

**R. Kiplin Guy**  
**St. Jude Children's Research Hospital**  
**Department of Chemical Biology and Therapeutics**

**Curriculum Vitae**

**CURRENT TITLE AND DEPARTMENT**

Chairman and Member, Department of Chemical Biology and Therapeutics, SJCRH

**SECONDARY APPOINTMENTS,**

Adjunct Professor of Pharmaceutical Chemistry and Cellular and Molecular Pharmacology, UCSF;  
Adjunct Professor of Biochemistry, Vanderbilt University

**EDUCATION**

|                    |   |                |
|--------------------|---|----------------|
| <b>1996 - 1998</b> | University of Texas Southwestern Medical Center<br><i>Postdoctoral Fellowship in Cellular Biology with Drs. Brown and Goldstein</i> | Dallas, TX     |
| <b>1991 - 1996</b> | The Scripps Research Institute<br><i>Ph. D. in Organic Chemistry with Dr. K. C. Nicolaou</i>  | La Jolla, CA   |
| <b>1995</b>        | The Woods Hole Research Institute<br><i>Physiology: Cellular and Molecular Biology Course</i>                                       | Woods Hole, MA |
| <b>1986 - 1990</b> | Reed College<br><i>B. A. in Chemistry</i>   | Portland, OR   |

**SPECIALTY; SUBSPECIALTY**

*Synthetic organic chemistry:* synthesis of terpenes and peptides, parallel and combinatorial synthesis, laboratory automation

*Cellular biology:* lipid homeostasis, nuclear hormone receptors, protein interactions

*High throughput screening:* quantitative assays, data analysis methods

**ACADEMIC AND PROFESSIONAL POSITIONS HELD**

**9/05-:** Member and Chairman, St Jude Children's Research Hospital, Memphis, TN.

**2/05-9/05:** Professor I, UCSF, San Francisco, CA.

**7/04-2/05:** Assistant Professor VI, UCSF, San Francisco, CA.

**1/03-9/05:** Executive Director, Bay Area Screening Center

**7/02-6/04:** Assistant Professor V, UCSF, San Francisco, CA.

**1/02-9/05:** Director, Center for Chemical Diversity

**7/00-6/02:** Assistant Professor IV, UCSF, San Francisco, CA.

**9/98-6/00:** Assistant Professor III, UCSF, San Francisco, CA.

**9/96-9/98:** Postdoctoral Fellow, Cellular Biology, UTSWMC, Dallas, TX.

**9/91-9/96:** Graduate Student, Synthetic Organic Chemistry, TSRI, La Jolla, CA.

**6/90-8/91:** Contract Chemist, IBM-Almaden Research, San Jose, CA.

**MEMBERSHIPS IN SCIENTIFIC, PROFESSIONAL AND SCHOLARLY SOCIETIES**

American Chemical Society, American Society for Cell Biology

**HONORS AND AWARDS**

**6/00-5/04:** NSF CAREER Award

**7/98-7/00:** Sidney Kimmel Cancer Research Foundation Scholar.

**9/96-9/98:** The Helen Hay Whitney Postdoctoral Fellowship.

**6/95-8/96:** George Hewitt Medical Research Foundation Fellowship.

**6/94-6/95:** American Chemical Society - Organic Chemistry Graduate Fellowship.

**6/94:** Roche Award for Excellence in Organic Chemistry.

**4/94:** Arthur Scott Lecturer, Reed College.

**8/91-6/94:** Office of Naval Research Graduate Fellowship.

**6/90:** American Institute of Chemists Student Award.

**6/90:** Phi Beta Kappa.

**86-90, annually:** Commended by the faculty for academic excellence.

**8/86-5/90:** John Hauberg Scholarship.

**RESEARCH AND CREATIVE ACTIVITY*****Synopsis of Research Program***

Research in the Guy laboratory centers on the development of new techniques and reagents for chemical biology – particularly those involving high throughput and systems orientation – and the application of these techniques to understanding and controlling signal transduction pathways. The two major focuses of the laboratory are the study of combinatorial protein interactions as a regulatory element in intracellular signal transduction cascades and the development of novel therapeutic agents for orphan diseases, particularly those of the third world. In the past five years, we have built proteomics models of transcription activation by nuclear hormone receptors, developed inhibitors of protein interactions that are active *in vitro* and in cellular systems, and discovered new leads for treatment of malaria.

***High Throughput Synthesis, Purification, and Assay Technology Development***

As the majority of our projects depend upon the production and use of chemical libraries, a substantial portion of our effort has been focused upon the development and implementation of automation and data handling technologies to enable the production, purification, storage, and use of these libraries. In the past few years, we have built a complete facility for the production, purification, and analysis of high purity parallel libraries of hundreds to thousands of compounds that allows the routine production of libraries, with full quality control data, on the 10 to 50 mg level. The facility is also capable of producing smaller libraries (tens of compounds) on the gram scale. The facility has been made available to the UCSF community as the Center for Chemical Diversity. In the past two years faculty from UCSC, UCD, and UCSF have used the facility for producing high quality libraries.

In late fall 2002, the Guy group took over a high throughput-screening center at the Gallo center and began the process of moving it into the California Institute for Quantitative Biomedical Research. The resulting Bay Area Screening Center is available as a regional resource for the biomedical community and currently includes equipment necessary to execute essentially any type of cellular or biochemical screen and compound holdings of approximately 150,000 compounds. As of October of 2003, the facility became fully operational in temporary space in Genentech Hall. As an offshoot of this facility, some members of the Guy group are now actively engaged in developing methods for automated analysis of HTS data and generation of predictive models of structure activity relationships based upon that data.

### ***Studying Signaling Pathways by Modulation of Protein-Protein Interactions using Novel Proteomimetics***

Intracellular signaling pathways often depend upon careful modulation of protein interactions for faithful transmission of signal from origin to effector. One major research focus of the laboratory is the dissection of these interactions, which often involve the potential interaction of one family of proteins with another but paradoxically provide for precise selectivity *in vivo*. Our program is based upon a combination of **quantitative proteomics** and **proteomimetic inhibitors of interactions**.

*Quantitative Proteomics.* Often critical protein interactions in signaling involve the interaction of one family of factors with another. In this context, simply identifying the relevant players can be a significant challenge, as is evidenced by assembly of transcriptional activation complexes by the nuclear hormone receptors (NR's). The NR's are a superfamily of DNA binding proteins that regulate target gene transcription in response to circulating non-peptide hormones. NR's exert their effects by nucleating the formation of a multiprotein regulatory complex with many accessory proteins including coactivators, corepressors, and the basal transcription machinery. The NR's are structurally dynamic proteins that adopt discrete conformations in the unliganded state or when bound to an agonist or antagonist ligand. These changes in conformation alter the interactions with other proteins in the complex, particularly coactivators and corepressors and thereby induce the different signaling effects of agonist and antagonist. Unfortunately, a precise understanding of the mechanisms by which the receptors exert their effects is still lacking. We have developed a set of high throughput assays that allow determination of which co-regulatory protein is recruited to a given receptor in a particular state. We are taking a forward biochemical approach to identifying candidate co-regulatory proteins for particular receptor state (including receptor, ligand, and promoter) *in vitro* and then testing if successful candidate are recruited to the appropriate system in cellular models. The work in the NR field has allowed us to describe the first quantitative model of co-regulator interactions for the thyroid hormone receptor. Additionally, in collaboration with several other labs at UCSF, we have been able to refine the model of the molecular steps involved in activating androgen signaling. Similar approaches are underway for other systems such as the PDZ domain containing adaptor proteins. As these systems have matured, we have begun to develop microarray-based methods for determining which response elements are activated *in situ* in order to allow full study of the systems involved. The goal is to eventually be able to map the circuitry underlying hormonal signaling using data enriched inferential modeling methods.

*Proteomimetic inhibitors of interactions.* The highly dynamic protein interactions in signaling pathways are often mediated by small contact areas of highly defined structure – usually common secondary structures such as turns, helicies, or strands. We have focused upon the design and synthesis of generally useful mimetics of such protein secondary structures and the evolution of these general scaffolds towards high affinity and selectivity for particular protein interactions. We use a two-phase strategy, beginning with a constrained peptide and following up in successful systems with a designed small molecule peptidomimetic. Our first approach to alpha helical proteomimetics has delivered useful and highly selective inhibitors of the interaction of the estrogen and thyroid receptors with their co-regulatory proteins. Studies are currently underway to convert these to small molecules. The same approach has recently produced small molecule inhibitors of the binding of carboxy terminal beta strand ligands to PDZ modular protein interaction motifs that are active in cellular models and prevent function of the targeted PDZ module in context. An important underlying theme in this program is experimental validation of particular computational design methods and intensive use of parallel chemical synthetic techniques that inherently drives advances in library synthesis methodologies. Such studies remain ongoing in the NR, PDZ and p53 systems.

*Moderate Resolution Structure Determinations.* It is often the case that proteins of interest do not easily afford a structure by either crystallographic or NMR methods. For that reason, we pursued a

collaborative project to determine moderate resolution structures by the combination of chemical crosslinking, mass spectrometry, and computation. A collaboration had existed for this purpose between the Gibson and Kuntz groups at UCSF, but was hindered by the lack of appropriate crosslinking reagents and process difficulties regarding the biochemistry and analytical chemistry. We took the lead by securing long term funding for the project and producing a suite of custom built crosslinking reagents for this purpose. The synthetic portions of this project have been completed and the process brought near to maturity. We expect to have one of the mass spectrometry groups involved in the consortium to take the lead in the near future.

### ***Drug Development for Orphan Diseases and Diseases of the Third World***

In the last two years, a new research direction has developed within the Guy group: the discovery of new therapeutic leads for orphan diseases. A number of diseases that cause a significant burden upon worldwide human health do not enjoy the benefits of industrially targeted drug development – predominantly due to unfavorable market analysis on the part of pharmaceutical companies. For the most part, these diseases are characterized as either being an orphan disease, one in which there are fewer than 200,000 patients worldwide, or as a disease of the third world. Both of these conditions lead to unprofitable market: the former through small numbers of patients, the latter through their inability to pay for treatment.

Utilizing the capacities for high throughput chemistry and screening that we have built at UCSF, we have initiated programs aimed at producing candidate compounds for several of these diseases: malaria, prion disease, cystic fibrosis, and Chagas' disease. These efforts are being carried out in the context of a consortium of investigators from UCSF, UCB, and SRI who are deliberately pooling our efforts to bridge the "translation gap" between target identification and completion of pre-clinical studies of potential new therapies. Our group has focused on applying high throughput chemistry and high throughput screening methods to target discovery, target validation, lead discovery, and lead optimization. Our general strategy is to use a scaffold based chemical approach to produce highly diverse screening libraries based upon "privileged scaffolds," to screen these libraries for lead compounds, and to follow up the leads through focused library production and screening. Our initial work focused on developing parallel synthetic routes to quinolines, phenothiazines, acridines, and thiosemicarbazones for these purposes. Based upon these preliminary studies, we have now begun the synthesis of large (several thousand compound) discovery libraries in the quinoline and acridine series – which we expect to finish by the middle of 2005. Further route development continues in the phenothiazine and thiosemicarbazone series; we have also begun to explore aspartyl and metalloprotease inhibitor scaffolds. Important early results have included the discovery of novel quinolines that are active against drug resistant strains of *Plasmodium falciparum* and the optimization of a protease inhibitor to provide compounds highly active against *Trypanasoma brucei*.

**RESEARCH AWARDS, FELLOWSHIPS AND EXTRAMURAL GRANTS****Summary:**

I have raised a sum total of roughly 12.5 million dollars in direct funding from a variety of sources including private foundations, NIH, NSF, and the DOD. Current grants include 1 R01; 3 projects in P01's; 1 project in a U01; and an NSF CRC as well as several smaller grants. I have mentored graduate and postdoctoral fellowships from external agencies for a total of \$260,000.

**Prior Funding:**

- 3/1/99:** PI, UCSF Academic Senate, "Shared Equipment Grant for Parallel Synthesis Apparatus," \$29,700 total direct funding.
- 11/98-11/99:** PI, UCSF Academic Senate, "Inhibition of hTRB1/GRIP1 Binding," \$30,000 total direct funding.
- 7/99-7/00:** PI, UCSF Cancer Center, ACS Award, Inhibition of p53/mdm2 binding, \$20,000 total direct funding.
- 7/99-7/00:** PI, Sandler Program in Basic Sciences, Alpha Helical Mimetics, \$50,000 total direct funding.
- 7/98-7/00:** PI, Sidney Kimmel Foundation for Cancer Research, Structural Proteins as Drug Targets, \$173,000 total direct funding.
- 6/00-5/03:** Mentor, Department of the Army, Breast Cancer Research Program Pre-Doctoral Traineeship for Timothy Geistlinger, "Evaluation of the Estrogen Receptor•Coactivator interface as a Target for Breast Cancer Chemotherapeutic Drug Design," \$65,523 total direct funding.
- 7/00-6/01:** Co-PI, Sandler Program in Basic Sciences, MS-3D: Low Resolution Protein Structure by Chemical Crosslinking and Mass Spectrometry, \$100,000 total direct funding.
- 7/00:** PI, UCSF REAC "Purchase of a Shared High Throughput Fluorescence Polarization Platereader," \$60,000 total direct funding.
- 7/00-6/01:** Mentor, California Breast Cancer Research Program Post-Doctoral Fellowship for Thomas Robertson, "A New Class of Drugs to Treat Breast Cancer," \$40,000 total direct funding.
- 9/00-8/01:** Investigator (PI B. Gibson), NIH 1 S10 RR14601-01, "LCQ-Deca Ion-Trap HPLC/MS System," \$261,890 total direct funding
- 9/1/00-8/31/01:** PI, NIH R55 DK58080-01 (J. A. Shannon Director's Award), "Novel Inhibitors of Nuclear Receptor Function," \$80,000 total direct funding.
- 4/01-3/02:** PI, Sandler Program in Basic Sciences, Seed Grants for Priority Basic Science Projects, "A Facility for the Parallel Synthesis, Purification, and Characterization of Combinatorial Libraries of Discrete Substances," \$416,000 total direct funding
- 5/01-4/02:** Co-PI (with Joe DeRisi), Sandler Program in Basic Sciences, "Genomic Structure Activity Relationships," \$46,000 total direct funding
- 6/01-5/02:** Co-PI (with Robert Fletterick), UCSF Prostate Cancer Research Program, "Novel Inhibitors of Androgen Receptor Function," \$50,000 total direct funding
- 1/02-12/03:** Co-PI (with Robert Fletterick), CAPCure, "Novel Inhibitors of Androgen Receptor Function," \$100,000 total direct funding
- 7/02-6/03:** PI, UCSF Stewart Trust, "Chemical Genetics of PDZ Domains," \$50,000 total direct funding
- 6/00-5/04:** PI, NSF-CHE 9984227, "Total Synthesis of Phalloidin and Amanitin," \$360,500 total direct funding.
- 6/01-5/04:** Mentor, Department of the Army, Breast Cancer Research Program Pre-Doctoral Traineeship for Jamie Moore, "Structure and Dynamics of Nuclear Receptor Coactivator Interactions," \$65,523 total direct funding.
- 6/02-5/04:** Co-PI with Robert Fletterick, NIH R21 CA095324, "Inhibition of Androgen Receptor Activation," \$200,000 total direct funding
- 4/02-3/04:** PI, Cystic Fibrosis Foundation Guy02x0, "Medicinal Chemistry for Cystic Fibrosis Drug

Discovery,” \$81,000 total direct funding

**4/02-3/05:** Project Co-Director (with Cliff Berkman, SFSU and Charles Craik, UCSF), PI Mac Roach, UCSF, NIH U56 CA096216, “Combinatorial Approaches for Studying Substrate Recognition and Developing Inhibitors of PMSA,” \$96,000 total direct funding

**8/00-7/05:** Core C Co-Director (PI, Robert Fletterick), NIH-NIDDK DK58390-01, “Structure and Dynamics of Nuclear Receptors,” \$3,471,937 total direct funding; \$888,614, total direct Core C funding.

**1/04-12/04:** PI, Prostate Cancer Foundation, “Novel Inhibitors of Androgen Receptor Funding,” \$75,000 total direct funding

**1/04-1/06:** PI, QB3 Opportunity Award, “Bay Area Screening Center,” \$120,000 total direct funding

**4/04-4/06:** PI, Sandler New Technologies Fund, “Bay Area Screening Center,” \$690,000 total direct funding

**6/04-6/06:** PI, SOP Dean’s Account, “Bay Area Screening Center,” \$120,000 total direct funding

**8/04-8/06:** PI, Buck Institute, “Bay Area Screening Center,” \$120,000 total direct funding

**7/01-6/06:** Chemistry Core Director (PI, James McKerrow), Sandler Program in Basic Sciences, “Basic Research in Parasitic Diseases,” \$560,000, total direct Core C funding.

**Active Funding:**

**9/01-8/11:** PI, NIH 1 R01 DK58080-01 A1, “Novel Inhibitors of Nuclear Receptor Function, \$1,250,000 total direct funding (current period).

**9/01-8/06:** PI (co-investigators I. D. Kuntz & B. Gibson), NSF CHE “Moderate Resolution Protein Structures by Chemical Crosslinking and Mass Spectrometry,” \$1,333,000 total direct funding

**9/02-8/07:** Co-Director Chemistry Core, NIH 2 P01 GM56531-06, “Structure, Biology, and Targeted Drug Design AIDS,” \$7,500,000 total direct funding, \$1,500,000 total direct funding (Core C)

**9/02-8/07:** Co-PI with Joe DeRisi, NIH 5 U01 AI053862 “Novel Anti-Malarials by Combinatorial Pharmacogenomics,” \$2,500,000 total direct funding

**12/02-11/07:** Project PI, NIH P01 AG021601 “Novel Therapeutics for Prion Disease,” \$20,000,000 total direct funding, \$1,700,000 Core C Total Direct Funding

## TEACHING

I am not currently responsible for teaching any direct courses. My prior teaching experience is outlined below. I also directed and taught a course in chemical biology for the new European Consortium which was hosted at the Gulbenkian Institute this year and is expected to be hosted at Goteburg University next year.

### Formal Scheduled Classes for UCSF Students

| Academic Year and Quarter | Course Number | Course Title                     | Nature of Contribution                                   | Hrs/Qtr of Instruction                                      | Total Students Enrolled |
|---------------------------|---------------|----------------------------------|--|---|-------------------------|
| 1999-2005 Fall            | PC 121        | Endocrine and Immunologic Agents | Instructor (1999-)<br>Course Director (2004-             | 8 hours of lecture (1999-203)<br>22 hours of lecture (2004- | 125                     |
| 2000 Fall                 | Biochem 200A  | Macromolecules                   | Discussion Group Leader                                  | 20 hours of conference                                      | 10                      |
| 1999-2005 Winter          | PC 242        | Bioorganic Chemistry             | Instructor (1999-2002; 2004-)<br>Course Director (2000-) | 20 hours of lecture   | 10-15                   |
| 1999-2001 Spring          | PC 203        | Synthetic Organic Chemistry      | Instructor   | 5 to 15 hours of lecture                                    | 5-10                    |

### Short Courses

| Academic Year and Quarter | Course Title            | Nature of Contribution                        | Location                             | Hrs/Qtr of Instruction | Total Students Enrolled |
|---------------------------|-------------------------|---|--------------------------------------|------------------------|-------------------------|
| 2004-Summer               | Chemical Genetics       | Course Director (2004-)<br>Instructor (2004-) | Gulbenkian Institute (Portugal)      | 8 hours of lecture     | 14                      |
| 2006-Summer               | Biology of the Parasite | Instructor                                    | Woods Hole Marine Biology Laboratory | 3 hours of lecture     | 16                      |

### MENTORING

I am actively involved in direct teaching and mentoring of students. Most quarters the laboratory hosts 1 to 2 rotation students, and on average 1 to 3 of those join the laboratory each year to complete their doctoral dissertations. We also host a summer undergraduate each summer and for the last two years have hosted two interns from the SFWorks program each year. Finally, two European Master's degree students have completed their dissertation work in my laboratory.

#### Summer Research Students:

| Name             | Summer | School             | Project                                   |
|------------------|--------|--------------------|---|
| Thuy Vo          | 1999   | UC - Berkeley      | Synthesis of a spin label analog to FLASH |
| Allison Chambers | 2000   | CSU – Bakersfield  | Synthesis of 2-carboxyindoles             |
| Chinedu Mmeje    | 2001   | UC - Santa Barbara | Synthesis of ER and TR selective peptides |
| LaWanda Johnson  | 2002   | Fort Lewis College | Mass Spectrometry in Three Dimensions     |
| Sarah Chui       | 2003   | UC – Berkeley      | Expression of LXR $\alpha$                |
| Lillian Seu      | 2004   | Barnard            | Synthesis of Biaryl ethers                |
| Christina Roels  | 2006   | Whitman            | Synthesis of KSHV Protease Inhibitors     |

#### Rotation Students:

| Name  | Rotation Period     |
|---|---------------------|
| Timothy Geistlinger, PC<br>Holly Field, PIBS                        | Winter Quarter 1999 |
| Timothy Geistlinger, PC<br>Walter Novak, PC<br>Kathleen Pendola, PC | Spring Quarter 1999 |
| Denise Kinski, BPS<br>Felice Lu, CCB                                | Fall Quarter 1999   |
| Anita Engh, Biophysics<br>John Deuber, PIBS                         | Winter Quarter 2000 |
| Jamie Moore, PSPG<br>Stephanie Truhlar, CCB<br>Jen Paulsen, PIBS    | Spring Quarter 2000 |
| Sarah Stowers, CCB<br>Anang Shelat, CCB                             | Fall Quarter 2000   |
| Michael Cohen, CCB<br>Peter Madrid, CCB                             | Spring Quarter 2001 |
| Edwin Tan, CCB<br>Jennifer Garrison, CCB                            | Fall Quarter 2001   |
| Ashwini Jambhekar, PIBS<br>Lisa Van Hoozer, CCB                     | Winter Quarter 2002 |
| Cory Ocasio, CCB  | Spring Quarter 2002 |
| Nicolas Mills, CCB  | Winter Quarter 2003 |
| Caleb Bashor, Biophysics  | Spring Quarter 2003 |
| David Smithson, CCB   | Fall Quarter 2003   |
| Jeremy Mallari, CCB   | Winter Quarter 2004 |

|                      |                     |
|----------------------|---------------------|
| Samantha Cooper, BMI | Spring Quarter 2004 |
| Jeff Henise, CCB     | Fall Quarter 2003   |

### Masters Dissertations Completed under Mentorship

| Name  | Years in Lab | Program                             | Project                                 |
|---|--------------|-------------------------------------|---|
| Ian Maulhardt<br>(Co-supervised with Joe DeRisi)<br>Terminal Masters Degree | 1999-2001    | UCSF<br>Pharmaceutical<br>Chemistry | Genomic SAR of Benomyl                  |
| Gerlof Kruidhof<br>(Co-supervised with B. Feringa)                          | 2002         | U. Groningen<br>Chemistry           | Alpha Helical Peptidomimetics           |
| Sabina Gerber   | 2002-2003    | U. Strausberg                       | Parallel Synthesis of<br>Phenothiazines |

### Doctoral Dissertations Completed under Mentorship

| Name   | Years in Lab | Program | Project   |
|--|--------------|---------|---|
| Timothy Geistlinger<br>(DOA-BCRP Pre-Doctoral<br>Fellow) | 1998-2004    | CCB     | Inhibition of NR $\alpha$ p160 Binding                                      |
| Kathleen Pendola   | 1999-2004    | PC      | Inhibition of PDZ Domain<br>Ligand Interactions                             |
| Jamie Moore<br>(DOA-BCRP Pre-Doctoral<br>Fellow)         | 2000-2004    | CCB     | Structure and Dynamics of<br>Nuclear Receptor Coactivator<br>Interactions   |
| Felice Lu<br>(Co-supervised with Tack<br>Kuntz)          | 2000-2005    | CCB     | Design and Synthesis of<br>Inhibitors of the Interaction of<br>p53 and mdm2 |
| Peter Madrid   | 2001-2005    | CCB     | Parallel Synthesis of Quinolines  |
| Anang Shelat<br>(Co-supervised with Tack<br>Kuntz)       | 2001-2005    | CCB     | Automated High Throughput<br>Data Mining                                    |
| Nicholas Mills   | 2003-2007    | CCB     | Applications of Constrained<br>Alpha Helical Peptides                       |

### Present Graduate Students under Mentorship

| Name            | Years in Lab | Program | Project  |
|-----------------|--------------|---------|--|
| Jeremy Mallari  | 2004-        | CCB     | Synthesis of Antiprotozoal<br>Cysteine Protease Inhibitors |
| David Smithson  | 2004-        | CCB     | Synthesis of Antiprotozoal<br>Aspartyl Protease Inhibitors |
| Samantha Cooper | 2004-        | BMI     | Circuit Analysis of Nuclear<br>Hormone Receptor Responses  |

**Professional Research Personnel, Postgraduate Personnel, and Postdoctoral Fellows**

**Professional Research Personnel**

| Name              | Years in Lab       | Title  | Current Position                                     |
|-------------------|--------------------|--|--|
| Edward Olsen      | 1998-1999          | Laboratory Helper, UCSF                          | Medical Student - Albert Einstein School of Medicine |
| Karen Tuttle      | 1999-2000          | Laboratory Helper, UCSF                          | Student SFCC   |
| Sarah Galicia     | 2001-2003          | Junior Specialist, UCSF                          | HTS Facility Director, Mt. Sinai, Toronto            |
| Andrea McReynolds | 2001-2005          | Staff Research Associate I, UCSF                 | Staff Research Associate II, UCSF                    |
| Daniel Grundig    | 2002               | Staff Research Associate, UCSF                   | Research Associate, Berlix                           |
| Kim Carter        | 2003               | SFWorks Intern, UCSF                             | Staff Research Associate, UCSF                       |
| Valerie Smith     | 2003               | SFWorks Intern, UCSF                             | Student CCSF   |
| John Sherrill     | 2003-2005          | Junior Specialist, UCSF                          | Staff Research Associate I, UCSF                     |
| Naoaki Fujii      | 2002-2005          | Professional Researcher, UCSF                    | Assistant Member, SJCRH                              |
| Martina Sigal     | 2003-2005<br>2005- | Specialist, UCSF<br>Laboratory Supervisor, SJCRH | --   |
| Janice Williams   | 2003-2005          | Specialist, UCSF                                 | Specialist, UCSF                                     |
| Ovidio Velasquez  | 2004               | SFWorks Intern, UCSF                             | Lab Assistant I, UCSF                                |
| Abdul Mahrat      | 2004               | SFWorks Intern, UCSF                             | Student CCSF   |
| Hong Yu           | 2004-2005          | Staff Research Associate II, UCSF                | Staff Research Associate II, UCSF                    |
| Michael Bingen    | 2004-2005          | Staff Research Associate I, UCSF                 | Staff Research Associate I, UCSF                     |
| Brian Wolff       | 2004-2005          | Staff Research Associate I, UCSF                 | Staff Research Associate I, UCSF                     |
| Linda Hicks       | 2004-2005          | Staff Research Associate I, UCSF                 | --   |
| Alexander Arnold  | 2005-              | Senior Research Technologist, SJCRH              | --   |

**Postdoctoral Fellows:**

| Name   | Years in Lab | Project   | Current Position                             |
|--|--------------|---|--|
| Thomas Robertson<br>(CBCR Fellow)                          | 1999-2001    | Synthesis of Designed Inhibitors of Nuclear Receptor Function | Research Scientist, University of Queensland |
| Prudencio Herradura  | 1999-2001    | Total Synthesis of Phalloidin                                 | Senior Scientist, Vicuron Pharmaceuticals    |
| Chris Collins<br>(UCSF Biochemistry Training Grant Fellow) | 2000-2001    | Synthesis of Novel Protein Crosslinking Reagents              | Researcher, SRI International                |
| Naoaki Fujii   | 2000-        | Synthesis of Beta Strand                                      | Professional Researcher,                     |

|  |           |  |                                     |
|--|-----------|--|-------------------------------------|
| (Visiting Scientist, Fujisawa Pharmaceuticals) | 2001      | Peptidomimetics  | UCSF                                |
| Wenchen Luo                                    | 2001-2004 | Synthesis of Designed Alpha Helical Peptidomimetic Inhibitors of Nuclear Receptor Function | Scientist, Pharmacyclics            |
| Marc Anderson                                  | 2001-     | Total Synthesis of Phalloidin  | Researcher, SFSU                    |
| A. "Leggy" Arnold                              | 2002-     | Synthesis of Designed Alpha Helical Peptidomimetics  | Senior Research Technologist, SJCRH |
| Chun Chow                                      | 2004-     | Synthesis of Aspartyl Protease Inhibitors  | Senior Scientist, Anadys            |

## PROFESSIONAL ACTIVITIES

### Service to Scholarly or Professional Societies

**6/99:** Organizer and Chair, Symposium on Chemical Biology, 54th Northwest Regional Meeting of the American Chemical Society.

**5/00-present:** Reviewer, Petroleum Research Fund, ACS

**2/04:** Organizer and Chair, CHI Library Design and Organic Synthesis Meeting, Target Oriented Synthesis vs. Diversity Oriented Synthesis Section

**5/04:** Organizer and Chair, QB3 "High Throughput High Return Studies for Biomedical Sciences,"

**7/04-7/06:** Vice-Chair (2005) and Chair (2006) Gordon Research Conference on Combinatorial Chemistry

**7/05-present:** Scientific Advisory Board, National University of Singapore

**1/05-present:** Steering group on Genomics and Drug Discovery, TDR, WHO

### Service to Industry

**5/99-present:** Due Diligence Consultant, Versant Venture Capital

**8/00-present:** SAB Orphagen Pharmaceuticals

**8/01-8/04:** SAB Genospectra, Inc.

**2/04-5/06:** SAB Zorphion Pharmaceuticals

**8/05-present:** SAB Advanced Genetic Systems

### Service to Scholarly and Professional Journals

**10/99-present:** Reviewer, *Bioorganic and Medicinal Chemistry Letters*

**7/01-present:** Reviewer, *Journal of Combinatorial Chemistry*

**6/02-present:** Reviewer, *Journal of the American Chemical Society*

**10/03-present:** Reviewer, *Journal of Organic Chemistry*

**2/04-present:** Reviewer, *Organic Letters*

**1/07-1/09:** Editorial Advisory Board, *Journal of Combinatorial Chemistry*

### Invited Lectures and Seminars

1. **4/00:** UCSF Cancer Center, "Alpha Helical Peptidomimetics"

2. **10/00:** UCSF Tetrad Graduate Program Symposium, "Alpha Helical Peptidomimetics"

3. **11/00:** UCSF Department of Anesthesia, "Alpha Helical Peptidomimetics"

4. **11/00:** UCSF/Harvard Symposium on Herbal Therapies and Dietary Supplements, “How does an herb become a drug? Taxol as a case study”
5. **01/01:** California State University Los Angeles, Department of Chemistry, “Alpha Helical Peptidomimetics”
6. **02/01:** Orphagen, Inc. “High Throughput Assay of Nuclear Hormone Receptor • Co-regulator Interactions”
7. **3/01:** Karo Bio USA, “Inhibitors of Thyroid Hormone Receptor Transcriptional Activation Complex Formation”
8. **3/01:** UCSF Prostate Cancer Retreat, “Interrupting assembly of nuclear hormone receptor transcriptional activation complexes: Implications for drug development”
9. **5/01:** Twelfth World Molecular Engineering Network Conference, Cabo San Lucas, Mexico “Alpha Helical Peptidomimetics Targeting the Nuclear Receptor Coregulator Interface”
10. **6/01:** GenoSpectra, “Applications of Chemical Genomics”
11. **7/01:** Structural Genomix, “Inhibitors of Thyroid Hormone Receptor Transcriptional Activation Complex Formation”
12. **9/01:** Karo Bio, Sweden, “Inhibitors of Thyroid Hormone Receptor Transcriptional Activation Complex Formation”
13. **9/01:** ACS National Meeting, “Inhibitors of Thyroid Hormone Receptor Transcriptional Activation Complex Formation”
14. **10/01:** Plexxicon, “Systems Approaches to Signaling Research Using Chemical Inhibitors of Protein Interactions”
15. **4/02:** UC - Davis, Department of Chemistry, “Alpha Helical Proteomimetics”
16. **5/02:** San Diego State University, Department of Chemistry, “Alpha Helical Proteomimetics”
17. **5/02:** UC – Santa Barbara, Department of Chemistry, “Alpha Helical Proteomimetics”
18. **4/02:** San Diego State University, Department of Chemistry, “Alpha Helical Proteomimetics”
19. **7/02:** Gordon Conference in Combinatorial Chemistry, Oxford, England, “A Tale of Two Helicies”
20. **7/02:** IUPAC Conference on Organic Chemistry, Christchurch New Zealand, “Application of Parallel Synthesis in the Production of Functional Alpha Helical Peptidomimetics”
21. **7/02:** Baker Medical Research Institute, Melbourne, Australia, Department of Cardiovascular Medicine, “The Inhibition of the Formation of Nuclear Hormone Receptor Transcriptional Activation Complexes Using Peptidomimetics”
22. **7/02:** University of Queensland, Brisbane, Australia, Department of Chemistry, “Insights into Function of the Nuclear Hormone Receptor Transcriptional Activation Complex through Chemical Techniques”
23. **7/02:** University of Sydney, Sydney, Australia, Department of Chemistry, “Interrupting the Function of Signaling Regulatory Complexes with Peptidomimetics”
24. **9/02:** Stanford Research Institute, “Alpha Helical Peptidomimetics”
25. **12/02:** Banbury Conference, Cold Spring Harbor, “Functional Probes of Glucocorticoid Receptor”
26. **1/03:** The Scripps Research Institute, Department of Chemistry, “Chemical Proteomics Approaches to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
27. **3/03:** Sandia National Laboratories, Livermore, CA, “Chemical Proteomics Approaches

- to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
28. **4/03:** UCSF Professional and Academic Success Skills Seminar, “Writing, Publishing, and Creating Open Access to Scientific Literature”
  29. **4/03:** Washington State University, Department of Chemistry, “Chemical Proteomics Approaches to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
  30. **4/03:** Arbor Vita Corporation, Redwood City, CA, “Chemical Approaches to Understanding and Regulating PDZ Domain Function”
  31. **5/03:** Roche Pharmaceuticals, Palo Alto, CA, “Chemical Proteomics Approaches to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
  32. **5/03:** Thirteenth World Molecular Engineering Network Conference, Cabo San Lucas, Mexico “Chemical Approaches to Regulating the PTEN, mdm2, p53 Tumor Suppressor Oncoprotein Network”
  33. **5/03:** UC – Santa Cruz, Department of Chemistry, “Chemical Proteomics Approaches to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
  34. **6/03:** Gordon Research Conference on Hormones and Development, New London, CT “Chemical Proteomics Approaches to Understanding Transcriptional Activation by Nuclear Hormone Receptors,”
  35. **6/03:** Array Biopharma, Boulder, CO “The UCSF Cystic Fibrosis Drug Development Program”
  36. **6/03:** UCSF Symposium on Entrepreneurship, “Walking the Tightrope: Balancing your Business and Academic Interests, Consultant Panel”
  37. **8/03:** Gilead Pharmaceuticals, Foster City, CA “Chemical Approaches to Understanding and Regulating PDZ Domain Function”
  38. **8/03:** Gilead Pharmaceuticals, Foster City, CA “HTS Cheminformatics”
  39. **9/03:** University of Southampton, Southampton, England, “Chemical Proteomics Approaches to Understanding Regulation of Transcription by Nuclear Hormone Receptors”
  40. **9/03:** Proteomic, Combinatorial, and Other Strategies for Drug Discovery, London, England, “Chemical Approaches to Understanding and Regulating PDZ Domain Function”
  41. **10/03:** CVRI Retreat, “Inhibitors of PDZ Domain Function,”
  42. **10/03:** NSF Symposium on Collaborations in Chemistry, Washington, DC “MS3D – Moderate Resolution Protein Structures by Chemical Crosslinking, Mass Spectrometry, and Computation”
  43. **11/03:** Saint Jude Children’s Research Hospital, Memphis, TN “Inhibitors of PDZ Domain Protein Interactions”
  44. **12/03:** CCB and Biophysics Joint Retreat, “Heterocycle Libraries as Lead Discovery Tools for Malaria”
  45. **2/04:** IBM – Alamaden Research Institute, San Jose, CA “Chemical Proteomics Approaches to Understanding Nuclear Hormone Receptor Signaling”
  46. **2/04:** CHI Library Design and Organic Synthesis, San Diego, CA, “Target Oriented Synthesis of Heterocycles - Microwaves, Parallel Purification, and Design”
  47. **5/04:** AstraZeneca, Wilmington DE, “Chemical Proteomics Approaches to Understanding Nuclear Hormone Receptor Signaling”
  48. **6/04:** U Washington, Seattle WA, “Drug Discovery for Malaria,”
  49. **7/04:** Myriad Pharmaceuticals, Salt Lake City, UT, “Inhibitors of PDZ Domain Protein Interactions”

50. **8/04:** Gordon Conference in Combinatorial Chemistry, Oxford, England, "Lead Discovery and Optimization for Antimalarials"
51. **9/04:** UCSF Tetrad Retreat, Lake Tahoe, CA, "Targeting Neglected Diseases"
52. **9/04:** Trypanosome Drug Development, Seattle, WA, "Compound Validation for Trypanosomal Disease Therapeutics"
53. **11/04:** Vanderbilt University, Nashville, TN. "Lead Discovery and Optimization for Antimalarials,"
54. **1/05:** UC Irvine, Irvine, CA, "Screening and Synthesis for Antimalarials,"
55. **2/05:** Lawrence Livermore National Laboratories, Livermore, CA, "Designed Generic Libraries – Rapid Lead Discovery for Orphan Diseases,"
56. **3/05:** Goteborg University, Goteborg Sweden, "Library Design for Academic Screening Facilities"
57. **4/05:** Keystone Symposium on Drugs against Protozoal Parasites, Copper Mountain, CO "Lead Discovery for Malaria,"
58. **5/05:** Society for Biomolecular Screening, Redwood City, CA, "Screening and Synthesis for Antimalarials,"
59. **7/05:** Bay Area Parasite Consortium, San Francisco, CA, "Screening and Synthesis for Antimalarials,"
60. **9/05:** Vanderbilt University, Nashville, TN, "Lead Discovery for Malaria,"
61. **10/05:** Buck Institute, Novato, CA, "Chemical Proteomics of Nuclear Hormone Receptors,"
62. **5/06:** International Symposium on Chemistry, Biology, and Medicine, Patpos, Cyprus, "Regulation of the Assembly of the Thyroid Receptor Transcriptional Regulatory Complex,"
63. **6/06:** Gordon Research Conference on Host-Parasite Biology, Newport, RI, "Lead Discovery for Malaria"
64. **6/06:** Conference on Drug Discovery for AIDS, Bethesda, MD "Inhibition of the Interaction of HIV-Rev Protein and the Rev Response Element"
65. **7/06:** Biology of the Parasite Short Course, Woods Hole, MA., "Discovery and Development of New Drugs for Parasitic Diseases"
66. **8/06:** University of Southampton, England "Novel Inhibitor of Thyroid Hormone Signaling"
67. **8/06:** University of Goteborg, Sweden "Novel Inhibitor of Thyroid Hormone Signaling"

## UNIVERSITY AND PUBLIC SERVICE

### **St Jude Children's Research Hospital Service**

**4/05-present:** Faculty Appointments and Promotions Committee

**4/05-present:** Biosafety Committee

**4/05-present:** Executive Committee

**4/05-2/06:** Strategic Planning Committee

**7/06-present:** Cancer Center Advisory Board

**10/06-present:** Management Council

### **University of California Service**

#### University-Wide

**7/00-7/02:** Alternate Delegate for UCSF, Academic Senate

**4/04-9/05:** UCSF Delegate to Regional Translational Research Planning Committee

**8/04-9/05:** Pharmastart Steering Committee

#### Campus-Wide

**9/98-9/00:** UCSF Mission Bay Design, Chemistry User Group Section

**7/99-11/99:** Co-Organizer, Second Annual UCSF Chemistry and Cancer Meeting

**3/00-6/01:** Chancellor's Ad Hoc Committee for the Supportive Work Environment Initiative

**6/00-9/05:** UCSF Chemical Safety Committee

**9/00-6/01:** Chancellor's Advisory Committee on Housing

**12/00-9/05:** Mission Bay Operations and Services Committee

- 12/00-present: Member, User's Subcommittee

- 6/01-present: Co-Chair, User's Subcommittee

- 9/01-present: Member, Core Planning Committee

**12/00-9/05:** Conflict of Interest Advisory Committee

**10/02-9/05:** UCSF Committee on the Library

**1/03-9/05:** Program in Population Sciences and Global Health, Education Subcommittee

**9/03-9/05:** Chair, UCSF Transportation Advisory Committee

**9/05-present:** Member, Strategic Planning Management Committee, SJCRH

**9/05-present:** Member, Executive Committee, SJCRH

**9/05-present:** Member, Faculty Appointments and Promotions Committee, SJCRH

**9/05-present:** Member, Institutional Biosafety Committee, SJCRH

#### School of Pharmacy

**9/00-8/01:** School of Pharmacy Informatics/Library Committee

**9/01-9/05:** School of Pharmacy Safety Committee

#### Department of Pharmaceutical Chemistry

**9/98-6/99:** Department of Pharmaceutical Chemistry Faculty Search

**10/98-12/99:** Department of Pharmaceutical Chemistry, Seminar Committee.

**10/01-9/05:** Department of Pharmaceutical Chemistry Faculty Search

#### Graduate Program in Biological Sciences

##### *Qualifying Examinations*

**10/98:** Member, Hikari Yoshihara, Program in Biological Sciences

**3/00:** Member, David Carroll, Program in Biological Sciences

**5/01:** Member, Jennifer Paulson, Program in Biological Sciences

Graduate Program in Biophysics

*Qualifying Examinations*

**2/01:** Chair, Zach Serber

**3/01:** Chair, Nilesh Shah

*Thesis Committees*

**2/01-7/03:** Zach Serber

**8/03-9/05:** Eric Slika

**12/03-present:** Eugene Hur

Graduate Program in Chemistry and Chemical Biology (Pharmaceutical Chemistry)

**6/00-12/00:** Retreat Committee, Chemistry and Chemical Biology Graduate Program

**11/99-5/01:** Admissions Committee, Chemistry and Chemical Biology Graduate Program

**9/04-12/04:** Retreat Committee, Chemistry and Chemical Biology Graduate Program

*Qualifying Examinations*

**2/00:** Member, Tao Shi

**5/00:** Member, Giselle Knudsen

**6/00:** Member, Sami Mahrus

**12/00:** Chair, Ngoc-Ha Nguyen

**3/01:** Member, Nicola Clegg

**3/01:** Chair, Andrew Verras

**6/01:** Member, Natasja Brooijmans

**8/01:** Member, Steph Truhlar

**11/01:** Member, Kevin Masukawa

**4/02:** Member, Mike Gage

**4/02:** Member, Michael Cohen

**5/02:** Member, Zachary Knight

**8/02:** Member, Justin Blethrow

**2/03:** Member, Theresa Downing

**4/03:** Member, Edwin Tan

**5/03:** Member, Raynard Bateman

**11/03:** Cory Ocasio

*Thesis Committees*

**6/00-6/04:** Giselle Knudsen

**3/01-4/05:** Ha Nguyen

**8/01-5/05:** Nicola Clegg

**10/1-9/05:** Andrew Verras

**12/01-3/05:** Steph Truhlar

**4/01-present:** Kevin Masukawa

**5/02-present:** Michael Cohen

**5/02-8/05:** Alan Marnett

**4/03-2/05:** Mike Gage

**4/03-9/05:** Nathan Sallee  
**9/03-present:** Theresa Downing  
**1/04-9/05:** Cory Ocasio

Graduate Program in Medical Information Sciences

*Qualifying Examinations*

**5/01:** Member, Jose Haresco, Medical Information Sciences

*Thesis Committees*

**6/01-6/03:** Jose Haresco, Medical Information Sciences

Graduate Program in Biopharmaceutical Sciences

*Qualifying Examinations*

**11/01:** Member, Valerie Ng, Program in Biological Sciences

*Thesis Committees*

**4/02-9/05:** Member, Valerie Ng, Program in Biological Sciences

Graduate Program in Quantitative Biology

**2/01-5/01:** Program in Quantitative Biology Curriculum Committee

**Service to Educational, Governmental, and Other Agencies**

Austrian National Research Council

**10/98-present:** Reviewer, Molecular Genetics Subsection, National Research Grants

**11/00-present:** Reviewer, Division of Lipid Biology, National Research Grants

University of Vienna, Department of Biochemistry

*Thesis Committees*

**4/01-:** Isabella Halama, (locally supervised by Peter Walters)

National Science Foundation

**4/02-present:** Reviewer, National Science Foundation, Panel on Nanotechnology

National Institutes of Health

**5/02:** Ad Hoc Member, Bioorganic and Natural Products Chemistry Study Section

**4/04-present:** Member, Special Emphasis Panel, Zebrafish Genetics and Screening Study Section

**5/05-present:** Member, Drug Discovery Special Emphasis Panel

**3/06-present:** Member, Advisory Committee on Compound Acquisition for the Roadmap

**6/06-:** Ad Hoc Member, Nuclear Dynamics and Transport Study Section

## Bibliography

### Summary

I am the author of 80 papers and book chapters and 8 issued patents.

### Journal Articles

#### Papers from work at IBM (Industrial Technician)

1. Guy, R. K.; DiPietro, R. A. "A Facile One-Pot Synthesis of Symmetrical and Unsymmetrical Acetaldehyde Acetals from Primary Alcohols," *Synth. Commun.* **1992**, *22*, 687-692.
2. Ito, H.; Dalby, C.; Pomerantz, A.; Sherwood, M.; Sato, R.; Sooriyakumaran, R.; Guy, K.; Breyta, G. "Monomer Reactivities and Kinetics in Radical Copolymerization of Hydroxystyrene Derivatives and *tert*-Butyl (Meth)acrylate," *Macromol.* **2000**, *33*, 5080.

#### Papers from Nicolaou Laboratory (Graduate School)

1. Nicolaou, K. C.; Liu, J. J.; Hwang, C. -K.; Dai, W. -M.; Guy, R. K. "Synthesis of a Fully Functionalized CD Ring System of Taxol," *J. Chem. Soc. Chem. Commun.* **1992**, 1118-1120.
2. Nicolaou, K. C.; Dai, W. -M.; Guy, R. K. "The Chemistry and Biology of Taxol," *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 15-44.
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5. Nicolaou, K. C.; Guy, R. K.; Wrasidlo, W.; Pitsinos, E. "A Water-Soluble Prodrug of Taxol with Self-Assembling Properties," *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1583-1587.
6. Nicolaou, K. C.; Couladouros, E. A.; Nantermet, P. G.; Renaud, J.; Guy, R. K. "Synthesis of C-2 Taxol Analogs," *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1581-1583.
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9. Nicolaou, K. C.; Liu, J. -J.; Yang, Z.; Ueno, H.; Sorensen, E. J.; Claiborne, C. F.; Guy, R. K.; Hwang, C. -K.; Nakada, M.; Nantermet, P. G. "Total Synthesis of Taxol. 2. Construction of A and C Ring Intermediates and Initial Attempts to Construct the ABC Ring System," *J. Am. Chem. Soc.* **1995**, *117*, 634-644.
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Papers from Brown and Goldstein Laboratory (Postdoctoral Fellowship)

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Papers from Guy Laboratory (UCSF)

1. Herradura, P. S.; Pendola, K. A.; Guy, R. K. "Copper-Mediated Cross-Coupling of Aryl Boronic Acids and Alkyl Thiols," *Org. Lett.* **2000**, *2*, 2019-22.
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