
BIOGRAPHICAL SKETCH

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NAME GUY, Rodney Kiplin.	POSITION TITLE		
eRA COMMONS USER NAME (credential, e.g., agency login) KIPGUY	Member and Chair		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Reed College, Portland, OR	B.A.	05/90	Chemistry
The Scripps Research Institute, La Jolla, CA	Ph.D.	06/96	Organic Chemistry
UT-Southwestern Medical Center, Dallas, TX	PostDoc	09/98	Cell Biology

A. Personal Statement

I have extensive experience in the discovery and development of novel small molecule inhibitors for novel targets -- including protein-interaction, enzymatic, and nucleotide targets -- and in the development of these inhibitors for use in animal models. Additionally, I have experience in modification of a wide range of inhibitors in order to improve their adsorption, distribution, metabolism, and excretion profile. Finally, I manage a large, multidisciplinary department whose major purpose is the development of small molecules for preclinical models.

B. Positions and Honors

Positions and Employment

1990-1991 Chemist, IBM-Almaden Research, San Jose, CA
1998-2005 Assistant Professor of Pharmaceutical Chemistry and Cellular and Molecular Pharmacology, UCSF
2000-2005 Director, UCSF Center for Chemical Diversity
2003-2005 Executive Director, Bay Area Screening Center
2005-2005 Professor of Pharmaceutical Chemistry and Cellular and Molecular Pharmacology, UCSF
2005-present Chairman and Member of Chemical Biology and Therapeutics, St Jude Children's Research Hospital, Memphis, TN
2005-present Adjunct Professor of Pharmaceutical Chemistry and Cellular and Molecular Pharmacology, UCSF
2006-present Adjunct Professor of Biochemistry, Vanderbilt University, Nashville, TN
2008-present Adjunct Professor of Pharmaceutical Sciences, University of Tennessee, Memphis, TN

Honors

1994 Roche Award for Excellence in Organic Chemistry
1995-1996 George Hewitt Medical Research Foundation Fellowship
1996-1998 The Helen Hay Whitney Postdoctoral Fellowship
1998-2000 Sidney Kimmel Cancer Research Foundation Scholar Award
2005-present Scientific Advisory Board for Medicinal Chemistry, National University of Singapore
2006-present Expert Scientific Advisory Committee, Medicines for Malaria Venture
2007-2009 Editorial Advisory Board, Journal of Combinatorial Chemistry
2009-present Fellowship Award Committee, Damon Runyon Walter Winchell Cancer Research Foundation

C. Selected peer-reviewed publications (in chronological order). (Of a total of 103 papers and 14 patents)

Geistlinger TR, Guy RK. An inhibitor of the interaction of thyroid hormone receptor beta and glucocorticoid interacting protein 1. J Am Chem Soc 123:1525-1526, 2001.
Geistlinger TR, Guy RK. Novel selective inhibitors of the interaction of individual nuclear hormone receptors with a mutually shared steroid receptor coactivator 2. J Am Chem Soc 125:6852-6853, 2003.
Fujii N, Haresco JJ, Pendola-Novak KA, Stokoe D, Kuntz ID, Guy RK. A selective irreversible inhibitor targeting a PDZ protein interaction domain. J Am Chem Soc 125:12074-12075, 2003.

- Estébanez-Perpiñá E, Moore JMR, Mar E, Nguyen P, Delgado-Rodrigues E, Baxter J, Buehrer BM, Webb P, Fletterick RJ, Guy RK. The mechanism of ligand dependent transactivation by the androgen receptor. *J Biol Chem* 280:8060-8068, 2005.
- Krylova IN, Sablin EP, Williams JD, Williams SP, Moore JMR, Xu RX, Waitt GM, Juzumiene D, Bynum JM, Montana V, Guy RK, Thornton JW, Fletterick RJ, Willson TM, Ingraham HA. Structural analyses of NR5 orphan receptors reveal a potential role as nuclear phospholipid sensors. *Cell* 120:343-355, 2005.
- Arnold LA, Estebanez-Perpina E, Togashi M, Jouravel N, Shelat A, McReynolds AC, Mar E, Nguyen P, Baxter JD, Fletterick RJ, Webb P, Guy RK. Discovery of small molecule inhibitors of the interaction of thyroid hormone receptor with transcriptional coregulators. *J Biol Chem* 280(52):43048-43055, 2005.
- Lu F, Chi SW, Kim DH, Han KH, Kuntz ID, Guy RK. Proteomimetic libraries: design, synthesis, and evaluation of p53-mdm2 inhibitors. *J Combi Chem* 8(3):315-325, 2006.
- Mills NL, Daugherty MD, Frankel AD, Guy RK. An α -helical inhibitor of the HIV-1 Rev-RRE interaction. *J Am Chem Soc* 128(11):3496-3497, 2006.
- Laurie NA, Donovan SL, Shih C-S, Zhang J, Mills N, Fuller C, Teunisse A, Lam S, Ramos Y, Mohan A, Johnson D, Wilson M, Rodriguez-Galindo C, Quarto M, Francoz S, Mendrysa SM, Guy RK, Marine J-C, Jochemsen AG, Dyer MA. Inactivation of the p53 pathway in retinoblastoma. *Nature* 444(7115):66-69, 2006.
- Fujii N, You L, Xu Z, Uematsu K, Shan J, He B, Mikami I, Edmondson LR, Neale G, Zheng J, Guy RK, Jablons DM. An antagonist of Dishevelled protein-protein interaction suppresses b-catenin dependent tumor cell growth. *Cancer Res* 67(2):573-579, 2007.
- Arnold A, Kosinski A, Estebanez-Perpina E, Fletterick RJ, Guy RK. Inhibitors of the interaction of thyroid hormone receptor and coactivators: Preliminary structure activity relationships. *J Med Chem* 50(22):5269-5280, 2007.
- Estebanez-Perpina E, Arnold A, Webb P, Nguyen P, Delgado-Rodrigues E, Mar E, Bateman R, Pallai P, Shokat KM, Baxter JD, Guy RK, Fletterick RJ. A surface on the androgen receptor that allosterically regulates coactivator binding. *Proc Natl Acad Sci USA* 104(41):16074-16079, 2007.
- Mallari JP, Shelat AA, O'Brien T, Caffrey CR, Kosinski A, Connelly M, McKerrow JH, Guy RK. Development of potent purine-derived nitrile inhibitors of the trypanosomal protease TbCatB. *J Med Chem* 51(3):545-552, 2008.
- Jones JO, Bolton EC, Huang Y, Feau C, Guy RK, Yamamoto KR, Hann B, Diamond MI. Ligand independent androgen receptor inhibition in vitro and in vivo. *Proc Natl Acad Sci USA* 106(17):7233-7238, 2009. PMID: PMC2678452
- Reed D, Ying S, Shelat A, Mills N, Smithson D, Arnold A, Otieno S, Regni C, Zhu F, Kriwacki R, Schulman B, Guy RK, Dyer MA. Identification and characterization of a small molecule inhibitor of MDMX. *J Biol Chem* (in press), 2009. PMID: PMC Journal – In Process

D. Research Support

Ongoing Research Support

MMV FDN (YR 1) (GUY) 01/01/2009-04/30/2010
MEDICINES FOR MALARIA VENTURE
Discovery of Novel Anti-malarial Lead Series

The goal of this project is to discover series of compounds (Lead Series) that meet MMV criteria as suitable for further Lead Optimization (LO) studies in an effort to identify novel compounds to treat or prevent *Plasmodium falciparum* and/or *Plasmodium vivax* malaria, with a focus on compound series demonstrating high potency against known resistant strains. This will be accomplished through Hit-to-Lead (H2L) studies on novel chemical structures resulting from an intensive whole-cell high throughput screening (HTS) effort undertaken and complete in the laboratories of Dr. Kip Guy at St. Jude.

1 R21NS066460-01 (WILLIAMS) 09/30/2009-08/31/2010
NINDS
Synergy Screening of BCR-ABL-driven Lymphoid Leukemia

The central goal of this grant is to further develop and configure cell-based assays for High-Throughput Screening (HTS) studies, with the goal of identifying known FDA-approved drugs and novel small molecules

that will both overcome cytokine-dependent 'protection' and synergize with dasatinib to efficiently induce killing of engineered leukemia cells.

5 U01AI075517-03 (GUY) 08/01/2007-07/31/2012

NIAID

Development of Antimalarial Preclinical Candidates

Develop five lead series with divergent chemotypes and presumptive mechanisms of action. Simultaneously optimize efficacy against drug resistant *P. falciparum* in vitro and favorable in vitro cellular and biochemical pharmacological profiles for each series. Optimize up to five promising validated lead series, using in vivo rodent efficacy, pharmacokinetic, and toxicology models. Optimize up to three promising late stage lead series using in vivo simian efficacy, pharmacokinetic, and toxicology models. Select two preclinical candidates from these series.

5 R01DK058080-08 (GUY) 09/30/2000-12/31/2011

NIDDK

Novel Inhibitors of Nuclear Receptor Function

Discovery of Novel Inhibitors of Nuclear Hormone Receptor Function

CERN P3 YR 3 (GUY) 07/01/2007-06/30/2012

COLLABORATIVE MED RESEARCH LLC

CERN P3: Molecular Targeted Drug Development

Comprehensive cancer research and related biomedical research and clinical applications dedicated to treatment, education, and prevention of cancer.

Completed Research Support

WHO-TDR FELLOWSHIP (GUY) 12/15/2005-04/30/2008

WHO

WHO-TDR Chemistry Workstation

Provide a "workstation" for up to two postdoctoral fellows that will be selected by the WHO.

1 U01AI053862 (GUY) 08/01/2005-07/31/2007

UCSF

Novel Anti-Malarials by Combinatorial Pharmacogenomics

To synthesize focused libraries of quinolines and package and distribute libraries for screening.

5 R01AG021601-05 (GUY) 06/01/2005-05/31/2008

UCSF

Novel Therapeutics for Prion Diseases

Synthesis of a series of acridine derivatives as potential prion therapeutics

5 R01GM056531-10 (GUY) 09/01/2005-08/31/2007

UCSF

Structure Biology and Targeted Drug Design for AIDS

Structure Biology and Targeted Drug Design for AID

2 P30CA021765-30 DEV FUND (DYER) 06/14/2008-02/28/2013

NCI

Retinoblastoma and the Rb Family

To enhance translational research in the treatment of retinoblastoma.

CERN P3 (GUY)

07/20/2007-06/30/2012

CERN

CERN P3: Molecular Targeted Drug Development

CERN Project 3: Molecular Targeted Drug Development