

*CURRICULUM VITAE***VERN LEE SCHRAMM**

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Personal Information:

Date of Birth:	November 9, 1941
Place of Birth:	Howard, South Dakota
Citizenship:	U.S.A.
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Education:

Sept 1959 – June 1963	B.S. in Bacteriology (chemistry emphasis), South Dakota State College
Sept 1963 – June 1965	Masters Degree in Nutrition (biochemistry emphasis), Harvard University Research Advisor, Dr. R.P. Geyer
Oct 1965 – April 1969	Ph.D. in Mechanism of Enzyme Action, Department of Biochemistry, Australian National University Research Advisor, Dr. John Morrison

Postdoctoral Experience:

Aug 1969 – Aug 1971	NRC-NSF Postdoctoral Research Associate at NASA Ames Research Center, Biological Adaptation Branch
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Appointments:

July 1999 – Present	University Professor of the Albert Einstein College of Medicine
July 1995 – Present	Ruth Merns Endowed Chair of Biochemistry
Aug 1987 – Present	Professor and Chairman, Department of Biochemistry, Albert Einstein College of Medicine
July 1981 - July 1987	Professor of Biochemistry, Temple University School of Medicine
July 1976 - June 1981	Associate Professor of Biochemistry, Temple University School of Medicine
Aug 1971 - July 1976	Assistant Professor of Biochemistry, Temple University School of Medicine

Fields of Interest:

Enzymatic Transition State Analysis, Transition State Inhibitor Design, Biological Targets for Inhibitor Design, Mechanisms of N-ribosyltransferases

National Committees and Service:

- Elected to the National Academy of Sciences, 2007
- Associate Editor, Journal of the American Chemical Society, 2003-Present
- Chair, Division of Biological Chemistry, American Chemical Society, 2002-2004
- Chair, Search Committee, Executive Officer of ASBMB, 2003-2004
- Program Co-Chair ASBMB National Meeting 2003, San Diego, CA
- Program Committee ASBMB National Meeting 2002, New Orleans, LA
- Organizer, 17th Winter Enzyme Mechanisms Conference, 2001
- ASBMB Elected Council Member, 2000-2002
- Chair, Gordon Research Conference, Isotopes in Chemistry and Biology, 2000; and Co-Chair, 1998
- Advisory Board, National Research Resource for Accelerator Mass Spectrometry, Livermore Research Laboratory, 2000 - Present
- Chair, FASEB Consensus Committee for 1998 and 1999 NSF budgets
- FASEB Representative to House Appropriations Subcommittee for 1997 NSF Budget
- Co-Editor, *Methods in Enzymology* Volume 308, Academic Press, 1999
- Editorial Board, *Vitamins and Hormones*, 1994-2001
- Advisory Board, National Tritium Laboratory, Berkeley Lawrence Laboratory, 1995 - 2001
- Invited participant, Institute of General Medical Sciences, NIH Council discussion on innovative research funding, 1993
- Ad Hoc Member, Council, Institute of General Medical Sciences, NIH – 1993, 1995, 1997, 2001
- Editorial Board, *Journal of Biological Chemistry*, 1986-1991; 1993-1996, 1997-1998
- Councilor, Biological Chemistry Division of the American Chemical Society, 1993-1996
- Program Chairman, American Chemical Society, Division of Biological Chemistry, 1991 National Meeting, New York
- External Review Committee, University of Minnesota, Department of Biochemistry, 1990
- Editorial Board, *International Journal of Purine and Pyrimidine Research*, 1990-1993
- Co-Chairman (with Dr. J. Klinman) of Gordon Conference, Enzymes, Coenzymes and Metabolic Pathways, 1989
- Nominating Committee, American Chemical Society, Division of Biological Chemistry, 1988
- Member, Biochemistry Study Section of NIH, 1981-1985
- Chaired initial meeting of Medical Biochemistry Study Section of NIH, 1981

Teaching, Research and Service Awards:

- Repligen Award, American Chemical Society, Division of Biological Chemistry, 2006
- Merit Research Award, GM Council of NIH, 1998-2008 for Transition State Analysis of Enzymatic Reactions
- Elected Fellow of the AAAS for research in enzymatic transition states, 1999
- Awarded the Rudi Lemberg Award by the Australian Academy of Science, 1999
- Named as University Professor, Albert Einstein College of Medicine, 1999
- Distinguished Medical Research Award, Young Men's Division of the Albert Einstein College of Medicine, 1997
- Harry Eagle Award for Outstanding Basic Science Teaching, Albert Einstein College of Medicine, 1996
- Elected to the Leo M. Davidoff Society at the Albert Einstein College of Medicine for "distinguished, caring and committed teaching", 1992
- Distinguished Faculty Service Award, Temple University, 1986

- George A. Sowell Award for Excellence in Teaching, 1983. Basic sciences teaching at the Temple University School of Medicine
- Awarded the Christian R. and Mary F. Lindback Foundation Award for distinguished teaching in graduate and medical courses in 1982
- Awarded the Golden Apple Teaching Award for 1977 and the 1981 academic years teaching to Medical Students

National Societies:

- The Harvey Society of New York
- American Society for Biochemistry and Molecular Biology
- American Association for the Advancement of Science
- American Chemical Society, Divisions of Biological and Medicinal Chemistry
- American Society of Biochemistry and Molecular Biology of FASEB

Selected Recent Invited Presentations:

- 2005 Eminent Scholar Series, University of Arizona
- 2005 Vanderbilt Institute of Chemical Biology, Vanderbilt University
- 2005 Keystone Symposium on Drugs Against Protozoan Parasites
- 2005 Department of Chemistry, City College of New York
- 2005 Gordon Research Conference on Carbohydrate Chemistry
- 2005 Isotopes 2005 International Conference – Invited Speaker - Bath, England
- 2005 Gordon Research Conference, Enzymes, Coenzymes & Metabolic Pathways
- 2005 Distinguished Speaker Lecture Series, NCI, Frederick, MD
- 2005 13th European Carbohydrate Symposium – Bratislava, Slovakia
- 2005 PacificChem Bioorganic Reaction Mechanisms – Honolulu, HI
- 2006 Cornell University, Pharmacology Seminar Series
- 2006 Case Western MSTP Winter Retreat – Student Invited Speaker
- 2006 Johns Hopkins University, Department of Chemistry
- 2006 University of Maryland, Baltimore Co., Department of Chemistry and Biochemistry
- 2006 University of Florida, Center for Structural Biology Seminar Series
- 2006 University of Kansas – Symposium on Drug Design, Lawrence, Kansas
- 2006 Simon Fraser University, Merck Frosst Lecturer – British Columbia, Canada
- 2006 University of California, Berkeley – Structural and Quantitative Biology Seminar Series
- 2006 Structural Biology Network 10th Annual Conference Tallberg, Sweden
- 2006 Fox Chase Cancer Center – Distinguished Lecture Series
- 2006 University of Guelph – Ontario, Canada
- 2007 University of Kentucky – Naff Symposium on Chemistry & Molecular Biology
- 2007 University of CA, Santa Barbara, B.R. Baker Lecture
- 2007 Isotopes 2007 – Castellón, Spain
- 2007 EMBO Symposium – Hamburg, Germany
- 2007 12th Int'l Symposium on Purine & Pyrimidine Metabolism in Man – Chicago, IL
- 2007 South Dakota State University – Brookings, SD
- 2007 Wyeth Annual Scientific Symposium (Chemical & Screening Sciences) – Collegeville, PA
- 2007 Stony Brook University, Institute for Chemical Biology & Drug Discovery
- 2007 University of South Florida, Symposium on Molecular Diversity in Drug Design, Discovery And Delivery - Tampa, FL
- 2008 Northeastern University, Department of Chemistry – Boston, MA
- 2008 Texas A&M University – Frontiers in Chemical Research – College Station, TX
- 2008 Universite de Montreal, Department of Chemistry – Montreal, Canada
- 2008 ASBMB Annual Meeting – Program Planning Committee – San Diego, CA
- 2008 Gordon Research Conference – Bioorganic Chemistry – Andover, New Hampshire
- 2008 Institut Pasteur - FRANCE

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- 2008 Trends in Enzymology – St. Malo, FRANCE
- 2008 International Conf on Physical Organic Chemistry – Santiago de Compostela, Spain
- 2008 Fisher Seminar – University of South Carolina
- 2008 AstraZeneca Infection Symposium – Waltham, MA
- 2008 EMBL Conference on Chemical Biology – Heidelberg, Germany
- 2009 Boehringer Ingelheim Lecture – University of British Columbia
- 2009 MIT Lectures – MIT Department of Chemistry
- 2009 The Ohio State University – Depts of Physics, Chemistry and Biochemistry
- 2009 29th Symp in Pharmacological Sciences & Biorelated Chemistry – University of Michigan
- 2009 Spring ACS National Meeting – Salt Lake City, UT
- 2009 University of CA, Davis
- 2009 Stanford University – Frontiers in Biology
- 2009 University of CA, San Francisco – Biophysics/Chemistry & Chemical Biology
- 2009 ISOTOPES 2009 – Cluj-Napoca, Romania
- 2009 Univ of Copenhagen – Protein Science, Summer School 2009 – Spetses, Greece
- 2009 13th Int'l Symp on Purine & Pyrimidine Metabolism in Man – Stockholm, Sweden
- 2009 42nd IUPAC Congress: Chemistry Solutions – Glasgow, Scotland
- 2009 Georgia State University – Molecular Basis of Disease Areas of Focus Lecture Series
- 2009 10th Latin-American Conference on Physical Organic Chemistry – Florianopolis, Brazil
- 2009 Combio Conference – Bio societies from Australia & New Zealand – Christchurch, NZ
- 2010 ET Seminar Series – Walter Reed Army Institute of Research – Silver Spring, MD
- 2010 Gordon Research Conference - Isotopes In Biological & Chemical Sciences – Galveston, TX
- 2010 Memorial Sloan-Kettering Cancer Center - MSKCC MPC Research Seminar – New York
- 2010 Volcano Conference in Chemical Biology – University of Washington
- 2010 Hunter College – New York, NY
- 2010 Gordon Research Conference – Proteolytic Enzymes & Their Inhibitors – Lucca, Italy
- 2010 Sheffield University – Sheffield, Wales
- 2010 University of Bristol – Bristol, Wales
- 2010 Cardiff University – Cardiff, UK
- 2010 European Symposia in Biological & Organic Chemistry 2010 – Gregynog, United Kingdom
- 2010 Gordon Research Conference – Enzymes Coenzymes & Metabolic Pathways – Waterville Valley, NH
- 2010 25th International Carbohydrate Symposium – Tokyo, Japan
- 2010 Case Western Reserve University – Hanson Symposium – Cleveland, OH
- 2010 Vanderbilt University – Discovery Lecture – Nashville, TN
- 2010 Marquette University, Milwaukee, WI
- 2010 Mexican Biochemical Society Biannual Meeting – Symposium “Proteins: Structure, Dynamics and Function” – Chiapas, Mexico
- 2010 PacifiChem 2010 – Honolulu, HI
- 2011 2011 Enzyme Mechanisms Conference – St. Pete Beach, FL
- 2011 Northwestern University – Evanston, IL
- 2011 Florida State University – Tallahassee, FL
- 2011 University of Tennessee – Knoxville, TN
- 2011 Translational Approahces in Cancer Therapeutics Conference – University of CA, Irvine
- 2011 University of CA, Irvine, Department of Biochemistry Seminar – University of CA, Irvine
- 2011 Isotopes 2011 – Provence-Alpes-Cote d’Azur, France
- 2011 Gordon Reseach Conference – Nucleosides, Nucleotides and Oligonucleotides – Newport, RI
- 2011 Wesleyan University – Middletown, Connecticut
- 2011 University of Alberta – 2011 Reuben Benjamin Sandin Lectures – Edmonton, Canada
- 2011 Virginia Tech – Blacksburg, Virginia
- 2011 2011 Michael Laskowski Lecture – Purdue University – West Lafayette, IN
- 2011 NYC Emerging Technologies Summit – Cornell University – New York, NY
- 2011 Pharmacology & Chem Biology Seminar – University of Pittsburgh, School of Med – PA
- 2011 Temple University, Department of Chemistry Seminar – Philadelphia, PA

Consultancies:

2008 – Present Pico Pharmaceuticals, Scientific Co-founder
2006 – Present Metabalon Biochemistry Advisory Board
2004 – Present Sirtris Scientific Advisory Board
2000 – Present Consultant, BioCryst Pharmaceuticals

Original Research Publications:

Schramm, V.L. and Morrison, J.F. "Purification, Properties and Allosteric Activation of Nucleoside Diphosphatase" *Biochemistry* 7, 3642-3652 (1968).

Schramm, V.L. and Morrison, J.F. "Kinetic Studies on the Mechanism and Allosteric Activation of the Reaction Catalyzed by Nucleoside Diphosphatase" *Biochemistry* 8, 3821-3828 (1969).

Schramm, V.L. and Morrison, J.F. "Studies on an Aged Preparation of Nucleoside Diphosphatase, Kinetics and Reaction Mechanism" *Biochemistry* 9, 671-676 (1970).

Schramm, V.L. and Morrison, J.F. "Studies on the Allosteric Modification of Nucleoside Diphosphatase Activity by Magnesium Nucleoside Triphosphates and Inosine Diphosphate" *Biochemistry* 10, 2272-2277 (1971).

Schramm, V.L. and Hochstein, L.I. "Stabilization of AMP Nucleosidase by Inorganic Salts, Substrate, and Allosteric Activator" *Biochemistry* 10, 3411-3417 (1971).

Schramm, V.L. and Hochstein, L.I. "Purification, Crystallization and Subunit Structure of Allosteric AMP-nucleosidase" *Biochemistry* 11, 2777-2783 (1972).

Schramm, V.L. and Leung, H. "Regulation of Adenosine Monophosphate Levels as a Function of Adenosine Triphosphate and Inorganic Phosphate. A Proposed Metabolic Role of Adenosine Monophosphate Nucleosidase from *Azotobacter vinelandii*" *J. Biol. Chem.* 248, 8313-8315 (1973).

Schramm, V.L. "A Large, Efficient and Inexpensive Bacterial Growth Chamber" *Analytical Biochemistry* 56, 377-382 (1974).

Plaut, G.W.E., Schramm, V.L. and Aogaichi, T. "Action of Magnesium Ion on Diphosphopyridine Nucleotide-Linked Isocitrate Dehydrogenase from Beef Heart" *J. Biol. Chem.* 249, 1848-1856 (1974).

Schramm, V.L. "Kinetic Properties of the Allosteric Adenosine Monophosphate Nucleosidase from *Azotobacter vinelandii*" *J. Biol. Chem.* 249, 1729-1736 (1974).

Schramm, V.L. and Lazorik, F.C. "The Pathway of Adenylate Catabolism in *Azotobacter vinelandii*. Evidence for Adenosine Monophosphate Nucleosidase as the Regulatory Enzyme" *J. Biol. Chem.* 250, 1801-1808 (1975).

Jomain-Baum, M., Schramm, V.L. and Hanson, R.W. "The Mechanism of 3-Mercaptopicolinic Acid Inhibition of Hepatic Phosphoenolpyruvate Carboxykinase (GTP)" *J. Biol. Chem.* 251, 37-44 (1976).

Schramm, V.L. "Comparison of Initial Velocity and Binding Data for Allosteric Adenosine Monophosphate Nucleosidase" *J. Biol. Chem.* 251, 3417-3424 (1976).

Schramm, V.L. and Fullin, F.A. "Kinetics of Adenosine Monophosphate Nucleosidase Inactivation by Phosphate and Protection by Substrate and Allosteric Activator" *J. Biol. Chem.* 253, 2161-2167 (1978).

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- Jomain-Baum, M. and Schramm, V.L. "Kinetic Mechanism of Phosphoenolpyruvate Carboxykinase (GTP) from Rat Liver Cytosol" *J. Biol. Chem.* 253, 3648-3659 (1978).
- Leung, H.B. and Schramm, V.L. "The Role of Adenosine Monophosphate Nucleosidase in the Regulation of Adenine Nucleotide Levels in *Azotobacter vinelandii* during Aerobic-Anaerobic Transitions" *Arch. Biochem. Biophys.* 190, 46-56 (1978).
- Schramm, V.L. and Leung, H.B. "Adenosine Monophosphate Nucleosidase from *Azotobacter vinelandii* and *Escherichia coli*" *Methods Enzymol.* 51, 263-271 (1978).
- DeWolf, W.E., Jr. and Schramm, V.L. "Synthesis of a New 8-Spin Labeled AMP and Its Interaction with AMP Nucleosidase" *J. Biol. Chem.* 254, 6215-6217 (1979).
- DeWolf, W.E., Jr., Fullin, F.A. and Schramm, V.L. "The Catalytic Site of AMP Nucleosidase. Substrate Specificity and pH Effects with AMP and Formycin 5'-PO₄" *J. Biol. Chem.* 254, 10868-10875 (1979).
- Schramm, V.L. and Reed, G.H. "The Interaction of Mn²⁺ and MnATP²⁻ with the Allosteric Sites of AMP Nucleosidase" *J. Biol. Chem.* 255, 5795-5801 (1980).
- DeWolf, W.E., Jr., Markham, G.D. and Schramm, V.L. "Evidence for Substantial Separation of the Catalytic and Allosteric Sites of AMP Nucleosidase" *J. Biol. Chem.* 255, 8210-8215 (1980).
- Leung, H.B. and Schramm, V.L. "Adenylate Degradation in *Escherichia coli*. The Role of AMP Nucleosidase and Properties of the Purified Enzyme" *J. Biol. Chem.* 255, 10867-10874 (1980).
- Brinkworth, R.I., Hanson, R.W., Fullin, F.A. and Schramm, V.L. "Mn²⁺ Sensitive and Insensitive Forms of Phosphoenolpyruvate Carboxykinase (GTP)" *J. Biol. Chem.* 256, 10795-10802 (1981).
- Schramm, V.L., Fullin, F.A. and Zimmerman, M.D. "Kinetic Studies of the Interaction of Substrates, Mn²⁺ and Mg²⁺ with the Mn²⁺-Sensitive and -Insensitive Forms of Phosphoenolpyruvate Carboxykinase" *J. Biol. Chem.* 256, 10803-10808 (1981).
- Leung, H.B. and Schramm, V.L. "A Mutant AMP Nucleosidase. Purification, Properties and *in vivo* Turnover of the Protein" *J. Biol. Chem.* 256, 12823-12829 (1981).
- Ash, D.E. and Schramm, V.L. "Determination of Free and Bound Manganese(II) in Hepatocytes from Fed and Fasted Rats" *J. Biol. Chem.* 257, 9261-9265 (1982).
- Wilson, D.F., Erecinska, M. and Schramm, V.L. "Evaluation of the Relationship Between the Intra- and Extramitochondrial [ATP]/[ADP] Ratios Using Phosphoenolpyruvate Carboxykinase" *J. Biol. Chem.* 258, 10464-10473 (1983).
- Schramm, V.L., McCluskey, R.A., Emig, F.F. and Litwack, G. "Kinetic Studies and Active Site Binding Properties of Glutathione S-Transferase using Spin-Labeled Glutathione, A Product Analogue" *J. Biol. Chem.* 259, 714-722 (1984).
- Leung, H.B. and Schramm, V.L. "The Structural Gene for AMP Nucleosidase. Mapping, Cloning and Overproduction of the Enzyme" *J. Biol. Chem.* 259, 6972-6978 (1984).
- Zlotnik, H., Schramm, V.L. and Buckley, H.R. "Purification and Partial Characterization of an Extracellular Protease from *Nocardia brasiliensis*" *J. Bacteriol.* 157, 627-631 (1984).

- Parkin, D.W. and Schramm, V.L. "Effects of Allosteric Activation on the Primary and Secondary Kinetic Isotope Effects for Three AMP Nucleosidases" *J. Biol. Chem.* 259, 9411-9417 (1984).
- Parkin, D.W., Leung, H.B. and Schramm, V.L. "Synthesis of Nucleotides with Specific Radiolabels in Ribose: Primary ¹⁴C and Secondary ³H Kinetic Isotope Effects on Acid-Catalyzed Hydrolysis of AMP, dAMP and Inosine" *J. Biol. Chem.* 259, 9418-9425 (1984).
- Barrett, J.F., Schramm, V.L. and Shockman, G.D. "Hydrolysis of Soluble, Linear, Uncrosslinked Peptidoglycans by Endogenous Bacterial N-Acetylmuramoylhydrolases" *J. Bacteriol.* 159, 520-526 (1984).
- Barrett, J.F., Dolinger, D.L., Schramm, V.L. and Shockman, G.D. "The Mechanism of Soluble Peptidoglycan Hydrolysis by an Autolytic Muramidase. A Processive Exo-dissacharidase" *J. Biol. Chem.* 259, 11818-11827 (1984).
- Schramm, V.L. and Baker, D.C. "Spontaneous Epimerization of (S)-Deoxycytoformycin and Interaction of (R)-Deoxycytoformycin, (S)-Deoxycytoformycin and 8-Ketodeoxycytoformycin with Adenosine Deaminase" *Biochemistry* 24, 641-646 (1985).
- Cornell, N.W., Schramm, V.L., Kerich, M.J. and Emig, F.A. "Subcellular Location of Phosphoenolpyruvate Carboxykinase in Hepatocytes from Fed and Fasted Rats" *J. Nutrition*, 116, 1101-1107 (1986).
- Giranda, V.L., Berman, H.M. and Schramm, V.L. "Crystallization and Preliminary X-ray Study of AMP Nucleosidase" *J. Biol. Chem.* 261, 15307-15309 (1986).
- DeWolf, W.E., Jr., Emig, F.A. and Schramm, V.L. "AMP Nucleosidase. Kinetic Mechanism and Thermodynamics" *Biochemistry* 25, 4132-4140 (1986).
- Parkin, D.W. and Schramm, V.L. "Catalytic and Allosteric Mechanism of AMP Nucleosidase from Primary, Beta Secondary, and Multiple Heavy Atom Kinetic Isotope Effects" *Biochemistry* 26, 913-920 (1987).
- Mentch, F., Parkin, D.W. and Schramm, V.L. "Transition State Structures for N-Glycoside Hydrolysis of AMP by Acid and by AMP Nucleosidase in the Presence and Absence of Allosteric Activator" *Biochemistry* 26, 921-930 (1987).
- Markham, G.D., Parkin, D.W., Mentch, F. and Schramm, V.L. "A Kinetic Isotope Study and Transition State Analysis of the S-Adenosylmethionine Synthetase Reaction" *J. Biol. Chem.* 262, 5609-5615 (1987).
- Merkler, D.L. and Schramm, V.L. "A Preparative Method for the Enzymatic 5'-Monophosphorylation of Nucleosides" *Anal. Biochem.* 167, 148-153 (1987).
- Giranda, V.L., Berman, H.M. and Schramm, V.L. "Crystal Structure of Formycin 5'-Phosphate: An Explanation for its Tight Binding to AMP Nucleosidase" *Biochemistry* 27, 5813-5818 (1988).
- Dolinger, D.L., Schramm, V.L. and Shockman, G.D. "Covalent Modification of the β -1,4-N-Acetylmuramoylhydrolase of *Streptococcus faecium* with 5-Mercaptouridine Monophosphate" *Proc. Natl. Acad. Sci. USA* 85, 6667-6671 (1988).
- Leung, H.B., Meyer, S.L., Kvalnes-Krick, K.L., DeRiel, J.K. and Schramm, V.L. "Structure and Regulation of the AMP Nucleosidase Gene (*amn*) from *Escherichia coli*" *Biochemistry* 28, 8728-8733 (1989).

- Meyer, S.L., Kvalnes-Krick, K.L. and Schramm, V.L. "Characterization of *AMD*, the AMP Deaminase Gene in Yeast. Production of *amd* Strain, Cloning, Nucleotide Sequence and Properties of the Protein" *Biochemistry* 28, 8734-8743 (1989).
- Giranda, V.L., Berman, H.M. and Schramm, V.L. "Crystallographic Quaternary Structural Analysis of AMP Nucleosidases from *Escherichia coli* and *Azotobacter vinelandii*" *J. Biol. Chem.* 264, 15674-15680 (1989).
- Merkler, D.J., Wali, A.S., Taylor, J. and Schramm, V.L. "AMP Deaminase from Yeast. Role in AMP Degradation, Large Scale Purification, and Properties of the Native and Proteolyzed Enzyme" *J. Biol. Chem.* 264, 21422-21430 (1989).
- Merkler, D.J. and Schramm, V.L. "Catalytic and Regulatory Site Composition of Yeast AMP Deaminase by Comparative Binding and Rate Studies. Resolution of the Cooperative Mechanism" *J. Biol. Chem.* 265, 4420-4426 (1990).
- Ash, D.E., Emig, F.A., Chowdhury, S., Satoh, Y. and Schramm, V.L. "Mammalian and Avian Liver Phosphoenolpyruvate Carboxykinase. Alternate Substrates and Inhibition by Analogs of Oxaloacetate" *J. Biol. Chem.* 265, 7377-7384 (1990).
- Merkler, D.J., Brenowitz, M. and Schramm, V.L. "The Rate Constant Describing Slow-Onset Inhibition of Yeast AMP Deaminase by Coformycin Analogs is Independent of Inhibitor Structure" *Biochemistry* 29, 8358-8364 (1990).
- Wente, S. R., Villalba, M., Schramm, V.L. and Rosen, O.M. "The Mn²⁺ Binding Properties of a Recombinant Protein Tyrosine Kinase Derived from the Human Insulin Receptor" *Proc. Natl. Acad. Sci. USA* 87, 2805-2809 (1990).
- Chen, C.-Y., Sato, Y. and Schramm, V.L. "Isotope Trapping and Positional Isotope Exchange with Rat and Chicken Liver Phosphoenolpyruvate Carboxykinases" *Biochemistry* 30, 4143-4151 (1991).
- Parkin, D.W., Mentch, F., Banks, G.A., Horenstein, B.A. and Schramm, V.L. "Transition State Analysis of a V_{max} Mutant of AMP Nucleosidase by the Application of Heavy-Atom Kinetic Isotope Effects" *Biochemistry* 30, 4586-4594 (1991).
- Chen, C.-Y., Emig, F.A., Schramm, V.L. and Ash, D.E. "Inactivation of Chicken Mitochondrial Phosphoenolpyruvate Carboxykinase by o-Phthalaldehyde" *J. Biol. Chem.* 266, 16645-16652 (1991).
- Parkin, D.W., Horenstein, B.A., Abdulah, D.R., Estupinan, B. and Schramm, V.L. "Nucleoside Hydrolase from *Crithidia fasciculata*. Metabolic Role, Purification, Specificity and Kinetic Mechanism" *J. Biol. Chem.* 266, 20658-20665 (1991).
- Horenstein, B.A., Parkin, D.W., Estupinan, B. and Schramm, V.L. "Transition State Analysis of Nucleoside Hydrolase from *Crithidia fasciculata*" *Biochemistry* 30, 10788-10795 (1991).
- Kline, P.C. and Schramm, V.L. "Purine Nucleoside Phosphorylase. Inosine Hydrolysis, Tight-Binding of the Hypoxanthine Intermediate and Third-the-Sites Reactivity" *Biochemistry* 31, 5964-5973 (1992).
- Sollitti, P., Merkler, D.J., Estupinan, B. and Schramm, V.L. "Yeast AMP Deaminase. Catalytic Activity in *Schizosaccharomyces pombe* and Chromosomal Location in *Saccharomyces cerevisiae*" *J. Biol. Chem.* 268, 4549-4555 (1993).

Kvalnes-Krick, K., Labdon, J.E., Nieves, E. and Schramm, V.L. "Mutagenic Analysis of AMP Nucleosidase from *E. coli*. Deletion of a Region Similar to AMP Deaminase and Peptide Characterization by Mass Spectrometry" *J. Biol. Chem.* 268, 8717-8726 (1993).

Merkler, D.J. and Schramm, V.L. "Catalytic Mechanism of Yeast AMP Deaminase. Zinc Content, Substrate Specificity, pH Studies and Solvent Isotope Effects" *Biochemistry* 32, 8717-8726 (1993).

Horenstein, B.A. and Schramm, V.L. "The Electronic Nature of the Transition State for Nucleosidase Hydrolase. A Blueprint for Inhibitor Design" *Biochemistry* 32, 7089-7097 (1993).

Horenstein, B.A. and Schramm, V.L. "Correlation of the Molecular Electrostatic Potential Surface of an Enzymatic Transition State with Novel Transition State Inhibitors", *Biochemistry* 32, 9917-9925 (1993).

Horenstein, B.A., Zabinski, R.F. and Schramm, V.L. "A New Class of C-Nucleoside Analogues. 1-(S)-aryl-1,4-dideoxy-1,4-imino-D-ribitols, Transition State Analogue Inhibitors of Nucleoside Hydrolase" *Tet. Lett.* 34, 7213-7216 (1993).

Merkler, D.J., Kline, P.C., Weiss, P. and Schramm, V.L. "Transition State Analysis of AMP Deaminase" *Biochemistry* 32, 12993-13001 (1993).

Kline, P.C. and Schramm, V.L. "Purine Nucleoside Phosphorylase. Catalytic Mechanism and Transition State Analysis of the Arsenolysis Reaction" *Biochemistry* 32, 13212-13219 (1993).

Boutellier, M., Horenstein, B.A., Semenyaka, A., Schramm, V.L. and Ganem, B. "Amidrazon Analogue of D-Ribofuranose as Transition State Inhibitors of Nucleoside Hydrolase" *Biochemistry* 33, 3994-4000 (1994).

Rising, K. and Schramm, V.L. "Enzymatic Synthesis of NAD⁺ with the Specific Incorporation of Atomic Labels" *J. Am. Chem. Soc.* 116, 6531-6536 (1994).

Ehrlich, J.I. and Schramm, V.L. "Electrostatic Potential Surface Analysis of the Transition State for AMP Nucleosidase and for Formycin 5'-PO₄, a Transition State Inhibitor" *Biochemistry* 33, 8890-8896 (1994).

Kline, P.C. and Schramm, V.L. "Electrostatic Potential Surfaces of the Transition State for AMP Deaminase and for (R)-Cofomycin, a Transition State Inhibitor" *J. Biol. Chem.* 269, 22385-22390 (1994).

Estupinan, B. and Schramm, V.L. "Guanosine-Inosine Preferring Nucleoside N-Glycohydrolase from *Crithidia fasciculata*" *J. Biol. Chem.* 269, 23068-23073 (1994).

Kline, P.C. and Schramm, V.L. "Pre-Steady-State Transition State Analysis of the Hydrolytic Reaction Catalyzed by Purine Nucleoside Phosphorylase" *Biochemistry* 34, 1153-1162 (1995).

Boutellier, M., Ganem, B., Horenstein, B.A., and Schramm, V.L. "Design and Synthesis of D-Ribofuranoamidrazones as Inhibitors of Nucleoside Processing Enzymes" *Synlett*, 510-512 Special Issue (1995).

Parkin, D.W. and Schramm, V.L. "Binding Modes for Substrate and a Proposed Transition State Analogue of Protozoan Nucleoside Hydrolase" *Biochemistry* 34, 13961-13966 (1995).

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Schramm, V.L., and Horenstein, B. "Transition State Inhibitors for Nucleoside Hydrolase", Filed February 2, 1998, U.S. Application No. 017,917, Issued 6,121,296.

Current Support

NIH R37 GM41916 "Transition State Analysis of Enzymatic Reactions", Principal investigator V.L. Schramm; project period 08/01/89 through 07/31/12. Current annual direct budget of \$370,824. The research goals are to explore transition state structures of nucleoside hydrolases and purine nucleoside phosphorylases by kinetic isotope effects, crystallographic and novel inhibitor design techniques. Isozyme-specific transition state inhibitors will be designed and synthesized. Initial review group, Biochemistry 1, score 3.0 percentile, Awarded as a "Merit Award" by GM Council. Renewed as RO1 GM41916 to 07/31/12 with IRG priority score 2.2 percentile.

NIH RO1 CA72444. "Ricin: Mechanism, Transition State & Inhibitor Design", Principal Investigator V.L. Schramm. Project period 09/30/07-07/31/12. Current year annual direct support of \$226,962. The research goals are to solve the transition state and chemical mechanism for ricin A-chain. The information will be used to design and synthesize transition state inhibitors for ricin A-chain. These may find application as rescue agents in ricin immunochemotherapy directed against specific cancers and to serve as antidotes for ricin poisoning. IRG priority score 0.3 percentile.

NIH RO1 AI49512 "Purine pathways and inhibitor design in *Plasmodium*" Principal investigator V.L. Schramm. The goal of the program is to define the pathways of purine salvage and metabolism in *P. falciparum* under normal conditions and when specific steps of the pathways are interrupted. Transition state inhibitors for malarial purine nucleoside phosphorylase and HGXPRT are a focus. Project period 04/1/01-04/30/13. Renewed as RO1 to 04/30/13 with IRG priority score 0.3 percentile. Current annual direct cost \$295,690.

NIH P01GM068036 "Protein Dynamics in Enzymatic Catalysis" PI. Robert H. Callender, P.I. Project II Vern L. Schramm "Coordination of Protein Dynamics and Chemistry in PNP". To describe and coordinate changes in protein structure as the chemical reaction progresses along the reaction coordinate. Project period 05/01/09-04/30/14. Direct cost for Project II 05/01/10-04/30/11 is \$162,259.

NIH CA135405 "Transition State Analogues as Modulators of DNA Regulation." Specific aims for this proposal are to evaluate the effects of a transition state analogue inhibitor of human methylthioadenosine on human cancer xenografts in mice with focus on lung cancer. Project period 09/11/08-07/31/13. Current annual direct cost \$162,651.