

Daniel Romo, Professor

Synthetic and Biomechanistic Investigations of Complex Marine Natural Products; Asymmetric Synthesis, Novel Transformations, and Applications of β -Lactones; Natural Product Receptor Isolation Studies (Chemical Genetics)

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Graduate Students

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Henry Nguyen	Morgan Shirley
Gang Liu	Takahiro Nago

Post-Doctoral Students

Dr. Carolyn Leverett	Dr. Yonggang Wang
Research Associate:	Dr. Jing Li

Undergraduates

Kevin Arendt	Alice Cole
Daniel Sanders	Luke Watson

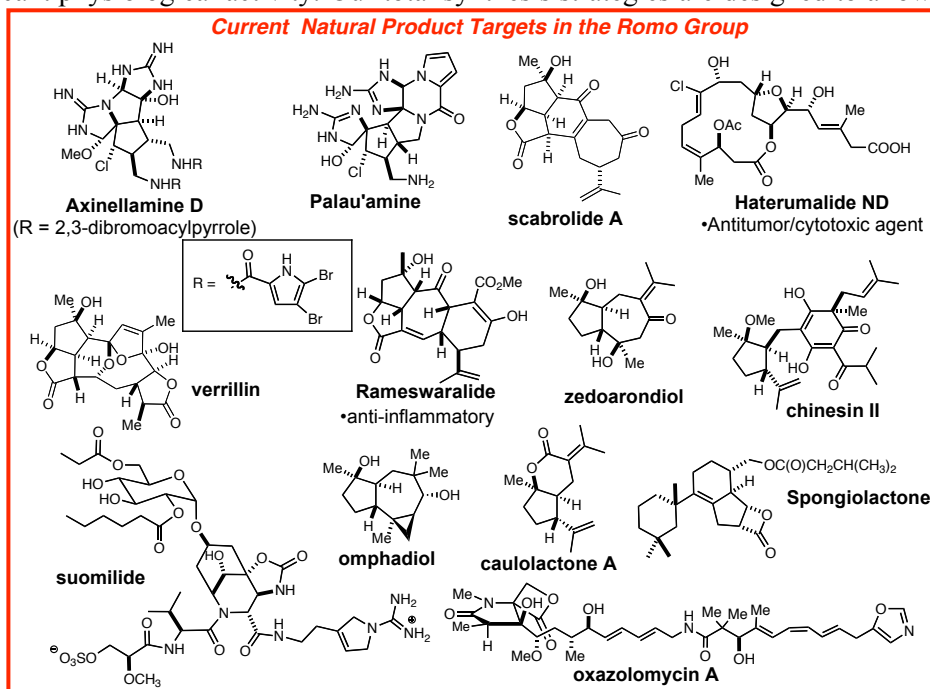
At the heart of our research interests are the chemistry and biology of natural products. These are unique and often structurally complex molecules that are designed to interact in highly specific ways with various cellular receptors and by homology those found in humans. Our interest in a particular synthetic target begins by an awe of the structural complexity and/or the presence of β -lactones or functionality derivable from β -lactones in addition to interesting biological activity. Thus, our group is engaged in developing novel synthetic strategies towards these naturally occurring compounds or derivatives that in turn serve as useful leads for inquiries into protein function.

•Structural, Synthetic, and Biomechanistic Investigations of Bioactive Marine Natural Products

One focus of our research efforts is the structure elucidation, total synthesis, and determination of the mode of action of marine natural products that display significant physiological activity. Our total synthesis strategies are designed to allow efficient access to the natural product in addition to structural derivatives and conjugates for studies aimed at elucidating their mechanism of action.

•Asymmetric Synthesis, Novel Transformations, and Applications of 2-Oxetanones (β -Lactones).

We are interested in developing diastereoselective and enantioselective methods for the preparation of β -lactones, underutilized heterocycles, employing 1) chiral amine catalyzed aldol-lactonization (NCAL) reactions of ketene and carbonyl compounds and 2) tandem Mukaiyama aldol-lactonization (TMAL) reactions. In addition, we are interested in developing new transformations of these strained systems and ultimate application to natural and unnatural product synthesis (e.g. spongiolactone, belactosin C, and Omuralide/salinoporamide derivatives). We recently initiated a project with Jeff Smith at the Burnham Institute (La Jolla) targeting fatty acid synthase (thioesterase domain) as a therapeutic target for cancer. This involves synthesis of Orlistat® derivatives employing the TMAL reaction.



•**Natural Products-Based Drug Discovery Center at TAMU (New Methodologies for Chemical Genetics/Functional Genomics)** This recently established center is focusing on the development of strategies and methodologies to more rapidly couple a natural product with its cellular protein target. The strategy bypasses the usual bottleneck of complete natural product structure determination. Our strategy involves mild reactions that enable simultaneous arming (with an alkyne for subsequent conjugate to various cellular probes) and SAR studies of bioactive natural products (to determine a suitable site for probe attachment). We recently described our first approach involving Rh(II) catalyzed OH insertions with natural products.

SELECTED RECENT PUBLICATIONS

- Peddibhotla, S.; Romo, D. "Simultaneous Arming and Structure/Activity Studies of Natural Products Employing O-H Insertions: An Expedient and Versatile Strategy for Natural Products-Based Chemical Genetics" *J. Am. Chem. Soc.* **2007**, *129*, 12222-12231. (Featured in *Chem. & Eng. News*, October 1, 2007)
- Low, W.-K.; Dang, Y.; Bhat, S.; Romo, D.; Liu, J. O. "Substrate-Dependent Targeting of Eukaryotic Translation Initiation Factor 4A by Pateamine A: Negation of Domain-Linker Regulation of Activity" *Chem. & Biol.* **2007**, *14*, 1.
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- Mitchell, T. A.; Cunziang, Zhao, C.; Romo, D. "Highly Diastereoselective, Tandem, Three-Component Synthesis of Tetrahydrofurans from Ketoaldehydes via Silylated β -Lactone Intermediates: Application to a Colopsinol B Fragment", *Angew. Chem. Int. Ed.*, **2008**, 5026-5029 .
- "Concise Synthesis of Spirocyclic, Bridged γ -Butyrolactones via Stereospecific, Dyotropic Rearrangements of β -Lactones Involving 1,2-Acyl and δ -Lactone Migrations" Purohit, V. C.; Matla, A. S.; Romo, D. *J. Am. Chem. Soc.* **2008**, *130*, 10478-10479.
- Wang, S.; Romo, D. "Enantioselective Synthesis of (+) Monobromophakellin and (+)-Phakellin: A Concise Phakellin Annulation Strategy Applicable to Palau'amine" *Angew. Chem., Int. Ed.* **2008**, *47*, 1284-1286.
- Liu, G.; Romo, D. "Enantioselective Synthesis of Schulzeines B and C via a β -Lactone-Derived Surrogate for Bis-homoserine Aldehyde" *Org. Lett.*, **2009**, *11*, 1143-1146.
- Kuznetsov, G.; Xu, Q.; Rudolph-Owen, L.; TenDyke, K.; Liu, J.; Towle, M.; Zhao, N.; Marsh, J.; Agoulnik, S.; Twine, N.; Parent, L.; Chen, Z.; Shie, J.; Jian, Y.; Zhang, H.; Du, H.; Boivin, R.; Wang, Y.; Romo, D.; Littlefield, B. "Potent In Vitro and In Vivo Anticancer Activities of Des-methyl, Des-amino Pateamine A, A Synthetic Analogue of Marine Natural Product Pateamine A" *Mol Cancer Ther.* **2009**, *8*, 1250-1260.
- Duffy, R. J.; Morris, K. A.; Vallikati, R.; Zhang, W.; Romo, D. "Unexpectedly Stable Spiroepoxy- β -Lactones: Synthesis, Structure, and Reactivity Including Facile Conversion to Optically Active Tetrionic Acids Applied to the Synthesis of (+)-Maculalactone A" *J. Org. Chem.*, **2009**, ASAP.

PUBLICATIONS IN PRESS/ACCEPTED

- Duffy, R. J.; Morris, K. A.; Romo, D. "Synthesis of Unusually Strained Spiro Heterocyclic Ring Systems and Their Exploits in Synthesis" *Tetrahedron* **2009**, *in press*.

CURRENT POSITIONS OF FORMER GROUP MEMBERS

Post-doctoral Students: Dr. Helene Shea (1994-6): Albermarle, Baton Rouge, LA; Dr. Kaapjoo Park (1996-7): Wyeth Research, PA; (2000-2): Eli Lilly & Co., Indianapolis, IN; Dr. Shukun Li (2002-04): Shanghai Institute of Materia Medica; Dr. Paul Dransfield (2002-5): Amgen, San Francisco, CA; Dr. Andy Skauge (2004-5): Cisco Jr. College, Cisco, TX; Dr. Ziad Moussa (2003-6): Tiabah University, Saudi Arabia; Dr. Ananth Swaramakrishnan (2004-6): ParmaCare, High Point, NC; Dr. Huda Henry-Riyad (2005-6): CEO The Key Publishing House, Inc., Toronto, Canada; Dr. Krishan Ponnampereuma (2004-6): Senior Lecturer, Texas A&M University; Dr. Satyamaheshwar Peddibhotla (2005-7): Burnham Institute, Orlando, FL; Dr. Gil Ma (2005-07): Lundbeck Research USA, Inc., Paramus, NJ; Dr. Liang Tang (2005-7): Anatrace Inc.; Maumee, OH; Dr. Xinhong Lai (2007-8): Schering-Plough; Dr. Wei Wang (2006-8), Senior Res. Scientist, AMRI, Albany, NY.

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