Donald B. Stierle, Ph.D.

Research Professor
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EDUCATION:

Southern Methodist University, B. S., Chemistry, 1973

University of California, Riverside, CA, Ph.D., Chemistry, 1978. Thesis Project: *Halogenated Monoterpenes from the Red Alga Plocamium.*

Scripps Institution of Oceanography, Postdoctoral Research Chemist, 1978-79. Compounds from Marine Sponges.

PERSONAL STATEMENT:

Research in our lab focuses on the isolation and characterization of secondary metabolites produced by microorganisms from unique ecological niches. One of strengths of Natural Products Chemistry is its adaptability. Diverse biological assays can direct compound isolation efforts from diverse source organisms. We are studying the secondary metabolites of two populations of microorganisms: the extremophilic microbes in Berkeley Pit Lake, an abandoned open pit copper mine and the symbiotic bacteria of the human intestine. 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-Developmental Therapeutics Program for evaluation in their 60 human cancer cell-line screen and to Memorial Sloan Kettering for evaluation as chemotherapeutic agents. Caspase-1 inhibiters 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.

HONORS:

2009 Rose and Ann Busch Outstanding Faculty Award

2006-2011 Rose and Anne Busch Endowed Chair in Mathematics and Sciences

COURSES TAUGHT:

BMED 615: (KEITH PARKER) 2 lectures, Fall 2012, MOLECULAR PHARMACOLOGY. *Fall 2012*

CHEM 595: Structural elucidation: *Fall 2011*
BMED 615:(KEITH PARKER) 2 lectures, MOLECULAR PHARMACOLOGY, *FALL 2010*

TRAINEES MENTORED:

8/20/10 – 5/1/11 - Shea Snyder and David Curran
8/20/11 – 5/1/12 – Sarah Hamblock on the Berkeley Pit Project
8/20/12- 5/1/13 – Michelle Nemetchek and Andrew Crompton
8/20/12 - 5/1/13 – Karina Oliveira
5/1/13 – 8/10/13 – Artur Bosco
8/20/12- present – Kaitelyn Kammers

PROFESSIONAL SERVICE: *(Last 3 years)*

Scientific Manuscript Reviews

Journal of Natural Products
Organic Letters
Journal of Organic Chemistry

Professional Affiliations

American Chemical Society
American Society of Pharmacognosy
Clark Fork Watershed Education Program

COMMUNITY SERVICE:

Visiting Naturalist in the Schools
Five Valleys Audubon Society
Clark Fork Native Plant Society
Co-Director/ Founder, *Montana Mind Expansion Science and Art Center for Children* 2000-2004
Pintler Audubon Society

BIBLIOGRAPHY:

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.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.

Andrea A. Stierle, Donald B. Stierle, Grant G. Mitman, Shea Snyder, Christophe Antczak and Hakim Djaballah. **2013**. *Phomopsolides and Related Compounds from the Alga-associated Fungus, Penicillium clavigerum*. *Natural Products Communications*, in press.

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-β 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.

GRANTS:

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

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

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

NSF-SBIR Phase II (C. Bradley, Montana Bioagriculture 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.

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-1β 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.