirable of habitats may provide important resources if we search them appropriately. We are also studying the secondary metabolites of symbiotic gut microbes and of specific Ayurvedic plants, and the metabolites of gut microbes grown in liquid culture containing Ayurvedic plant material.

We select for inhibitors of the signaling enzymes matrix metalloproteinase-3, caspase-1, caspase-3, and XIAP. MMP-3 inhibitors block the onset and metastasis of certain tumors. Caspase-1 inhibitors target autoimmune, neurodegenerative, and inflammatory disorders and inflammation-associated cancers. Caspase-3 inhibitors mitigate the damaging repercussions of stroke and XIAP inhibitors enhance apoptosis of tumors. Novel enzyme inhibitors have been sent to the *NIH-NCI-Developmental Therapeutics Program* for evaluation in their 60 human cancer cell-line screen and to *Memorial Sloan Kettering Cancer Center* and *Eisai, Inc.* for evaluation as chemotherapeutic agents. Caspase-1 inhibitors are evaluated for their ability to mitigate IL-1B production in the intact inflammasome. All of the compounds we have isolated have shown low-micromolar to nanomolar activity against specific human cancer cell lines.

We are also working with Montana BioAgriculture, Inc., to design a biochemical control system to protect forests from Mountain Pine Bark Beetle.

### ***Awards***

- *Rose and Ann Busch Outstanding Faculty Award*- 2009
- *Charles and Anne Morrow Lindbergh Merit Award* - 2009

- *Montana Tech Outstanding Achievement Award* - 2008
- *Montana Tech Distinguished Researcher Award* - 2008

### ***TEACHING EXPERIENCE***

- *FALL 2010*  
MOLECULAR PHARMACOLOGY: BMED 615 (KEITH PARKER) 2 lectures  
NATIVE AMERICAN MEDICINE AND HEALTH: PHAR 395 (RUSTEM MEDORA) 1 lecture
- *SPRING 2011*  
MEDICINAL CHEMISTRY: MED CHEM 624 (NICK NATALE)  
Antiviral Drugs (3 lecture periods)  
Natural Products in Drug Discovery (3 lecture periods)
- *Fall 2012*  
MOLECULAR PHARMACOLOGY: BMED 615 (KEITH PARKER) 2 lectures

### ***Trainees mentored***

#### **Undergraduate Researchers at Montana Tech: 8/15/2009 - 5/15/2010**

From August 2009 through May 2010 I was at Montana Tech every Friday and weekends as I continued to mentor two undergraduate research students and two High School Science Fair students who had been working with me in the lab. The Stierle lab has been a research home to almost 100 undergraduate students over the years and I wanted to complete my work with Jonathan Cloonan and Marissa Darvis who were working on Berkeley Pit microbes in our laboratory. Our RO1 provided the funding for these students and I wanted to see them through their projects until they graduated in May 2010. Both students presented their work at the Montana Tech Undergraduate Research Fair in Butte and at the Montana American Chemical Society regional meeting.

#### **Undergraduate Researchers at UM-Missoula: 8/20/2010- present**

8/20/10 - 5/01/11 - Shea Snyder and David Curran  
8/20/11 - 5/01/12 - Sarah Hamblock on the Berkeley Pit Project  
8/20/12 - 5/01/13 - Michelle Nemetchek and Andrew Crompton  
8/20/12 - 5/01/13 - Karina Oliveira  
5/01/13 - 8/10/13 - Artur Bosco  
8/20/12- 5/10/13 - Kaitelyn Kammers  
8/20/14 - 5/10/15 - Monique de Carvahlo de Santana

#### **Graduate Student**

10/01/15 - present Kelly McGrath, Department of Biomedical and Pharmaceutical Sciences

#### **Graduate Students Mentored**

10/1/09 - 2014 - John Hoody, Department of Chemistry  
10/2014 - present Nick Wageling, Department of Chemistry

### ***Professional Service***

#### ***JOURNAL REVIEWS***

- *Journal of Natural Products*

- *Journal of Organic Chemistry*
- *Phytochemistry*
- *Organic Letters*
- *Journal of Microbial Ecology*
- *Tetrahedron Letters*

#### **PROFESSIONAL AFFILIATIONS**

- *American Chemical Society*
- *American Society of Pharmacognosy*
- *Sigma Xi*
- *International Society of Microbial Ecology*
- *Clark Fork Watershed Education Program*

#### **COMMUNITY SERVICE**

##### **MISSOULA**

*Five Valleys Audubon Society - Secretary*

Visiting Naturalist with the *Naturalist in the Schools Program (Montana Natural History Center)*

Raptor banding with Rob Domenech, *Raptors Research*

*Peregrine Watch*

Audubon Society - Christmas Bird Counts

##### **BUTTE**

*St. James Community Hospital (Butte, Montana) Board member and member of the Executive Committee*

*Butte Silver Bow County Planning Board*

*Citizens for Preservation and Revitalization Historic Improvement Program Board Member*

*Clark Fork Watershed Environmental Program (Board Member and Educator)*

*Southwest Montana Science Teachers Program Instructor*

*Audubon Society- Christmas Bird Counts*

*Audubon Society- Spring Birdathon*

##### ***Recent Patents***

- *A yeast isolate that sequesters metals from low ph, high metal content aqueous solutions, Andrea A. Stierle and Donald B. Stierle, submitted September 2011.*

##### ***Selected Publications - last ten years***

A Stierle, D Stierle **2016** *Secondary Metabolites of Acid Mine Waste Fungi. In "Topics in Biodiversity and Conservation", D Hawksworth, RRM Patterson (Eds), Springer, in press*

A Stierle, D Stierle, D Decato **2015** *Redetermination and absolute configuration of berkeleydione. Acta Crystallographica Section E. Structure Reports Online. E71, o248.*

A Stierle, D Stierle, D Decato **2015** *Determination of the absolute configuration of preaustinoid A1. Acta Crystallographica Section E. Structure Reports Online. E71, o596-597.*

A Stierle, D Stierle, T Girtsman, T.C. Mou, C Antczak, H Djaballah **2015** *Azaphilones from an Acid Mine Waste Extremophilic Isolate of Pleurostomophora sp., manuscript in press, J Nat Prod*

A Stierle, D Stierle **2015** *Bioactive secondary metabolites produced by the fungal endophytes of conifers. Nat Prod Commun, 10(10): 1671-1682*

A Stierle, D Stierle, D Decato **2015** *The berkeleylactones, new antibiotic macrolides from a Berkeley Pit fungal co-culture, manuscript in preparation, J Nat Prod*

A Stierle, D Stierle **2014** *Bioactive Secondary Metabolites of Acid Mine Waste Extremophiles. Nat Prod Commun, 9(7), 1037-1044.*

A Stierle, D Stierle, G Mitman, S Snyder, SC Antczak, H Djaballah (2014) *Phomopsolides and related compounds from the algae-associated fungus Penicillium clavigerum. Nat Prod Commun. 9(1), 87-90.*

A.A. Stierle, D.B. Stierle, G.G. Mitman, S. Snyder, S, C. Antczak, H. Djaballah. **2014**. *Phomopsolides and related compounds from the alga-associated fungus, Penicillium clavigerum. Nat Prod Commun. 9(1), 87-90.*

A.A. Stierle, D.B. Stierle. **2014**. *Bioactive Secondary Metabolites of Acid Mine Waste Extremophiles. Nat.Prod.Commun., 9(7), 1037-1044.*

Andrea Stierle and Donald Stierle. **2013**. *Bioprospecting in the Berkeley Pit: the Use of Signal Transduction Enzyme Inhibition Assays to Isolate Bioactive Secondary Metabolites from the Extremophilic Fungi of an Acid Mine Waste Lake. In: "Bioactive Natural Products" Atta-Ur-Rahman, Ed.; Elsevier Science Publishers: Amsterdam. pp. 1-47.*

A. Stierle, D. Stierle, T. Girtsman. **2012**. *Caspase-1 Inhibitors from a Deep Water, Acid Mine Waste Extremophilic Fungus with Specific Cytotoxicity Towards Leukemia Cell Lines. J.Nat. Prod. 75, 344-350.*

D. Stierle, A. Stierle, T. Girtsman, K. McIntyre, J. Nichols. **2012**. *Caspase-1 and 3 Inhibiting Drimane Sesquiterpenoids From the Extremophilic Fungus, Penicillium solitum. J. Nat. Prod. 75, 262-266*

R. N. Kharwar, A. Mishra, S. K. Gond, A.Stierle\*, D.Stierle. **2011**. *Anticancer compounds derived from fungal endophytes: their importance and future challenges. Nat. Prod. Rep., 28(7), 1208 - 1228.*

D. Stierle, A. Stierle, B. Patacini, K. McIntyre, R. Girtsman, E. Bolstad. **2011**. *Berkeleyones and Related Meroterpenes From a Deep Water Acid Mine Waste Fungus That Inhibit the Production of Interleukin 1- $\beta$  from Induced Inflammasomes J. Nat. Prod. 74, 2273-2277.*

Andrea A. Stierle, Donald B. Stierle, Briana Patacini, **2008**. *The Berkeleyamides: Four New Amides From Penicillium rubrum, a Deep Water Acid Mine Waste Fungus. J. Nat. Prod. 71(5), 856-860.*

Stierle, D. B.; Stierle, A. A.; Patacini, B. **2007**. The Berkeleyacetals, Three Meroterpenes from a Deep Water Acid Mine Waste *Penicillium*. J. Nat. Prod. 70(11); 1820-1823.

A. Stierle, D. Stierle, and K. Kelley, **2006**. *Berkelic Acid, A Novel Spiroketal with Highly Specific Anti-tumor Activity from an Acid-Mine Waste Fungal Extremophile*. 2006. J. Org. Chem. 71: 5357-5360.

Andrea Stierle, **2006**. *Bioprospecting in the Berkeley Pit: The Search for Valuable Natural Products from a Most Unnatural World*. Montana, The Magazine of Western History. 56 (4): 71.

Andrea Stierle and Donald Stierle. *Bioprospecting in the Berkeley Pit: Bioactive Metabolites from Acid Mine Waste Extremophiles*. In: "Bioactive Natural Products", Volume 32, Atta-Ur-Rahman, Ed.; Elsevier Science Publishers: Amsterdam. **2005**.

D. Stierle, A. Stierle, J. David Hobbs, Janalee Stokken, and J. Clardy. **2004**. *Berkeleydione and Berkeleytrione, New Bioactive Metabolites from an Acid Mine Organism*. Organic Letters 6(6): 1049-1052.

A. Stierle, D. Stierle, and K. Kemp, **2004**. *Novel Sesquiterpenoid Matrix Metalloproteinase-3 Inhibitors from an Acid Mine Waste Extremophile*. in August 2004 D. John Faulkner and Paul Scheurer memorial issue of J. Nat. Prod. 67(8): 1392-1395.

### ***Presentations and News Stories***

Authors: Stierle, Andrea. A.; Stierle, Donald B.

Title: *Computational Modeling Directed Synthesis of More Potent Inhibitors of Molecular Pathways Associated with Epithelial Mesenchymal Transition as Novel Tools and Potential Chemotherapies*

Conference/Event: CBSD Research Retreat

Location: Double Arrow Conference Center, Montana

Date: 09/06/2015

Author: Stierle, Andrea

Title: *Richest Hills Symposium: Finding Value in a Toxic Landscape*

Conference: Keynote Speaker, National Endowment for the Humanities: Richest Hills Symposium

Location: Archives, Butte, Montana

Date: 07/30/15

Author: Stierle, Andrea

Title: *Richest Hills Symposium: Mining for Microbes: Unexpected Treasures from a Toxic Landscape*

Conference: Keynote Speaker, National Endowment for the Humanities: Richest Hills Symposium

Location: Finlen Hotel, Butte, Montana

Date: 07/16/15

Authors: Stierle, Andrea. A.; Stierle, Donald B.

Title: *Mining for Microbial Metabolites That Inhibit Enzyme Pathways Associated with Inflammation and Metastasis*

Conference/Event: Cellular and Molecular Biology Seminar

Location: University of Montana  
Date: 01/26/2015

Authors: Stierle, Andrea. A.; Stierle, Donald B.  
Title: *Search for MMP-3 and Caspase-1 Inhibitors from Extremophilic Fungi*  
Conference/Event: Invited speaker  
Location: University of Aberdeen, Aberdeen, Scotland  
Date: 11/21/2014

Authors: Stierle, Andrea. A.; Stierle, Donald B.  
Title: *Bioprospecting in the Berkeley Pit: Unique Microbes, Unique Chemistry*  
Conference/Event: Keynote, Natural Product Biotechnology International Conference  
Location: Inverness, Scotland  
Date: 11/20/2014

Authors: Stierle, Andrea. A.; Stierle, Donald B.  
Title: *Computational Modeling Directed Synthesis of More Potent Inhibitors of Molecular Pathways Associated with Epithelial Mesenchymal Transition as Novel Tools and Potential Chemotherapies*  
Conference/Event: CBSD Seminar  
Location: University of Montana  
Date: 11/06/2014

Authors: Stierle, Andrea. A.; Stierle, Donald B.  
Title: *Bioprospecting in the Berkeley Pit: Unique Microbes, Unique Chemistry*  
Conference/Event: Biomedical Pharmaceutical Sciences Seminar  
Location: University of Montana  
Date: 11/7/2014

- *Northwest Regional Meeting American Chemical Society Invited Speaker* -June 25, 2014
- *CoBRE CBSD Research retreat presentation* - September 6, 2014
- *CBSD seminar* - November 6, 2014.
- *BMED Departmental seminar* - November 7, 2014
- *Center for Biomolecular Structure and Dynamics Research seminar* - 11/15/2012.
- *Molecular Pharmacology lecture* - 10/18/2012.
- *Center for Biomolecular Structure and Dynamics Research Retreat* - 09/24/2012.
- *Research View*, summer 2012, *A Scientific Marriage*, 14(2), 4-5.
- *Failure Magazine*, Fall 2011, *The Berkeley Pit*.
- *Harkins-Fusion* High School presentation - December 14<sup>th</sup>, 2011
- *Great Conversations* - Helena Education Foundation - November 16<sup>th</sup>, 2011
- *Montana Natural History Conference* - October 19<sup>th</sup>, 2011
- Carnegie Mellon University's student run radio station, WRCT 88.3 FM Pittsburgh: *The World Revealed*, 2010.
- Medicinal Chemistry Colloquium, University of Montana - September, 2010
- *RadioLab*, WNYC, New York, "OOPs" - September 2010

- Health Effects of Metal Mining Symposium, sponsored by the CDC and Harvard School of Public Health, Bozeman, MT - May 2010
- The University of Montana School of Pharmacy - January 2010
- NISBRE Conference - National IDeA Symposium of Biomedical Research Excellence, Bethesda, MD, July 16 - 18, 2010
- International Fungal Biology Conference and the National Congress, Ensenada, Mexico - December, 2009
- American Society of Pharmacognosy, Honolulu, HI - July, 2009
- Montana Audubon Society, Helena, MT - January 2009

### ***RESEARCH GRANTS***

**NIH-NCRR-CoBRE Center for Biomolecular Structure and Dynamics Junior Investigator Award**  
(NIGMS 8P20GM103546-04) PI: Steve Sprang 08/01/2014 - 07/31/2016.

*Computational Modeling Directed Synthesis of More Potent Inhibitors of Molecular Pathways Associated with Epithelial Mesenchymal Transition as Novel Tools and Potential Chemotherapies.*

Project Location: The University of Montana  
Total award amount: Stierle subaward - \$300,000  
Person months/year: Acad. Year: 6.0  
Role: Project Investigator

**NSF-SBIR Phase II** (PI: C. Bradley, Montana BioAg, LLC) 09/15/13 - 09/14/15.

*Combining fungal metabolites and fungal insect pathogens for cost effective control of bark beetles in forestry*

Project Location: The University of Montana  
Total award amount: \$425,000; Stierle subaward - \$79,000  
Person months/year: Acad. Year: 4.0

1. Define baseline efficacy of the fungal pathogen against bark beetles
2. Identify fungal metabolites that act as boring deterrents
3. Determine a commercially scalable process for producing selected metabolites
4. Assess regulatory approval of selected metabolites.

MMP will collaborate with University of Montana scientists who have expertise in isolation and characterization of fungal metabolites and in bark beetle biology to identify fungal metabolites that act as boring deterrents, to assess the compatibility of boring deterrents with the bark beetle fungal pathogen, to develop larger scale production of desired metabolites, and to assess fungal pathogen/boring deterrent metabolite synergy.

**R01CA139159-01- NIH**

5/01/09-02/01/13

\$650,000

*Signal Transduction Enzyme Inhibitors as Novel Anticancer Agents from Acid Mine Waste Extremophilic Microbes*

The goal of this study is to use signal transduction enzyme inhibition assays to guide the isolation of compounds from a population of acid mine waste extremophilic microbes, to determine the structure of these compounds, and to evaluate their efficacy against cancer cell lines.

Role: PI

**IIP-1142411-**

**NSF-SBIR**

01/01/12 - 12/30/12

\$35,000

Combining fungal metabolites and fungal insect pathogens for cost effective control of bark beetles in forestry

This goal of this study is to determine the efficacy of the application of specific secondary metabolites and the fungus *Beauveria bassiana* to Ponderosa pine trees to mitigate infestation of the mountain pine beetle in treated trees.

Role: university collaborator

**8P20GM103546-02 NIH**

11/15/11-07/31/12

\$25,000

The Use of Caspase-1 Inhibition and the Mitigation of Interleukin-1 $\beta$  Production by Induced Inflammasomes to Isolate Compounds with Anti-inflammatory and Anticancer Activity from Symbiotic Bacteria of the Human Gut Microbiome

This was a small pilot study funded by a NIGMS-CoBRE grant awarded to the *Center for Biomolecular Structure and Dynamics*. The goal of this pilot study was the isolation and structural characterization of anti-inflammatory and anticancer compounds from symbiotic gut bacteria.

Role: pilot project leader

***Certification***

Montana Natural History Center (MNHC) Master Naturalist Spring 2011-2014