

# CURRICULUM VITAE

Richard J. Bridges

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## PERSONAL DATA:

Birthdate: November 16, 1955  
Place of Birth: Zweibrucken, Germany  
Citizenship: U.S.A.

## EDUCATION:

B.S.: University of California, Davis, (Biochemistry), 1977  
Ph.D.: Cornell University Graduate School of Medical Sciences, (Biochemistry), 1984

## RESEARCH INTERESTS:

Glutamate Transport and Metabolism, Excitatory Amino Acid Receptor Pharmacology, Mechanisms of Excitatory Amino Acid-Mediated Neurotoxicity, Gliotoxicity, Glial Tumors

## POSITIONS HELD:

2011- Regents Professor, Department of Biomedical & Pharmaceutical Sciences, Skaggs School of Pharmacy, University of Montana, Missoula  
2008-2015 Chair, Department of Biomedical & Pharmaceutical Sciences, University of Montana  
2000-2008 Director, NIH COBRE Center for Structural and Functional Neuroscience Dept. of Biomedical & Pharmaceutical Sci., University of Montana  
1998- Professor, Department of Pharmaceutical Sciences, School of Pharmacy and Allied Health Sciences, University of Montana, Missoula  
1993-1998 Associate Professor, Department of Pharmaceutical Sciences, School of Pharmacy and Allied Health Sciences, University of Montana, Missoula  
1995-1998 Clinical Associate Professor, Department of Neurology, California College of Medicine, University of California, Irvine  
1993-1995 Associate Professor in Residence, Department of Neurology, California College of Medicine, University of California, Irvine  
1987-1993 Assistant Professor in Residence, Department of Neurology, California

College of Medicine, University of California, Irvine

1984-1987 NIH Postdoctoral Fellow, Dr. Carl Cotman, Department of Psychobiology, University of California, Irvine

1977-1984 Predoctoral Fellow, Dr. Alton Meister, Biochemistry Department, Cornell University Medical College

Winter 1977 Teaching Assistant, Dr. J.P. Preiss, Department of Biochemistry and Biophysics, University of California, Davis

1975-1977 Research Assistant, Dr. I.H. Segel, Department of Biochemistry and Biophysics, University of California, Davis

**AWARDS, HONORS, & NOTABLE PROFESSIONAL SERVICE:**

1978-1979 Blau Fellow, Cornell University Medical College

1985-1987 National Research Service Award, NIH

1991-1993 Board of Directors, Paralysis Project of California

1991- 2002 Scientific Advisory Committee, Paralysis Project of California

1992-2002 Editorial Board of the *Journal of Spinal Cord Medicine*

1992 First Step Service Award Paralysis Project of California

1995 Burroughs-Wellcome International Travel Fellow, Institute of Psychiatry, London

1995 Merit Award, University of Montana

1997 Instructor of the Year Award, Univ. of Montana School of Pharmacy

1997 Merit Award, University of Montana

1998 NIH NLS-2 Study Section, Ad-hoc Member

1998-Present Founding Member, Board of Directors, *Montana Neuroscience Institute*

2001 Merit Award, University of Montana

2002 NIH MDCN4 Study Section Ad-hoc Member

2003 COBRE Special Emphasis Panel Member

2003 Mershon Award, Scientific Contributions, Montana Academy of Sciences

2003 Merit Award, University of Montana

2004 NIH MDCN Study Section Special Emphasis Panel Member

2004 University of Montana, Provost's Distinguished Faculty Lecturer

2004-2011 Founding Member, Board of Directors, Montana BioScience Alliance

2004-2012 Univ. of Alaska-SNRP Basic Neuroscience Center Program Advisory Committee, Current Chair

2005 NIH NTRC Study Section, Ad-hoc Member

2006 Organizing Committee and Session Chair, National IDeA Symposium of Biomedical Research Excellence, Washington, DC

2007 Merit Award, University of Montana

2007-2009 Member, RCMI/IDeA Program Review and Advisory Panel, NIH

2007-Present Board of Directors, *Montana Neuroscience Institute*

2008-Present Univ. of North Dakota, COBRE Neuroscience Center Program Advisory Committee

2008 Dennison Presidential Faculty Award, University of Montana

2009 NIH NTRC Study Section, SEPA panel member

2010 NIH MDN Study Section SEPA panel reviewer

2010 Merit Award, University of Montana

2010 Brain Science Institute, SPCD Review Panel, Johns Hopkins School of Medicine

2011 Regents Professor, University of Montana  
2014 NIH ZRG1 MDCN-B SEPA Reviewer and Session Chair  
2014 Affiliate Director Project Lead the Way STEM Biomedical Sciences Initiative

**PUBLISHED WORKS:**

- Griffith, O.W., Bridges, R.J., and Meister, A. (1978) Evidence that the  $\gamma$ -glutamyl cycle functions *in vivo* using intracellular glutathione; effects of amino acids and selective inhibition of enzymes, *Proceedings of the National Academy of Sciences, U.S.*, **75**, 5405.
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- Anderson, M.E., Bridges, R.J., and Meister, A. (1980) Direct evidence for interorgan transport of glutathione and that the non-filtration renal mechanism for glutathione utilization involves  $\gamma$ -glutamyl transpeptidase, *Biochemical and Biophysical Research Communications*, **96**, 848.
- Bridges, R.J., Griffith, O.W., and Meister, A. (1980) *Threo*-L-( $\beta$ -methyl)glutamyl-L- $\alpha$ -aminobutyrate, a specific substrate of  $\gamma$ -glutamyl cyclotransferase: *in vivo* inhibition by  $\beta$ -aminoglutaryl-L- $\alpha$ -aminobutyrate, *Journal of Biological Chemistry*, **256**, 10, 10787 .
- Griffith, O.W., Bridges, R.J., and Meister, A. (1981) Formation of  $\gamma$ -glutamylcyst(e)ine *in vivo* is catalyzed by  $\gamma$ -glutamyl transpeptidase, *Proceedings of the National Academy of Sciences, U.S.*, **78**, 2777 .
- Abbott, W.A., Bridges, R.J., and Meister, A. (1983) Extracellular metabolism of glutathione accounts for its disappearance from the basolateral circulation of the kidney, *Journal of Biological Chemistry*, **259**, 15393 .
- Bridges, R.J., and Meister, A. (1985)  $\gamma$ -Glutamyl amino acids: transport and conversion to 5-oxoproline in the kidney, *Journal of Biological Chemistry*, **260**, 7304 .
- Bridges, R.J., Abbott, W.A., Murata, K., and Meister, A. (1985) Enzymatic synthesis of isotopically-labeled glutathione by means of an immobilized cell matrix, in Methods in Enzymology, **113**, 567, (A. Meister ed.) Academic Press, NY, NY.
- Bridges, R.J., Hearn, T.J., Monaghan, D.T., and Cotman, C.W. (1986) A comparison of AP4 receptors and  $^3\text{H}$ -AP4 binding sites in the rat brain, *Brain Res.*, **375**, 204 .
- Bridges, R.J., Nieto-Sampedro, M., Kadri, M., and Cotman, C.W. (1987) A novel chloride-dependent  $^3\text{H}$ -L-glutamate binding site in astrocyte membranes, *Journal of Neurochemistry*, **48**, 1709-1715 .

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- Bridges, R.J., Kesslak, J.P., Nieto-Sampedro, M., Broderick, J.T., Yu, J., and Cotman, C.W. (1987) A  $^3\text{H}$ -L-glutamate binding site on glia: an autoradiographic study on implanted astrocytes, *Brain Research*, **415**: 163-168.
- Bridges, R.J., Kadri, M., Monaghan, D.T., Nunn, P.B., Watkins, J.C., and Cotman, C.W. (1988) Inhibition of  $^3\text{H}$ - $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) by the excitotoxin  $\beta$ -N-oxalyl-L- $\alpha,\beta$ -diaminopropionic acid. *Eur. J. Pharmacol.* **145**, 357-359 .
- Cotman, C.W., Bridges, R.J., Geddes, J.W., Monaghan, D.T., and Cahan L.D. (1988) Anatomical organization and plasticity of excitatory amino acid receptors in the rodent and human brain: predictions on their functional state in neurodegenerative diseases. in Inhibitory and Excitatory Amino Acid Transmitters, (E. Costa ed) FIDIA,.
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- Monaghan, D.T., Bridges, R.J., and Cotman, C.W. (1989) The excitatory amino acid receptors: their classes, pharmacology, and distinct properties in the function of the central nervous system. *Ann. Rev. of Pharmacol. and Toxicol.* **29**, 365-402 .
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- Bridges, R.J. and Cotman, C.W. (1991) The balance between EAA plasticity and pathology: the potential role of glutamate transport. in Transmitter Amino Acid Receptors: Structure, Transduction and Models for Drug Development E.A. Barnard and E. Costa, eds. FIDIA Research Foundation; Thieme, NY. pp. 423-436.
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- Etoga, J.G., Ahmed, S.K., Patel, S., Bridges, R.J., and Thompson, C.M. (2010) Conformationally-Restricted Amino Acid Analogues Bearing a Distal Sulfonic Acid Show Selective Inhibition of System X<sub>c</sub>- over the Vesicular Glutamate Transporter, *Bioorganic & Medicinal Chemistry Letters*, **20** (18), 2680-2683.



- Seib, T.M., Patel, S. and Bridges, R.J. (2011) Regulation of the System xc<sup>-</sup> cystine/glutamate exchanger by intracellular glutathione levels in rat astrocyte primary cultures, *Glia*, **59** (10), 1387-1401
- Pathmajeyan, M.S., Patel, S.A., Seib, T.M., Striebel, J.F, Bridges, R.J. and Chesebro, B. (2011) Increased excitatory amino acid transport into p 1 rion protein knockout astrocytes, *Glia*, **59** (11), 1684-1694
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- Bridges, R.J., Natale, N., and Patel, S. (2012) System xC<sup>-</sup> cystine/glutamate antiporter, an update on molecular pharmacology and roles within the CNS, *British Journal of Pharmacology*, 165(1), 20-34
- Sontheimer H, Bridges RJ (2012) Sulfasalazine for brain cancer fits. *Expert Opinions on Investigational Drugs*;21(5), 575-8.
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- Newell JL, Keyari CM, McDaniel SW, Diaz PJ, Natale NR, Patel SA, Bridges RJ. (2014) Novel di-aryl-substituted isoxazoles act as noncompetitive inhibitors of the system xc<sup>-</sup> cystine / glutamate exchanger. *Neurochem Int*. **73**:132-8. (PMID: 24333322)

## Recently Published Abstracts

- Patel, S.A., Newell, J., Braden, M., Gerdes, J.M., Natale, N.R., and, Bridges, (2012) Structure-function of the system xc<sup>-</sup> glutamate/cystine exchanger: Identification of xct residues participating in binding and translocation. *Center for Biomolecular Structure and Dynamics Retreat*, Seeley Lake, MT.
- Gerdes J, Ahmed S, Danoon S, Braden M, Bridges R, Rothstein J, Sattler R, VanBrocklin H. (2012) Discovery of a novel PET tracer for the Excitatory Amino

Acid Transporter 2 (EAAT2) in the CNS, Society for Nuclear Medicine. *Journal of Nuclear Medicine*, 53(S1):1639.

Gerdes J, Bridges R, Braden M, Ahmed S, Patel S, VanBrocklin H, Dannon, S, Rothstein J, Sattler R. (2012) PET Imaging of the Excitatory Amino Acid Transporter 2 in an Amyotrophic Lateral Sclerosis Rat Model, Neuroreceptor Mapping Symposium, Johns Hopkins, Baltimore, MD. *J Cerebral Blood Flow & Metabolism*, 32(S1):26-27.

Sattler, R., Ayukawa, Y., Gerdes, J., Ahmed, S., Bridges, R., Patel, S., Rothstein, J. (2012) *In Vivo* Rodent Studies for Discovery of an Excitatory Amino Acid Transporter 2 (EAAT2, GLT-1) PET Imaging Tracer to Biomark ALS. ALS Association: Drug Discovery for ALS, Washington DC.

Dannon, S.; Braden, M.; Bridges, R.; Rothstein, J.; Sattler, R.; Vanbrocklin, H. (2012) , Discovery of a novel PET tracer for the Excitatory Amino Acid Transporter 2 (EAAT2) in the CNS Society for Nuclear Medicine, Miami Beach, FL

Patel, S.A., Newell, J., Diaz, P.J., Natale, N.R., Bridges, R.J. (2012), Effect of lipophilic binding domains on substrate transport and kinetics of the System xc- cystine/ glutamate antiporter *Society for Neuroscience Abstracts*, 38, 332.03

J. Gerdes, J., VanBrocklin, H., Sattler, R., Bridges, R., (2012) Progress Towards an EAAT2 PET Imaging Tracer For Monitoring ALS Therapy and Astroglia: From Chemicals To Rodents To Humans. Packard Center ALS Research Symposium, Baltimore, MD

Bridges, R.J., Patel, S.A., Natale, N.R., Diaz, P., Braden, M. (2013) Pharmacological Specificity of the System xc- Cystine/Glutamate Antiporter", International Society for Neurochemistry - American Society for Neurochemistry, 24th Biennial Joint Meeting, Cancun, Mexico,

Gerdes, J., VanBrocklin, H., Sattler, R., Bridges, R., (2013) Translational Progress of the ALS EAAT2 PET Imaging Tracer Packard Center ALS Research Symposium, Baltimore, MD

Patel, S.A., Newell, J., Braden, M., Keyari, C., Diaz, P.J., Natale, N.R., Bridges, R.J., (2013) Mapping substrate binding domains on the System xc- cystine/ glutamate antiporter *Society for Neuroscience Abstracts*, 39, 703.06.

Bridges, R.J., Igual, M.O., Capeletti Da Silva, L., Patel, S.A., Braden, M., Duncan, N., Weaver, M., Natale, N.R. (2014) Naphthyl-3-isoxazole analogs of 2,6-dibromo tyrosine (NIM-DBT) synthesis and System Xc- activity, Northwest Regional Meeting of the American Chemical Society, Missoula MT, abstract **NORM153**.

Patel, S.A., Newell, J., Braden, M., Diaz, P.J., Natale, N.R., Bridges, R.J. (2014) Structural comparisons of isoxazole-based non-competitive and competitive inhibitors of the system xc- antiporter *Society for Neuroscience Abstracts*, 40, 127.08

VanBrocklin, H.F., Bridges, R.J., Sattler, R., Pomper, M., Gerdes, J.M., (2015) IND Enabling Efforts and Accomplishments for the ALS EAAT2 PET Imaging Tracer, Packard Center ALS Research Symposium, Baltimore, MD

Bridges, R.J., Chase, L., Patel, S.A., Hewett, S.J. (2015) The System xc- glutamate / cysteine exchanger: consequences of the revolving door, Winter Conference on Brain Research, Big Sky, MT

#### **GRADUATE STUDENTS SUPERVISED:**

Colleen Baker; MS in Pharmaceutical Sciences, 9/95

Wallace Webster; MS Pharmaceutical Sciences, 8/98

Liping Liu; MS Pharmaceutical Sciences, 7/98 (Co-supervision with C. Eyer)

Richard Bartlett; PhD in Pharmaceutical Sciences, 5/99

Hans Koch; PhD in Pharmaceutical Sciences, 6/99

Sarj Patel; Ph.D., in Pharmaceutical Sciences 9/99

Kristin Reed, M.S. , in Pharmaceutical Sciences, 6/01

Brady Warren; Ph.D. in Pharmaceutical Sciences, 5/04

Todd Seib, M.S in Biological Sciences 7/04

Wes Smith; Ph.D. in Pharmaceutical Sciences, 1/07

Shailesh Agarwal; Ph.D. in Pharmaceutical Sciences, 5/07

Ran Ye; Ph.D. in Chemistry, 4/09

Todd Seib, Ph.D. in Pharmaceutical Sciences, 8/10

Jayme Newell, M.S. in Pharmaceutical Sciences 5/14

#### **POSTDOCTORAL SUPERVISION**

Munaf Kadri, MD

Sean Esslinger, Ph.D. (Shared supervision with C. Thompson, Chemistry)

Michael Anderson; MD

Colin Willis; Ph.D

Sarj Patel, Ph.D.

#### **RECENT INVITED LECTURES:**

##### *Regional*

Montana BioScience Alliance (10/11)

St. Patrick Hospital, Montana Neuroscience Institute Retreat, Missoula, MT (12/11)

University of Montana, Provost's Distinguished Lecture (12/12)

Montana State Science Fair Keynote lecture, Univ. of Montana (3/14)  
UM, High School Science Students Harkins Fusion Lecture series (11/14)  
St. Patrick Hospital Montana Cancer Institute, Missoula, MT (3/15)

*National*

National Acad. of Sci. Committee, Review of EPSCoR & IDeA Programs, Wash. DC (9/12)  
Dept. of Pharmacology, University of Washington School of Medicine, Seattle, WA (3/13)  
Neuroscience Program, Vanderbilt, Nashville, TN (10/13)  
Winter Conference on Brain Research (Session Organizer), Big Sky, MT (1/15)

*International*

University of Pereira, Pereira, Columbia (3/13)  
International Soc. for Neurochemistry (Organizing Committee), Cancun, Mexico (4/13)

**PATENTS**

U.S. Patent No. 5,942,537, Issues Aug 24, 1999  
Inventors; Chamberlin, A.R., Cotman, C.W., Stanley, M., and Bridges, R.J.  
Methods of inhibiting the transport of L-glutamate to treat CNS disorders  
UC Case No. 89-036-2

U.S. Provisional Patent Application Docket UMT-110P  
Inventors: Esslinger, C.S., Bridges, R.J., and Kavanaugh, M.P.  
3-Alkylaryl aspartate compounds and their use for selective enhancement of synaptic transmission

U.S. Provisional Patent Application Docket No. UMT-120P, Serial No. 61/089,484  
Inventors: Natale, N.R.; Bridges, R.J.; Patel, S.; Rajale, T.  
Isoxazoles with in vivo anti-convulsive activity  
Serial No. 61/089,484, U.S. August 15, 2008.

US Provisional Patent, UM Ref 2011-035-01  
Inventors: J. Gerdes, S. Ahmed, S. Patel, R. Bridges  
*"Novel Aspartylamide Inhibitors of Excitatory Amino Acid Transporters"*  
Filed March 2012

US Provisional Patent, 62/015,178  
Inventors: N. Natale, R. Bridges, S. Patel  
Isoxazoles as allosteric inhibitors of system xc- transporter  
Filed June 20, 2014

U.S. Patent submission PRO10495P00121US  
Inventors: N. Natale, R. Bridges, S. Patel., N. Duncan, M. Weaver, M. Gajewski  
Novel Inhibitors of System Xc-  
Filed June 19, 2015

## COMPLETED RESEARCH FUNDING

- NIH RO1: Bridges: PI  
*Excitotoxicity, the role of non-NMDA receptors,*  
Grant Period: 1989-1992
- NIH RR-11796: Bridges: Project Director (Paden, MSU: Co-PI)  
*Advancement of neuroscience in Montana*  
Grant Period: 9/30/96 - 8/31/99
- Paralysis Project: Bridges: PI  
*The role of glutamate transporters in spinal cord injury*  
12/15/96-12/14/97:
- NIH P20 RR10169 (IDEAS): Bridges: PI,  
*Development of a CNS tissue culture facility,*  
3/1/95-2/28/98,
- NIH: NSRA Postdoctoral Fellowship for Sean Esslinger  
Bridges: Research Supervisor (Thompson co-advisor).  
*CNS glutamate analogues: distal COOH substitutions.*  
Grant Period: 1/1/97 - 12/31/98
- NIH (AREA): Bridges: Collab. Invest., (PI: Eyer)  
*Are the glutamate systems target in trimethyltin toxicity?*  
Grant Period: 7/95-11/97
- EPSCoR MONTS Award: Bridges: Program Director,  
*Fluorescent detection of oxidative damage to the central nervous system.,*  
2/1/94-8/31/94
- Paralysis Project: Bridges: Collab. Investigator (S. Queen, U.M.: PI),  
*Glutamate transporters: targets in spinal cord injury?*  
12/15/98-12/14/99
- NIH P20 RR15583-01: Bridges: PI, (Thompson, Ross, Gerdes Co-PI)  
*COBRE Equipment Supplement*  
9/1/02-8/31/03
- Montana Board of research and Technology Commercialization  
Bridges: PI, (Poulsen Co-PI)  
*Enhancement of Applied Research in Biomedicine*  
7/1/03 - 6/30/10  
Competitive renewal (Kavanaugh Co-PI)  
7/1/10 -6/30/11  
Competitive renewal (Kavanaugh, Fanguy Co-PI)  
7/1/13 -6/30/14
- NIH R21 NS42077: Bridges: PI,  
*Vesicular glutamate transport; neurosteroid regulation*  
7/1/01-6/30/02, Total costs: ≈ \$130,000  
Grant Period: 7/1/01-6/30/03

Murdock Charitable Trust: Bridges, PI, (Collab: Coffin, Kavanaugh)  
*Functional Assessment for Animal Models of Human Disease*  
10/1/06 – 7/1/07

NIH P20 RR15583: Bridges: PI, (PI changed to M. Kavanaugh, 5/1/08)  
*COBRE Center for Structural and Functional Neuroscience*  
Grant Period: 10/1/01-4/31/10

NIH: RO1 NS 27600: Bridges: Collab. Investigator (A.R. Chamberlin, U.C. Irvine: PI),  
*Receptor specific excitatory amino acid analogues,,*  
Grant Period: 4/1/98-3/31/08

NIH RO1 NS38248: Bridges: Co-Investigator (C.M. Thompson, U.M.: PI),  
*Vesicular glutamate transport: pharmacophore elucidation*  
Grant Period: 9/1/99-8/31/08

NIH RO1 NS30570: Bridges: PI,  
*Properties and roles of excitatory amino acid transport,*  
Grant Period: 7/1/96-12/31/08

Robert Packard ALS Foundation: Bridges: Co-PI (J. Gerdes, UM, PI)  
*Cerebral PET imaging agents for monitoring ALS therapy*  
10/1/06 - 5/31/09 (Yearly Competitive Renewal)

NIH 5R21NS067466: Bridges: Co-PI (Natale, Co-PI)  
*Fluorescent-based Probes for the Glutamate/Cystine Exchanger System Xc-*  
10/1/09-9/30/12

NIH P20GM103546 Pilot Project: Bridges: Co-PI (S. Patel, UM, Co-PI)  
*Structure-function of the system xc- glutamate/cystine exchanger: Identification of xct  
residues participating in binding and translocation*  
11/1/11 - 7/31/12

P2 ALS Foundation: Bridges: Co-PI (J. Gerdes, UM, PI)  
*Cerebral PET imaging agents for monitoring ALS therapy*  
1/1/09 - 12/31/13 (Yearly Competitive Renewal)

#### **CURRENTLY ACTIVE RESEARCH FUNDING**

Montana Board of Research and Technology Commercialization  
Enhancement of applied research in biomedicine  
Bridges: Co-PI, (Kavanaugh, Fanguy Co-PIs)  
7/1/14- 6/30/16

NIH R15 NS088899, Bridges: PI,  
*Molecular Pharmacology of the System xc- Glutamate/Cystine Antiporter*  
7/1/14 - 6/30/16